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Video-Assisted Thoracoscopic Surgery versus open approach for systematic mediastinal lymph node dissection as surgical staging in major pulmonary resections for lung cancer

Garcia Fernandez Jose Luis, Moreno Balsalobre Ramon, Milian Goicoechea Hector, Cal Vazquez Isabel, Rofso Raboso Paloma, De la Fuente Alejandra

Department of Thoracic Surgery, University Hospital La Princesa, Autonomous University of Madrid (UAM), Spain

Correspondence: Jose Luis Garcia Fernandez, Department of Thoracic Surgery, University Hospital La Princesa, Autonomous University of Madrid (UAM), Spain, Email jlgf7478@gmail.com

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Abstract

Introduction

Oncological pulmonary resection should include ipsilateral hilar and mediastinal systematic lymphatic dissection allowing adequate pathological staging. Video-Assisted Thoracoscopic Surgery (VATS) has been proposed as an appropriate surgical procedure for treatment of early-stage lung cancer patients. This study aims to compare VATS versus Thoracotomy lymph node dissection in patients who underwent pulmonary resection for lung cancer.

Methods

This is a retrospective analysis of prospectively collected data from 585 patients operated at La Princesa University Hospital in Madrid (Spain) from December 2007 to January 2018. All included patients underwent complete major pulmonary resection, lobectomy or bilobectomy, and mediastinal lymph node dissection. Patients were divided in two groups, VATS group with 290 patients and thoracotomy group (TT) with 295 patients.

Results

The number of lymph nodes resected in each group did not present significant differences. VATS-group was 13.4 and TT-group was 14.1. We did not appreciate any significant difference regarding the identification of positive hilar lymphadenopathies in VATS-group versus TT-group, 36 and 41 patients respectively. However, we observed differences in patients with mediastinal lymph node metastasis (N2 disease). 34 cases (11.7%) in VATS-group and 28 cases (9.5%) in the TT-group. Lymphadenectomy 2R and 4R stations was equivalent in both groups and did not show any statistically significant difference. In the same way, there was no difference in the number of lymph nodes for levels 7R and 8R. Hilar lymphadenectomy (10R and 11R) was performed in both procedures in an equivalent manner obtaining 3.4 lymphadenopathies in VATS-group and 3.3 lymphadenopathies in TT-group. Regarding lymphadenectomy on the left side, we did not observe any difference between both groups at 5L or 6L levels. Otherwise, subcarinal lymphadenectomy on the left side showed differences when this was performed by VATS in comparison to open surgery. 3.2 lymph nodes in the VATS-group versus 4.9 lymph nodes in TT-group. This difference was statistically significant ($p < 0.01$). There was no difference in at the level of 8L and 9L stations. Hilar lymphadenectomy at 10L and 11L levels was superior in VATS-group, 4.4 lymphadenopathies, respect to TT-group, 3.1 lymph nodes. This difference was statistically significant ($p < 0.01$).

Conclusions

VATS seems to be at least equivalent to thoracotomy for pulmonary major resections in terms of oncological and staging criteria.

Keywords: lobectomy; lung cancer; lymphadenectomy; lymphadenopathies; Video-Assisted Thoracoscopic Surgery (VATS).

Introduction

Minimally invasive surgery for lung cancer has been carried out since the 80's. This technique has been imposed over last decade and there are numerous studies supporting videothoracoscopy as the best approach in terms of safety, postoperative hospital stay and earlier recovery.[1–4]

Oncological pulmonary resection should include ipsilateral hilar and mediastinal systematic lymphatic dissection allowing adequate pathological staging.[2] In this way, there are numerous articles in the literature comparing Video-Assisted Thoracoscopic Surgery (VATS) with open surgery. Following the international guidelines for the treatment of lung cancer, VATS has been proposed as an appropriate surgical procedure for the treatment of early-stages lung cancer patients.[5]

Guidelines recommend systematic Mediastinal Lymph Node Sampling (MLNS) or systematic Mediastinal Lymph Node Dissection (MLND) in patients with resectable primary lung cancer in order to achieve an accurate staging.[6] In ACOSOG Z0030, a protocol of systematic sampling was followed: for tumors in the right lung, stations 2R, 4R, 7, and 10R were sampled while in the left lung sampling was performed at stations 5, 6, 7, and 10L. Based on this trial, it can be concluded that either systematic MLNS or MLND are adequate for lymph node staging for T1 or T2 tumors.[7]

Either systematic sampling or lymph node dissection, actually the question is: VATS or thoracotomy? This study aims to compare VATS versus Thoracotomy Lymph Node Dissection in patients who underwent pulmonary resection for lung cancer.

Methods

Patients selection

We performed a retrospective analysis of prospectively collected data from 585 patients operated at La Princesa University Hospital in Madrid (Spain) from December 2007 to January 2018.

All included patients underwent complete major pulmonary resection, lobectomy or bilobectomy, and MLND. Patients who underwent sleeve resections were excluded. Anatomical localization of lymphadenopathies was taken on the distribution of diagram taken from IASLC 2009.[8]

Patients were divided in two groups, VATS-group with 290 patients and thoracotomy-group (TT) with 295.

Preoperative cardiopulmonary assessment of patients was carried out following the European guideline of preoperative evaluation for radical therapy in lung cancer patients including FEV1, DLCO and stress test with maximum oxygen consumption when any of the predicted values of respiratory function was less than 80%. All patients underwent a preoperative anesthesia evaluation.

Clinical staging was carried out according to the 2017 classification.[9]

Surgical technique

All patients underwent general anesthesia with double-lumen tube. Thoracic epidural catheter was inserted for postoperative pain control. Posterolateral thoracotomy was performed at the level of the fifth intercostal space with preservation of Serratus muscle.

VATS was approached through two or three ports. A 3 cm port was located anteriorly in the mid-axillary line in fourth intercostal space. Another 10 mm port was located in the mid-axillary line in the eighth intercostal space. Sometimes, a third assistance port was placed in the eighth intercostal space at the scapular line. After surgery, patients were transferred to the postoperative recovery room where they remained for 24 hours.

In both groups, we performed an individualized dissection of the hilar structures as well as systematic ipsilateral hilar and mediastinal lymphadenectomy. Lymphadenopathies were measured and classified by the main surgeon. Other intraoperative parameters such as surgical time or blood loss were measured by the anesthesiologist.

Statistical analysis

Data were entered in a database in the statistical system SPSS (version 15.0 for Windows). Means and standard deviations of the continuous variables, and number and percentages of the categorical variables were given by using descriptive statistics. Categorical data were compared using the chi-squared test. To test the significant differences between the groups, the Shapiro-Wilk test was used to test the normality of the variables. One-way analysis of variance (ANOVA) followed by Tukey's test was used for normally distributed variables, and the Kruskal-Wallis test was used for variables that were not distributed normally. A p-value of less than or equal to 0.05 was considered as statistically significant.

Results

Most of the patients were males, with a mean age of 69 years old for VATS-group and 65 years for TT-group. The assessment of the ASA (American Society of Anesthesiologists) scale was 2 in both groups. Both groups presented similar values of diffusion and expiratory volume in preoperative study. In VATS-group, 16 patients had received chemotherapy preoperatively, while 29 in TT-group (9.8%). (Table 1).

Table 1 Characteristics of the resected patients

	VATS	TT
N	290	295
Age (95 % CI)	69.2 (56.5-77.6)	65.1 (60.2-72.3)
Sex (male)	174 (60%)	180 (61%)
ASA	2 (1-4)	2 (1-4)
DLCO % (mean +/- SD)	68 (46-116)	71 (51-112)
FEV1 % (mean +/- SD)	73 (49-109)	72 (50-109)
Preoperative chemotherapy	16 (5.5 %)	29 (9.8 %)

VATS: Video-Assisted Thoracoscopy; TT: Thoracotomy; FEV1: forced expiratory volume in one second; DLCO: diffusing capacity of the lung for carbon- monoxide; ASA: American Society of Anesthesiologists

Table 2 describes the distribution of resected pulmonary lobes in both groups. In VATS-group, the most frequently resected lobe was the right upper lobe followed by left upper lobe. Similar for TT-group.

Table 2 Resected pulmonary lobes

	VATS	TT
RUL	91	87
RML	29	33
RLL	48	36
RUL + RML	2	8
RML + RLL	3	7
LUL	59	70
LLL	290	54

RUL: right upper lobe; RML: right middle lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe

Description of the operative data is seen in Table 3. Surgical time was 151 minutes for VATS-group and 172 minutes in TT-group. Although this difference is not significant, there is a lower operative time for the VATS group.

Table 3 Operative data

	VATS	TT	p-value
Operation time (min) [95% CI]	151 [144-161]	172 [160-188]	0.1
Intraoperative blood loss (ml) [95% CI]	110 [100-120]	180 [160-190]	<0.01
Injury esophagus	0	1 (0.3%)	-
Injury NLR	6 (2.1 %)	6 (2%)	0.44
Injury great vessel	8 (2.6 %)	5 (1.7 %)	0.05
Deaths	0	1 (0.3 %)	-

VATS: video-assisted thoracoscopy; TT: thoracotomy

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Intraoperative blood loss was significantly different between the two groups. VATS-group had an average loss of 110 ml per surgery while TT-group had a loss of 180 ml. This difference was significant with p <0.01.

Only one intraoperative death occurred in the TT-group. This was a patient with myocardial involvement. Intraoperative complications were an esophageal injury in TT-group. In both groups, 6 recurrent laryngeal nerve injuries occurred due to level 5 lymphadenectomy.

In TT-group, 5 (1.7%) lesions of large vessels required the blood transfusion. 8 lesions of large vessels required the blood transfusion in the VATS-group. This difference presented statistical differentiation.

30 days postoperative data analysis is shown in Table 4. VATS-group patients had lower drainage (260 ml) in comparison to TT-group patients (800 ml). This difference was significant (p<0.01).

Patients who underwent VATS lobectomy presented a median hospital stay of 4 days. Patients underwent a thoracotomy was 7 days. Supraventricular tachyarrhythmias had higher incidence with 37 patients in TT-group versus 16 in VATS-group.

In both groups, patients presented equivalent episodes of atelectasis or pneumonia. However, there is also a significant difference regarding the duration of thoracic drainage. In VATS-group, patients presented a median of 2 days while in TT-group median was 5 days. There was no difference the incidence of prolonged air leakage of more than 7 days.

Table 5 shows TNM classification after the pathological analysis.[10]

Table 6 describes our data on lymphadenectomy performed in both groups. The Number of nodes resected in each group did not present significant differences. VATS-group was 13.4 and in TT- group 14.1.

Table 4 Perioperative data

	VATS	TT	p-value
Postoperative drainage (ml) [95% CI]	260 [190-350]	800 [750-950]	<0.01
Length of stay (days) [95% CI]	4 [2-6]	7 [5-9]	<0.01
Atrial Tachyarrhythmia	16 (5.5 %)	37 (12.5%)	<0.01
Chylothorax	2 (0.7 %)	3 (1 %)	0.44
Atelectasis/pneumonia	9 (3.1 %)	12 (4.1 %)	0.1
Days with chest tube [95% CI]	2 [1-4]	5 [3-7]	<0.01
Prolonged Air leak (>7 days)	8 (2.7 %)	6 (2 %)	0.32

VATS: video-assisted thoracoscopy; TT: thoracotomy

We did not appreciate any significant difference in the identification of positive hilar lymphadenopathies in VATS- group with 36 patients or in TT-group with 41. However, we observed relevant differences in patients with mediastinal lymph node metastasis (N2 disease). 34 cases (11.7%) in VATS-group and 28 cases (9.5%) in the TT-group.

Regarding the anatomical location of the lymphadenopathies. Lymphadenectomy for 2R and 4R stations was equivalent in both groups and did not show any statistically significant difference. In the same way, there was no difference in the number of lymph nodes for levels 7R and 8R. Hilar lymphadenectomy (10R and 11R) was performed in both procedures in an equivalent manner obtaining 3.4 lymphadenopathies in VATS-group and 3.3 lymphadenopathies in TT-group.

Table 5 Pathological tumor stage

	VATS	TT
Ia	138	119
Ib	65	66
IIa	33	37
IIb	20	45
IIIa	34	28

VATS: video-assisted thoracoscopy; TT: thoracotomy

Table 6 Comparison MLND

MLND	VATS (95% CI)	TT (95% CI)	p-value
Average node number	13.4 (12.5-15.7)	14.1 (13.2-6.8)	0.15
Ganglion metastasis N1 (%)	36 (12.4)	41 (13.9)	0.12
Ganglion metastasis N2 (%)	34 (11.7)	28 (9.5)	<0.01
2R+4R	4.1 (3.7-5.1)	4.7 (3.9-5)	0.35
7R	5 (4.1-6)	5.3 (4.4-6.8)	0.41
8R+9R	3.1 (2-3.9)	3.5 (2.8-4)	0.36
10R+11R	3.4 (2.4-4.3)	3.3 (2-4.1)	0.44
5L+6L	5.2 (4.1-6.3)	5.1 (3.9-6.1)	0.31
7L	3.2 (2.8-5)	4.9 (4-6)	<0.01
8L+9L	3.1 (2.6-4.2)	3.3 (1.9-4.6)	0.6
10L+11L	4.4 (3.5-5.1)	3.1 (2.2-4.1)	<0.01

Regarding lymphadenectomy on the left side, we did not find any difference between both groups at 5L or 6L levels. Otherwise, subcarinal lymphadenectomy on the left side showed differences when this was performed by VATS in comparison to open surgery. 3.2 lymph nodes in the VATS-group versus 4.9 lymph nodes in TT-group. This difference was statistically significant (p < 0.01). There was no difference in at the level of 8L and 9L stations. Hilar lymphadenectomy at 10L and 11L levels was superior in VATS-group -4,4 lymphadenopathies- than in TT-group -3.1 lymph nodes-. This difference was statistically significant (p <0.01).

Discussion

Lymphadenectomy is a cornerstone for surgical staging in lung cancer patients. VATS has been gradually incorporated to perform major pulmonary resections in most surgical groups. There are numerous studies that aimed to analyze the suitability of minimally invasive surgery for proper treatment and adequate staging in lung cancer patients. Today, international guidelines recommend VATS for lung cancer surgery as first option. Most surgical procedures can be carried out using this surgical approach basically depending on surgeon experience.

Palade et al.[11] published a randomized and controlled prospective study about the effectiveness of mediastinal lymphadenectomy performed

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by VATS. Authors did not find significant differences between open and VATS surgery in the number of resected lymph nodes, stations explored or perioperative complications.

Zhang et al.[12] reported 497 patients with lobectomy and mediastinal lymphadenectomy. One group with 242 patients who underwent surgery through minimally invasive procedures and 255 patients by thoracotomy. They concluded that systematic lymphadenectomy by VATS has an earlier recovery than open surgery, less post-operative complications and similar hospital stay. However, thoracotomy resects more lymphadenopathies from level 7 L.

Our surgical operative data revealed that surgical time and intraoperative complications between both procedures are equivalent. There is no statistically significant difference regarding the injury of neighboring structures such as esophagus, recurrent laryngeal nerve or vessel. However, we found statistically significant difference regarding surgical time VATS group was 110 minutes compared to 180 minutes in the TT-group ($p<0.01$).

In the same way, there was significant difference in terms of less volume drainage, days with chest tube, postoperative hospital stay and incidence of supraventricular tachyarrhythmias in favor of VATS-group. These results agree with those published by other authors.[13–15]

The statistical analysis comparing systematic mediastinal lymphadenectomy for both approaches also reveals differences. Both groups resected a similar number of lymphadenopathies (13.4 in VATS-group versus 14.1 in TT-group). The incidence of hilar metastasis (N1) between both groups was also equivalent (36 patients in minimally invasive surgery group versus 41 patients in the open surgery group). The number of lymph nodes obtained in the lymphadenectomy of the right hemithorax at levels 2R + 4R, 7R, 8R and 9R was equivalent in the two approaches. This data is similar to Palade et al.[11] and Zhang et al.[12] In case of systematic mediastinal lymphadenectomy on the left side, the number of nodes resected at the level 5L + 6L or 8L + 9L were also similar. However, 7L station lymphadenectomy by thoracotomy seemed to be superior, 4.9 lymphadenopathies compared to 3.2 in VATS-group. Palade also found significant difference in lymphadenectomy in open surgery versus VATS at 7L level. Our results coincide with data published. Probably, difference between both groups is due to a greater difficulty at the time of exploration of subcarinal level from the left side. However, we found the difference in hilar and peribronchial levels (10L and 11L) in favor of VATS-group compared to TT-group. This difference could be explained by systematic use of the ultrasound energy device at the time of hilar lymphadenectomy. This type of energy allows an optimal hilar and peribronchial lymphadenectomy due to great visualization of the hilar structures thanks to high definition cameras.

Conclusions

VATS seems to be at least equivalent to thoracotomy for pulmonary major resections in terms of oncological and staging criteria. VATS it appears superior since it has lower incidence of perioperative complications and shorter hospital stay compared to conventional surgery.

Conflict of interest: none declared.

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Ethical Statement: The study is approved by the institutional ethical committee.

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