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ORIGINAL ARTICLE

Long-term outcomes of video-assisted thoracoscopic surgery lobectomy vs. thoracotomy lobectomy for stage IA non-small cell lung cancer

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Abstract

Objectives Video-assisted thoracoscopic surgery (VATS) lobectomy is performed widely for patients with clinical stage I non-small cell lung cancer (NSCLC) because of its superior short-term outcomes to those of thoracotomy lobectomy. However, the long-term outcomes of VATS lobectomy vs. thoracotomy lobectomy remain controversial.

Methods We reviewed the clinical data of 202 consecutive patients who underwent lobectomy for clinical stage IA NSCLC at our institution between January, 2008 and December, 2013. Stage IA NSCLC was confirmed pathologically in 162 of these patients, 60 of whom underwent VATS lobectomy and 102 of whom underwent thoracotomy lobectomy. We compared the perioperative clinical factors and outcomes of these two groups, using a propensity score-matched analysis.

Results In an analysis of 58 matched cases, the VATS group showed less blood loss, a shorter duration of chest tube placement, a shorter postoperative hospital stay, and a lower peak C-reactive protein value, despite a longer operative time. The VATS group also had significantly longer survival than the thoracotomy group [5-year overall survival, 100% vs. 87%, respectively ($p=0.01$); 5-year disease-free survival, 100% vs. 86% ($p=0.03$)].

Conclusions These findings suggest that VATS may have better long-term as well as short-term outcomes than thoracotomy for patients with early-stage NSCLC.

Keywords Video-assisted thoracoscopic surgery (VATS) · Lobectomy · Non-small cell lung cancer (NSCLC) · C-reactive protein (CRP) · Long-term outcome

Introduction

Video-assisted thoracoscopic surgery (VATS) lobectomy is often thought to be inferior to thoracotomy lobectomy in terms of long-term outcomes, including recurrence and the overall survival (OS) of patients with non-small cell lung cancer (NSCLC). This is because the restricted handling of surgical instruments in VATS lobectomy can make complete oncologic resection difficult in patients with NSCLC. Although the short-term advantages of VATS lobectomy for early-stage NSCLC, including lower rates of postoperative complications and a shorter hospital stay, are well documented [1–3], there are few reports on the long-term outcomes of VATS lobectomy being equivalent to those of thoracotomy lobectomy for patients with clinical stage I NSCLC [4, 5]. However, the long-term outcomes, especially the oncologic efficacy of VATS lobectomy in comparison to thoracotomy lobectomy, should be evaluated and discussed.

In this retrospective study, we used a propensity score-matched analysis to compare the short- and long-term outcomes of patients who underwent VATS lobectomy or thoracotomy lobectomy for stage IA NSCLC. The study population was limited to patients with clinical and pathological stage IA disease, because there are several different populations of patients with clinical stage I NSCLC. We investigated the medical records of patients with clinical and pathological stage IA NSCLC to deliver an unbiased

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rating of both surgical approaches. The results of this study may provide better indications regarding the best surgical approach for early-stage NSCLC.

Patients and methods

Patients

We reviewed the clinical data of 202 consecutive patients with clinical stage IA NSCLC who underwent lobectomy at Nagoya City University hospital between January, 2008 and December, 2013. The data of 162 of these patients, with clinical and pathological stage IA NSCLC, were collected for this study. Of the 162 patients, 60 underwent VATS lobectomy and 102 underwent thoracotomy lobectomy. The preoperative staging was established by bronchoscopy, computed tomography (CT) of the body with contrast enhancement, positron emission tomography, and magnetic resonance imaging of the brain. The seventh edition of the TNM lung cancer staging system was used in this study [6]. The study was approved by the Institutional Review Board of Nagoya City University Hospital and each patient gave written consent for the use of their clinicopathological data for research.

Surgical procedure

The procedures were performed under general anesthesia and thoracic epidural anesthesia. All patients were managed with one-lung ventilation and were then positioned in the lateral decubitus position. For the VATS procedures, we used three or four 1.2-cm incisions for trocar introduction and finally extended one incision to 3.0–4.0 cm for retrieval of the organ. All VATS procedures were performed under monitor vision alone, without rib spreading. Thoracotomy was performed via one 1.2-cm incision for trocar introduction and an access incision of 7.0–15.0 cm, mainly under direct vision. All thoracotomy procedures were performed with the use of a rib spreader through the access incision.

Postoperative management

Regardless of the surgical approach, the chest tube was removed without any air leakage, postoperative bleeding, chylothorax, or increase in the amount of pleural effusion. The chest tubes were kept in the pleural space with a suction pressure of 10 cm H_2O until the drainage over a 24-h period was <200 ml. For postoperative pain control, a continuous epidural infusion of 0.2% ropivacaine was administered at 4 ml/h until the chest tubes were removed. Loxoprofen sodium was administered regularly three times a day in addition to epidural anesthesia and the dosage was gradually decreased.

Data collection and follow-up evaluation

We analyzed the clinical data on patient characteristics, operative details, and postoperative outcomes. The operative mortality data included all of the patients who died within the first 30 days after surgery or during hospitalization. The postoperative morbidity data included all patients who experienced complications during hospitalization and after discharge from the hospital. All complications were graded according to the Clavien–Dindo classifications [7]. The complete follow-up data were obtained from the records of post-discharge visits and from regular radiographic follow-up assessments. For most of the patients, CT scans of the body were obtained 6 and 12 months postoperatively, and thereafter at yearly intervals.

Statistical analysis

Fisher's exact test was used to compare the nominal variables between the VATS and thoracotomy groups. The Mann–Whitney *U* test was used to compare the continuous variables. Survival curves were generated using the Kaplan–Meier method, and the log-rank test was used to assess the significance of the differences between groups. Two-sided p values of <0.05 were considered to indicate a significant difference. All of the data were analyzed using the EZR software program [8].

To minimize the bias caused by the non-randomized allocation of patients to VATS or thoracotomy, a retrospective propensity score-matched analysis was performed to adjust the confounding variables. The propensity score was calculated by a multivariate logistic regression model that included age, gender, smoking status, preoperative carcinoembryonic antigen (CEA), solid component size of the tumor, and histology as independent variables and the caliper was set at 0.1. This analysis was performed using R version 3.3.3 with the "matching" and "survival" libraries.

Results

Table 1 summarizes the clinical characteristics of the patients in the VATS and thoracotomy groups. In the non-matched analysis, the VATS group had younger patients (median age 64 vs. 68 years), a female predominance, a smaller solid component size of the tumor, and a higher frequency of adenocarcinoma than the thoracotomy group. The smoking status, CEA level, tumor size and pathologic invasiveness of the tumor were significantly higher in the thoracotomy group than in the VATS group. There were no

Table 1 Demographic data

Variable	Non-matched analysis			Matched analysis		
	VATS ($n=60$)	Thoracotomy ($n=102$)	p value	VATS ($n=58$)	Thoracotomy ($n=58$)	p value
Age (year)						
Median (range)	64 (43–79)	68 (32–86)	0.01	64 (43–79)	65 (32–80)	0.89
Gender						
Male	26 (43.3%)	62 (60.8%)	0.04	24 (41.4%)	25 (43.1%)	1.00
Female	34 (56.7%)	40 (39.2%)		34 (58.6%)	33 (56.9%)	
ECOG performance status						
0/1	60 (100%)	101 (99.0%)	1.00	58 (100%)	58 (100%)	1.00
2	0	1 (1.0%)		0	0	
Preoperative comorbidities						
Hypertension	12 (20.6%)	19 (18.6%)	0.84	12 (20.7%)	6 (10.3%)	0.20
Other cancer	9 (15.0%)	13 (12.7%)	0.81	9 (15.5%)	6 (10.3%)	0.58
Diabetes mellitus	8 (13.3%)	6 (5.9%)	0.15	8 (13.8%)	2 (3.4%)	0.09
Heart disease	2 (3.3%)	5 (4.9%)	1.00	2 (3.4%)	0	0.50
Collagen disease	0	5 (4.9%)	0.16	0	2 (3.4%)	0.50
Liver disease	3 (5.0%)	1 (1.0%)	0.14	3 (5.2%)	1 (1.7%)	0.62
Kidney disease	0	2 (2.0%)	0.53	0	3 (5.2%)	0.24
Number of preoperative comorbidities						
$\geqq 2$	8 (13.3%)	7 (6.9%)	0.26	8 (13.8%)	4 (6.9%)	0.36
<1	52 (86.7%)	95 (93.1%)		50 (86.2%)	54 (93.1%)	
Smoking status (pack year)						
Median (range)	0 (0–125)	40 (0–169)	<0.01	0 (0–125)	23 (0–90)	0.47
FVC(L)						
Median (range)	3.2 (1.8–5.2)	3.1 (1.4–5.2)	0.48	3.2 (1.8–4.6)	2.9 (1.5–5.2)	0.15
FEV1.0 (L)						
Median (range)	2.3 (1.2–4.1)	2.2 (1.0–3.9)	0.26	2.3 (1.2–3.5)	2.3 (1.4–3.9)	0.33
GPS						
0	60 (100%)	99 (97.1%)	0.30	58 (100%)	58 (100%)	1.00
1	0	3 (2.9%)		0	0	
NLR						
<5	58 (96.7%)	100 (98.0%)	0.63	56 (96.6%)	57 (98.3%)	1.00
$\geqq 5$	2 (3.3%)	2 (2.0%)		2 (3.4%)	1 (1.7%)	
PLR						
<150	36 (60.0%)	83 (81.4%)	<0.01	35 (60.3%)	51 (87.9%)	0.01
$\geqq 150$	24 (40.0%)	19 (18.6%)		23 (39.7%)	7 (12.1%)	
CEA (ng/ml)						
Median (range)	2.1 (0.1–13.8)	3.1 (0.1–64)	<0.01	2.2 (0.1–13.8)	2.3 (0.1–10.2)	0.66
Tumor size (major axis: mm)						
Median (range)	16 (7–29)	20 (5–30)	<0.01	17 (7–29)	20 (5–30)	<0.01
Solid component size of the tumor (major axis: mm)						
Median (range)	12 (0–29)	15 (0–30)	<0.01	12 (0–29)	10 (0–29)	0.69
Histology						
Adenocarcinoma	55 (91.7%)	73 (71.6%)	<0.01	54 (93.1%)	51 (87.9%)	0.52
Others	5 (8.3%)	29 (28.4%)		4 (6.9%)	7 (12.1%)	
Pathologic invasiveness						
Lymphatic invasion	3 (5.0%)	17 (16.7%)	0.04	3 (5.2%)	3 (5.2%)	1.00
Vascular invasion	2 (3.3%)	17 (16.7%)	0.01	2 (3.4%)	3 (5.2%)	1.00

VATS Video-assisted thoracoscopic surgery, *ECOG* Eastern Cooperative Oncology Group, *FVC* forced vital capacity, *FEV1.0* forced expiratory volume in 1 s, *CEA* carcinoembryonic antigen, *GPS* Glasgow prognostic score, *NLR* neutrophil lymphocyte ratio, *PLR* platelet lymphocyte ratio

differences between the groups with respect to performance status, preoperative comorbidities or pulmonary function. In the propensity score-matched analysis, although the VATS group patients had a smaller tumor size (median major axis 17 mm vs. 20 mm), the size of the solid component of the tumor did not differ between the groups. Similarly, there were no differences between the groups with respect to age, gender, smoking status, CEA level, histology, or the pathological invasiveness of the tumor. There were no differences in the Glasgow prognostic score (GPS) or neutrophil lymphocyte ratio (NLR) between the groups. The platelet lymphocyte ratio (PLR) was significantly higher in the VATS group than in the thoracotomy group. Positron emission tomography was performed in 103 (64%) patients (37 from the VATS group and 66 from the thoracotomy group). The maximal standardized uptake value (SUV) was significantly lower in the VATS group than in the thoracotomy group in the non-matched analysis (median 2.3 vs. 3.2, $p < 0.01$). However, there was no difference in the maximal SUV between the groups in the matched analysis (median 2.3 vs. 1.7, $p = 0.87$).

Table 2 summarizes the perioperative details. All patients in both groups underwent complete resection (R0) and none of the VATS procedures required conversion. The VATS group showed significantly less blood loss, a shorter postoperative hospital stay, and a lower peak C-reactive protein (CRP) level than the thoracotomy group in both analyses, despite the longer operative time. The VATS group showed a lower CRP level on postoperative day (POD) 1 in the non-matched analysis and a shorter duration of chest tube placement in the matched analysis. The CRP levels of almost all patients peaked on POD3. There were no differences in the perioperative treatment variables of the two groups with regard to the order of interrupting the pulmonary vessels, mediastinal lymphadenectomy and postoperative adjuvant chemotherapy in either of the analyses.

Table 3 summarizes the postoperative complications. There were no cases of operative mortality or intraoperative complications in either group. Nine patients had a collective nine complications in the VATS group, while 17 patients had a collective 18 complications in the thoracotomy group in the non-matched analysis. In the matched analysis, eight patients had eight complications in the VATS group, while five patients had five complications in the thoracotomy group. There were no significant differences in the incidence of each postoperative complication, the overall incidence of postoperative complications, or the incidence of grade ≧ III complications (Clavien–Dindo) in either of the analyses.

In the non-matched analysis, after a median follow-up period of 60 months (range 7–96 months for the VATS

Table 2 Perioperative outcomes

Variable	Non-matched analysis			Matched analysis		
	VATS ($n=60$)	Thoracotomy ($n=102$)	p value	VATS ($n=58$)	Thoracotomy ($n=58$)	p value
Order of interrupting pulmonary vessels						
Artery-first	15 (25.0%)	22 (21.6%)	0.70	15 (25.9%)	16 (27.6%)	1.00
Vein-first	45 (75.0%)	80 (78.4%)		43 (74.1%)	42 (72.4%)	
Mediastinal lymph node dissection						
Yes	42 (70.0%)	73 (71.6%)	0.86	40 (69.0%)	33 (56.9%)	0.25
No	18 (30.0%)	29 (28.4%)		18 (31.0%)	25 (43.1%)	
Operative time (min)						
Median (range)	210 (123–332)	173 (80–332)	<0.01	210 (123–332)	166 (104–289)	<0.01
Blood loss (ml)						
Median (range)	84 (5–482)	116 (5–1431)	<0.01	84 (5–482)	105 (13–498)	0.04
Chest tube duration (days)						
Median (range)	3 (2–24)	4 (2–20)	0.12	3 (2–24)	4 (2–16)	0.01
Postoperative hospital stay (days)						
Median (range)	8 (5–35)	9 (4–64)	0.03	8 (5–35)	9 (4–23)	0.03
CRP on POD1 (mg/dl)						
Median (range)	4.6 (0.4–10.7)	5.0 (1.3–11.4)	0.04	4.6 (0.4–10.7)	5.0 (1.3–9.5)	0.06
CRP at peak (mg/dl)						
Median (range)	5.6 (2.6–14.0)	8.5 (2.4–21.5)	<0.01	5.6 (2.6–14.0)	7.9 (2.5–21.5)	0.01
Postoperative adjuvant chemotherapy						
Yes	11 (18.3%)	11 (10.8%)	0.23	11 (19.0%)	4 (6.9%)	0.09
No	49 (81.7%)	91 (89.2%)		47 (81.0%)	54 (93.1%)	

VATS Video-assisted thoracoscopic surgery, *CRP* C-reactive protein, *POD* postoperative day

Table 3 Postoperative complications

Complication	Non-matched analysis			Matched analysis		
	VATS ($n=60$)	Thoracotomy ($n=102$)	p value	VATS ($n=58$)	Thoracotomy ($n=58$)	p value
Air leak	5 (8.2%)	6 (5.8%)	0.54	4 (6.9%)	2 (3.4%)	0.68
Chylothorax	1 (1.7%)	3 (2.9%)	1.00	1 (1.7%)	3 (5.2%)	0.62
Wound infection	1 (1.7%)	1 (1.0%)	1.00	1 (1.7%)	0	1.00
Thoracic empyema	1 (1.7%)	1 (1.0%)	1.00	1 (1.7%)	0	1.00
Bleeding requiring surgical treatment	1 (1.7%)	0	0.37	1 (1.7%)	0	1.00
Atelectasis	0	1 (1.0%)	1.00	0	0	1.00
Hoarseness	0	1 (1.0%)	1.00	0	0	1.00
Delirium	0	1 (1.0%)	1.00	0	0	1.00
Atrial fibrillation	0	2 (1.9%)	0.53	0	0	1.00
Pneumonia	0	1 (1.0%)	1.00	0	0	1.00
Hypoxia	0	1 (1.0%)	1.00	0	0	1.00
All complications	9 (15.0%)	18 (17.6%)	0.83	8 (13.7%)	5 (8.6%)	0.56
All severe complications (Clavien–Dindo grade III or greater)	2 (3.3%)	4 (3.9%)	1.00	1 (1.7%)	0	1.00

VATS Video-assisted thoracoscopic surgery

group and 0.5–111 months for the thoracotomy group), the 5-year OS rate was 100% in the VATS group vs. 86% in the thoracotomy group ($p<0.01$, Fig. 1a). The 5-year disease-free survival (DFS) rates in the VATS and thoracotomy groups were 100% and 81%, respectively ($p<0.01$, Fig. 1b). In the matched analysis, after a median follow-up period of 60 months (range 7–96 months), the 5-year OS rate in the VATS group was 100%. In contrast, after a median follow-up period of 66 months (range 0.5–104 months), the 5-year OS rate in the thoracotomy group was 87% ($p=0.01$, Fig. 2a).

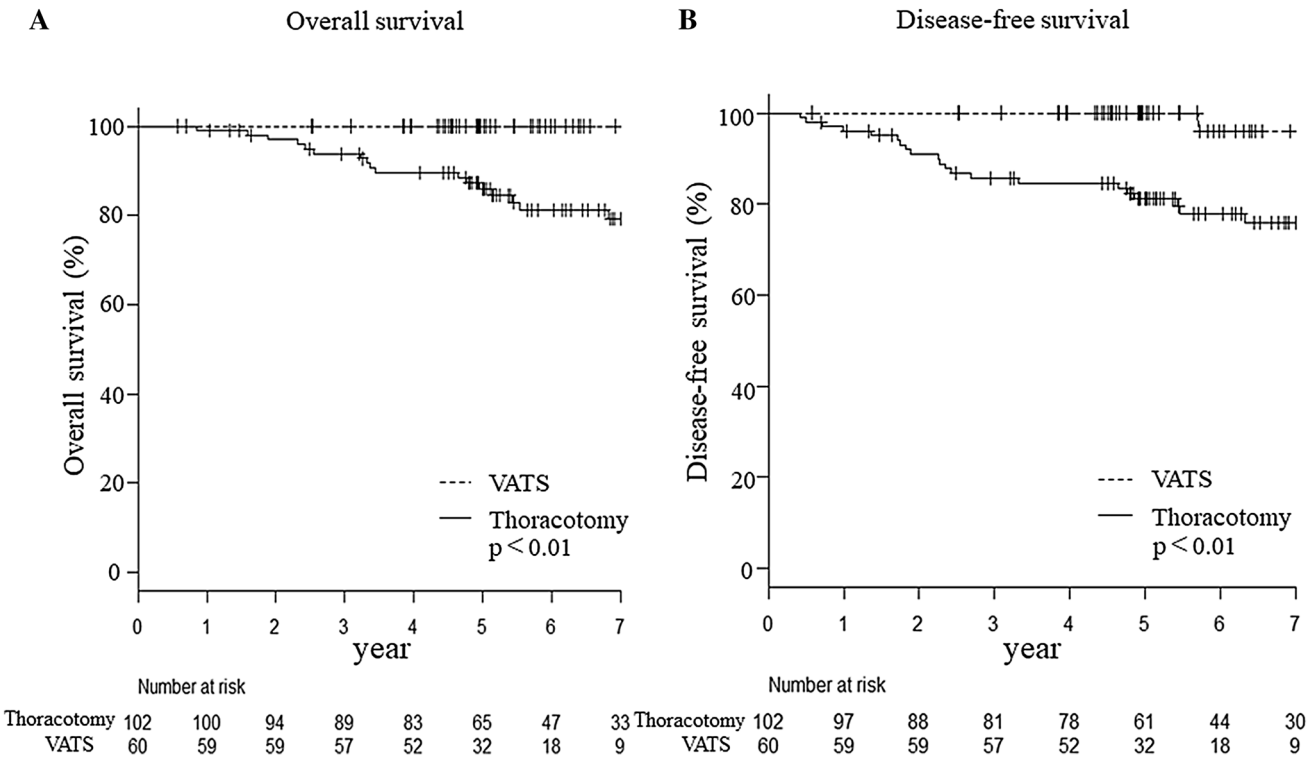

Fig. 1 Overall (**a**) and disease-free (**b**) survival of patients after video-assisted thoracoscopic surgery or thoracotomy in the non-matched analysis

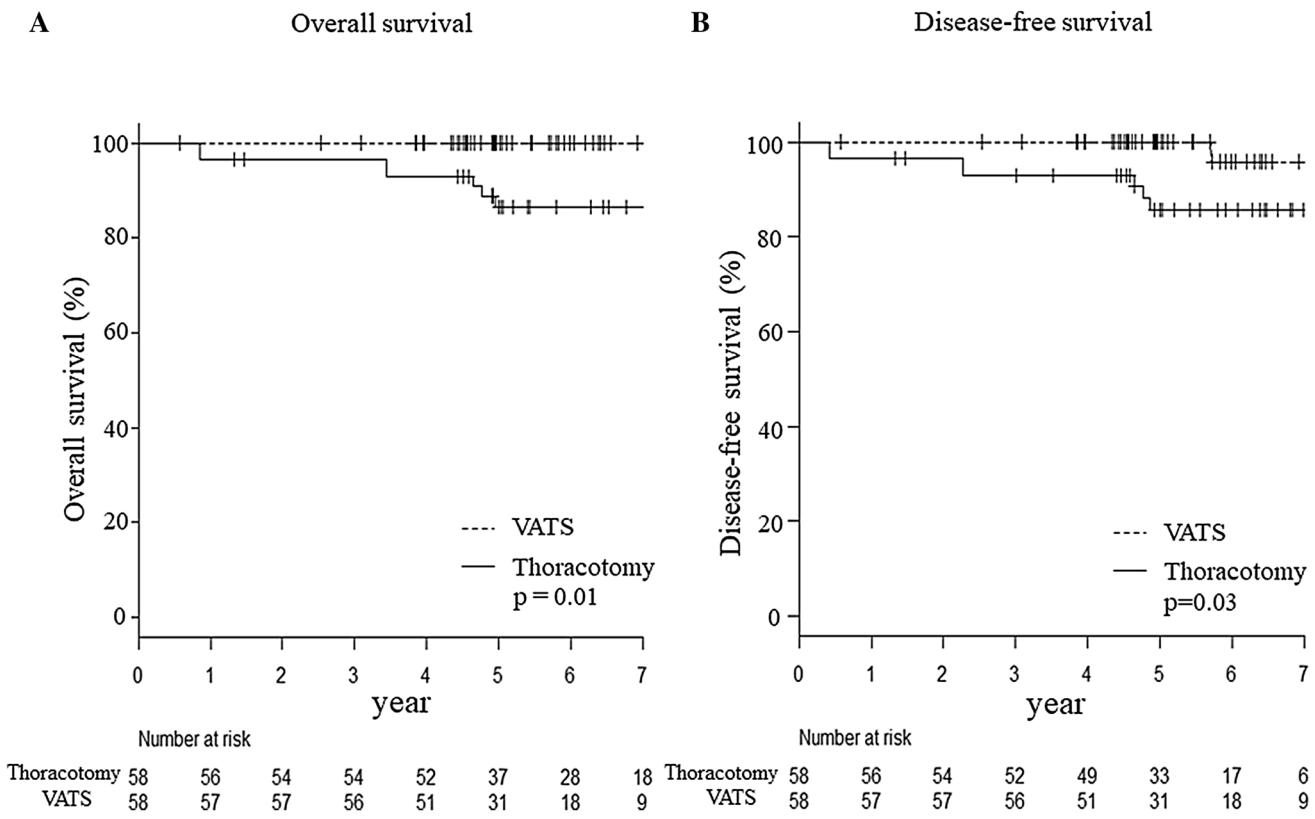

Fig. 2 Overall (**a**) and disease-free (**b**) survival of patients after video-assisted thoracoscopic surgery or thoracotomy in the matched analysis

The 5-year DFS rates in the VATS and thoracotomy group were 100% and 86%, respectively ($p = 0.03$, Fig. 2b).

Recurrence developed in 16 patients (15.7%) in the thoracotomy group and one patient (1.7%) in the VATS group. The recurrence sites in the thoracotomy group were local ($n = 10$), distant ($n = 2$), and both ($n = 4$) (Table 4). There were 18 deaths, all of patients from the thoracotomy group, including 12 lung cancer-related deaths and six deaths from

Table 4 Recurrence sites and time to recurrence

Variable	Non-matched analysis			Matched analysis		
	VATS ($n = 60$)	Thoracotomy ($n = 102$)	p value	VATS ($n = 58$)	Thoracotomy ($n = 58$)	p value
Recurrence patterns						
Local (total)	0	10 (9.8%)	0.01	0	3 (5.2%)	0.24
Ipsilateral lung	0	6	0.09	0	1	1.00
Mediastinal or hilar nodal stations	0	3	0.30	0	2	0.50
Dissemination	0	1	1.00	0	0	1.00
Distant (total)	0	2 (2.0%)	0.53	0	0	1.00
Liver	0	1	1.00	0	0	1.00
Carcinomatous meningitis	0	2	0.53	0	0	1.00
Local and distant (total)	1 (1.7%)	4 (3.9%)	0.65	1 (1.7%)	2 (3.4%)	0.50
Lung and carcinomatous meningitis	0	1	1.00	0	0	1.00
Nodal stations and bone	0	3	0.30	0	2	0.50
Nodal stations and brain	1	0	0.37	1	0	1.00
Total	1 (1.7%)	16 (15.7%)	< 0.01	1 (1.7%)	5 (8.6%)	0.21

VATS Video-assisted thoracoscopic surgery

other disease. In the matched analysis, five patients (8.6%) in the thoracotomy group and one patient (1.7%) in the VATS group suffered recurrence. The five patients with recurrent disease showed a higher rate of smoking, a larger solid component, and a higher incidence of lymphatic invasion than the 53 patients without recurrence in the thoracotomy group. The one patient with recurrent disease in the VATS group was found to have a brain metastasis and mediastinal lymph node metastasis at a routine follow-up examination 70 months after the operation.

Discussion

There are several different populations of patients with clinical stage I NSCLC. These include patients with nodal upstaging as well as those with pathologic stage I disease. Even after optimal preoperative staging, 10–25% of patients with clinical stage I NSCLC are found to have unforeseen positive lymph nodes in the final pathological examination [9, 10]. Several investigators have reported lower rates of N1 upstaging after VATS lobectomy than after thoracotomy lobectomy, due to unsystematic hilar node dissection [10, 11]. As the subjects of this study were limited to patients with clinical and pathological stage IA, there may have been more patients with undiscovered positive nodes in the VATS group than in the thoracotomy group. Thus, it was expected that the VATS group would have lower survival rates than the thoracotomy group; however, the VATS group showed better survival than the thoracotomy group in both the matched and non-matched analyses.

Regarding the perioperative outcomes in the matched analysis, although the operative time for the VATS group was longer than that for the thoracotomy group, the VATS group had significantly less blood loss and lower peak CRP levels. Several investigators have found that less blood loss and lower postoperative CRP levels are associated with better postoperative OS of NSCLC patients [12, 13]. Blood loss commonly depends on the size of the chest wound, the extent of resection, and the skill of the operator. The patients in the present study, limited to those with clinical and pathological stage IA disease, were thought to show a uniform extent of resection. Although poor endoscopic surgical skill is associated with a longer operative time, the reason for the decreased blood loss in the VATS group may include the precision of surgery, attributed to the magnified view, as well as the smaller size of the chest wound than in the thoracotomy group. CRP is an acute-phase response marker associated with postoperative complications such as respiratory distress syndrome and multiple organ failure [14]. Several studies have shown that VATS lobectomy causes less inflammatory response than open lobectomy [2, 15]. The elevated GPS, NLR, and PLR have also been associated with poor prognosis in patients with lung cancer [16–18]. Although the PLR in the VATS group was significantly higher than that in the thoracotomy group in this study, the VATS procedure was associated with a good prognosis. The VATS group did not include more patients in good preoperative condition (Table 1). Therefore, the better prognosis of the VATS group cannot be explained by preoperative selection bias. Our results for CRP suggest that VATS was associated with less tissue damage and consequently, reduced acute-phase associated mediator activity. This suppression of the perioperative inflammatory response that is associated with VATS procedures may contribute to reducing the recurrence of NSCLC by maintaining an adequate immune reaction against circulating tumor cells, whereas in thoracotomy, the tumor cells may diffuse into the vascular and lymphatic vessels by directly touching the tumor.

VATS is associated with shorter chest tube duration than thoracotomy [2, 3]. In this study, the matched analysis showed a shorter chest tube duration in the VATS group than in the thoracotomy group, despite no significant difference between the groups in the non-matched analysis. Because chest tube duration was not a variable of the propensity score, a significant difference might not be revealed in this study. The causes of the discrepancy may be associated with the lack of postoperative fast-tracking protocols in our institution in that period [19], however, now chest tube duration is becoming uniformly shorter than before in our institution, with the recent recommendation of early chest tube removal [20].

Although many studies have shown that the rates of postoperative complications after VATS lobectomy are lower than those after thoracotomy lobectomy [3], this study indicated no differences between the groups. The postoperative complication rate of the thoracotomy group in this study was approximately 15%, which is lower than that reported in previous studies (approximately 30%) [1, 2, 4]. The relatively low rate of postoperative complications in the thoracotomy group may be attributed to the fact that we limited the subjects to patients with early-stage disease (clinical and pathological stage IA) and also because the length of the access incision (7.0–15.0 cm) in thoracotomy was shorter than in previous reports.

Although the risk factors of recurrence after surgery are unclear, several studies have shown that they include age, gender, cardiac comorbidities, smoking status, histology, angiolymphatic invasion, tumor size, and another primary malignancy [21, 22]. In the analysis of our matched thoracotomy group, the five patients with recurrent disease had a higher incidence of smoking, higher CEA levels, a larger solid component size, and a greater incidence of lymphatic invasion than the 53 patients without recurrence. Although many investigators have reported a $\geqq$30% incidence of recurrence after surgery for stage I NSCLC is [21–23],

recurrence was found in only one patient in our VATS group. Although a few cases of port site recurrence and recurrence of dissemination caused by VATS procedures have been reported [24], none of the patients in our VATS group was found to have recurrence in the pleural space or wound site. Several reports have shown that dissecting the pulmonary veins before the pulmonary arteries might reduce the dissemination of malignant tumor cells through circulation [25]. We could not find any differences between the two groups in the order of vascular treatment.

Although the tumor size in the thoracotomy group was significantly larger than that in the VATS group ($p < 0.01$), the solid component size in the two groups was comparable in the matched analysis. As the solid component size of the tumor is reported to be more related to the prognosis rather than the tumor size [26, 27], it is possible that there were no patient-related factors that affected the rate of recurrence or the prognosis of the patients in the two groups. There were some deaths from other diseases, including pneumonia and other cancers in the thoracotomy group. The better prognosis of the VATS group could be attributed in part to the less severe perioperative inflammatory response inhibiting the exacerbation of other disease.

This retrospective study had several limitations. Although we tried to match the patients' characteristics and tumor progression in the two groups to reduce bias, the small patient population remained its main limitation. We also could not match the operating surgeons in the two groups. The propensity-score matching process using a logistic regression model was reported to be effective for adjusting for significant confounders and reducing potential biases in retrospective studies; however, unlike randomized controlled trials, its limitation lies in that it does not reduce the biases caused by unobserved covariates [28]. Longer follow up may be necessary for the comparison because the VATS group had smaller tumors than the thoracotomy group after matching, although the median follow-up period was 60 months in the both groups. One of the problems of this study was that we only investigated certain parameters including CRP, GPS, NLR, and PLR as an acute phase-associated mediator. To ensure and prove the invasiveness of VATS procedures more universally, we should investigate other acute phase-associated mediators. Next, we will conduct a clinical study to clarify the positive survival outcomes of VATS by objectively analyzing the perioperative blood and pleural effusion during surgery to scientifically prove VATS is less invasive.

In conclusion, we found that VATS was associated with better long-term and short-term outcomes than thoracotomy for selected patients with clinical and pathological stage IA disease. Our next study aims to scientifically clarify the objective data to support that VATS is less invasive than thoracotomy.

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Compliance with ethical standards

Conflict of interest We have no conflicts of interest to declare.

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