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Transition from a multiport technique to a single-port technique for lung cancer surgery: is lymph node dissection inferior using the single-port technique?†

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Abstract

OBJECTIVES: The feasibility and radicalism of lymph node dissection for lung cancer surgery by a single-port technique has frequently been challenged. We performed a retrospective cohort study to investigate this issue.

METHODS: Two chest surgeons initiated multiple-port thoracoscopic surgery in a 180-bed cancer centre in 2005 and shifted to a single-port technique gradually after 2010. Data, including demographic and clinical information, from 389 patients receiving multiport thoracoscopic lobectomy or segmentectomy and 149 consecutive patients undergoing either single-port lobectomy or segmentectomy for primary non-small-cell lung cancer were retrieved and entered for statistical analysis by multivariable linear regression models and Box–Cox transformed multivariable analysis.

RESULTS: The mean number of total dissected lymph nodes in the lobectomy group was 28.5 ± 11.7 for the single-port group versus 25.2 ± 11.3 for the multiport group; the mean number of total dissected lymph nodes in the segmentectomy group was 19.5 ± 10.8 for the single-port group versus 17.9 ± 10.3 for the multiport group. In linear multivariable and after Box–Cox transformed multivariable analyses, the single-port approach was still associated with a higher total number of dissected lymph nodes.

CONCLUSIONS: The total number of dissected lymph nodes for primary lung cancer surgery by single-port video-assisted thoracoscopic surgery (VATS) was higher than by multiport VATS in univariable, multivariable linear regression and Box–Cox transformed multivariable analyses. This study confirmed that highly effective lymph node dissection could be achieved through single-port VATS in our setting.

Keywords: Single port • Video-assisted thoracoscopic surgery • Lobectomy • Segmentectomy • Lymph node dissection

INTRODUCTION

Adequate lymph node dissection is a fundamental procedure in lung cancer surgery both for staging and for local control. The result correlates well with the prognosis and also acts as guidance for adjuvant treatment. Various concepts and techniques have been debated for years regarding the influence of different stages and image findings on therapeutic strategy [1–5]. With rapid progress in the development of endoscopic surgical instruments and techniques, single-port video-assisted thoracoscopic surgery (VATS) has become popular and well accepted. Most studies published regarding single-port thoracoscopic surgery have focussed on lung resection [6–8]; however, only a few of these articles mentioned the technical issues and the efficacy of lymph node dissection by this approach [9–14]. Cooperation between the surgeon and team members with regard to performing adequate lymph node dissection through the single-port technique can be quite a challenge, and the learning curve remains unclear. In addition, multiple factors may contribute to the outcome of lymph node dissection, including clinical cancer staging, comorbidities, the ability and assertiveness of the surgeon to do the dissection and the experience of the pathologist analysing the specimens. As a result, heterogeneous results on lymph node dissection have been observed [15, 16].

Our team has published our previous experience with single-port surgery for lung cancer, which commenced in 2010. We established our single-port lymph node dissection-based technique based on previous experience by the multiport technique [11] and performed a propensity-matched comparison study between single- and multiport VATS with a limited number of cases [12, 13]. Herein, we would like to update and expand on our

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data and performed a comparison between the single- and the multiport technique on a larger scale to the entire cohort, not just selected cases by highly matched pairs. Moreover, the learning curve on surgical outcome through the multiport and the single-port technique by year, multivariable analysis for the prediction of outcomes and quality of lymph node dissection by the single-port approach will be described in detail.

MATERIALS AND METHODS

Surgical technique

Two surgeons adopted the multiport VATS technique for lung cancer in 2005 in a 180-bed cancer centre, with a transition to single-port VATS for lung cancer in 2010 by one surgeon, followed by the other in 2014. Single-port VATS become standard procedure of choice in our hospital after 2015. Early-stage young female patients and straightforward cases may be picked up during the initial learning curve; the same for both transition periods, from the open technique to the multiport technique in 2005 and also from the multiport technique to the single-port technique in 2010. Each new technique requires a learning curve at the beginning, but the single-port technique is now nearly routine. The techniques regarding lymph node dissection were documented previously [11]. Major modifications in the single-port approach compared with the multiport technique included instrument modification and adoption of a specific manoeuvre to facilitate exposure of the left-side subcarinal space.

Data sources

We retrieved data from our prospective surgical database established in 2000. A total of 604 patients undergoing VATS for primary non-small-cell lung cancer between May 2005 and December 2014 were identified. Demographic data and clinical variables included age, sex and comorbidities, including chronic obstructive pulmonary disease (COPD), diabetic mellitus (DM) and tuberculosis (TB), the year of the surgery, laterality and location of the cancer, clinical stage and the pathological stage. Histological typing was established according to the World Health Organization classification. TNM stage was determined according to the American Joint Committee on Cancer staging system, 7th Edition. We further categorized the patients into Stage I and others because of the fact that Stage I disease is dominant in the patient population compared with other stages. Also, there is a potentially different strategy on lymph node dissection; lobe-specific or systemic sampling techniques were adopted for Stage I cancer patients after 2014, while the other stages did not have such changes in technique. Surgical outcomes included type of surgery, length of the surgical wound, operative time, operative blood loss, number of total dissected lymph nodes and the length of the hospitalization. The study was approved by the institutional review board of Koo Foundation Sun Yat-Sen Cancer Center.

Patient selection

From May 2005 to December 2014, 604 patients underwent thoracoscopic resection for primary lung cancers, according to our surgical database. To highlight the general practice of lymph node dissection, we intentionally removed the data obtained from wedge resection ($n = 54$), bilobectomy ($n = 9$) and pneumonectomy ($n = 3$). Thus, 538 patients (149 in the single-port group and 389 in the multiport group) who underwent either VATS lobectomy ($n = 442$) or segmentectomy ($n = 96$) were entered into the study.

Statistical analysis

Demographic data and clinical information were compared between those receiving single-port VATS and those receiving multiport VATS for lung cancer. For comparison of these two techniques, we further stratified study individuals into a lobectomy group and a segmentectomy group. Surgical outcomes (number of total dissected lymph nodes, operative blood loss, length of hospitalization, length of surgical wound and operative time) were compared. Continuous variables were expressed as mean ± standard deviation, and differences between data were compared using independent *t*-tests. Categorical data between the two groups were compared using the χ^2 test or Fisher's exact test.

Next, we performed multivariable linear regression to control for potential confounders and test the association between surgical outcomes with key predictor variables. We decided not to use a propensity-score matching for this analysis so that we could include as many sample patients as possible, to show a learning curve from the initiation of the procedures and to stratify and compare patients in different subgroups, including lobectomy and segmentectomy. The selection of predictor variables in the models was based on previous studies and clinical judgement. We controlled for the following dummy confounding variables: the type of surgery (0: lobectomy, 1: segmentectomy), age (0: ≤65 years, 1: >65 years), sex (0: female, 1: male), antecedents of tuberculosis and diabetic mellitus (0: no, 1: yes) and pathological stage (0: Stage I, 1: stage more advanced; this was performed because dichotomizing the sampled patients into Stage I and non-stage I gives a similar number of patients in each group).

The following assumptions of the linear regression models were tested: linearity in a plot of residuals versus predicted values; normality of the error distribution; statistical independence of the errors (evaluated using the Durbin Watson test) and the homoscedasticity of the errors (evaluated using the White test). The goodness of the fit of each model was evaluated by calculating the R^2 and the adjusted R^2 values.

Because the outcome variables only have positive values, we tested different Box–Cox transformation functions and then compared the models before and after transformation with the skewness and kurtosis coefficients. In addition, we constructed a regression model to predict the number of total lymph nodes dissected among patients receiving single-port VATS.

To demonstrate the learning curve, we plotted the number of patients and mean number of lymph nodes dissected over time in line graphs. We used four lines (lobectomy/multiport, lobectomy/single-port, segmentectomy/multiport and segmentectomy/single-port) to show the specifics of each group. Other surgical outcomes presented in the same manner included the mean length of wound, mean operative time, mean blood loss and mean duration of hospital stay. To present in detail the quality of mediastinal lymph node dissection in single-port VATS, we generated box-and-whisker plots to show the distribution of the number of dissected lymph nodes in the main nodal stations (R234, R7, R89, L456, L7 and L89) among patients who received lobectomy and segmentectomy, respectively.

Table 1: Characteristics of patients by type of surgery (lobectomy and segmentectomy) and number of ports (single/multiple) (n = 538)

Patient characteristics	Lobectomy			Segmentectomy		
	Single port	Multiport		Single port	Multiport	
	n = 100 n (%)	n = 342 n (%)	P-value	n = 49 n (%)	n = 47 n (%)	P-value
Demographic variables						
Gender			0.388			**0.004**
Female (n = 323)	61 (61.0)	192 (56.1)		42 (85.7)	28 (59.6)	
Male (n = 215)	39 (39.0)	150 (43.9)		7 (14.3)	19 (40.4)	
Age			**0.012**			**0.004**
≤65 (n = 363)	79 (79.0)	225 (65.8)		37 (75.5)	22 (46.8)	
>65 (n = 175)	21 (21.0)	117 (34.2)		12 (24.5)	25 (53.2)	
Clinical characteristics						
Adenocarcinoma versus other						
No (n = 105)	18 (18.0)	71 (20.8)	0.671	5 (10.2)	11 (23.4)	0.104
Yes (n = 433)	82 (82.0)	271 (79.2)		44 (89.8)	36 (76.6)	
Stage I versus other			0.329			**0.007**
No (n = 344)	62 (62.0)	230 (67.2)		20 (40.8)	32 (68.1)	
Yes (n = 194)	38 (38.0)	112 (32.8)		29 (59.2)	15 (31.9)	
Location			0.100			0.870
RUL (n = 185)	33 (33.0)	141 (41.2)		7 (14.3)	4 (8.5)	
RML (n = 49)	15 (15.0)	34 (9.9)		–	–	
RLL (n = 102)	23 (23.0)	66 (19.3)		7 (14.3)	6 (12.8)	
LUL (n = 129)	11 (11.0)	61 (17.8)		28 (57.1)	29 (61.7)	
LLL (n = 71)	18 (18.0)	39 (11.4)		7 (14.3)	7 (14.9)	
Double lung cancer (n = 1)	–	–		0 (0.0)	1 (2.1)	
Other (n = 1)	0 (0.0)	1 (0.3)		–	–	
Laterality			0.874			0.738
Left (n = 201)	29 (29.0)	102 (29.8)		35 (71.4)	35 (74.5)	
Right (n = 337)	71 (71.0)	240 (70.2)		14 (28.6)	12 (25.5)	
Preoperative treatment			0.140			0.742
None (n = 514)	94 (94.0)	326 (95.3)		48 (98.0)	46 (97.9)	
Induction CT (n = 14)	2 (2.0)	11 (3.2)		0 (0.0)	1 (2.1)	
Induction CRT (n = 1)	1 (1.0)	0 (0.0)		–	–	
Previous treatment with residual disease (n = 2)	0 (0.0)	2 (0.6)		–	–	
Previous treatment with recurrence (n = 1)	0 (0.0)	1 (0.3)		–	–	
Target (n = 5)	2 (2.0)	2 (0.6)		1 (2.0)	0 (0.0)	
Previous CT with residual disease (n = 1)	1 (1.0)	0 (0.0)		–	–	
Chronic obstructive pulmonary disease			0.326			0.460
No (n = 496)	95 (95.0)	315 (92.1)		45 (91.8)	41 (87.2)	
Yes (n = 42)	5 (5.0)	27 (7.9)		4 (8.2)	6 (12.8)	
Tuberculosis			**0.010**			0.490
No (n = 526)	94 (94.0)	337 (98.5)		49 (100.0)	46 (97.9)	
Yes (n = 12)	6 (6.0)	5 (1.5)		0 (0.0)	1 (2.1)	
Diabetic mellitus			0.848			**0.002**
No (n = 472)	89 (89.0)	302 (88.3)		47 (95.9)	34 (72.3)	
Yes (n = 66)	11 (11.0)	40 (11.7)		2 (4.1)	13 (27.7)	

CT: chemotherapy; CRT: chemoradiotherapy; RUL: right upper lobe; RML: right middle lobe; RLL: right lower lobe; LUL: left upper lobe; LLL: left lower lobe.
P values less than 0.05 were marked in bold.

Differences were considered statistically significant when the probability (P) value was below 0.05. Data analysis was performed using SAS 9.1 (SAS Institute, Inc., Cary, NC, USA).

RESULTS

From May 2005 to December 2014, 538 patients undergoing either VATS lobectomy or segmentectomy in Koo Foundation Sun Yat-Sen Cancer Center were identified and entered into this study. There were 149 patients in the single-port group and 389 in the multiport group; a comparison of demographic data from the two groups is presented in Table 1. Among patients receiving VATS lobectomy for primary lung cancer, patients undergoing single-port VATS were significantly younger (P = 0.012), and the prevalence of TB was higher compared with the multiport group (P = 0.010). Other parameters, such as gender, comorbidities other than TB, laterality and location of the cancer, treatment before surgery, and clinical and pathological stage, did not differ between the groups. Among patients receiving segmentectomy, the single-port group comprised significantly more female patients, younger patients, patients with a history of DM and patients with pathological stage I cancer. However, no differences in laterality and location of the lung cancer, comorbidity with COPD, TB and usage of chemoradiotherapy before the surgery were observed.

Table 2: Surgical outcomes by type of surgery (lobectomy and segmentectomy) and number of ports (single/multiple) (n = 538)

Outcome variables	Lobectomy			Segmentectomy		
	Single port	Multiport		Single port	Multiport	
	n = 100 Mean ± SD	n = 342 Mean ± SD	P-value	n = 49 Mean ± SD	n = 47 Mean ± SD	P-value
Total dissected lymph node number	28.47 ± 11.77	25.23 ± 11.30	**0.013**	19.47 ± 10.79	17.91 ± 10.28	0.472
Blood loss	55.68 ± 52.81	78.28 ± 84.99	**0.001**	63.88 ± 79.60	59.36 ± 50.23	0.739
Hospital stay	5.96 ± 1.69	6.80 ± 3.56	**0.001**	5.76 ± 1.98	6.83 ± 2.21	**0.014**
Length of wound	3.92 ± 1.81	4.70 ± 0.77	**<0.001**	3.66 ± 0.77	4.50 ± 0.56	**<0.001**
Operative time	2.99 ± 0.87	3.47 ± 1.06	**<0.001**	3.34 ± 0.93	3.45 ± 0.92	0.542
Residual tumour condition (%)			1.000			0.232
R0	98 (22.8)	331 (77.2)		48 (52.7)	43 (47.3)	
Microscopic residual tumour	2 (16.7)	10 (83.3)		1 (25.0)	3 (75.0)	
Macroscopic residual tumour				0 (0.0)	1 (100.0)	
Complications			0.167			0.117
No	92 (92.0)	295 (86.3)		46 (93.9)	39 (83.0)	
Yes	8 (8.0)	47 (13.7)		3 (6.1)	8 (17.0)	

SD: standard deviation. P values less than 0.05 were marked in bold.

Surgical outcomes

The results of the surgical outcomes from the univariable linear analysis are presented in Table 2. Among patients receiving lobectomy, the single-port VATS group was significantly associated with a higher number of lymph nodes removed (mean 28.47 vs 25.23; $P = 0.013$), smaller surgical wound (mean length 3.92 vs 4.70 cm; $P < 0.001$), less blood loss (mean 55.68 vs 78.28 ml; $P = 0.001$), shorter operative time (mean 2.99 vs 3.47 h; $P \leq 0.001$) and shorter hospital stay (mean 5.96 vs 6.80 days; $P = 0.001$). The status of the surgical margin did not differ significantly between the two groups.

Among patients receiving VATS segmentectomy, the single-port group was also significantly associated with smaller surgical wound (mean length 3.66 vs 4.50 cm; $P < 0.001$) and shorter hospital stay (mean 5.76 vs 6.83 days, $P = 0.014$) compared with the multiport group. However, the number of total lymph nodes dissected, blood loss during surgery, operative time and surgical margin after surgery did not differ significantly between the two groups.

The complication rate, with regard to hoarseness, chylothorax, arrhythmia, pneumonia and wound infection, was statistically similar in the lobectomy and segmentectomy groups by the single- and multiport approach, although there was a trend of it being lower in the single-port group (Table 2).

Since age, gender, comorbidity with TB or DM, pathological stage I cancer differed between patients with different types of VATS lung resection (lobectomy and segmentectomy, respectively) by single-port and multiport technique in our sample, these were potential confounders of the association between usage of single-port VATS and better surgical outcome. We therefore carried out multivariable linear analysis to control for these factors (Table 3). In the multivariable analysis, after controlling for age, gender, comorbidity (TB, DM), operation type (lobectomy/segmentectomy) and stage I cancer, use of the single-port VATS technique for lung cancer remained associated with a higher number of total lymph nodes dissected through a smaller surgical wound, less operative time and shorter hospital stay. However, the amount of blood loss during surgery was not significantly associated with the use of single-port VATS for lung cancer in the multivariable analysis. Also for Stage I lung cancer, the number of total dissected lymph nodes was lower and associated with smaller wound, shorter operative time and shorter hospital stay. For lobectomy patients, the number of total dissected lymph nodes was associated with slightly shorter operative time compared with the segmentectomy group.

The results of multivariable linear regression of the surgical outcomes are presented in Table 3. The Cox–Box transformed models are presented in Table 4. The results using transformed models are similar to the linear regression models. The variables that were significant in the transformed models and non-transformed linear regression models are almost identical. In the square root model, the fact that a patient had a single-port or multiport VATS ($P = 0.017$) and the type of surgery ($P < 0.001$) remain significant when adjusting for the other covariables. The sex of the patient still influenced the blood loss ($P = 0.004$), as well as the age of the patient ($P = 0.020$) in the logarithm model. We noted the same following significant variables in the linear and reciprocal models on analysing the number of days of hospital stay: the number of ports during the operation ($P = 0.002$), age ($P < 0.001$) and antecedents of tuberculosis ($P = 0.018$), when adjusting for the other covariables included in the model. The stage of the patient became significant at the 5% level ($P = 0.038$). Comparing the linear and reciprocal square root models, the number of ports and patient sex remain highly significant when adjusting for the other covariables ($P < 0.001$ for each variable). Similar to the results for the total number of lymph nodes dissected, the stage becomes significant in our new model ($P = 0.010$). Finally, the type of surgery becomes significant ($P = 0.008$) when the duration of the surgery was assessed in the logarithm model.

Learning curve and quality of single-port mediastinal lymph node dissection

As shown in Fig. 1, we started using single-port VATS lobectomy and segmentectomy for lung cancer in early 2010. Despite the use of different techniques within the study period by the two surgeons, there was a crossover on the growth curves of single-port over multiport VATS in 2012 for segmentectomy and in 2013 for

Table 3: Multivariable linear regression analysis for surgical outcomes ($n = 538$)

	Outcome variables									
	Total number of LNs dissected		Blood loss		Hospital stay		Length of wound		Operative time	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Single-port VATS	3.088***	0.848; 5.328	−12.261*	−27.436; 2.915	−0.807***	−1.398; −0.216	−0.747***	−0.949; −0.544	−0.343***	−0.537; −0.148
Lobectomy	7.831***	5.222; 10.440	5.337	−12.336; 23.010	−0.003	−0.692; 0.685	0.188*	−0.048; 0.424	−0.215*	−0.442; 0.012
Younger than 65	−0.255	−2.332; 1.823	−16.073**	−30.147; −1.999	−0.928***	−1.476; −0.380	−0.103	−0.291; 0.085	−0.120*	−0.301; 0.060
Female	−0.555	−2.539; 1.429	−21.688***	−35.127; −8.249	−0.369*	−0.892; 0.155	−0.291***	−0.471; −0.112	−0.343***	−0.515; −0.171
Previous history of TB	−4.310*	−10.821; 2.201	31.042*	−13.063; 75.146	4.134***	2.417; 5.852	0.244	−0.346; 0.833	0.677**	0.111; 1.242
Previous history of DM	−0.367	−3.338; 2.605	−0.300	−20.430; 19.829	0.159	−0.625; 0.943	0.142	−0.127; 0.411	0.093	−0.165; 0.351
Stage I cancer	−2.174*	−4.211; −0.137	0.056	−13.743; 13.856	−0.472*	−1.010; 0.065	−0.143*	−0.328; 0.041	−0.264***	−0.441; −0.087
R^2		0.080		0.044		0.090		0.154		0.090
Adjusted R^2		0.068		0.031		0.078		0.142		0.078
White test (P-value)		0.073*		<0.001***		0.052		0.001		0.056*
Durbin Watson D		1.958		1.650		2.017		1.847		1.962
No. of observations		538								

Standard errors are reported in parentheses. *, ** and *** indicate confidence at the 80, 95 and 99% levels, respectively.
CI: confidence interval; VATS: video-assisted thoracoscopic surgery; DM: diabetic mellitus; TB: tuberculosis; LNs: lymph nodes.

lobectomy. In 2014, 78% of lobectomies and 90% of segmentectomies were carried out using single-port VATS. As shown in Fig. 2, during the very beginning of the learning curve (2010–11) for the single-port technique, mean length of wound, operative time, blood loss and hospital stay appeared similar to the multiport technique, except for hospital stay for the first segmentectomy patients; 1 patient with emphysematous lung undergoing left common basal segmentectomy stayed longer for COPD control. Of note, the mean operative time for segmentectomy by both single- and multiport techniques increased in 2014, being related mainly to more complex atypical segmentectomies (e.g. superior segmentectomy of the right upper lobe and anterior basal segmentectomy of the lower lobe) performed over the period. However, we found the number of total dissected lymph nodes to be lower in the beginning, that is, in 2010–11 (Fig. 3), probably as a result of the learning curve with limited experiences in that period. After modifying our technique and instruments, we were able to dissect more lymph nodes, especially during attempts of radical dissection in the lobectomy group. The mean number of dissected lymph nodes peaked in 2013 for lobectomy (a mean of 29.64 lymph nodes dissected) and in 2012 for segmentectomy (a mean of 24.17 lymph nodes dissected). The decline in the number of lymph nodes dissected in 2013 and 2014 noted in the segmentectomy group could be related to our modified strategy on lymph node dissection for Stage I lung cancer, such as lobe-specific lymph node dissection and systemic lymph node sampling, or even none for pure ground-glass opacity (GGO) lung cancer with sizes less than 2 cm.

To present in detail the quality of mediastinal lymph node dissection, we applied box-and-whisker plots (Fig. 3) to show the distribution of the number of dissected lymph nodes in the main nodal stations during single-port VATS. The median dissected mediastinal lymph node station by the single-port approach was 3.4 on the left and 3.5 on the right side by lobectomy and 3.2 for the left and 2.1 for the right side by segmentectomy.

We also applied multivariable analysis to evaluate factors related to the number of total lymph nodes dissected among patients receiving single-port VATS ($n = 149$). The results are in Table 5. Lobectomy, compared with segmentectomy, was significantly associated with a higher number of dissected lymph nodes ($P < 0.001$); Stage I cancer was associated with a lower number of lymph nodes being dissected ($P = 0.017$) than any other stage of lung cancer. Laterality of the cancer (left/right) was not associated with the number of lymph nodes dissected after controlling for lobectomy/segmentectomy and the stage of lung cancer.

DISCUSSION

Performing lymph node dissection through the single-port technique remains challenging. Despite a number of published studies on single-port surgery for lung cancer [6–8], few have focused on lymph node dissection. Moreover, the quality of lymph node dissection using the single-port approach has not yet been described in detail. Not only in single-port studies [14] but also in studies using multiport or open techniques [15], large differences in overall performances and quality of lymph node dissection have been observed despite the current knowledge on the importance of lymph node dissection and various well-established guidelines [4, 5]. We previously published a comparison study investigating the number of lymph nodes harvested using propensity-matched scores by single-port versus multiport techniques, and concluded

Table 4: Multivariate analysis for the surgical outcomes after Box–Cox transformations ($n = 538$)

Outcome variables	Total number of LNs dissected		Blood loss		Hospital stay		Length of wound		Operative time	
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI
Single-port VATS	0.285**	0.052; 0.518	−0.132*	−0.300; 0.037	0.014***	0.005; 0.024	0.053***	0.045; 0.061	−0.108***	−0.163; −0.053
Lobectomy	0.857***	0.586; 1.128	0.074	−0.122; 0.270	−0.001	−0.011; 0.010	−0.007*	−0.017; 0.003	−0.070**	−0.134; −0.006
Younger than 65	0.051	−0.165; 0.267	−0.186**	−0.342; −0.030	0.021***	0.012; 0.030	0.006*	−0.001; 0.014	−0.025	−0.076; 0.026
Female	−0.001	−0.216; 0.196	−0.221***	−0.370; −0.072	0.007*	−0.001; 0.015	0.016***	0.009; 0.023	−0.090***	−0.139; −0.041
Antecedent of TB	−0.542*	−1.219; 0.135	0.362*	−0.127; 0.851	−0.032**	−0.059; −0.006	−0.017*	−0.041; 0.007	0.184**	0.025; 0.344
Antecedent of DM	−0.023	−0.332; 0.286	0.053	−0.170; 0.276	−0.003	−0.015; 0.010	−0.008*	−0.019; 0.003	0.024	−0.049; 0.097
Stage I cancer	−0.191*	−0.402; 0.021	0.009	−0.144; 0.162	0.009**	<0.001; 0.017;	0.010***	0.002; 0.017	−0.067***	−0.117; −0.017
R^2		0.084		0.044		0.097		0.319		0.086
Adjusted R^2		0.071		0.031		0.085		0.310		0.074
White test (*P*-value)		0.176*		0.026**		0.945		0.253		0.451
Durbin Watson D		1.960		1.723		1.831		1.864		1.980
λ		0.5		0		−1		−0.5		0
No. of observations		538								

Standard errors are reported in parentheses; *, ** and *** indicate confidence at the 80, 95 and 99% levels, respectively.
CI: confidence interval; VATS: video-assisted thoracoscopic surgery; DM: diabetic mellitus; TB: tuberculosis; LNs: lymph nodes.

that the single-port technique led to the harvesting of more lymph nodes [12, 13]; however, this did not include the entire cohort in our database. In this article, we report updated data on single-port results and performed multivariable regression analysis to compare the results between single- and multiport VATS lymph node dissection, with both arms assessing from the beginning of the learning curve until the end of this study. We again documented that compared with multiport surgery for lung cancer, lymph node dissection by the single-port technique tends to harvest more lymph nodes through a smaller surgical wound, with less operative times and shorter hospital stays.

Fragmentation is sometimes inevitable, but we prefer to dissect the lymph nodes in an en bloc fashion, particularly in mediastinal lymph node dissection; this is why we put on links to YouTube videos, and also show the number of harvested lymph nodes in each station to document the quality of lymph node dissection. The method the pathologists use to calculate the number of lymph nodes is counting the specimens they see, whether in pieces (counted as one if they were obviously connected) or in an en bloc style (the pathologist must dissect the specimen and count the lymph node numbers in each station as a standard operating procedure for cancer surgery). This method used by pathologists has not changed with time or changed with the transition from the multiport to the single-port technique.

Unlike lobectomy or segmentectomy through a single port, lymph node dissection does not need bulky instruments like the endocutter, nor does it run any risk related to handling of vascular structures; the working port was dilated even more during the specimen retrieval process, which allowed more room for us to perform the mediastinal lymph node dissection. Furthermore, with the rapid progress in the development of high-resolution video systems and refined energy delivery systems (e.g. Teflon coating of the blade of ultrasonic scissors, additional bipolar coagulation function, wireless design), we think that lymph node dissection by a single-port approach is actually much easier to adapt than lobectomy by a single port; as shown, blood loss and operative time in our learning period were no different from those of the multiport approach in the period 2010–11 (Fig. 2). However, some tricks and tips are necessary to harvest more lymph nodes including the use of modified instruments such as longer and curved suckers and double-joint thoracoscopic or laparoscopic instruments to avoid clashing of instruments. In fact, for right-side lymph node dissection and left-side superior mediastinal lymph node dissection, the technique is similar to the multiport technique. However, it is sometimes quite challenging to expose the left-side subcarinal area by the single-port technique. We developed a specific 'Liu's maneuver' [17] to solve this problem: A non-elastic nylon tape was applied via the wound protector into the anterior hilum, hooked onto the lower lobe bronchus through the space between the left main bronchus and the left inferior pulmonary vein and, coming out from the posterior hilum, pulled outside of the wound, eventually being fixed with a clamp on the edge of the wound protector; through proper traction tension on this tape, the left lower lung could be retracted away from the posterior mediastinum and towards the operator. Further dissection of the subcarinal space would be straightforward without the need to grasp the left lung with another retractor or grasper. After cutting the feeding vessels from the oesophagus and the bronchial artery, subcarinal lymph nodes can be removed thoroughly and safely. The deep-seated right pleura, right main bronchus and right inferior pulmonary vein can be easily identified through this technique.

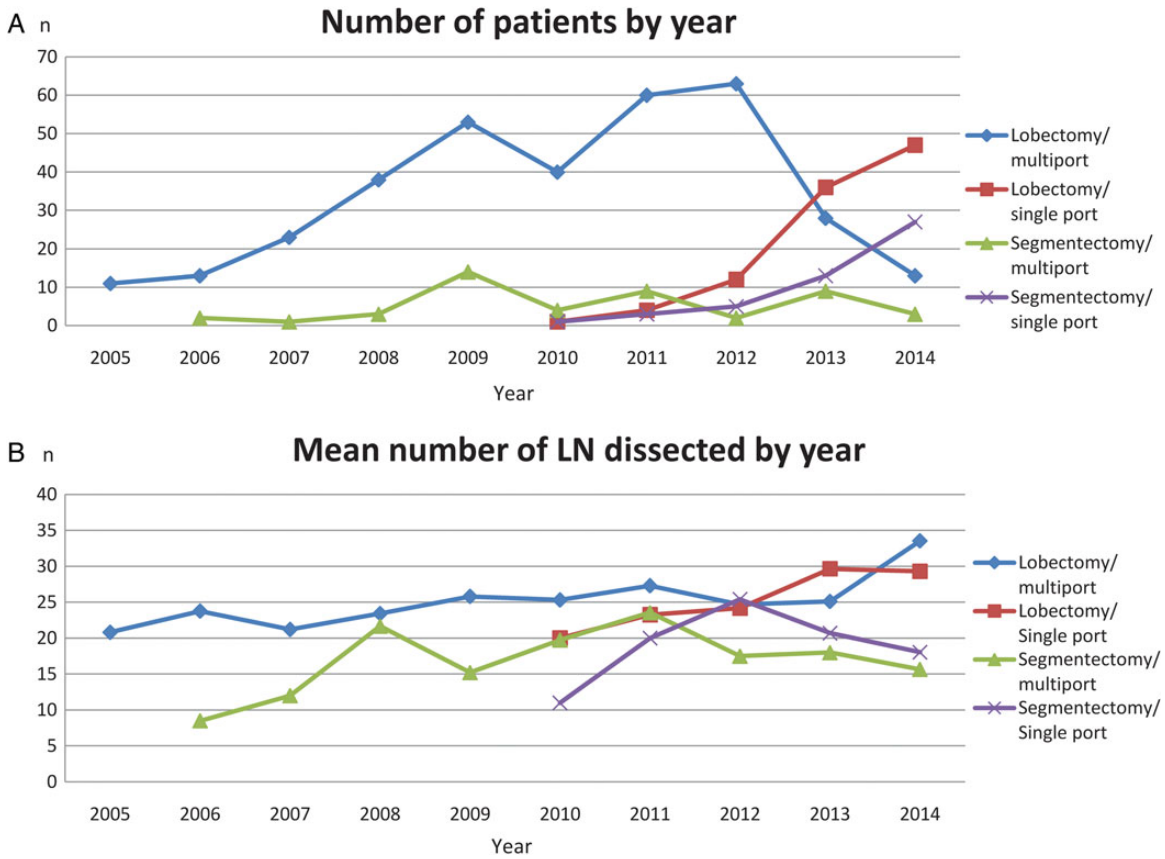

Figure 1: (**A**) Number of cases (**B**) Mean number of total dissected lymph nodes by year, for patients undergoing lobectomy or segmentectomy using the single-port or the multiple-port VATS technique. VATS: video-assisted thoracoscopic surgery.

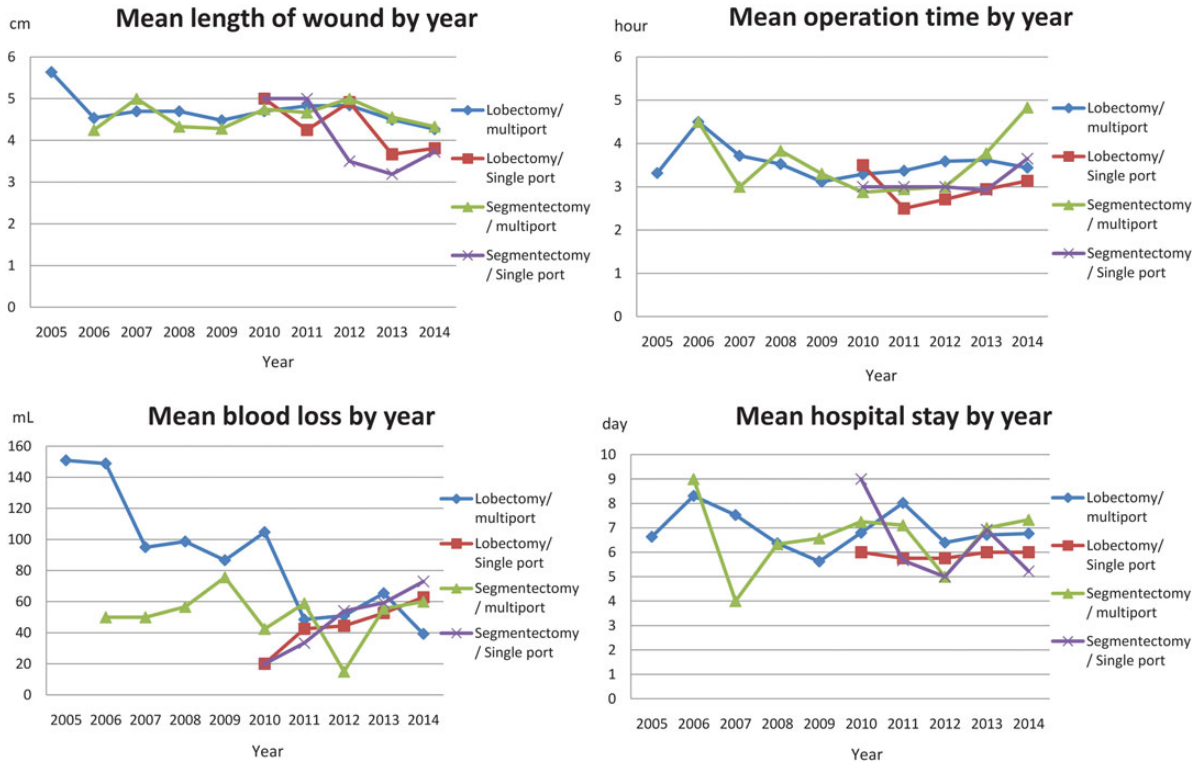

Figure 2: Means of wound length, operative time, blood loss and hospital stay by year, for patients undergoing lobectomy or segmentectomy using the single-port or the multiple-port VATS technique. VATS: video-assisted thoracoscopic surgery.

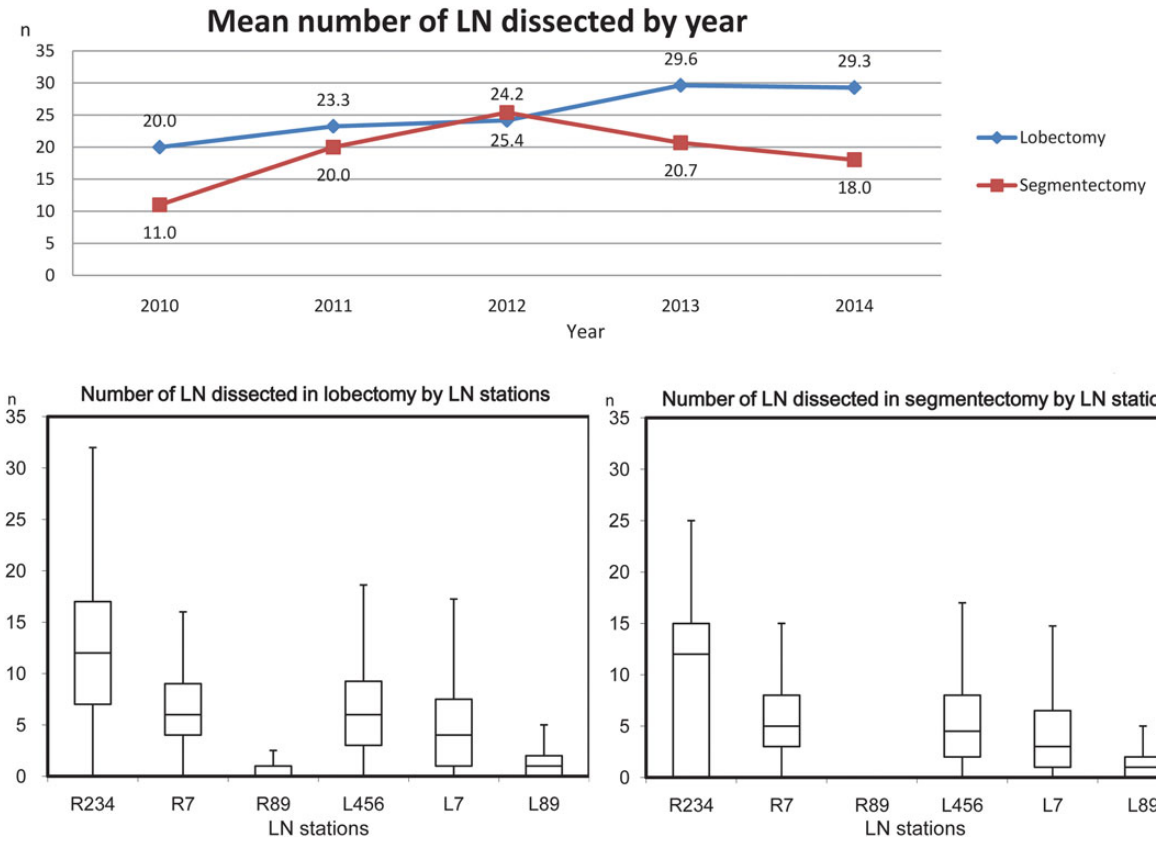

Figure 3: Learning curve and quality of lymph node dissection by the single-port technique for primary lung cancer—total dissected lymph node number in a single operation by year (upper panel) and the number of dissected lymph nodes in individualized mediastinal nodal stations by single-port VATS lobectomy (left lower panel) and segmentectomy (right lower panel). VATS: video-assisted thoracoscopic surgery.

Table 5: Regression analysis of the total number of lymph nodes dissected among single-port VATS for lung cancer patients (n = 149)

	Total number of LNs dissected		
	β	SE	P-value
Lobectomy	7.434	2.171	**<0.001**
Right-side cancer	1.465	2.020	0.468
Stage I cancer	−4.464	1.878	**0.017**
Constant	21.693	2.010	**<0.001**

VATS: video-assisted thoracoscopic surgery; LNs: lymph nodes. P values less than 0.05 were marked in bold.

Despite lack of a camera port from the lower intercostal space, a thoracoscope inserted through the single port provides the operator with a better ergonomic view [18, 19] than the side view from the lower intercostal port, and it is even easier to reach the retrocaval space or even the left side of the upper mediastinum during an extended right-side upper mediastinal lymph node dissection in our experience [20]; this could be very difficult if the camera was inserted through a lower and more posterior intercostal space.

The paradigm shift in lung cancer presentation and surgical management has been quite obvious over the recent 20 years. More and more younger female patients without a smoking history are diagnosed with early-stage lung adenocarcinoma by low-dose chest computer tomography (CT) scan; these patients were staged more accurately with positron emission tomography–computer tomography (PET-CT) scan and/or endobronchial ultrasound-guided trans-bronchial needle aspiration (EBUS/TBNA) and visited our clinic for curative treatment. Despite lobectomy with radical lymph node dissection remaining the gold standard of operable lung cancer surgery, sublobar resection, combined with lobe-specific lymph node dissection or systemic lymph node sampling [21, 22], is emerging as an alternative and equivalent treatment option for Stage I lung cancer. We have also started adopting lobe-specific lymph node dissection and systemic lymph node sampling following the ACOSOG Z0030 protocol for clinical stage I lung cancer, sometimes even omitting lymph node dissection for pure GGO lesions with sizes less than 2 cm. These modifications of our lymph node dissection strategy have led to a decline in the total dissected lymph node number after 2013, especially in the segmentectomy group treated for early lung cancer (Table 5). We believe that in the future, precise cancer staging will not only be based on surgery alone but also on our knowledge of the tumour characteristics as observed on chest CT images [23, 24], preoperative functional imaging such as PET-CT scan, EBUS/TBNA with navigation system and even combined with molecular analysis to predict tumour biology. Hence, the value and extent of lymph node dissection in different clinical scenarios should be investigated thoroughly to control the disease and, in the meantime, be minimized to reduce trauma in these patients.

The length of the wound is smaller in the single-port group, when compared with the multiport group. We believe it is because of our accumulated experience aiming to reduce the trauma and also to

challenge ourselves. Incision wounds as small as 2–3 cm were possible in some cases, particularly for right middle lobe lesions (smaller specimens to retrieve), early-stage lung cancer (tumours of smaller size to pass the intercostal space) and segmentectomy (smaller with regard to both tumour size and specimen size).

We analysed the time trend with a dichotomous variable (=0 if the year of the surgery is between 2005 and 2009 before the introduction of the single port; and =1 if the surgery is after the start of the use of the single port). The *P*-value in the multivariable linear regression analysis for time trend is significant in the models for the following outcome variables: blood loss ($P < 0.001$) and total number of lymph nodes dissected ($P = 0.048$); and is not significant for the other outcome variables: hospital stay ($P = 0.122$), length of wound ($P = 0.616$) and operation time ($P = 0.491$).

This indicates that there is indeed a time trend or upward learning curve that was associated with better surgical outcomes, at least in some of the outcome variables. That being said, the variable single port in these models remained significant in predicting better surgical outcomes after the introduction of a time-trend variable. Therefore, we are confident that, in addition to the accumulation of experience, the single-port technique was associated with an equivalent or better surgical outcomes. In the concept of this article, we would like to present that lymph node dissection was not compromised by the single-port technique and, in fact, the total number of dissected lymph nodes grew even higher through the modification of the technique and on the basis of previous experience with the multiport technique.

In summary, by merely reducing one or two ports and solving some minor issues such as clashing of instruments and modification of surgical techniques, we believe that single-port surgery has now become a relevant, alternative way of performing VATS, based on former experience with the multiport technique. In our hands, it did not prove too difficult to adopt the single-port technique for thorough lymph node dissection, with quantity and quality equal, if not superior, to the multiport technique.

The limitation of this study is its retrospective nature, with different study periods for the single- and multiport techniques. The concept and technique of the single-port technique were based on previous experience with the multiport technique, and other factors such as modification of surgical techniques and refinement of endoscopic instruments by the industry may also have contributed to our results. As for the strength of this study, we documented that lymph node dissection using the single-port technique for lung cancer in our case series was not compromised, being at least as effective as the multiport technique in our hands.

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