Lymph Node Evaluation Achieved by Open Lobectomy Compared With Thoracoscopic Lobectomy for N0 Lung Cancer

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Background. Controversy remains regarding the adequacy of the lymph node evaluation achieved by video-assisted thoracic surgery (VATS) lobectomy for lung cancer. This study compared the completeness of the lymph node dissection or sampling for patients undergoing lobectomy by open thoracotomy vs VATS for clinical N0 lung cancer.

Methods. This study was a retrospective review of 129 patients who underwent lobectomy for clinical N0 lung carcinoma from December 2008 to January 2012.

Results. Lobectomy was an open procedure in 69 patients (53.5%) and by VATS in 60 (46.5%). The VATS and open groups were well matched for age (p = 0.50) and forced expiratory volume in 1 second percentage predicted (p = 0.16). The mean pathologic tumor sizes were not significantly different (2.9 ± 0.26 vs 3.4 ± 0.25 cm, respectively; p = 0.14). The mean number of nodes dissected in the open group was significantly higher (14.7 ± 1.3 vs. 9.9 ± 0.8 nodes; p = 0.003). In the open lobectomy group, 24.6% of the patients were upstaged to pathologic N1 or N2 compared with 10% in the VATS group (p = 0.05). The Kaplan-Meier 3-year survival was similar between the groups.

Conclusions. In our hands, significantly more lymph nodes were dissected, and a higher percentage of patients were upstaged to N1/N2, during open lobectomy compared with VATS lobectomy in patients with clinical stage N0 lung cancer. Although this did not translate into improved survival at 3 years, concern is raised about the adequacy of lymph node dissection during VATS lobectomy.


Lung carcinoma remains the leading cause of cancer-related death in North America [1]. Most commonly, patients with clinical stage I non-small cell lung carcinoma (NSCLC) are managed with lobectomy and lymph node sampling or lymphadenectomy through an open thoracotomy incision. In recent years, video-assisted thoracic surgery (VATS) lobectomy has emerged as the technique of choice at some centers for patients with stage I NSCLC. Multiple studies analyzing the results of VATS lobectomy have established with reasonable certainty the advantages of less postoperative pain, less postoperative morbidity, and shorter hospital stay compared with open lobectomy [2–5].

Despite the purported benefits of VATS lobectomy, there have been conflicting reports on the adequacy of the lymph node dissection or sampling achieved during VATS lobectomy compared with open lobectomy. A number of authors have demonstrated no difference in the completeness of lymph node sampling or dissection for VATS lobectomy compared with open lobectomy [6–8]. In contrast, Denlinger and colleagues [9] demonstrated that VATS lobectomy was associated with fewer mediastinal lymph nodes being dissected compared with open lobectomy [9]. In a large The Society of Thoracic Surgeons database review of 11,500 patients, Boffa and colleagues [10] reported that VATS lobectomy had a lower rate of N1 upstaging, which may serve as a surrogate for completeness of lymph node evaluation [10].

Noninvasive staging modalities for lung carcinoma, such as computed tomography (CT) and positron-emission tomography (PET), have limited sensitivity and specificity in identifying lymph node metastasis. The importance of complete surgical nodal staging during lobectomy cannot be overemphasized, given the proven benefit of adjuvant chemotherapy in patients with nodal-positive lung carcinoma [11–13]. Furthermore, there is little doubt that complete surgical removal of lymph nodes with malignant involvement provides an improved chance for cure.

Given this background, we compared the completeness of the lymph node evaluation/excision in our hands during VATS lobectomy and open lobectomy in patients with clinical N0 NSCLC. We also determined the rate of nodal upstaging to N1 or N2 and the 3-year survival rates between the two groups.

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Patients and Methods
The Stanford University Institutional Review Board approved this study protocol. A waiver for informed consent was granted, and patient information was protected. This is a retrospective review of 129 patients who underwent lobectomy for clinical N0 lung carcinoma from December 2008 to January 2012. Patient demographics, progress notes, imaging studies, operative reports, discharge summaries, and pathology reports were obtained from the electronic medical records, clinic records, and the Division of Thoracic Surgery’s prospective database.

The study excluded patients who underwent lobectomy for carcinoid tumors, secondary lung carcinoma, or benign diagnoses and those who underwent induction therapy, chest wall resection, sleeve resection, sublobar resection, or pneumonectomy. Importantly, patients with clinically suspected N1 or N2 nodal metastasis were also excluded on the basis of any lymph node with shortest diameter greater than 1 cm on CT scan or a standardized uptake value maximum greater than 2.5 on a PET scan. All patients underwent CT scans and all except 1 patient in each group underwent preoperative PET/CT. Patients were classified as clinical T1a N0, T1b N0, T2a N0, T2b N0, or T3 N0 according to the current NSCLC classification system [14].

The selection of VATS vs open lobectomy operative technique was at the discretion of the individual surgeon. We usually offer VATS lobectomy for patients with peripheral lung tumors that are 3 cm or smaller and without evidence of N2 nodal disease on imaging or mediastinoscopy. A routine lymph node evaluation was performed in every patient; however, the decision to perform a complete lymph node dissection vs a lymph node sampling was the choice of the individual surgeon. Lymph node stations that were typically sampled or dissected were 4R, 7, 11R, 10R, and 9R for right-sided procedures and 5, 6, 11L, 7, 10L, and 9L for left-sided procedures.

The VATS lobectomy procedures were performed using two or three 1-cm to 2-cm incisions and an anterior access incision no larger than 6 cm in length, without rib-sparing, as described in the Cancer and Leukemia Group B 39802 study [15]. The fissure is typically divided as the final step during VATS lobectomy, which is described as the “fissure-less” technique. When the fissure is complete in some cases, the pulmonary artery branches are dissected and divided initially.

Patient demographic data collected included age, sex, comorbidities, preoperative forced expiratory volume in 1 second percentage predicted, pack-years of smoking, and clinical stage. Postoperative complications recorded included pneumonia, respiratory failure, prolonged air leak (> 5 days), atrial fibrillation, myocardial infarction, and pulmonary embolism. A postoperative death was recorded if it occurred within 30 days of the procedure or in the hospital before discharge home.

The number of hilar and mediastinal lymph nodes that were removed at the time of lobectomy was recorded from the final pathology report. Additional lymph nodes that were removed from the lobectomy specimen by the pathologist were also included in the lymph node count. The same core group of pathologists reviewed all of the pathology specimens in the VATS and open lobectomy groups. Lymph nodes that were collected in fragments were usually counted as a single node from the respective nodal station; however, some fragmented nodes could possibly have been counted as single nodes in the VATS or open lobectomy groups. Nodal upstaging was reported as the percentage of patients who were found to have lymph node metastasis in the surgical specimen after being clinically staged as N0 based on preoperative CT and PET scans and upon mediastinoscopy in those patients who underwent mediastinoscopy.

Categoric variables were analyzed with the $\chi^2$ test and continuous variables with an unpaired $t$ test. Arithmetic mean values are reported with the standard error of the means. The overall survival rates of the VATS and open lobectomy groups were estimated by the Kaplan-Meier method. The statistical analyses were performed using MedCalc software (MedCalc Software, Mariakerke, Belgium). Differences were considered significant when the probability of a false-positive result was 0.05 or less. The biostatistics department at Stanford University was consulted for review of statistical methods.

Results
From December 2008 to January 2012, 129 patients underwent lobectomy for clinical N0 lung carcinoma at Stanford University Hospital. Of these, 69 (53.8%) underwent open lobectomy and 60 (46.2%) underwent VATS lobectomy. In the open lobectomy group, 18 (26%) underwent preoperative mediastinoscopy—nearly identical to the 15 (25%) in the VATS lobectomy group ($p = 0.94$).

The preoperative patient characteristics are listed in Table 1. There were no statistically significant differences between the groups on any of the examined variables. The clinical stage of the patients based on CT and PET scans and selective mediastinoscopy is listed in Table 2. The VATS lobectomy group had slightly more T1 lung carcinomas than the open lobectomy group (68.3% vs 52.2%; $p = 0.09$) and slightly fewer T2 ($p = 0.27$) and T3...
Table 1. Preoperative Patient Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>VATS Lobectomy (n = 60)</th>
<th>Open Lobectomy (n = 69)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>67 ± 1.2</td>
<td>68 ± 1.4</td>
<td>0.5</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>28 (46.7)</td>
<td>31 (44.9)</td>
<td>0.98</td>
</tr>
<tr>
<td>Females</td>
<td>32 (53.3)</td>
<td>38 (55.1)</td>
<td>0.98</td>
</tr>
<tr>
<td>FEV₁ % predicted</td>
<td>95.7 ± 2.1</td>
<td>91.4 ± 2.2</td>
<td>0.16</td>
</tr>
<tr>
<td>Smoking, pack-years</td>
<td>25.8 ± 3.2</td>
<td>20.5 ± 2.8</td>
<td>0.2</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>0.97 ± 0.03</td>
<td>0.98 ± 0.036</td>
<td>0.8</td>
</tr>
<tr>
<td>COPD</td>
<td>2 (3.3)</td>
<td>10 (14.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>CAD</td>
<td>8 (13.30)</td>
<td>11 (15.9)</td>
<td>0.87</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2 (3.3)</td>
<td>6 (8.7)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

* Categoric data are shown as number (%) and continuous variables as mean ± standard deviation.

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; FEV₁ = forced expiratory volume in 1 second; VATS = video-assisted thoracoscopic surgery.

tumors (p = 0.38), but these differences did not reach statistical significance. Furthermore, the mean pathologic tumor size was 2.9 ± 0.25 cm in the VATS group compared with 3.4 ± 0.25 cm in the open group, which was not significantly different (p = 0.14). The median pathologic tumor size in the VATS lobectomy group was 2.5 cm compared with 2.8 cm in the open lobectomy group. The distribution of lobectomy location was similar between the two groups (Table 2).

Postoperative complications are listed in Table 4. There were no (0%) 30-day or in-hospital deaths in the VATS lobectomy group and 1 death (1.4%) in the open lobectomy group. The mean length of stay in the VATS group was 4.5 ± 0.3 days compared with 5.1 ± 0.3 days in the open group (p = 0.14). The open lobectomy group had an insignificantly higher rate of respiratory complications. Atrial fibrillation rates were essentially the same.

The mean numbers of lymph nodes counted by the pathologists per lobectomy are listed in Table 5. Significantly more overall lymph nodes were dissected during open lobectomy than in VATS lobectomy. The total mean number of N2 nodes dissected was significantly higher in the open lobectomy group, but the total mean numbers of N1 nodes dissected were similar between the two groups. The percentage of nodal upstaging from N0 to N1 or N2 was significantly higher in the open lobectomy group than in the VATS group (24.6% vs 10%; p = 0.05; Table 6).

The mean follow-up time in the VATS lobectomy group was 16 ± 1.3 months compared with 22.6 ± 1.3 months in the open lobectomy group. Adjuvant chemotherapy was administered to 13.3% (8 of 60) of the patients in the VATS group compared with 28.9% of the patients in the open group (p = 0.05). Distant recurrent lung carcinoma was detected during follow-up in 11.7% (7 of 60) of the VATS lobectomy patients compared with 11.6% (8 of 69) in the open lobectomy patients. A locoregional recurrence was documented in an N2 lymph node 1 patient (1.7%) in the VATS group and in the ipsilateral pleura or in a separate ipsilateral lobe in 4 patients (5.8%) in the open lobectomy group.

The Kaplan-Meier overall survival curves are illustrated in Figure 1. The overall 3-year survival was 89.9% for the VATS lobectomy group and 84.7% for the open lobectomy group (log-rank test p = 0.6).

Comment

We compared the completeness of the lymph node evaluation between VATS lobectomy and open lobectomy in patients with clinical N0 NSCLC. A number of reports have demonstrated that VATS lobectomy can be performed with minimal complications and a shorter length of stay compared with open lobectomy [2-5]. Unfortunately, none of these reports gave a detailed

Table 2. Clinical Stages

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>VATS Lobectomy (n = 60) No. (%)</th>
<th>Open Lobectomy (n = 69) No. (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>cT1 N0</td>
<td>41 (68.3)</td>
<td>36 (52.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>cT2 N0</td>
<td>17 (28.3)</td>
<td>27 (39.1)</td>
<td>0.27</td>
</tr>
<tr>
<td>cT3 N0</td>
<td>2 (3.4)</td>
<td>6 (8.7)</td>
<td>0.38</td>
</tr>
</tbody>
</table>

* VATS = video-assisted thoracoscopic surgery.

Table 3. Anatomic Location of the Lobectomy

<table>
<thead>
<tr>
<th>Anatomic Location</th>
<th>VATS Lobectomy (n = 60) No. (%)</th>
<th>Open Lobectomy (n = 69) No. (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right lobe</td>
<td>22 (36.7)</td>
<td>24 (34.7)</td>
<td>0.95</td>
</tr>
<tr>
<td>Middle</td>
<td>5 (8.3)</td>
<td>2 (2.9)</td>
<td>0.93</td>
</tr>
<tr>
<td>Lower</td>
<td>6 (10.0)</td>
<td>11 (15.9)</td>
<td>0.47</td>
</tr>
<tr>
<td>Left lobe</td>
<td>14 (23.3)</td>
<td>18 (26.1)</td>
<td>0.87</td>
</tr>
</tbody>
</table>

VATS = video-assisted thoracoscopic surgery.

Table 4. Postoperative Complications

<table>
<thead>
<tr>
<th>Complication</th>
<th>VATS Lobectomy (n = 60) No. (%)</th>
<th>Open Lobectomy (n = 69) No. (%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>3 (5)</td>
<td>6 (8.7)</td>
<td>0.6</td>
</tr>
<tr>
<td>Air leak (&gt; 5 days)</td>
<td>5 (8.3)</td>
<td>4 (5.8)</td>
<td>0.8</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>2 (3.3)</td>
<td>5 (7.2)</td>
<td>0.56</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>0</td>
<td>4 (5.8)</td>
<td>0.2</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>11 (18.3)</td>
<td>12 (17.4)</td>
<td>0.9</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>0</td>
<td>1 (1.4)</td>
<td>0.9</td>
</tr>
<tr>
<td>Pulmonary Embolus</td>
<td>0</td>
<td>1 (1.4)</td>
<td>0.9</td>
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VATS = video-assisted thoracoscopic surgery.
analysis of the number of lymph nodes or lymph node stations that were dissected during VATS lobectomy. Despite these benefits of VATS lobectomy for stage I lung carcinoma, the completeness of lymph node evaluation during the procedure has been questioned.

Lymph node sampling or dissection remains an important component of lobectomy performed for resection of lung carcinoma. In the Cancer and Leukemia Group B 9781 prospective trial, D’Cunha and colleagues [16] demonstrated that 27.5% of patients with clinical stage I lung carcinoma were upstaged to N1 or N2 after lobectomy. This study illustrates the limitations of noninvasive preoperative staging with CT and PET scanning. Given the fairly poor correlation between clinical and pathologic staging for clinical stage I lung NSCLC, the importance of a complete lymph node evaluation becomes even greater to ensure accurate staging, which has implications on the use of adjuvant chemotherapy.

A number of studies have investigated the ideal extent of the lymph node dissection during lobectomy and the effect of the nodal evaluation on survival for lung carcinoma. Currently, the ideal, requisite number of lymph nodes that should be resected during a lobectomy for lung carcinoma remains unknown and controversial. In an attempt to establish a guideline for the number of lymph nodes to be dissected during a resection for lung carcinoma, Ludwig and colleagues [17] reviewed 16,800 patients from the Surveillance, Epidemiology and End Results database who underwent resection of clinical stage I lung NSCLC to evaluate the correlation between overall survival and the number of lymph nodes removed. They determined that patients who had 8 to 16 lymph nodes removed at the time of surgical resection demonstrated statistically better overall survival than those with less nodes evaluated/removed [17].

The much-anticipated American College of Surgeons Oncology Group Z30030 randomized clinical trial compared mediastinal lymph node dissection with systematic mediastinal lymph node sampling in patients with clinical N0 or N1 lung carcinoma. Darling and colleagues [18] demonstrated that the 5-year disease-free survival was similar between the groups, and only 4% of the patients in the mediastinal lymph node dissection group had occult N2 disease. The results of this randomized study, however, may have been influenced by the rigorous systematic lymph node sampling protocol that the trial required for randomization.

Even without a clear survival benefit for mediastinal lymph node dissection, it is plausible to conclude that the probability of a pathologic staging error (missing positive lymph nodes during lobectomy) decreases incrementally with a greater number of lymph nodes evaluated in the

<table>
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<th>Table 5. Mean and Median Number of Lymph Nodes Dissected</th>
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<tr>
<td>Nodes Dissected</td>
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<tr>
<td></td>
</tr>
<tr>
<td>Overall number</td>
</tr>
<tr>
<td>Total nodes</td>
</tr>
<tr>
<td>N2</td>
</tr>
<tr>
<td>N1</td>
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</table>

SD = standard deviation; VATS = video-assisted thoracoscopic surgery.

<table>
<thead>
<tr>
<th>Table 6. Percentage of Lymph Node Upstaging</th>
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<tbody>
<tr>
<td>Nodal Upstaging</td>
</tr>
<tr>
<td>Overall</td>
</tr>
<tr>
<td>N1</td>
</tr>
<tr>
<td>N2</td>
</tr>
</tbody>
</table>

VATS = video-assisted thoracoscopic surgery.

Fig 1. Kaplan-Meier survival curve comparing the overall survival rates for patients who underwent video-assisted thoracoscopic surgery (VATS, solid line) lobectomy and open lobectomy for clinical N0 lung carcinoma (OPEN, dotted line). The overall 3-year survival was 89.9% for the VATS lobectomy group compared with 84.7% for the open lobectomy group (log-rank test, p = 0.6).
pathology specimen. Beyond the possibility of achieving cure with complete removal of involved nodes with resection itself, the detection of occult N1 and N2 nodal metastases will in addition identify appropriate candidates for adjuvant chemotherapy, which has a proven survival benefit for stage II and stage IIIA resected NSCLC [11–13]. Our study found that a significantly greater mean number of lymph nodes were dissected during lobectomy by thoracotomy than during VATS lobectomy. In addition, the total mean number of N2 lymph nodes that were dissected during open lobectomy was significantly higher than during VATS lobectomy; however, the mean number of N1 lymph nodes was similar between the groups, with only a trend toward more N1 nodes being resected during open lobectomy. The overall pathologic upstaging from N0 to N1 or N2 was significantly greater in the open lobectomy group, apparently because of the increase in the number of nodes evaluated.

Denlinger and colleagues [9] reported similar results in their retrospective study of lymph node evaluation achieved by VATS lobectomy compared with open lobectomy. Significantly more overall lymph nodes were dissected in the open group (8.9 ± 5.2 vs 7.1 ± 5.2 nodes; \( p = 0.006 \)) than in the VATS lobectomy group. Subset analyses demonstrated that significantly more N2 lymph nodes were dissected in the open lobectomy group; however, the mean number of N1 nodes dissected was similar between the two groups. This finding was attributed to the difficulty of accessing the subcarinal lymph node station during left-sided VATS procedures and difficult visualization of the level 5 and level 6 stations during VATS.

Boffa and colleagues [10] reported the results of lymph node evaluation by VATS and open approaches in 11,500 anatomic lung cancer resections from The Society of Thoracic Surgeons database. Their report demonstrated 14.3% nodal upstaging in the open group compared with 11.6% in the VATS lobectomy group (\( p = 0.0001 \)). The study also demonstrated that upstaging from N0 to N1 was significantly greater in the open group, whereas upstaging to N2 was similar between the groups. The report concluded that of the completeness of mediastinal lymph node dissection was similar between VATS and open lobectomy but that the peribronchial and hilar lymph node dissection was more complete in the open lobectomy group. They did not indicate if the patients underwent preoperative PET scanning for staging, which could have implications for the accuracy of the clinical N0 designation.

The observation in our report of a more effective mediastinal lymph node harvest by open lobectomy has a number of potential explanations. First, some believe that performing a complete mediastinal lymph node dissection with the VATS technique is more technically challenging due to deceased visualization of nodal tissue and the limited instrumentation available for the efficient and effective removal of lymph node tissue. We do believe that performing a complete lymphadenectomy by VATS requires a great deal of patience. In fact, after the publication of the American College of Surgeons Oncology Group Z0030 study demonstrating no difference in survival with systematic lymph node sampling compared with complete lymphadenectomy, the senior author (J.B.S.) switched to a technique of systematic sampling with frozen sections for VATS, while continuing to perform complete lymphadenectomy in open cases, and the first author (R.E.M.) performs sampling for both VATS and open lobectomies. As a result, a systematic mediastinal lymph node sampling, as opposed to a complete lymphadenectomy, was more likely to be performed during a VATS lobectomy in our study.

Despite the disparity in mediastinal lymph node evaluation between VATS lobectomy and open lobectomy, it is important to note that we did not observe a difference in 3-year overall survival between the two groups (Fig 1). A similar finding has been seen in other studies comparing the overall survival of VATS lobectomy with open lobectomy [4, 9, 19]. One must, nevertheless, wonder whether the equivalence of survival in our study represents a type II error due to insufficient power.

The interpretation of the results of our study is additionally limited by the retrospective study design, which introduces inherent selection bias. Although the demographics of the patient populations in the two groups are very similar and the patients underwent nearly identical preoperative staging, the VATS lobectomy group did contain a slightly higher number of clinical T1 tumors, although the median pathologic tumor sizes were similar (2.5 vs 2.8 cm). That this statistically insignificant difference in tumor size/T category between the groups could be the sole cause of the significant difference in nodal upstaging seems unlikely.

A critic of our study might also suggest that these results could be due to these particular VATS surgeons still being on the ascending limb of their learning curve for VATS lobectomy because the experience described in this study is modest in size. However, this would also seem to be unlikely because the senior author (J.B.S.) has been performing VATS lobectomies for 10 years and has performed more than 300 VATS lobectomies. A recent study evaluating the learning curve for VATS lobectomy suggested that peak skills arrive after approximately 30 to 60 procedures [20].

In an environment in which VATS lobectomies are likely achieving less complete lymph node evaluation than would have been completed by thoracotomy, it is critical that VATS lobectomies be performed primarily in clinical stage N0 patients who have minimal chance of harboring occult N1 or N2 disease. We believe that this should include only patients with peripheral tumors that are less than 3 cm in maximal diameter, and we believe that those with tumors exceeding 2 cm in diameter should likely undergo mediastinoscopy before being considered for VATS lobectomy.

In the future, it is possible that the time and effort required to perform a more complete mediastinal lymph node evaluation during VATS lobectomy will be reduced by improvements in VATS instrumentation to the point that it will be feasible for all surgeons to undertake this
effort. In addition, it may be time to consider a randomized phase III study to compare the long-term survival and the extent of lymph node resection between VATS lobectomy and open lobectomy.

References


DISCUSSION

DR DAVID R. JONES (Charlottesville, VA): Do you do your lymph node dissection first, or do you do your pulmonary resection first?

DR MERRITT: Initially, we used to perform the resection of the lobe first by dividing the pulmonary vein, the pulmonary artery branches, and the bronchus. We would then complete the lymph node dissection at the end of the case, but more recently, we started performing the lymph node dissection before the actual lobectomy.

DR JONES: Do you think it is the technique, meaning video-assisted thoracoscopic surgery (VATS) or thoracotomy, or do you think it is the surgeons and their willingness to do the dissection regardless of technique?

DR MERRITT: Well, I think the extent of the lymph node dissection is a direct correlate of the motivation of the individual surgeon. At Stanford, we participate in adjuvant chemotherapy clinical trials, so we are interested in performing a complete lymph node dissection to identify patients who are eligible for adjuvant chemotherapy, but it does take a great deal of patience and effort to do a very thorough lymph node clearance thoracoscopically compared with thoracotomy. And obviously, we all have our individual biases whether we perform a mediastinal lymph node sampling or a full mediastinal lymph node dissection.

DR JONES: Thank you.

DR SCOTT J. SWANSON (Boston, MA): I thought that was an excellent presentation. A couple of questions and a couple observations. One, is at least to date, none of the VATS lobectomy trials or the meta-analyses have ever shown a higher locoregional recurrence after VATS compared with open. So I would think if there is a lymph node issue, we would see that either in local recurrence or systemic, and that has never been shown. I would be interested in your take on that. Secondly, I noticed you did mediastinoscopy about a quarter of the time. That seemed a little low to me, and I was curious why that might be. And then the second question is in terms of the surgeons involved with the study, did both surgeons do equal numbers of VATS and open, and was there experience level going into this involved with the study, did both surgeons do equal numbers of VATS lobectomy and open lobectomy.


that might be part of where the difference is in this study. So I would be interested in the experience level of the surgeons that were doing this, and were they doing both.

DR MERRITT: Thanks Dr Swanson. The answer to the first and second question, whether or not the extent of lymph node dissection will affect local recurrence or distant recurrence, I think that for this particular cohort of patients, they had a complete preoperative staging with positron-emission tomography (PET) computed tomography (CT) scans, and a quarter of them had mediastinoscopy.

If we do detect nodal disease in these patients during lobectomy, it is going to be microscopic nodal disease and not gross nodal disease. So it is hard to really decipher if doing a complete lymph node clearance in these patients would result in decreased local recurrence or decreased distant recurrence. I think if it is true microscopic nodal disease, a complete nodal dissection may give you a more complete resection and lower the risk of having a local recurrence in the mediastinum. I am not sure if that will translate into increased long-term survival.

And then the answer to the third question about the experience of the surgeon with VATS lobectomy, the senior author on the paper has done hundreds of VATS lobectomies, so he is well above that learning curve. I am also beyond the learning curve, having performed more than 100 VATS lobectomies, but during the study period, I was going through that learning curve. I think that the experience of the surgeon performing a VATS lobectomy and also their individual volume does have an impact on how thorough or complete the lymph node evaluation will be.

DR SWANSON: Because I agree with what David Jones said, I think it is the interest of the surgeon—not the technology—that gets the lymph nodes out. There is nothing about VATS that prevents lymph node removal. It is sort of at the end of a case whether you want to go through that or not.

DR MERRITT: Right. I agree. I think the technique is not the limiting factor, but it is the motivation and skill level of the surgeon performing the technique that will impact the completeness of the lymph node dissection. But with that said, if we perform VATS lobectomies, we have to make sure that we perform a complete lymph node evaluation to identify patients that will benefit from adjuvant chemotherapy.

DR SWANSON: Seems like a good recommendation: take out the lymph nodes. I agree.

DR SHRAGER: As the “senior author,” I just want to comment that I think that the key issues are exactly the things you guys just identified. In my opinion, the VATS technique does make it a little harder to really clear out the nodes. I believe, even having done hundreds of VATS lobectomies, that you have to have the patience of a saint, I think, to really do the same lymph node dissection thoracoscopically that you do open. I think in the real world, very few of us have the patience to be able to do it exactly the same. So I think in the real world, you are not going to have the same complete lymphadenectomy by VATS as by open. I think that what we are demonstrating with this paper is we are showing a real-world issue.

It is also important to mention that there are a lot of papers that demonstrate trends towards a little bit better survival in the open lobectomy vs VATS group for N0 tumors. And so it may just be a type II error, that we just don’t have any gigantic enough studies that would show a statistically significant difference in survival even when that difference is small, but that is just a hypothesis.

DR GAIL DARLING (Toronto, Ontario, Canada): I have a comment and then a question. One of the things that shows up in these studies is that we are talking about numbers of lymph nodes and differences in numbers of lymph nodes but they don’t specifying lymph node stations, and we all know the difficulty in counting lymph nodes. Do you count fragments? Do you weigh them?

So maybe your center is different than mine, but I would say numbers of lymph nodes in my center are not a reliable indicator of my lymph node assessment, and I am just wondering if you have looked at lymph node stations. Did you sample the N2 stations as per the American College of Surgeons Oncology Group (ACSGO) protocol, or were they just N1 stations? And I think that is probably a more important metric than the actual number of lymph nodes. Could you comment on that?

DR MERRITT: I agree. I think it is hard to really decipher if we are counting fragments or whole lymph nodes, and the other metric is weighing the lymph nodes to see if they are adequate. I think there is a great deal of variability between institutions because there is no established protocol, and I think that does bias the data.

DR DARLING: Did you look at which lymph node stations were sampled?

DR MERRITT: Yes. That data I didn’t show today, but we did perform a cursory review of the different lymph node stations that we were actually sampling. And consistently for right-sided resections we usually would get lymph nodes from level 4, level 7, level 11R, and level 10. For left-sided resections in most cases, we would sample level 5, level 6, 10L, and then level 9. We did report the number of N2 nodes removed in the VATS group and the thoracotomy group.

DR DARLING: And were those the same for the VATS group and the open group?

DR MERRITT: I don’t have those data. We can go back and do that analysis, but for this study we didn’t do that. We think that the percentage of upstaging from N0 to N1 or N2 would serve as a better metric of measuring the extent of the lymph node dissection.

DR DARLING: Because it certainly raises the question: If you take out more nodes and you have more upstaging, why and how is the survival is the same? That’s sort of intriguing, isn’t it?

DR MERRITT: Absolutely. And it could be the issue of also the impact of micrometastatic nodal disease on overall survival, particularly long-term survival. This was a short-term analysis with just a 3-year follow-up.