STUDY ON ROBOTIC VIDEO-ASSISTED THORACIC LOBECTOMY FOR LARGE TUMOR LUNG CANCER

***Nguyen Viet Dang Quang*[1]*, Nguyen Van Nam*[2]*, Vu Huu Vinh*[1]**

Summary

Objectives: To evaluate the efficacy of robotic video-assisted thoracic lobectomy (r-VATS) in patients with locally advanced non-small cell lung cancer. ***Subjects and methods:*** r-VATS lobectomy was performed in 79 patients with non-small cell lung cancer treated at Cho Ray Hospital from July 2018 to June 2022. We divided 79 patients into two groups: Group 1 consists of 50 patients with tumors < 5 cm in diameter; group 2 consists of 29 patients with tumors ≥ 5 cm in diameter (cT3 and cT4). ***Results:*** The mean operative time of the tumor ≥ 5 cm group was longer than that of the other group (273.7 minutes vs. 255.5 minutes); however, the difference was not statistically significant. The rate of conversion to open surgery in group 2 was significantly higher than in group 1 (17.2% vs. 4.0%, p = 0.046). There was no statistically significant difference in post-operative complications in the two groups. There was no significant difference in the survival rate in the two groups (p = 0.272). ***Conclusion:*** r-VATS is effective in lobectomy for non-small cell lung cancer ≥ 5 cm in size (cT3 and cT4). With tumor size ≥ 5 cm, the surgical time, the rate of postoperative complications, and the post-operative recurrence rate did not increase; however, the conversion rate to open surgery increased.

** Keywords: r-VATS; Mini-invasive surgery; Lobectomy; Non-small cell lung cancer.*

[1]Thoracic Department, Cho Ray Hospital

[2]Cardiovascular - Thoracic Department, Military Hospital 103

Corresponding author: Nguyen Viet Dang Quang (drquang.choray@yahoo.com)

Date received: 23/02/2023

Date accepted: 28/3/2023

http://doi.org/10.56535/jmpm.v48i4.309

INTRODUCTION

It was reported that 27% of lung cancer patients were diagnosed with an advanced stage by the time of detection, with tumor enlargement and necrosis, mediastinal lymphadenopathy, pleural, vascular, or bronchial invasion, which challenges surgeons and compromises surgical oncological outcome [1]. Video-assisted thoracic surgery (VATS) in these cases is often very difficult and is occasionally converted to open surgery to ensure R0 resection and adequate lymph node dissection.

r-VATS has witnessed tremendous growth in the last two decades. For the treatment of non-small cell lung cancer, compared with VATS, r-VATS lobectomy has been reported to decrease the rate of conversion to open surgery, postoperative complications, and length of hospital stay [3, 4, 5]. r-VATS lobectomy benefits surgeons with the flexibility of robotic arms and intraoperative 3D imaging for better vascular and lymph node dissection, and therefore has been shown to be highly effective in advanced patients. The conversion rate to open surgery ranges from 8.6 - 17.3%. postoperative complications are encountered in 27.6 - 44.2% of the cases, and the 30-day mortality rate is approximately 1.9% [2].

In Vietnam, r-VATS has recently been developed. Currently, there are five Da Vinci Xi robotic surgery systems operating nationwide. In thoracic surgery, Binh Dan Hospital was the first to perform a r-VATS lobectomy in July 2017, but the number of operations is still limited. At Cho Ray Hospital, since our first case in July 2018, r-VATS lobectomy has been developed rapidly with an increasing number of patients. During the implementation of r-VATS, we changed the position of the robotic arms approaching in a triangular shape to suit the local conditions with the same approach criteria as VATS and reduced one robot arm. From July 2018 to July 2022, we performed r-VATS lobectomies for 79 lung cancer patients with stage I-IIIA disease. We conducted this study to: *Evaluate the efficacy of r-VATS lobectomy in patients with locally advanced non-small cell lung cancer.*

SUBJECTS AND METHODS

1. Subjects

79 patients with non-small cell lung cancer were treated at Cho Ray Hospital from July 2018 to June 2022.

We divided 79 patients into two groups:

- Group 1: 50 patients with tumors < 5 cm of diameter.

- Group 2: 29 patients with tumors ≥ 5 cm of diameter (cT3 and cT4).

** Inclusive criteria:*

- Patients who were diagnosed with clinical stage I, II, and IIIA (8th edition of TNM classification of the International Association of the Study of Lung cancer) via contrast chest CT scan, brain MRI and PET scan.

- Patients who were candidates for radical surgical resection (ASA 1-3).

* *Exclusion criteria:*

- Patients with severe heart disease, renal impairment, any other serious comorbidities according to the investigator, recent oncologic history (another malignant tumor within the last 2 years), and previous chest surgery.

- In stage cIIIA, we chose T3N1 and T4N0, and excluded T4 which invaded diaphragm, heart and main bronchus.

2. Methods

Pre-operative staging included contrast-enhanced total body CT and FDG-PET. The standard functional evaluation included an ECG, a cardiologic evaluation, pulmonary function tests, and a pre-anesthesia evaluation.

In cases of suspected mediastinal nodes, an EBUS or mediastinoscopy was performed before resection. A pre-operative diagnosis was obtained by CT-driven needle biopsy or endobronchial biopsy. In the absence of histology in the pre-operative diagnosis, intraoperative lung cancer was confirmed with a frozen section.

* *Operative approaches:*

All procedures were performed under general anesthesia with a double-lumen endotracheal tube to deflate the diseased lung with patients in the lateral decubitus position. The DaVinci Robotic System Xi was used with a 30° camera and standard endoscopic staplers. Our r-VATS technique was modified from the protocol posted by the American Chest Surgery Association to fit the circumstances in Vietnam. Robotic arms were set up as follows:

- In the case of right lung cancer:

+ Camera trocar: 8th intercostal space on the back, 1 cm from the posterior axillary line.

+ Arm 1: 5th intercostal space at the midpoint between the anterior axillary line and the midclavicular line.

+ Arm 2: 7th intercostal space on the back, 3 cm from the posterior axillary line.

+ Assistant trocar (1.5 cm): 7th intercostal space at the anterior axillary line.

- In the case of left lung cancer:

+ Camera trocar: 7th intercostal space at the midpoint between the anterior axillary and the midaxillary line.

+ Arm 1: 8th intercostal space on the back, 3 cm from the posterior axillary line.

+ Arm 2: 4th intercostal space at the midpoint between the anterior axillary line and the midclavicular line.

+ Assistant trocar: (1.5 cm): 9th intercostal space at the anterior axillary line.

In all cases, we used only the cadiere forcep and harmonic scalpel robotic arms which were further supported with thoracoscopic instruments through assistant trocars: the suction, Kelly forcep, stapler, etc. No CO_2 insufflation was needed. After lobectomy, N1 lymph nodes were routinely dissected. For N2, we performed lymphadenectomy to lymph nodes > 1 cm on CT scan or on intraoperative screen.

The early outcome was investigated by operative time, rate of intra-operative bleeding defined as blood loss > 500 mL due to vessel damage, the rate of conversion to an open procedure, the number of lymph nodes collected, the rate of post-operative complications, and mortality rate.

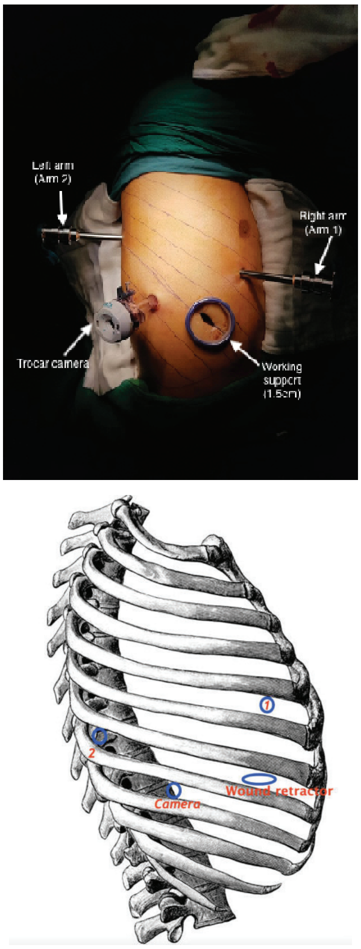

Figure 1: Trocar placement on the right side.

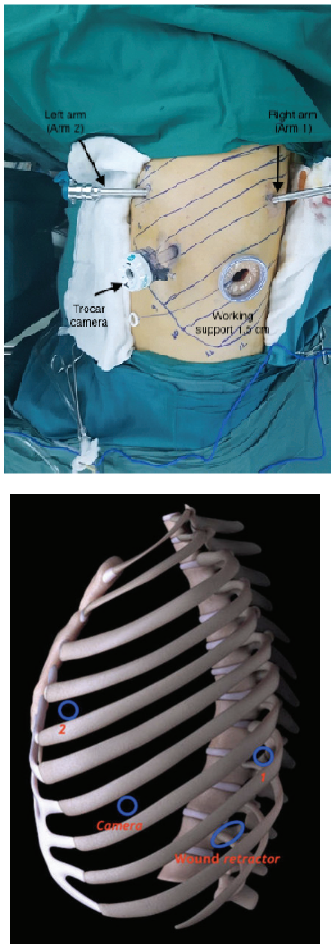

Figure 2: Trocar placement on the left side.

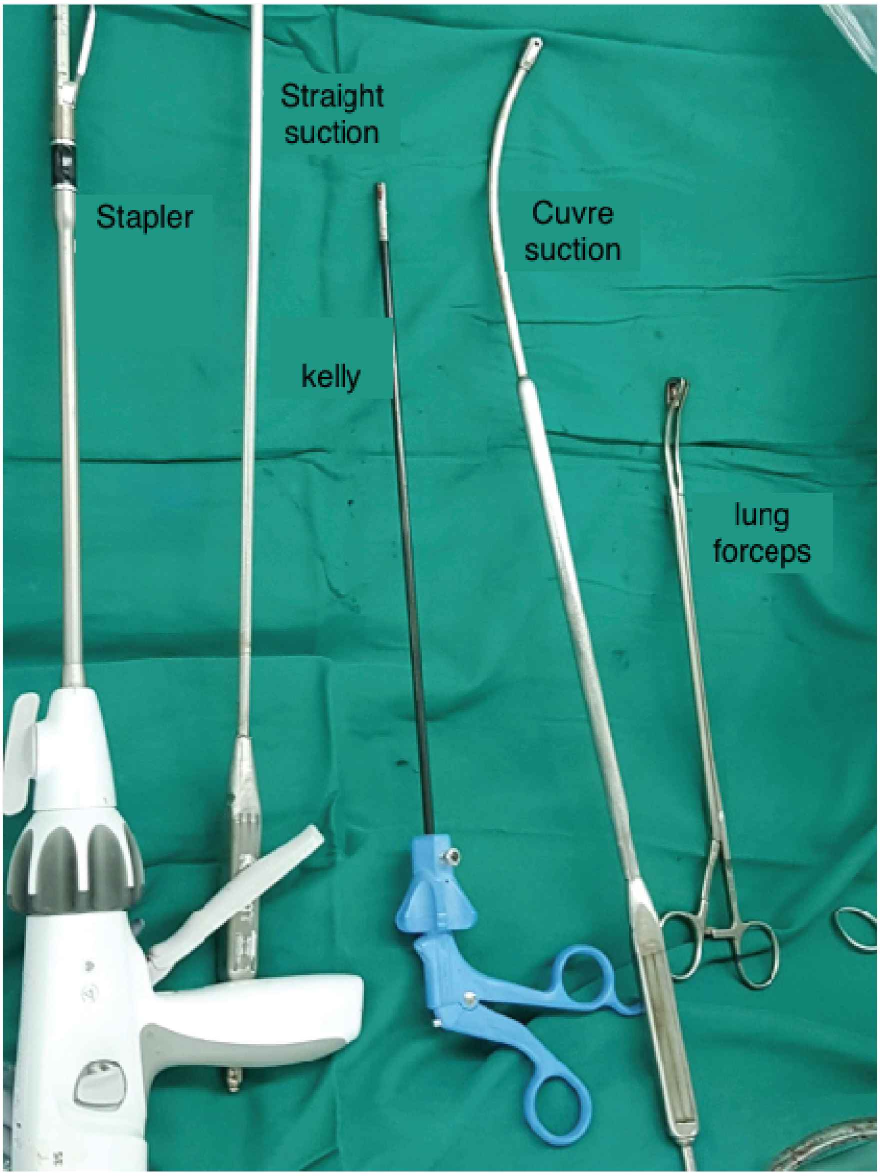

Figure 3: VATS instruments used via an assistant trocar.

* *Statistical analysis:*

The recorded data were collected and entered in a spreadsheet computer program (Microsoft Excel, 2010) and then exported to the data editor page of IBM SPSS version 22.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics and frequency distributions were calculated. A Chi-square test was used for bivariate associations. For all tests, the confidence interval and p-value were set at 95% and ≤ 0.05, respectively.

RESULTS

From July 2018 to July 2022, we performed r-VATS lobectomy on 79 non-small cell lung cancer patients.

Table 1: Characteristics of patients.

Characteristics		Group 1 (n = 50) n (%)	Group 2 (n = 29) n (%)	p-value
Gender	Male	33 (66.0)	21 (72.4)	0.55*
	Female	17 (34.0)	8 (27.6)	
Age (years)		61.2 ± 8.4	61.1 ± 9.6	0.92**
Tumor size (cm)		2.7 ± 0.9	6.1 ± 1.2	0.001**
Lymphadenopathy detected on CT scan	N1	18 (36.0)	19 (65.5)	0.03*
	N2	26 (52.0)	19 (65.5)	0.01*
Lobular lesion distribution	LUL	16 (32.0)	12 (41.4)	0.46*
	LLL	5 (10.0)	4 (13.8)	
	RUL	16 (32.0)	5 (17.2)	
	RML	2 (4.0)	0 (0)	
	RLL	11 (22.0)	8 (27.6)	
Location of tumor	Peripheral	44 (88.0)	25 (86.2)	0.81
	Central	6 (12.0)	4 (13.8)	
FEV1/FVC (%)		77.2 ± 11.4	73.7 ± 9.2	0.19**
TNM staging (cTNM/pTNM)	Stage I	34 (68.0)/ 31 (62.0)	0 (0) / 0 (0)	-
	Stage IIA	2 (4.0) / 0 (0)	0 (0) / (0)	
	Stage IIB	4 (8.0) / 10 (20.0)	10 (34.5) / 17 (58.7)	
	Stage IIIA	10 (20.0) / 8 (16.0)	19 (65.5) / 5 (17.2)	
	Stage IIIB	0 (0) / 1 (2.0)	0 (0) / 7 (24.1)	

** Chi-square test; ** T-test*

LUL: left upper lobe; LLL: left lower lobe; RUL: right upper lobe.

RML: right middle lobe; RLL: right lower lobe.

cTNM: clinical TNM; pTNM: pathologic TNM.

There were no statistically significant differences in gender, age, tumor location, and preoperative respiratory function between the two groups. In group 2, the clinical stage was mainly IIIA, accounting for 65.5%. On CT scan images, group 2 had a significantly higher percentage of enlarged N1 and N2 lymph nodes than group 1.

Table 2: Results of operation.

		Group 1 (n = 50) n (%)	**Group 2 (n = 29) n (%)**	**p-value**
Operative time (min)		255.5 ± 68.4	273.7 ± 88.5	0.31**
N2 lymphadenectomy		36 (72.0)	23 (79.3)	0.33*
Number of N2lymph nodes collected	Station 1	22 (61.1)	9 (39.1)	0.11*
	Station 2	10 (27.8)	7 (30.4)	
	Station 3	3 (8.3)	7 (30.4)	
	Station 4	1 (2.8)	0 (0)	
Intra-operative bleeding		1 (2.0)	1 (3.4)	0.6*
Conversion to open surgery		2 (4.0)	5 (17.2)	0.046*
Post-operative complications	Pneumonia	1 (2.0)	0 (0)	0.07*
	Stroke	1 (2.0)	0 (0)	
	Prolonged air leak (> 7 days)	2 (4.0)	6 (20.7)	
	Emphysema	0 (0)	1 (3.4)	
	Bronchial fistula	1 (2.0)	0 (0)	

(Chi-square test; ** T-test)*

The mean operative time of the tumor ≥ 5 cm group was longer than that of the tumor < 5 cm group (273.7 minutes vs. 255.5 minutes), but the difference was not statistically significant (p = 0.03). The rate of lymph node dissection implemented in the two groups was similar (group 1: 72% vs. group 2: 79.3%, p = 0.33). In group 2, the number of N2 lymphadenectomy performed at 2 or more stations accounted for 60.8%. The rate of intraoperative bleeding was similar in the 2 groups. The rate of conversion to surgery in group 2 was significantly higher than that in group 1 (17.2% vs. 4.0%, p = 0.046). In group 1, there were 2 cases of conversion to open surgery, one of which was due to arterial damage during dissection. In group 2, all 5 cases converted to elective open surgery were due to lack of space for manipulation or invasion of the bronchi/blood vessels. The most common postoperative complication was pneumothorax lasting > 7 days, group 2 had a complication rate of prolonged pneumothorax of 20.7%. There was no statistically significant difference in postoperative complications between the two groups.

Table 3: Results of oncology

		Group 1 (n = 50) n (%)	**Group 2 (n = 29) n (%)**	**p-value**
Pathologica l results	Adenocarcinoma	46 (92.0)	25 (86.2)	0.411*
	Squamous carcinoma	4 (8.0)	4 (13.8)	
Metastatic lymph node level N1		12 (24.0)	5 (17.2)	0.481*
Metastatic lymph node level N2		9 (18.0)	7 (23.1)	0.513*
Time of follow up (month)		26.2 ± 10.9	22.1 ± 9.4	0.323**
Recurrent lymph node		14 (31.8)	6 (27.3)	0.705*
Distant metastasis		17 (39.5)	10 (45.5)	0.674*

*: chi-quare test; **: T-test

The most pathology finding in the two groups was adenocarcinoma. The rate of lymph node metastasis to N1 and N2 in the 2 groups was significantly different. During post-operative follow-up, we found that the rates of lymph node recurrence and distant metastasis in the 2 groups had no statistically significant difference. In group 1, the survival rates after 1 and 2 years were 91.3% and 80.4%, respectively. In group 2, survival rates were 88% and 62.2%, respectively. There was no significant difference in the survival rate between the 2 groups (p = 0.272).

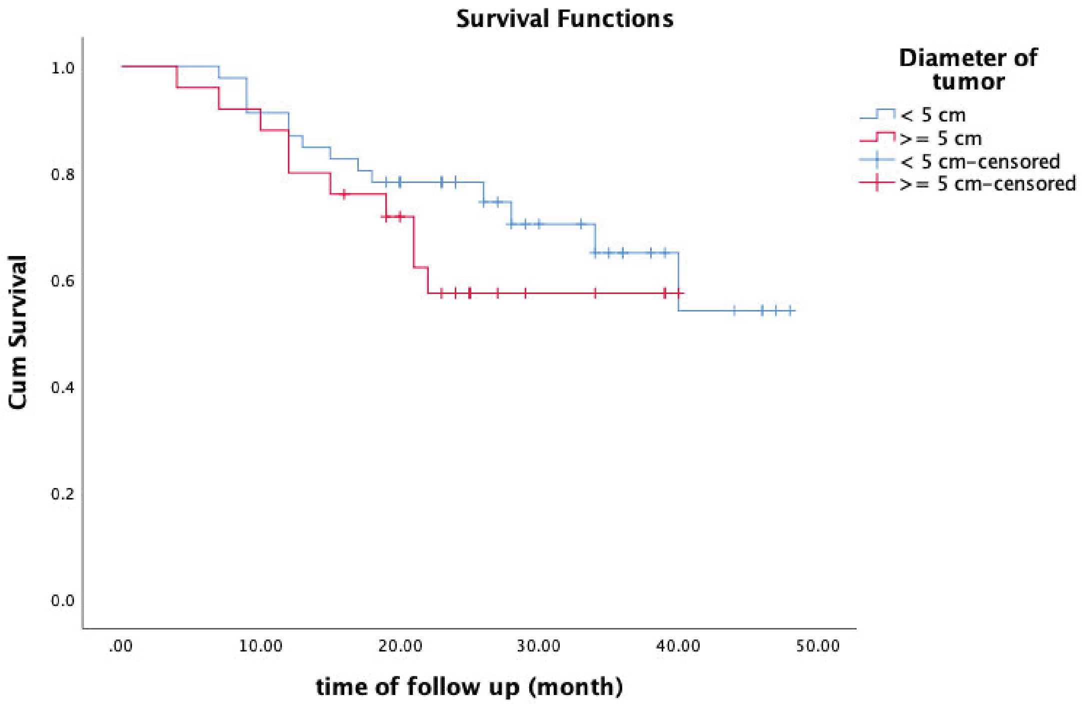

Figure 4: Kaplan-Meier of survival.

Table 4: Time of survival.

Time of survival	Group 1 (n = 50) n (%)	Group 2 (n = 29) n (%)	p-value
1 year	91.3	80.4	0.272*
2 year	88.0	62.2	

** log-rank (Mantel-Cox)*

DISCUSSION

First, we would like to discuss the modified triangular port placement in r-VATS lobectomy. Currently, there are 2 approaches in r-VATS: Total and partial approach with robotic arms. Parini et al. also reviewed that there were many approaches and positions of robotic arms to consider depending on the actual conditions at the centers, the generation of robots used, and surgeons' habits and experience [3]. To the best of our knowledge, many authors changed the trocar placement of the robotic arm with different approaches, as mentioned in a study by Veronesi G. [4]. At our center, we choose a partial-approach r-VATS with one 1.5 cm assistant trocar for conventional thoracoscopic instrument during surgery. With this modification, we saved 01 robotic arm, helping to reduce the cost of r-VATS (about 12 - 14 million VND per case). Surgeons are familiar with switching from VATS to r-VATS and take advantage of the flexible robotic arms in dissection and lobectomy.

There was no significant difference between the 2 groups in terms of operative time. The mean operative time in the group with tumors ≥ 5 cm was 273.7 minutes. Kneuertz P.J. recorded a mean operative time of 283.6 minutes with r-VATS lobectomy in 296 patients [6]. Nelson B.D. et al. reported their mean operative time on 106 patients was 226 minutes, significantly longer than conventional thoracoscopy with 173 minutes ($p < 0.001$) [7]. The issue of prolonged operative time with r-VATS has also been reported in many other multicenter studies.

A study by Mao J. et al. (2019) showed that r-VATS significantly took longer than thoracoscopic surgery ($p < 0.001$). However, reports in the last 5 years showed no statistically significant difference between the 2 surgical groups in terms of surgery time [8]. A meta-analysis by Ma J. reviewing 13 reports from 2015 - 2020 comparing the operative time between r-VATS and thoracoscopic surgery implied that there was no statistically significant difference ($p = 0.92$) [9].

In our study, the rate of conversion to open surgery in the group of tumors > 5 cm was 17.2%, all were due to large tumors and vascular invasion, which minimized manipulation space and made thoracoscopic dissection difficult and therefore, compromised the oncological outcome of the surgery. In the group of tumors < 5 cm, the rate of conversion to open surgery was 2/50 cases, one of which was due to pulmonary artery injury during dissection. The rate of conversion to surgery in group 2 was higher than that in group 1 (17.2% vs. 4%) with statistical significance (p = 0.046). Author Yang H.X. et al. (2016) reported the rate of conversion to open surgery was 9.2% (16 cases) in r-VATS for 172 patients, with 3 cases due to bleeding (1.7%), 5 cases due to adhesions in the pleural space, 3 cases of inadequate ventilation with a single lung, 2 cases due to incompetent assistant, 1 case with a limited intra-thoracic view, 1 case with an anesthesia machine error, and 1 case of bulky hilar lymph nodes [5]. Veronesi showed a conversion rate to open surgery of 15.2% of 223 patients with stage pIIIA non-small cell lung cancer [4]. Except for the conversion to open surgery due to vascular injury, the plan for an anticipated conversion due to large tumors or lymph node invasion should depend on the surgeons' level of experience. Planned open surgery will help reduce blood loss and ensure safety for the patients.

In our study, during post-operative follow-up, we found that the rates of lymph node recurrence and distant metastasis in the 2 groups had no statistically significant difference. The survival rates after 1 and 2 years for group 1 were 91.3% and 80.4%, respectively. In group 2, survival rates were 88% and 62.2%, respectively. There was no significant difference in survival rates between the 2 groups (p = 0.272). A report on robotic non-small cell lung cancer surgery on 249 patients by Toosi et al. showed a mean follow-up time of 18 months. The lung cancer survival rates by stage assessed after surgery at 1 year and 3 years were: Stage-I, 92% (87 - 97%) and 75% (63 - 87%); Stage-II, 83% (70 - 96%) and 73% (49 - 97%); Stage-III, 75% (63 - 87%) and 44% (26 - 62%); and Stage-IV, 67% (37 - 97%) and 0% [10]. The survival rate in our study is similar to that of other authors in the world.

CONCLUSION

r-VATS is effective in lobectomy for non-small cell lung cancer ≥ 5 cm in size. With a tumor size ≥ 5 cm, the surgical time, the rate of post-operative complications, the post-operative lymph node recurrence rate, and the metastasis rate did not increase. The rate of conversion to open surgery increased when the tumor is ≥ 5 cm, and the decision of conversion was within the plan.

REFERENCES

1. Morgensztern D., Ng S.H., Gao F., et al. (2010). Trends in stage distribution for patients with non-small cell lung cancer: A National Cancer Database survey. *J Thorac Oncol;* 5: 29-33.

2. Glover J., Velez-Cubian F.O., Toosi K., et al. (2016). Perioperative outcomes and lymph node assessment after induction therapy in patients with clinical N1 or N2 non-small cell lung cancer. *J Thorac Dis;* 8: 2165-2174. [Crossref] [PubMed].

3. Parini, S., Massera, F., Papalia, E., et al. (2022). Placement Strategies for Robotic Pulmonary Lobectomy: A Narrative Review. *J. Clin. Med*; 11: 2612. https://doi.org/10.3390/ jcm11092612.

4. Veronesi G., Abbas A.E., Murianna P. et al. (2021). Perioperative outcome of robotic approach versus manual videothoracoscopic major resection in patients affected by early lung cancer: resultss od a randomized multicentric study (ROMAN study). *Front Oncol;* 11: 726408.

5. Yang H.X., Woo K.M., Sima C.S., et al. (2016). Long term survival based on the surgical approach to lobectomy for clinical stage I nonsmall cell lung cancer: comparison of robotic, video-assisted thoracic surgery and thoracotomy lobectomy. *Ann Surg;*

6. Kneuertz P.J., Singer E., D'Souza H., et al. (2019). Hospital cost and clinical effective- ness of robotic-assisted versus video-assisted thoracoscopic and open lobectomy: A propensity score-weighted comparison. *J. Thorac. Cardiovasc. Surg;* 157: 2018-2026.e2.

7. Nelson D.B., Mehran R.J., Mitchell K.G., et al. (2019). Robotic-Assisted Lobectomy for Non-Small Cell Lung Cancer: A Comprehensive Institutional Experience. *Ann. Thorac. Surg;* 108: 370-376.

8. Mao J., Tang Z., Mi Y., et al. (2021). Robotic and video-assisted lobectomy/segmentectomy for non-small cell lung cancer have similar perioperative outcomes: A systematic review and meta-analysis. *Translational Cancer Research;* 10(9): 3883-3893. https://doi.org/10.21037/tcr-21-646.

9. Ma J., Li X., Zhao S., et al. (2021). Robot-assisted thoracic surgery versus video-assisted thoracic surgery for lung lobectomy or segmentectomy in patients with non - small cell lung cancer: A meta-analysis. *BMC cancer;* 21: 498. https://doi.org/10.1186/s12885-021-08241-5.

10. Toosi K., Velez-Cubian F.O., Glover J., et al. (2016). Upstaging and survival after robotic-assisted thoracoscopic lobectomy for non-small cell lung cancer. *Surgery*. http://dx.doi.org/ 10.1016/j.surg.2016.08.003.