Video-assisted mediastinoscopic lymphadenectomy is associated with better survival than mediastinoscopy in patients with resected non–small cell lung cancer

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Objectives: We aimed to analyze the accuracy of video-assisted mediastinoscopic lymphadenectomy (VAMLA) as a tool for preoperative staging and the impact of the technique on survival in patients with non–small cell lung cancer (NSCLC) undergoing pulmonary resection.

Methods: Between May 2006 and December 2010, 433 patients underwent pulmonary resection for NSCLC, 89 (21%) had VAMLA before resection and 344 (79%) had standard mediastinoscopy. The patients who had negative VAMLA/mediastinoscopy results underwent anatomic pulmonary resection and systematic lymph node dissection.

Results: The median and mean numbers of resected lymph node stations were 5 and 4.9 in the VAMLA group and 4 and 4.2 in the mediastinoscopy group ($P = .9$). The mean number of lymph nodes per biopsy specimen using standard mediastinoscopy was 10.1, whereas it was 30.4 using VAMLA ($P < .001$). VAMLA unveiled N2 or N3 disease in 30 (33.7%) and in 6 (6.7%) of patients, respectively. The negative predictive value, sensitivity, false-negative value, and accuracy of VAMLA were statistically higher in the VAMLA groups compared with those of standard mediastinoscopy. The 5-year survival was 90% for VAMLA patients and 66% for mediastinoscopy patients ($P = .01$). By multivariable analysis, VAMLA was associated with better survival (odds ratio, 1.34; 95% confidence interval, 1.1-3.2; $P = .02$).

Conclusions: VAMLA was associated with improved survival in NSCLC patients who had resectional surgery.
(J Thorac Cardiovasc Surg 2013;146:774-80)

The best treatment for non–small cell lung cancer (NSCLC) is dependent on correct staging of the disease. Nodal status provides a pivotal role in anatomic staging of lung cancer. Despite this fact, mediastinoscopy has been accepted as the gold standard method for preoperative mediastinal staging in patients with NSCLC, it has its inherent limitations, and the false-negativity rate can be as high as 10% and was equal to the false-negativity rate of endobronchial ultrasound-guided transbronchial needle aspiration.[1] Hürtgen and colleagues[2] developed a technique of radical video-assisted mediastinoscopic lymphadenectomy (VAMLA). The primary advantage of VAMLA over conventional mediastinoscopy or videomediastinoscopy is to reduce the false-negative rate.[2] However, the exact role of VAMLA has not been fully elucidated. Our study aimed to assess the accuracy of regional lymph node classification and its impact on survival for conventional mediastinoscopy and video-assisted mediastinoscopic lymphadenectomy.

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Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Aug 16, 2012; revisions received April 14, 2013; accepted for publication April 24, 2013; available ahead of print June 17, 2013.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2013.04.036

METHODS

Between May 2006 and December 2010, patients who had undergone pulmonary resection for NSCLC were analyzed. Mediastinal procedure selection is purely based on the surgeon's preference. All VAMLA procedures were performed by 1 surgeon (A.T.). However, mediastinoscopies in the study were performed by experienced surgeons (A.D. and K.K.). One surgeon (A.T.) only performed VAMLA in all consecutive patients. Of all patients, 89 underwent VAMLA before operation, whereas 344 underwent standard mediastinoscopic exploration. Two surgeons (A.D. and K.K.) only performed standard mediastinoscopy. This is a retrospective cohort study of prospectively recorded patients. The preoperative workup included routine blood tests, posteroanterior and lateral chest radiographs, bronchoscopy, pulmonary function tests, with or without diffusion capacity of lung for carbon monoxide and ventilation-perfusion lung scan, and blood gas analysis. Computed tomographic scans of the thorax, abdomen (or abdominal ultrasonography), and cranium (or cranial magnetic resonance imaging), and whole-body bone scintigraphy were performed in most patients for pretreatment staging. Positron emission tomography–computed tomography analysis was performed in a total of 401 patients. The patient characteristics are shown in Table 1. There was no death or major complication due to mediastinoscopy or VAMLA.

Mediastinal lymph node sampling through cervical mediastinoscopy at stations 2, 4 (both left and right), and 7 was performed in almost all patients. Preoperative mediastinal exploration was supplemented by left anterior mediastinotomy (n = 20) or extended mediastinoscopy (n = 13) in patients whose tumor lay in the left upper lobe or left main bronchus

Abbreviations and Acronyms

NSCLC = non–small cell lung cancer
TEMLA = transcervical extended mediastinal lymphadenectomy
VAMLA = video-assisted mediastinoscopic lymphadenectomy

and in those with enlarged anterior mediastinal or aorticopulmonary lymph nodes (ie, stations 5 and 6). In our institution, mediastinoscopy (VAMLA or standard mediastinoscopy) was performed routinely in patients with potentially operable histologically proven NSCLC. In all, 433 (94.3%) of 459 patients underwent mediastinoscopy or VAMLA. We used a Linder-Dahan videomediastinoscope (Richard Wolf, Knittlingen, Germany) for VAMLA and a standard mediastinoscope (Richard Wolf) for standard mediastinoscopy.

According to our institutional strategy, we did not operate on patients with N2-N3 disease without oncological treatment (ie, radiotherapy and/or chemotherapy) (Figure 1). Fifty patients who underwent VAMLA (VAMLA-negative patients) and 279 patients who underwent standard mediastinoscopy were operated on. The type of resection was decided based on anatomic tumor involvement. Pneumonectomy was performed in 88 patients (26.7%), sleeve lobectomy was performed in 14 patients (4.3%), bilobectomy was performed in 51 patients (15.5%), wedge resection/segmentectomy was done in 5 patients (1.5%), and (standard) lobectomy was performed in 195 patients (59.3%). For pneumonectomy and lobectomy, postoperative 30-day mortality rates were 6.8% (n = 6) and 3.5% (n = 9), respectively. *Complete resection* was defined as the removal of all detectable disease by the surgeon and histologic confirmation of tumor-free resection margins. Complete resection was achieved in 307 cases (93.3%). The time between VAMLA/mediastinoscopy and pulmonary resection was fewer than 30 days in almost all (97.6%) of patients (319 of 327 patients who had pulmonary resection). Patients with tumor-positive margins on final pathology review after complete gross resection at thoracotomy were classified as having undergone incomplete resection (n = 22). A systematic mediastinal lymphadenectomy was performed in every patient, in addition to anatomic lung resection (ie, all patients underwent uniform staging to determine a final surgical-pathologic stage, based on information obtained through thoracotomy and pathology examination).[3] The final surgical-pathologic stage of the patients who underwent resection before 2009 was reconstructed according to a recent staging system.[3] The CONSORT flow diagram of the study is shown in Figure 1.

Patients were grouped according to highest level of involved lymph node station. The mean number of lymph nodes resected and examined was 16 per patient (range, 2 to 67) for the N1 and N2 lymph node regions. In the N1 region, a mean of 9 lymph nodes (range, 2 to 37) was removed. All histologic specimens from patients were evaluated according to the World Health Organization classification.[4] Histopathologic tumor types included squamous carcinoma in 210 cases (63.8%), adenocarcinoma in 89 cases (27.0%), and other non–small cell carcinoma types in 30 cases (9.1%). An informed consent was obtained from every patient. The need for Institutional Review Board Approval was waived according to our country's law because the study is a retrospective cohort study.

The distribution of clinical T factors is balanced in the VAMLA and mediastinoscopy groups, despite the fact that the rate of T4 tumors was higher in patients who underwent VAMLA ($P = .29$) (Table 1). The surgical pathological T factors that were reconstructed using resected materials are also balanced between 2 groups (Table 2).

Statistical Analysis

A χ^2 test was used for distribution of the T factor. A Mann-Whitney *U* test was used for the comparison of biopsy specimen/resected lymph nodes. The negative predictive value, sensitivity, and specificity were calculated by the following formulas:

Negative Predictive Value = [(Number of True Negatives)/(Number of True Negatives + Number of False Negatives)] × 100

Sensitivity = [(Number of True Positives)/(Number of True Positives + Number of False Negatives)] × 100

Specificity = [(Number of True Negatives)/(Number of False Positives + Number of True Negatives)] × 100

Accuracy = [(Number of True Negatives + Number of True Positives)/(Number of True Negatives + Number of True Positives + Number of False Positives + Number of False Negatives)] × 100

Patient survival was expressed by analysis according to the Kaplan-Meier method, using time 0 as the date of thoracotomy and death as the end point. Perioperative deaths were included in survival analysis. We performed an intention-to-treat analysis, including all patients who had undergone resectional surgery during the study period. Prognostic factors were evaluated in completely resected patients. Differences in survival were determined using the log-rank test in the univariate analysis, and multivariate analysis was done using the Cox proportional hazards regression model. The mean follow-up time was 20.1 ± 20.1 months (range, 10 to 67 months). We also performed a propensity-matched analysis to compare the patients in the VAMLA and standard mediastinoscopy groups.

Propensity matching was performed to identify 2 similar groups within the standard mediastinoscopy and VAMLA groups. These groups were matched with regard to age, sex, forced expiratory volume in 1 second, and tumor histology clinical T stage. In this propensity analysis, 50 matched pairs were identified.

TABLE 1. Patients' clinical characteristics and distribution of clinical T stages according to preoperative invasive mediastinal staging modality

Parameter	Standard mediastinoscopy (n = 344)	VAMLA (n = 89)	P value
Age (range), y	60.3 (20-81)	59.7 (44-79)	>.05
Male/female ratio	290:54	70:19	>.05
Mean FVC (mL)	3210.5	3218.8	>.05
Mean FEV_1 (mL)	2394.4	2298.9	>.05
Predicted FEV_1, %	77.2	75.6	
FEV_1/FVC ratio	89.5	84.0	>.05
T stage, no. (%)			
cT1a	43 (12.5)	15 (16.9)	
cT1b	44 (12.8)	12 (13.5)	
cT2a	118 (34.3)	32 (36.0)	
cT2b	28 (8.1)	6 (6.7)	
cT3	105 (30.5)	20 (22.5)	
cT4	6 (1.7)	4 (4.5)	>.05

VAMLA, Video-assisted mediastinoscopic lymphadenectomy; *FVC*, forced vital capacity; *FEV_1*, forced expiratory volume in 1 second.

RESULTS

The median number of resected lymph node station was 5 in the VAMLA group (mean, 4.9), whereas the median number of station was 4 (mean, 4.1) in the mediastinoscopy group ($P = .9$). The mean number of lymph nodes per biopsy specimen using standard mediastinoscopy was 10.1 (range, 2-33), whereas it was 30.4 (range, 18-110) using VAMLA ($P < .001$). In the VAMLA group, lymph node dissection of stations 2R, 2L, 4R, 4L, 7, and 8 was achieved in

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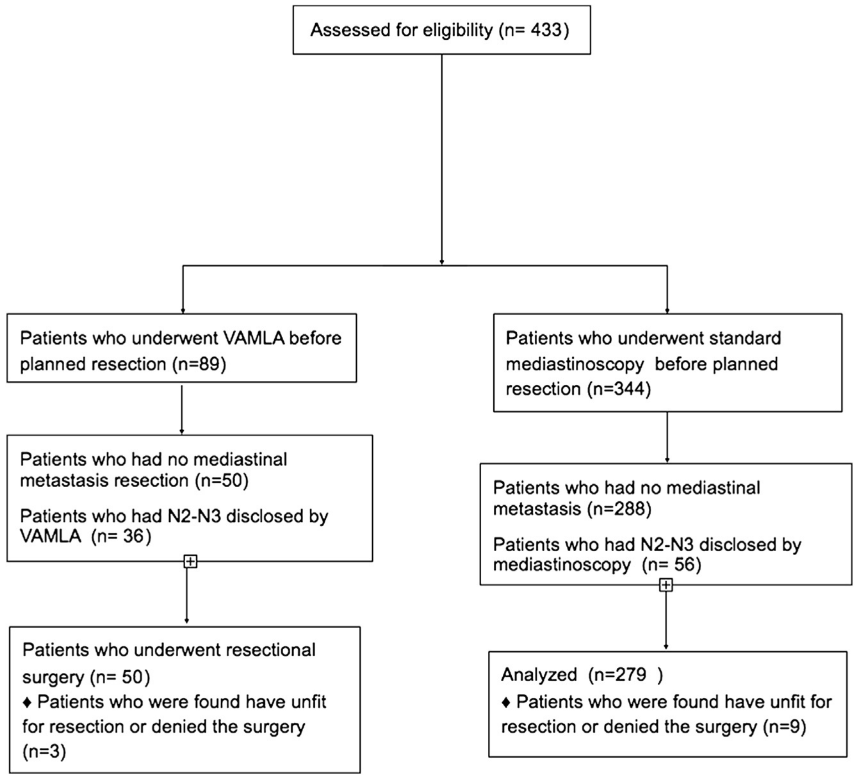

FIGURE 1. CONSORT 2010 diagram of the study. *VAMLA*, Video-assisted mediastinoscopic lymphadenectomy.

85 (95.5%), 60 (67.4%), 86 (96.7%), 85 (95.6%), 88 (98.9%), and 23 (25.8%) of the patients, respectively. In the standard mediastinoscopy group, 2R, 2L, 4R, 4L, 7, and 8 underwent biopsy in 190 (55.2%), 89 (25.9%), 296 (86.0%), 189 (54.8%), 215 (62.5%), and 0 of the patients, respectively. The difference was statistically significant ($P < .001$). VAMLA statistically significantly disclosed more disease ($P < .001$) (Table 3). The mean number of resected mediastinal lymph nodes during pulmonary resection was 8.3 (range, 0-32) or 4.0 (range, 0-11) in patients who underwent standard mediastinoscopy or VAMLA, respectively ($P < .001$). Dysphonia was notified in 8 (9.0%) of patients who had VAMLA, whereas the complication rate was 4.1% (13 dysphonia and 1 pneumothorax) in patients who underwent standard mediastinoscopy. The difference was statistically significant ($P = .03$). When comparing histopathologic staging from VAMLA with final pathology, there were 3 false-negative (1 patient with subcarinal, 1 patient with 2R, and 1 patient with 8R metastasis) results. In the standard mediastinoscopy group, 27 patients (12, 3, 2, 2, 1, 2, and 1 patient with 7, 4, 2, 5, 6, 8R, and 9R metastasis, respectively) had N2 disease after resection. The negative predictive value, sensitivity, false-negative value, and accuracy of VAMLA were statistically higher in VAMLA groups compared with those of the standard mediastinoscopy group (Table 3). All (n = 329) patients who had undergone complete resectional surgery had a 5-year survival of 66%, with a mean survival time of 50.6 months.

Kaplan-Meier estimation and log-rank comparison of the survival data revealed that the 5-year survival rate of patients who had VAMLA and subsequent pulmonary resection (n = 50) was 90.0%, whereas it was 66.4% in patients who underwent mediastinoscopy and pulmonary resection (n = 279) ($P = .01$) (Figure 2). N factor, T factor, type of mediastinoscopy (VAMLA or standard mediastinoscopy), sex, and type of operation were entered into the Cox proportional (multivariate) analysis. Multivariate Cox analysis showed that performing VAMLA, absence of nodal metastasis, and T factor were independently good prognostic elements in resected patients (Table 4).

TABLE 2. Pathologic T stages of patients who had undergone resectional surgery

Pathologic T stage, no. (%)	VAMLA (n = 50)	Standard mediastinoscopy (n = 279)	*P* value
pT1a	12 (24)	63 (22.5)	>.05
pT1b	9 (18)	28 (10)	>.05
pT2a	12 (24)	74 (27)	>.05
pT2b	4 (8)	23 (8)	>.05
pT3	11 (22)	88 (32)	>.05
pT4	2 (4)	3 (1)	>.05

Values are given as number (percentage). *VAMLA*, Video-assisted mediastinoscopic lymphadenectomy.

TABLE 3. N stages of patients disclosed by mediastinal staging modality ($P < .001$) and accuracy of mediastinal staging modalities according to final pathologic findings of resected lymph nodes

N status	Standard mediastinoscopy (n = 344)	VAMLA (n = 89)	P value
N0, no. (%)	288 (83.7)	53 (59.6)	.023
N2-3, no. (%)	56 (16.2)	36 (40.4)	<.001
Specificity	100.0	100.0	1
Sensitivity	67.5	95.5	.001
False-negative value	9.4	3.4	.04
Negative predictive value	90.6	94.3	.03
Accuracy	92.2	96.6	.04

Values are given as percentage, unless otherwise indicated. *VAMLA*, Video-assisted mediastinoscopic lymphadenectomy.

In addition, propensity matching was performed to identify 2 similar groups within the standard mediastinoscopy and VAMLA groups (n = 50 in each group) (Tables 5 and 6). As shown in Figure 3, survival was significantly better for the VAMLA groups: 86.5% at 5 years compared with 49.5% for the mediastinoscopy groups ($P = .002$). Cox regression confirmed that performing VAMLA provided independently better survival (Table 7).

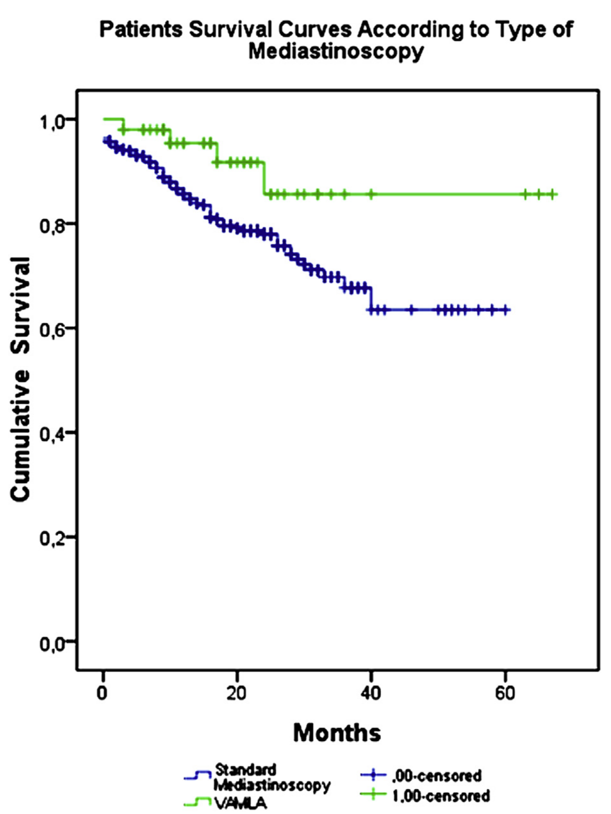

FIGURE 2. Survival curves of patients who underwent video-assisted mediastinoscopic lymphadenectomy (*VAMLA*) or standard mediastinoscopy.

TABLE 4. Cox regression (multivariable) model for death hazard estimation

Parameter	Hazard ratio	95% Confidence interval	P value
Mediastinal metastasis (N2)	2.39	1.273-4.501	.007
T	1.43	1.004-2.055	.047
VAMLA vs standard mediastinoscopy	1.34	1.116-3.212	.02

VAMLA, Video-assisted mediastinoscopic lymphadenectomy.

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DISCUSSION

VAMLA is feasible and can be performed safely.[2,4] Also, the probability of false-negative mediastinoscopy results is markedly decreased when more lymphoid tissue is resected via VAMLA. Our results confirmed that more N2 and N3 disease was found by VAMLA. Thus, VAMLA prevented more futile thoracotomies. These results were confirmed with previous studies.[2,4,5]

More important, VAMLA led to a longer survival rate in resected patients for NSCLC. Moreover, this impact of VAMLA was independent of T or N factor. A propensity analysis found that VAMLA provided better survival in patients with resected NSCLC. To our knowledge, this survival benefit was not reported before. The possible reasons for the survival benefit can be speculated: First, more accurate preoperative invasive staging could have caused less overlooked N2 disease; therefore, it could have helped us to operate on real N0 patients. Particularly, the subcarinal region can be completely dissected without suspicious lymph node tissue left behind. In our study, standard mediastinoscopy helped to disclose N2 disease in 16.2% of patients, whereas 40.4% of patients had N2 involvement, despite the 2 groups being well balanced in terms of T factor. The effectiveness of VAMLA was reported before.[2,5] In addition, we showed that VAMLA resulted in a higher sensitivity and negative predictive value and a lower false-negative rate. VAMLA provided a bilateral lymph node dissection before possible resectional surgery. This type of lymph node dissection is nearly impossible during left thoracotomy because of great vessels. During right thoracotomy, bilateral dissection of lymph nodes is technically challenging and time-consuming and usually necessitates median sternotomy.[6] The number of dissected lymph nodes in patients who underwent VAMLA was fewer than that of those who had undergone standard mediastinoscopy ($P < .001$) in our series. During VAMLA, paraesophageal lymph nodes can be sampled, whereas lymph nodes adjacent to pulmonary ligamentum could not be reached. In our study, number 8 lymph nodes were sampled in 26% of patients. We suggest that it is especially useful in patients with right-sided tumors who had an enlarged paraesophageal lymph node on positron emission tomography–computed tomography or computed tomography only. However, there are 2 technical

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TABLE 5. Patient characteristics and preoperative T-stage distribution in "propensity score–matched" patients

Parameter	Standard mediastinoscopy (n = 50)	VAMLA (n = 50)	P value
Age (range), y	57.6 (20-81)	59.2 (45-82)	>.05
Male/female ratio	47:3	45:5	>.05
Mean FVC	3079.3	3144.5	>.05
Mean FEV_1	2342.5	2299.4	>.05
Predicted FEV_1, %	76.1	75.3	
FEV_1/FVC ratio	92.7	82.3	.04
T stage, no. (%)			
cT1a	9 (18.0)	8 (16.0)	
cT1b	6 (12.0)	6 (12.0)	
cT2a	16 (32.0)	19 (38.0)	
cT2b	3 (6.0)	2 (4.0)	
cT3	14 (28.0)	11 (22.0)	
cT4	2 (4.0)	4 (8.0)	>.05

VAMLA, Video-assisted mediastinoscopic lymphadenectomy; *FVC*, forced vital capacity; *FEV_1*, forced expiratory volume in 1 second.

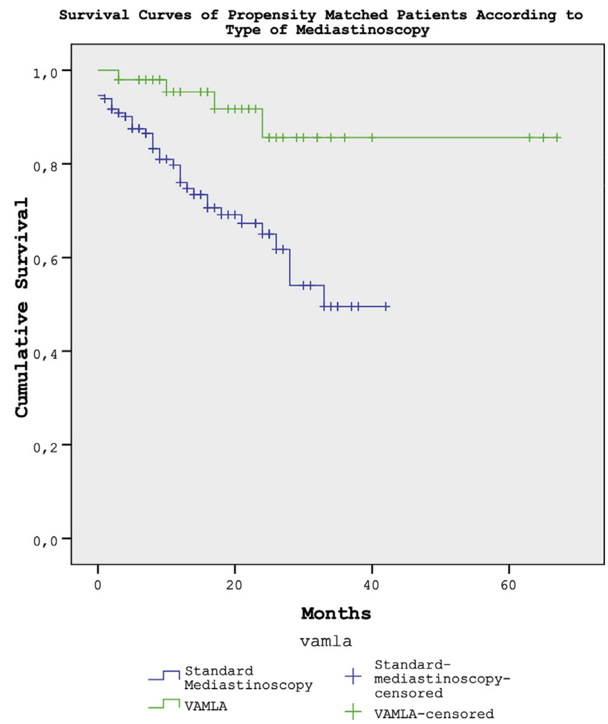

FIGURE 3. Survival curves of propensity-matched non–small cell lung cancer patients (n = 50) who underwent either video-assisted mediastinoscopic lymphadenectomy (*VAMLA*) or standard mediastinoscopy.

challenges: First, before further dissection toward the paraesophageal region, subcarinal lymph nodes must be completely dissected out and the right main pulmonary artery should be mobilized. Second, a mediastinoscope should be placed under the main pulmonary artery gently away from the arterial branches. However, dissection of all paraesophageal lymph nodes was not technically possible. A longer mediastinoscope could have helped us to solve this technical challenge.

The impact of radical lymphadenectomy was shown before.[7] Ludwig and colleagues[8] analyzed 16,800 patients and reported that patient survival after resection for NSCLC is associated with the number of lymph nodes evaluated during surgery. Their data support the conclusion that an evaluation of nodal status should include more than 11 lymph nodes. During VAMLA, we usually dissected more than 30 lymph nodes and our dissection could be somewhat equal to lymph node dissection performed during thoracotomy or videothoracoscopy.

TABLE 6. N stages of propensity-matched patients disclosed by mediastinal staging modality (*P* < .001) and accuracy of mediastinal staging modalities according to final pathologic findings of resected lymph nodes

N status	Standard mediastinoscopy (n = 50)	VAMLA (n = 50)
N0, no. (%)	41 (82.0)	33 (66.0)
N2-3, no. (%)	9 (18.0)	17 (34.0)
Specificity	100	100
False-negative rate	100	5
Sensitivity	92	96

Values are given as percentage, unless otherwise indicated. *VAMLA*, Video-assisted mediastinoscopic lymphadenectomy.

There are several advantages of VAMLA: VAMLA seemed to disclose more N2 disease than was discovered by standard mediastinoscopy. In our series, despite the 2 populations being balanced in terms of T factor, age, and sex, more N2 disease was discovered by VAMLA. We also have shown the effectiveness of VAMLA in propensity-matched groups. The other advantage of VAMLA is that it provides bilateral lymph node dissection before resectional surgery and it theoretically diminishes "lymph node dissection time" during pulmonary resection, because lymph node dissection, rather than lymph node biopsy, was performed during the procedure. It should be especially important in videothoracoscopic lobectomies. In our series, 5 thoracoscopic lobectomies were performed after VAMLA. During dissection, we virtually dissect no lymph nodes or fatty tissue at stations 2, 4, and 7 in these patients. For this reason,

TABLE 7. Cox regression (multivariable) model for death hazard estimation in propensity-matched patients

Parameter	Hazard ratio	95% Confidence interval	P value
Mediastinal metastasis (N2)	5.22	1.273-22.501	.003
T	1.21	0.911-4.593	.12
VAMLA vs standard mediastinoscopy	1.12	1.030-4.736	.04

VAMLA, Video-assisted mediastinoscopic lymphadenectomy.

we also found that the mean number of dissected lymph nodes in the VAMLA group is lower than that in the standard mediastinoscopy group ($P < .001$). More important, 2L and 4L lymph nodes can be completely dissected by VAMLA, whereas they cannot be completely dissected after video-assisted thoracic surgery lobectomy because it is technically demanding and it necessitates elevation of the aorta. In our series, we also realized that VAMLA facilitates dissection of proximal arterial branches and bronchus during video-assisted thoracic surgery and can reduce the operation time while increasing the completeness of lymph node dissection.

On the other hand, there are some disadvantages of VAMLA: It takes more than 30 minutes, which is longer than is necessary for standard mediastinoscopy . The longer operation time was confirmed by Witte and colleagues.[5] A frozen section analysis of lymph nodes that were dissected via VAMLA is time-consuming because the number of necessary sections is too high. For this reason, we started to send the specimen for standard histopathologic analysis instead of sending lymph nodes to ''frozen section'' analysis. The mean number of resected lymph nodes was 30.4 in the VAMLA group. This number is higher than the mean number of resected lymph nodes during thoracotomy in most patients who underwent mediastinoscopy. Also, we performed VAMLA in an outpatient setting. We also did not anticipate hilar fibrosis during dissection in patients who had undergone the VAMLA procedure.

In a well-designed ACOSOG Z0030 study, Darling and colleagues[9] concluded that if systematic and thorough preresection sampling of mediastinal and hilar lymph nodes is negative, mediastinal lymph node dissection does not improve survival in patients with stage I-II NSCLC.[9] The results of this study should not be considered proof of lack of the beneficial effect of lymph node dissection after surgical resection in patients with NSCLC because the patients had early-stage lung cancer and all patients had already undergone lymph node sampling.[9]

In 2004, Kuzdzal and colleagues[10] developed the technique of limited invasive bilateral mediastinal lymph node dissection, termed transcervical extended mediastinal lymphadenectomy (TEMLA). The TEMLA method enables complete resection of all nodes from stations 2L, 2R, 3, 4R, 4L, 5, 6, 7, 8, and 9.[10] It was an extremely accurate modality in NSCLC staging, with the additional advantage of a potentially curative effect of the radical lymphadenectomy.[10] However, TEMLA is time-consuming and technically demanding, and there is a need for a special sternum elevator. A study comparing these 2 lymph node dissection and mediastinal staging techniques is warranted.

There are some limitations of the study that must be addressed. This study is a retrospective cohort study without a randomization. Regarding the 2 surgeons' preference of standard mediastinoscopy, they believed that standard mediastinoscopy was appropriate and is a straightforward and quick method for preoperative mediastinal staging. For this reason, these surgeons (A.D. and K.K.) and a surgeon performing VAMLA (A.T.) operated on consecutive patients without any patient selection. There is also a possibility that the results of VAMLA could be confounded with a possible surgeon (A.T.)/skill effect that could not be separated from VAMLA results. This possible effect could be more understandable when considering that the number of resected lymph nodes is greater than the number published.[3,4] However, the optimal standards of mediastinoscopy or VAMLA remain unknown. The complication rate of VAMLA was higher than that of mediastinoscopy. This may be due to our higher rate of dissection of the 2L station. This higher rate may also be due to our early experience of VAMLA, in which the recurrent nerve was not identified before commencing left-sided dissection. It is important to start with identification of this nerve to reduce dysphonia. In addition, electromyographic monitoring could have reduced the dysphonia rate if we had used it. Fortunately, all but 1 case of dysphonia were resolved in 6 months. We put all our efforts into dissecting the 2L station in almost every patient possible. This is probably one of the reasons that dysphonia was higher in patients who underwent VAMLA. During VAMLA, nodal tissue rarely is extracted completely intact; instead, it comes out in fragments. For this reason, it could be possible that some of the lymph nodes in our data set were, in fact, fragments and the true number of lymph nodes analyzed may have been overestimated. This phenomenon is difficult to eliminate, and it was also mentioned to be inevitable by Ludwig and colleagues.[8]

In conclusion, VAMLA seemed to provide better preoperative invasive staging, with higher sensitivity, negative predictive value, and accuracy. It also independently prolonged survival in patients with operable NSCLC. Further randomized studies with a longer follow-up are warranted to confirm our results.

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