Unilateral Thoracoscopic Thymectomy for Thymoma: Does Side Matter? A Single Institutional Experience

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Abstract

Background Thoracoscopic thymectomy is increasingly performed for the treatment of early stage thymoma. It is characterized by shorter postoperative hospital stay, decreased intraoperative blood loss, and fewer complications compared with transsternal thymectomy. Unilateral video-assisted thoracic surgery (VATS) thymectomy can be easily performed from either side of the thorax, because thymus is located in the middle of mediastinum. However, the side that provides better outcomes remains controversial. The purpose of this study was to compare the efficacy of right and left approaches in performing unilateral thoracoscopic thymectomy for thymoma.

Methods Consecutive patients affected by thymoma who underwent VATS thymectomy on either side between February 2001 and March 2020 were enrolled in the study. Clinicopathologic, surgical, and oncological outcomes were retrospectively analyzed and compared among the two surgical approaches.

Results Unilateral VATS approaches were performed on 29 patients: 12 (41%) on the left side and 17 (59%) on the right side. The mean age was 63.1 ± 11.3 years and the female/male ratio was 1.73:1. The mean operative time and the hospital stay for the left-side VATS and right-side VATS groups were, respectively, 168 ± 49.5 versus 171 ± 47.9 minutes ($p = 0.9$) and 3 ± 1.03 days versus 3.65 ± 1.93 days ($p = 0.7$). Postoperative complications occurred in one patient (3%) for left-side VATS group and one patient (3%) for right-side VATS. The 5-year disease-free survival was comparable between two groups ($p = 0.74$).

Conclusion Unilateral VATS thymectomy in patients with thymoma can be safely and effectively performed by experienced surgeons in either side of the thorax with equivalent oncological outcomes.

Keywords
- myasthenia gravis
- VATS
- thymectomy
- outcomes
- thymoma

Introduction

Over the last two decades, many approaches have been described, extensively analyzed and published for the management of thymoma.[1–3] Total thymectomy via median sternotomy has been the preferred standard treatment for thymoma for a long time despite the fact that this technique causes long postoperative hospital stay, long-lasting postoperative pain, and poor cosmetic outcomes.[4,5]

In the last decade, minimally invasive techniques of thymectomy have been increasingly performed for early stages

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thymomas.[6] Minimally invasive thymectomy improves postoperative outcomes, including reduced postoperative pain, fewer postoperative complications, and shorter postoperative hospital stay. Furthermore, it provides equivalent oncological clinical outcomes when compared with standard sternotomy approach to the disease.[7–12] Several operative approaches for minimally invasive thymectomy have been described including unilateral video-assisted thoracic surgery (VATS), bilateral VATS, robotic video-assisted techniques, transcervical thymectomy, and subxiphoid thymectomy.[13–15] Unilateral thoracoscopic thymectomy is a simple procedure and oncologically feasible for thymoma at early stages.[16] However, controversies exist regarding the side that provides the best postoperative outcome. Unilateral VATS, performed on the right side, is generally preferred; in this technique, the landmark of the superior vena cava, where the left innominate vein converges, can be conveniently identified.[17,18] However, other researchers recommended left-sided VATS thymectomy.[19] This study presents our experience on unilateral VATS thymectomy, compares short-term and oncological outcomes, and identifies differences of unilateral VATS thymectomy conducted on both sides.

Methods

Between February 2001 and March 2020, 72 patients underwent surgery for thymoma in our unit with different surgical approaches. We retrospectively collected and reviewed data of 29 consecutive patients undergoing thoracoscopic thymectomy during that time period. All surgeries were performed by four general thoracic surgeons, who are fellowship trained in minimally invasive thoracic surgery and advanced minimally invasive surgery.

The study was approved by the local Ethics Committee. Patients with definitive histological diagnosis of thymic carcinoid, thymic hyperplasia, thymolipoma, primary thymic lymphoma, or thymic cyst were excluded from the study. Patients who received an open approach as well as patients who underwent nonsurgical treatments were also excluded. Clinicopathologic data, including gender, age at disease onset, date of surgery, clinical classification, medication, surgery information, morbidity, thymoma histology, maximum diameter, and position, were obtained from clinical and pathologic records. Comorbidities were defined according to the Charlson Comorbidity Index score.[20] The histologic type of neoplasm was classified according to the 2015 World Health Organization (WHO) Classification of Tumors of the Thymus.[21] The tumor stage was determined according to both Masaoka system[22] and tumor, node, and metastasis (TNM) classification system.[23,24] Postoperatively, all patients were checked for recurrence with an oncological follow-up.

The preoperative myasthenia gravis severity was evaluated according to the Myasthenia Gravis Foundation of America (MGFA) classification system.[25] The postoperative patients' clinical symptoms were evaluated during the hospitalization for thymectomy, and each patient had regular postoperative follow-up, which were performed at least two times per year. The therapeutic response to thymectomy was compared with the patient's preoperative status and assessed according to MGFA postintervention status.

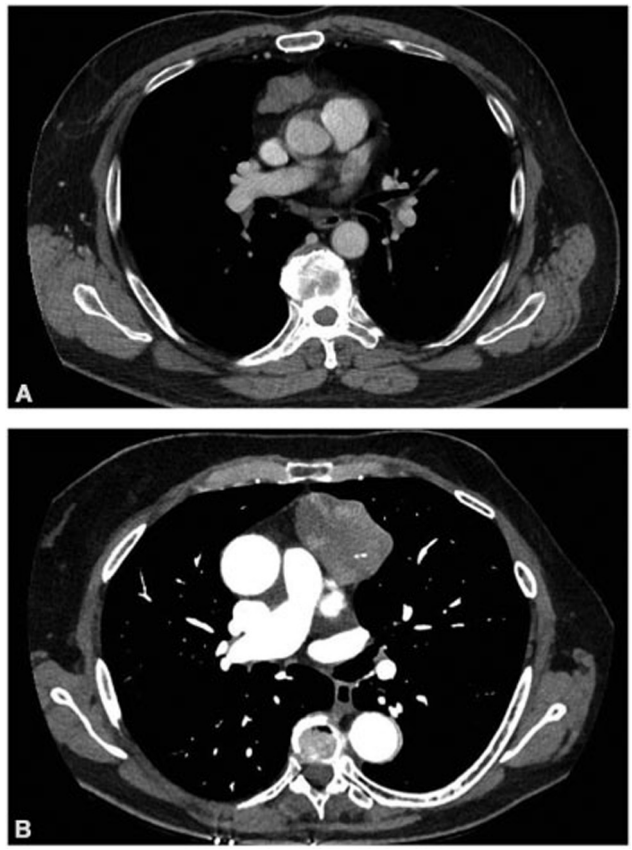

Fig. 1 Chest CT scans showing thymomas extending predominantly on le right side (**A**) or to the left side (**B**).

Surgical Technique

The access via left or right VATS was determined according to the position of the tumor, as noted on the preoperative chest computed tomography (CT) (►**Fig. 1**). Similar techniques for right- and left-sided VATS were performed. VATS was usually performed with the patient positioned in ~30 degrees semisupine position. The ipsilateral arm is placed naturally and secured by the side and below the chest wall on the padded board (►**Figure 2**). The operating surgeon, the assistant, and the scrub nurse stand along the same side. Three trocars were generally positioned between the third and sixth intercostal spaces following the submammary line. CO_2 insufflation was used to collapse the lung.

The mediastinal pleura overlying the lower ends of the main thymic lobes was dissected along the phrenic nerve, which has to be carefully preserved. The incision of the mediastinal pleura was continued at the upper edge to open the connection to the neck tissue. During further mobilization of the anterior mediastinal tissue portion by retrosternal incision down to the diaphragm, the arterial thymic supply was divided. The whole tissue portion was then mobilized from the pericardial surface. After complete exposure of the innominate vein all thymic veins were resected. Finally, the totally freed thymic tumor, thymic gland, and its accompanying mediastinal fatty tissues

Fig. 2 Patient's positioning and submammary incisions.

were brought out. Contralateral phrenic nerve was visualized only in case of large thymic tumors by means of opening the contralateral mediastinal pleura. Our treatment strategy for thymoma was to perform an extended thymectomy, including the excision of bilateral fat tissue, regardless of the presence of myasthenia gravis.

Statistical Analysis

For categorical variables, absolute and percentage frequencies were reported. In the presence of symmetry of the distributions, the variables were represented with the mean and standard deviation or, in the case of not-normal distribution, with the median value and interquartile range (IQR). Statistical comparisons of continuous variables were assessed using Student's t-test for normally distributed variables and using Mann–Whitney U test in case of not-normal distribution, while for categorical variables Pearson chi-squared test or Fisher's exact test were used depending on the minimal expected count in each crosstab. Disease-free survival (DFS), defined as freedom from recurrence in case of complete resection (R0) or as time-to-progression in case of incomplete recurrence (R1–R2), was calculated from the day of surgery. The disease-free follow-up, expressed in months, was evaluated over the 10 years after surgery. Survival analysis was undertaken using the Kaplan–Meier method. The comparison between groups was evaluated using the log rank test.

Results

Twenty-nine patients (11 males and 18 females) were enrolled in the study. The mean age was 63.1 ± 11.3 years and the female/male ratio was 1.73:1. Ten patients (34%) presented with myasthenia gravis. Left-side video-assisted thoracoscopic extended thymectomy was performed in 12 patients (41%), whereas right-side thoracoscopic extended thymectomy was performed in 17 patients (59%). Patients' characteristics are listed in ►**Table 1**. The median value of Charlson comorbidity score was 4 (IQR: 4–6) in the right approach group and 4 (IQR: 3–5) in the left approach group (p = . 0.248). With regard to the WHO classification, there were 4 type A, 10 type AB, 5 type B1, 7 type B2, one thymic carcinoma, and one micronodular thymoma without significant differences between two groups ($p = 0.999$). The mean tumor size of the resected specimens was 5.6 (± 2.5) cm for the right side and 5.4 (± 1.3) cm for the left side in diameter ($p = 0.490$). Most of the patients (86%) had Masaoka stage I or II tumors, none were in stage IV, but three patients (14%) were in stage III. Furthermore, no patient required conversion to open thymectomy.

As shown in ►**Table 2**, the mean operation time for the right-side VATS and groups left-side VATS was, respectively, 170.6 ± 47.9 versus 168.3 ± 49.5 minutes ($p = 0.903$). Curative resection (R0) was accomplished in 94% of cases in case of right VATS and 92% of cases of left VATS approach ($p = 0.798$). The mean duration of chest drain was 2 days in both groups ($p = 0.962$). The mean hospital stay was 3 days (IQR: 3–4) for the left-side VATS and 3 days (IQR: 3–4) for right-side VATS groups ($p = 0.723$). One patient (5.9%) required intensive care unit (ICU) postoperative ICU admission in the right-side group and two patients (16.9%) in the left-side group ($p = 0.533$).

Postoperative complications occurred in one patient (3%) for left-side VATS group with phrenic nerve lesion on the left side and one patient (3%) for right-side VATS with respiratory failure. The morbidity rate was similar in the two groups ($p = 0.99$). There was no surgery-related mortality in either group.

The mean follow-up time was 105 months (IQR: 72.5–150) for the left-side group and 40 months (IQR: 27–99.5) for the right-side group. There were two recurrences in the left-side VATS group and two recurrences in the right-side VATS group; all the recurrences were local on both sides. ►**Fig. 3** shows Kaplan–Meier estimate for DFS: there were no differences in the DFS between the two groups ($p = 0.7401$).

According to the MGFA postintervention status only one patient, in the left side group, was considered in complete stable remission, whereas the pharmacological remission in our study group was achieved in only three and one patients in the right- and left-side group, respectively (►**Table 3**). We also compared the postoperative outcome between the left-side surgical approach (6 patients) and the right-side approach (4 patients) and we found similar patterns of average operating time, mean length of hospitalization, and rates of complete resections.

In addition, we compared the postoperative outcome between myasthenic and nonmyasthenic patients as shown in ►**Table 4**. The only significant difference was found in ICU stay, which was more commonly needed in myasthenic patients ($p = 0.032$).

Table 1 Characteristics of 29 patients undergoing video-assisted thoracoscopic thymectomy for thymoma

Variable	Right approach (17)	Left approach (12)	*p*-Value
Age (y) mean (SD)	65.2 (12.6)	59.9 (9.3)	0.230
(range)	(42–84)	(45–71)	
Female, *n* (%)	8 (47.1)	10 (83.3)	0.047
Male, *n* (%)	9 (52.9)	2 (16.7)	0.064
Myasthenia gravis, *n* (%)	4 (23.5)	6 (50)	0.236
Preoperative MGFA clinical classification, *n* (%)			
–I	1 (5.9)	1 (8.4)	0.999
–II	2 (11.8)	2 (16.7)	0.999
–III	3 (17.6)	1 (8.4)	0.622
–IV	0	0	0.999
COPD, *n* (%)	3 (17.6)	0 (0)	0.124
Hypertension, *n* (%)	12 (70.6)	3 (25)	0.025
Diabetes, *n* (%)	2 (11.8)	0 (0)	0.218
Charlson comorbidity score (median) (IQR)	4[4 6]	4[3 5]	0.248
Tumor location on chest CT –Predominantly right side –Predominantly left side	17 (100)	12 (100)	0.999
WHO, *n* (%)			
A	2 (11.8)	2 (16.7)	0.999
AB	7 (41.2)	3 (25)	0.449
B1	2 (11.8)	3 (25)	0.624
B2	3 (17.6)	4 (33.3)	0.403
B3	1 (5.9)	0 (0)	0.999
Thymic carcinoma	1 (5.9)	0 (0)	0.999
Micronodular thymoma, *n* (%)	1 (5.9)	0 (0)	0.999
Tumor size (cm) mean, (SD)	5.9 (2.5)	5.4 (1.3)	0.490
Masaoka stage, *n* (%)			
I	8 (47.1)	7 (58.3)	0.710
II	8 (47.1)	3 (25)	0.273
III	1 (5.8)	2 (16.7)	0.553
IV	0 (0)	0 (0)	0.999
TNM stage, *n* (%)			
I	12 (70.6)	9 (75)	0.999
II	4 (23.5)	0 (0)	0.121
IIIA	0(0)	3 (25)	0.006
IIIB	1 (5.9)	0 (0)	0.999

Abbreviations: COPD, chronic obstructive pulmonary disease; CT, computed tomography; IQR, interquartile range; MGFA, Myasthenia Gravis Foundation of America; SD, standard deviation; TNM, tumor, node, and metastasis; WHO, World Health Organization.

Table 2 Postoperative features

Variable	Right access(17)	Left access (12)	*p*-Value
Complications, *n* (%)			
Bleeding	0 (0)	0 (0)	0.999
Phrenic nerve lesion	0 (0)	1 (8.3) left side	0.414
Respiratory failure	1 (5.9)	0 (0)	0.999
Operative time (min)	170.6 (47.9)	168.3 (49.51)	0.903
Complete resection, *n* (%)	16 (94.1)	11 (91.7)	0.798
Chest drain removal (postoperative days) Median (IQR)	2 (2.3)	2 (2.3)	0.962
Intensive care unit stay (no of patients)	1 (5.9)	2 (16.7)	0.533
Postoperative hospital stay (days) median (IQR)	3 (3.4)	3 (3.4)	0.723

Abbreviation: IQR, interquartile range.

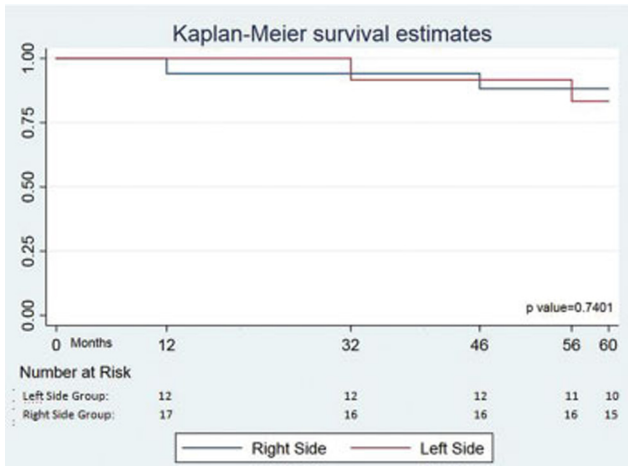

Fig. 3 Kaplan–Meier estimate for DFS.

Discussion

Traditionally, transsternal thymectomy has been the standard approach for thymomas. However, with the surgical advances, VATS thymectomy has become an effective method to treat early and small thymomas. Two recent large meta-analyses showed a significant reduction in postoperative blood loss and blood products requirements, reduction in postoperative pain scores, overall complications rates, and postoperative hospital stay with VATS thymectomy compared with open thymectomy.[26,27] Furthermore, the probability of achieving microscopically complete resection (i.e., tumor-free margins at pathologic examination) and locoregional recurrence rates was similar with either approach. In

Table 3 Outcomes of myasthenic patients considering the side of surgery

Myasthenic patients	Right-side approach (4)	Left-side approach (6)	*p*-Value
Complications, *n* (%)	1 (25)	0 (0)	0.40
Bleeding	0 (0)	0 (0)	0.99
Phrenic nerve lesion	0 (0)	1 (16.6)	0.40
Respiratory failure	1 (25)	0 (0)	0.40
Operative time (min)	172 min	181 min	
Complete resection, *n* (%)	3 (75)	5 (83.3)	0.74
Postoperative hospital stay (avg days)	5.5	3.6	
Intensive care unit stay (no of patients)	1 (25)	2 (33.3)	0.778
MGFA postoperative clinical status	0 Complete remission	1 Complete remission	0.40
	3 Pharmacological remission	1 Pharmacological remission	0.19
	0 Minimal manifestation	0 Minimal manifestation	–
	0 Improvement	1 Improvement	0.40
	0 Unchanged	0 Unchanged	–
	1 Worse	3 Worse	0.57

Abbreviation: MGFA, Myasthenia Gravis Foundation of America.

Table 4 Outcomes of myasthenic patients compared with nonmyasthenic patients

	Myasthenia gravis (10)	No myasthenia gravis (19)	*p*-Value
Complications, *n* (%)	1 (10)	0 (0)	0.344
Bleeding	0 (0)	0 (0)	0.999
Phrenic nerve lesion	1 (10)	0 (0)	0.344
Respiratory failure	1 (10)	0 (0)	0.344
Operative time (min)	177 min	165 min	
Complete resection, *n* (%)	8 (80)	19 (100)	0.118
Postoperative hospital stay (avg days)	4,4	3,0	
Intensive care unit stay, no of patients (%)	3 (30)	0 (0)	0.032

this study, no differences in terms of morbidity between the two groups were found.

Thymoma has $5+1$ subtypes according to the WHO classification: A, AB, B1, B2, B3, and thymic carcinoma that differ in prognostic values. The thymoma types A, AB, and B1 are considered at low risk of malignancy, whereas the types B2 and B3 have a high risk of malignancy. Thymic carcinoma is considered a malignant neoplasm, associated with a worse prognosis. In our study, most patients presented with the low-risk types A, AB, and B1 (66%), followed by high-risk types B2 and B3 (31%). Taking this into account, in clinical practice, preoperative estimation of the risk of malignancy is also important to determine the treatment strategy and surgical method (endoscopic vs. open surgery). Another important factor to be taken into consideration is the tumor stage. Agasthian[17] suggested that early-stage thymomas can be safely resected with VATS; our data showed that most of the patients had early-stage thymomas according to both Masaoka and TNM staging systems, respectively, in 90 and 86% of cases. As shown in our experience, the most important factor in the preoperative evaluation of patients undergoing minimally invasive thymectomy is local infiltration of the tumor rather than to tumor size. In fact, the mean size of tumors was 5.6 and 5.3 cm in the two groups.

During this study, we performed thymectomy via both left and right VATS. The choice of left or right VATS depended on the surgeon's experience and the anatomy of the tumor, which was normally assessed by preoperative chest CT. In our study, most thymomas (59%) extended to the right anterior mediastinum, making right VATS a better choice for complete thymectomy. The advantages of the right VATS are a better visualization and control of the superior vena cava, aorta, right atrium, and phrenic nerve, thereby a reduction in the potential risk of injury to these structures.[18] In our study, 41% of VATS thymectomies were performed using a left-side approach. The left-sided enables an extensive removal of fat allocated in the aortocaval groove, aortopulmonary window, and both pericardiophrenic sides.[19]

Nevertheless, this approach does have some disadvantages. When approaching from one side of the chest, it is difficult to identify the contralateral phrenic nerve. In our study, only one patient in the left side group had phrenic nerve palsy, which occurred on the same side of the operation.

Despite the small sample size, our favorable results confirm the safety and benefits of VATS thymectomy. Postoperative complications rate was low in line with literature (only 1 patient for each side).[18,19] The mean hospital stay was 3 days (IQR: 3–4) for the left-side VATS and 3 days (IQR: 3–4) for right-side VATS groups ($p = 0.723$); this was also in line with literature like the 3 days of Mineo et al[19] and 4 days by Mack et al.[28] A shorter period of hospitalization is partly due to the minimally invasive thoracoscopic technique that most of the time does not require a period in the ICU and therefore shorter hospital stay.

The tumor recurrence rate in the VATS group was relatively low in both groups, and all recurrences were local. These data suggest that VATS thymectomy does not increase the risk of pleural dissemination. We managed to completely remove the thymoma in most of the patients except in two cases where there were severe adhesions to the great vessels. In terms of oncologic outcome, there are several reports of the oncologic feasibility of VATS thymectomy for Masaoka stage I and II tumors. Jurado et al[8] reported no differences in terms of 5-year recurrence-free survival (RFS) and recurrence rates between VATS and transternal thymectomy patients. Sakamaki et al, comparing VATS and transternal approaches,[29] found that VATS improved the 5-year overall survival, whereas the 5-year RFS was not different between the groups. In the present study, both left and right approaches were easily manageable; the 5-year RFS comparison did not show significant difference between two groups.

With regard to clinical outcomes in myasthenic patients, our analysis did not find any statistical difference between patients who underwent the left and those who underwent the right one.

Limitations

This investigation represents a single institution's experience; the cohort of patients was assessed retrospectively with a small number of patients in each group and the follow-up period is relatively short for this type of tumor. Therefore, we acknowledge that there is inherent bias associated with this approach.

Conclusion

In conclusion, VATS thymectomy can produce satisfactory outcomes, reduce surgical risks perioperatively, and shorten the hospitalization time. Unilateral VATS thymectomy in patients with thymoma is a clinically acceptable procedure, and can be safely and effectively performed on either side of the thorax.

Conflict of Interest
None declared.

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