

Original
Article

Lymph Node Dissection in Surgery for Lung Cancer: Comparison of Open vs. Video-Assisted vs. Robotic-Assisted Approaches

Alper Toker, MD, Mehmet Oğuzhan Özyurtkan, MD, Özkan Demirhan, MD,
Kemal Ayalp, MD, Erkan Kaba, MD, and Elena Uyumaz, MD

Purpose: We compared open, video-assisted and robotic-assisted thoracoscopic surgical techniques in the dissection of N1 and N2-level lymph nodes during surgery for lung cancer.

Methods: This retrospective analysis is based on prospectively collected data of patients (excluding those with N2 or N3 diseases, and sleeve resections) undergoing mediastinal lymph node dissection via open (n = 96), video-assisted thoracoscopy (n = 68), and robotic-assisted thoracoscopy (n = 106). The groups are compared according to the number of lymph node stations dissected, the number of lymph nodes dissected, and the number of lymph nodes dissected by stations.

Results: Three techniques had similar results based on the number of the dissected N1 and N2-level lymph node stations. Robotic-assisted thoracoscopic surgery yielded significantly more lymph nodes in total (p = 0.0007), and in the number of dissected N1-level nodes (p < 0.0001). All techniques yielded similar number of mediastinal lymph nodes, whereas robotic-assisted thoracic surgery (RATS) yielded more station #11 and #12 lymph nodes compared to the other groups.

Conclusions: In this study, robotic-assisted thoracoscopic surgery has been shown to dissect more lymph nodes at N1 level. However, taking the open approach as standard, we could claim that both currently robotic and video-assisted techniques may provide similar number of dissected N1 and N2-level lymph node stations.

Keywords: lymph node dissection, lung cancer, video-assisted thoracoscopy, robotic surgery, thoracotomy

Introduction

The current guidelines recommend systematic mediastinal lymph node sampling (MLNS) or systematic mediastinal lymph node dissection (MLND) in patients with

resectable primary lung cancer for accurate staging and management.¹⁾ Mediastinal lymph node staging is also reported to be a prognostic factor in case of metastatic lung cancers, therefore either MLNS or MLND are advised for patients undergoing metastasectomies for some certain types of malignancies.²⁾ More than this, the dissection of N1-level lymph nodes are considered to be highly important due to (1) recurrence, (2) proper staging, and (3) for decision making of sleeve resection or pneumonectomy.

Anatomical pulmonary resections are performed either by thoracotomy or by minimally invasive approaches. Video-assisted thoracic surgery (VATS) and robotic-assisted thoracic surgery (RATS) are current surgical techniques in minimally invasive lung resections. Several authors compared thoracotomy to VATS in the dissection

Department of Thoracic Surgery, Istanbul Bilim University Medical Faculty and Group Florence Nightingale Hospitals, Istanbul, Turkey

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Corresponding author: Mehmet Oğuzhan Özyurtkan, MD. Department of Thoracic Surgery, Istanbul Bilim University and Group Florence Nightingale Hospital, Abide-i Hürriyet Cad. No: 166, Şişli-Istanbul, Istanbul, Turkey

Email: moozyurtkan@hotmail.com

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of N1 and N2-level lymph nodes.³⁻¹⁰ Besides, there are some reports comparing thoracotomy and RATS, and VATS and RATS.¹¹⁻¹⁴ Based on these studies, the results are controversial about the superiority of a “specific” surgical technique.

The above-mentioned studies, which are limited in number, compared only two modalities in the dissection of N1 and N2-level lymph nodes. Yet, there is not a specific study in the literature comparing open, video-assisted, and robotic approaches in the dissection of N1 and N2-level lymph nodes. This study was planned to compare these three modalities, taken the open approach as standard.

Materials and Methods

Patient selection

We performed a retrospective analysis on prospectively collected data of the patients with primary or metastatic lung cancers who underwent anatomic pulmonary resections and mediastinal and N1-level lymph node dissection via open, video-assisted or robotic approaches, from October 2011 to March 2016. Among the patients, those who had pathologically proven N2 and/or N3 diseases, and who underwent sleeve resections were excluded. The remaining 270 patients were included in this study. This study received Institutional Review Board Approval, with individual patient consent being waived.

The patients were grouped into three according to the type of the operative approaches: 96 patients underwent thoracotomy (T), 68 patients underwent VATS, and 106 patients underwent RATS. The choice of the operative approach (open vs. minimally invasive) was at the discretion of the surgical team in the preoperative meetings. The decision to offer the approach, either VATS or RATS, was made according to the healthcare insurance systems, and the patients’ willingness.

Surgical technique

All operations were performed by the same surgeon. In all operations, double lumen intubation tube was placed. Thoracotomies were performed from either anterior muscle sparing or posterolateral thoracotomies. VATS operations were performed either with 2 or 3 port techniques. RATS technique is described elsewhere,¹⁵ but generally 3 to 4 arm techniques were used including an access approach located at the 10th intercostal space posteriorly for upper lobes and anteriorly through the arm one (left side) or arm two (right side) as described by Veronesi and colleagues.¹²

Mediastinal and N1-level lymph node dissection were performed by similar technique in all types of the approaches, systematic MLND was preferred. Basically, the surrounding fat tissue was resected together with the lymph nodes en bloc. Mediastinal lymph node stations that were typically dissected were 2R, 4R, 7, 8, 9 for right-sided procedures, and 5, 6, 7, 8, 9 for left-sided procedures. N1-level lymph nodes, station #10, #11 and #12 were dissected separately according to the flow during the surgery. Lymph nodes that were retrieved en bloc with the specimen or during the preresection mediastinoscopy were not added to the lymph node counting. Lymph node counting was done as previously described.¹⁶ Fissures were divided by staplers or coagulation in all resections. Basically, for a segmentectomy operation level 11 and 12 nodes were dissected completely and sent for frozen section analysis. We defined #2 and #4 as superior mediastinal nodes, #5 and #6 as paraaortic nodes, #7 as subcarinal nodes, and #8 and #9 as inferior mediastinal nodes.¹⁷ N1-level lymph nodes were subdivided as hilar lymph nodes (#10) and level 11 and 12 lymph nodes.

Data collection

Patients demographics, operative reports, and final pathology reports were obtained from prospectively collected medical records. The type of the resection, the number of the lymph nodes and N1/N2 lymph node stations were recorded. Three groups were compared according to (1) the number of lymph node stations dissected, (2) the number of lymph nodes dissected, and (3) the number of lymph nodes dissected by stations. To evaluate lymph nodes more specific to an ipsilateral resection, right and left-sided operations were investigated separately.

Statistical analysis

Excel software (Microsoft Corp, Seattle, WA) was used to analyze the data. The means and standard deviations of the continuous variables, and number and percent of categorical variables were given by using descriptive statistics. Categorical data were compared using the chi-squared test. To test significant differences between the groups, 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 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.

Table 1 Characteristics of the patients

	T	VATS	RATS	p
N	96	68	106	
Age (mean ± SD), years	60 ± 12	63 ± 8	62 ± 11	0.21
Male (n, %)	82 (85%)	47 (69%)	76 (72%)	0.02
Right-sided procedure (n, %)	50 (52%)	39 (57%)	64 (60%)	0.50
Diameter of the lesion (mean ± SD), cm	4.8 ± 3.0	3.5 ± 2.4	2.8 ± 1.9	<0.0001
N1 positivity (n, %)	13 (14%)	1 (1%)	9 (8%)	0.02
Number of primary lung cancer (n, %)	91 (95%)	62 (91%)	99 (93%)	0.76
Stage I lung cancer (n, %)	25 (27%)	33 (53%)	59 (60%)	<0.0001
Histology (n, %)				
Adenocarcinoma	25 (26%)	37 (54%)	45 (42%)	0.0009
Squamous cell carcinoma	54 (56%)	16 (24%)	34 (32%)	<0.001
Carcinoid tumor	3 (3%)	4 (6%)	8 (8%)	0.39
Metastases	5 (5%)	6 (9%)	7 (7%)	0.66
Type of the resection (n, %)				
Segmentectomy	3 (3%)	20 (29%)	34 (32%)	<0.0001
Lobectomy	66 (69%)	45 (67%)	69 (65%)	0.86
Bilobectomy	10 (10%)	3 (4%)	1 (1%)	0.01
Pneumonectomy	17 (18%)	0 (0%)	2 (2%)	<0.0001

VATS: video-assisted thoracic surgery; RATS: robotic-assisted thoracic surgery; SD: standard deviation

Table 2 Number of lymph node stations dissected

	T	VATS	RATS	p
Overall number of nodal stations dissected	4.6 ± 1.4	4.6 ± 1.2	4.9 ± 1.5	0.32
N1-level	1.6 ± 0.6	1.7 ± 0.7	1.9 ± 0.7	0.16
N2-level	3.1 ± 1.1	3.0 ± 0.9	3.0 ± 1.0	0.82
Right-sided procedures				
Overall number of nodal stations dissected	4.5 ± 1.2	4.6 ± 1.3	4.7 ± 1.3	0.76
N1-level	1.5 ± 0.5	1.6 ± 0.7	1.8 ± 0.7	0.08
N2-level	3.2 ± 1.0	3.1 ± 0.8	3.0 ± 0.8	0.66
Left-sided procedures				
Overall number of nodal stations dissected	4.7 ± 1.6	4.8 ± 1.2	5.1 ± 1.7	0.31
N1-level	1.7 ± 0.7	1.9 ± 0.8	1.9 ± 0.8	0.57
N2-level	3.1 ± 1.3	2.9 ± 1.0	3.0 ± 1.4	0.89

Values are given in (mean ± SD). VATS: video-assisted thoracic surgery; RATS: robotic-assisted thoracic surgery; SD: standard deviation

Results

Table 1 outlines the characteristics of the patients in each group. The groups were similar with respect to age, site of the disease, and the rate of primary lung cancer. The VATS and RATS group had more stage I lung cancer than the T group (53% and 60% vs. 27%, $p < 0.0001$). While the mean pathological tumor size was similar in the VATS and RATS group, significantly larger lesions were resected in the T group ($p < 0.0001$). Besides, more patients in the T group had pathologically proven N1 disease compared to the other groups ($p = 0.02$). According to the histology of the disease, significantly more patients had squamous

cell carcinoma in the T group compared to the others ($p < 0.001$), while adenocarcinoma predominated in both VATS and RATS group compared to the T group ($p = 0.0009$). None of the patients in the VATS group underwent pneumonectomy, and the rate of pneumonectomy was only 2% in the RATS group. There were no significant differences between VATS and RATS group in terms of the type of the resection, but significantly more patients in the T group underwent pneumonectomy (18%, $p < 0.0001$). All three groups had nearly equal rate of lobectomies, but segmentectomies were more common in the minimally invasive (VATS and RATS) groups compared to T group ($p < 0.0001$). There were no significant differences between three groups in

Table 3 Number of lymph nodes dissected

	T	VATS	RATS	p
Overall number of lymph nodes dissected	12.0 ± 6.4	11.7 ± 4.7	14.9 ± 6.5	0.0007
N1-level	4.0 ± 2.7	3.8 ± 2.1	6.8 ± 3.7	<0.0001
N2-level	8.3 ± 5.4	8.1 ± 3.6	8.6 ± 4.3	0.79
Right-sided procedures				
Overall number of lymph nodes dissected	12.5 ± 6.4	12.8 ± 4.5	15.6 ± 6.9	0.03
N1-level	3.8 ± 3.1	3.6 ± 2.0	6.6 ± 4.0	<0.0001
N2-level	9.0 ± 4.7	9.5 ± 3.3	9.5 ± 4.3	0.81
Left-sided procedures				
Overall number of lymph nodes dissected	11.3 ± 6.6	10.2 ± 4.7	13.9 ± 6.0	0.03
N1-level	4.2 ± 2.3	4.1 ± 2.3	7.1 ± 3.4	<0.0001
N2-level	7.6 ± 6.0	6.3 ± 3.1	7.1 ± 4.0	0.56

Values are given in (mean ± SD). VATS: video-assisted thoracic surgery; RATS: robotic-assisted thoracic surgery; SD: standard deviation

Table 4 Number of lymph nodes dissected by mediastinal stations

	T	VATS	RATS	p
Right-sided procedures				
Superior mediastinal lymph nodes dissected	5.0 ± 3.6	5.6 ± 2.6	5.2 ± 3.1	0.64
Subcarinal lymph nodes dissected	3.5 ± 2.3	3.7 ± 2.0	3.8 ± 2.3	0.75
Inferior mediastinal lymph nodes dissected	0.6 ± 1.0	0.3 ± 0.5	0.5 ± 1.0	0.18
Left-sided procedures				
Paraortic lymph nodes dissected	2.7 ± 2.6	3.1 ± 1.6	2.8 ± 2.1	0.71
Subcarinal lymph nodes dissected	3.4 ± 3.3	2.4 ± 1.8	2.7 ± 1.8	0.24
Inferior mediastinal lymph nodes dissected	1.2 ± 1.4	0.8 ± 1.2	1.3 ± 1.8	0.39

Values are given in (mean ± SD). VATS: video-assisted thoracic surgery; RATS: robotic-assisted thoracic surgery; SD: standard deviation

terms of intraoperative complications like bleeding, hypotension or arrhythmia ($p > 0.05$).

As demonstrated in **Table 2**, three different approaches had similar results based on the number of the dissected N1 and N2-level lymph node stations, regardless of the site of the operation. Although more lymph node stations have been dissected, both from the left and the right, via RATS, the results were not significant ($p > 0.05$).

Table 3 outlines the details of the number of lymph nodes dissected, both during the right-sided and the left-sided resections. RATS yielded significantly more lymph nodes in total, compared to the T and VATS groups ($p = 0.0007$). There was also significant difference in the number of N1-level nodes dissected in the RATS group compared to the other groups ($p < 0.0001$). Regarding the operation site, the total number and number of N1-level lymph nodes dissected in the RATS group were significantly higher than the other approaches ($p < 0.05$). All the groups were same with regard to the number of overall

and N2-level lymph nodes dissected, either from the left or the right.

Overall, the mean numbers of the N1-level lymph nodes dissected during segmentectomy procedure in three different approaches were 5.0 ± 3.6 , 3.4 ± 1.9 , and 6.0 ± 3.0 , respectively ($p = 0.19$). Significantly more N1-level lymph nodes were dissected during lobectomy and bilobectomy procedures in the RATS group (4.1 ± 2.8 , 4.0 ± 2.2 , and 7.3 ± 4.0 , respectively with $p < 0.05$).

When examining specific mediastinal nodal stations for all patients, there was not a significant difference in the number of nodes dissected for stations #2, #4, #7, #8 and #9 for right-sided, and #5, #6, #7, #8 and #9 for left-sided operations (**Table 4**). **Table 5** demonstrated the number of lymph nodes dissected by N1-level stations. All three approaches resulted in similar numbers of hilar (#10) lymph nodes, but RATS yielded significantly more level 11 and 12 lymph nodes, compared to the other two approaches ($p < 0.0001$).

Table 5 Number of lymph nodes dissected by N1-level stations

	T	VATS	RATS	p
#10 dissected	1.3 ± 1.0	1.0 ± 0.9	1.2 ± 1.1	0.37
#11 dissected	2.4 ± 2.2	2.2 ± 1.8	4.1 ± 2.6	<0.0001
#12 dissected	0.4 ± 0.6	0.7 ± 0.9	1.6 ± 1.5	<0.0001
Sum of #11 and #12 dissected	2.8 ± 2.3	2.9 ± 1.9	5.7 ± 3.1	<0.0001

Values are given in (mean ± SD). VATS: video-assisted thoracic surgery; RATS: robotic-assisted thoracic surgery; SD: standard deviation

Discussion

The excision and pathological assessment of mediastinal and N1-level lymph nodes in lung cancer resections is important in the prognosis and treatment. Besides non-invasive techniques, several surgical approaches including open or minimally invasive techniques, have been performed to obtain the oncologic effectivity based on the completeness of lymph node dissection.¹⁸⁾

Systematic MLND is considered to be the single most effective technique to decide and evaluate the extension of the nodal disease. Excision of occult mediastinal nodal disease may be diagnosed with a proper MLND. The effectivity of a particular technique, especially a new one, should be able to provide the similar results at least as the common and standard one (which is thoracotomy in this situation). In this study, we aimed to analyze our capability at lymph node dissection with the robotic and videothoroscopic surgical techniques.

According to the literature, there exist several studies comparing T and VATS, T and RATS, and VATS and RATS approaches separately, based on the N1 and N2-level lymph node dissection. This study differs from the previous studies, because we investigated three different approaches (T, VATS, and RATS) at the same time, and to our knowledge, this is the first study comparing these three modalities.

Several studies on patients with stage I lung cancer, demonstrated that lymph node assessment can be performed as effectively by the VATS as by the T approach.^{3,4,6)} In a multicenter study, D'Amico et al.⁵⁾ compared 199 patients undergoing VATS with 189 patients undergoing T, and found similar results. Unlike the previous studies concerning of patients with N0 diseases, the latter one included also patients with N2 and N3 diseases. In our study, we excluded patients with pathologically proven N2 or N3 diseases, and included only patients with N0 and N1 diseases.

Three recent studies compared the completeness of the lymph node dissection in patients with clinical N0 primary

lung cancers, undergoing lobectomy via VATS or T. Both Denlinger et al.,⁹⁾ and Merritt et al.¹⁰⁾ investigated the patients with only stage I lung cancers, therefore Ramos et al.⁸⁾ also included patients with stage II lung cancers in their study. All three studies demonstrated that more lymph nodes (total and N2-level, but not N1-level) could be dissected with open approach. The authors concluded that thoracotomy was superior in lymph node dissection, because of the long learning curve of the VATS procedure.^{9,10)} It was claimed that in VATS, more experienced surgeon could perform a proper mediastinal lymph node dissection. Sato et al.¹⁹⁾ mentioned that it is easier, by using thoracotomy, to create efficient retraction of organs and sufficient working place to dissect lymph nodes located in deep groove between the superior vena cava and trachea, or between the two main bronchi and the esophagus.

However, in a multicenter study of 5620 patients undergoing lobectomy with lymphadenectomy (2703 VATS vs. 2917 T), Wang et al.⁷⁾ concluded that it was possible to dissect more lymph nodes using VATS, compared to T. The authors claimed that the thoracoscopic vision provides better surgical exposure and has a visual zoom effect to magnify the surgical field, and this helps to identify and expose clearly the hilar structures and mediastinal lymph node stations.

One of the benefits of robotic pulmonary resection is the superior and stable vision allowing the surgeon to perform an extensive lymphadenectomy.¹²⁾ Although the number of lymph nodes removed tended to increase with increasing experience, there were no significant differences between RATS and T in terms of lymph nodes removed even in the early experience.^{11,12)} Then it could be speculated that, in robotic MLND, even in the early experience, similar number of lymph nodes could be dissected. This superiority, provided by the capability of robotic instruments may help to solve the experience problem faced in VATS, as described above.^{9,10)} Louie et al.¹³⁾ and Lee et al.¹⁴⁾ also compared RATS and VATS, and concluded that both approaches were similar in lymph node dissection. However we believe that the lymph node dissection in robotic surgery requires

a sharp dissection unlike that in VATS, which is generally performed with blunt dissection.

Our team has been performing VATS lobectomy since 2006, and the surgeons have developed their capabilities of MLND with VATS. In our study, MLND capability developed on an old technique, which is VATS, was compared to the most recent one, which is robotic. It is interesting that the most recent technique provided the higher number of lymph node dissection of N1-level, but similar number of nodes were dissected at N2-level.

Our study demonstrated that, compared to T and VATS, RATS can yield more N1-level lymph nodes, in both from the right or left-sided procedures ($p < 0.05$). As mentioned above, RATS provided the surgeon greater confidence and capability in dissecting N1 lymph nodes adjacent to the pulmonary artery.¹³⁾ We believe that, there may be two explanations for such a higher number of N1-level lymph node dissection in RATS. As a first explanation, we speculate that, as the console surgeon and table surgeon are different, the console surgeon tries to provide a clear area around artery and bronchus for the table surgeon, who is going to staple these dangerous structures, and so, resects each lymph node around arteries and branches to be divided to provide a safer area. Contrary to this, in VATS and thoracotomy, the dissecting and stapling surgeons are the same persons, thus depending on the personal experience, the surgeon may not need to dissect all lymph nodes to provide a clear area around artery and bronchus. The second explanation may be the greater capability of the instruments used in RATS. Robotic instruments provide sharp surgical techniques and prevent the violation of the capsule of the lymph node, and by this way the number of nodes may increase.

We demonstrated that hilar (#10) lymph node dissection yielded similar results in three approaches. On the contrary, significantly more level 11 and 12 lymph nodes could be obtained by RATS, which increased the overall sum of the N1-level lymph nodes. The significant increase in the rate of segmentectomy procedures in the RATS group, was not correlated with the increased number of dissected N1-level lymph nodes.

Very few studies investigated lymph node dissection by specific nodal stations, up to now. Ramos et al.⁸⁾ found that using T, surgeon could dissect more N1-level lymph nodes on the left-sided operations compared to VATS, but did not give an explanation for this finding. Denlinger et al.⁹⁾ also demonstrated that, compared to VATS, T was advantageous significantly in the dissection of station #7, and insignificantly in that of station #5 and #6. They

concluded that it was challenging for VATS to dissect paraaortic lymph node region in lower lobectomy cases, since the visualization was at times difficult. We believe that all techniques are safe. We also believe that the standard technique should be the open technique. As long as a new technique provides similar number of lymph nodes with the classical open technique, then the innovative technique may be an acceptable alternative for the MLND.

In 2013, Palade et al.⁶⁾ published their study comparing VATS and open mediastinal lymphadenectomy. They classified N1 and N2-level lymph nodes into different zones, and made a detailed comparison between two approaches. They reported similar results with respect to the number of lymph nodes in each zone. They stated that although the visualization of the anatomical structures with the optic system was excellent, the subcarinal station posed the problem of a sufficient lung retraction and a clear exposure of the depth to dissect along the contralateral mainstem bronchus compared to open technique.

This study has several limitations. Being retrospective in nature is the first limitation, although the data were collected prospectively. Histology, stage and size of the tumors are different which may possibly affect the number of the dissected lymph nodes. The main limitation of our study is that the types of the operations were not uniform in three groups. But the abovementioned limitations have shown to be also valid for similar studies we have referenced, comparing the different modalities in the dissection of the N1 and N2-level lymph nodes.

Conclusion

This study analyzes prospectively collected data on N1 and N2-level lymph node dissection in patients with lung cancer, which compares three different approaches (T, VATS, and RATS). This study is the updated form of our previous study including 170 patients (T = 60 patients, VATS = 44 patients, and RATS = 66 patients), and presented before.²⁰⁾ In conclusion, our study shows that all three methods can provide similar numbers of N1 and N2-level lymph node stations, and there exist no significant difference in the number of lymph nodes dissected from specific nodal stations. But, using RATS, significantly more N1-level lymph node could be dissected. Considering this is the results of an early experience of RATS technique, we can claim that RATS may have a potential in the future of lung cancer surgery, if the choice will be a minimally invasive surgery. However, we still believe that this difference should not be overrated, and

should only be considered as a sign of similar capabilities of RATS technique compared to VATS and thoracotomy techniques in the current thoracic surgery practise.

Disclosure Statement

Alper Toker and other co-authors have no conflict of interest.

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