



# Minimally invasive surgery for thymic epithelial tumors: a single institutional experience

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**Background:** Minimally invasive surgery (MIS) is increasing to become the preferred surgical approach for anterior mediastinal tumors. This study reported our experience with MIS including video-assisted thoracoscopic surgery (VATS) and robot-assisted thoracoscopic surgery (RATS) for thymic epithelial tumors and compared the surgical results of MIS with those of conventional approaches (CAs).

**Methods:** Between March 2001 and December 2014, 129 patients underwent surgical treatment for thymic epithelial tumors at authors' institute. Fifty-nine patients underwent MIS including VATS and RATS (MIS group) and 70 patients underwent CA such as median sternotomy and thoracotomy (CA group). The clinical outcomes between two groups were compared.

**Results:** The surgical procedures in MIS group included extended thymectomy in 8, total thymectomy in 4, right hemi-thymectomy in 24, and left hemi-thymectomy in 23 patients. The surgical procedures in CA group included extended thymectomy in 11, total thymectomy in 56, right hemi-thymectomy in 2, and left hemi-thymectomy in 1 patient. The mean tumor size was 35.6 mm in MIS group and 49.2 mm in CA group. The tumor size in MIS group was significantly smaller than CA group ( $P=0.0011$ ). The number of patients with MG was 9 (15.3%) in VATS group and 11 (15.7%) in CA group, with no significant difference. The operating time, blood loss, duration of drainage, and length of hospital stay in MIS group were significantly less than those in CA group ( $P<0.0001$ ). There were no perioperative complications in MIS group. The operative mortality rate was 0% in MIS group, 1.4% in CA group. The tumor histology in MIS group was thymoma in 22, thymic cancer in 5, thymic cyst in 29, and thymic lipoma in 3 patients. In CA group, the tumor histology was thymoma in 57; thymic cancer in 8, thymic cyst in 4, and thymic lipoma in 1 patient. No recurrence was observed in MIS group but 5 patients in CA group had recurrence. In MIS group, 9 patients underwent RATS. There were extended thymectomy in 3, total thymectomy in 4, and hemi-thymectomy in 2 patients. The mean tumor size was  $32.8\pm 18.3$  mm in RATS. Patients with MG were 3 (33.3%). The mean operative time, blood loss, duration of drainage, and length of postoperative stay were  $204.3\pm 55.4$  min,  $44.1\pm 71.9$  mL,  $1.6\pm 0.5$  days, and  $7.0\pm 0.9$  days, respectively. The tumor histology in RATS was thymoma in 5 and thymic cyst in 4 patients. No conversion to VATS or CA occurred. There were no perioperative complications in RATS.

**Conclusions:** This study showed MIS was feasible and safe for thymic epithelial tumors. MIS including RATS can be standard surgical treatment of anterior mediastinal tumors.

**Keywords:** Video-assisted thoracoscopic surgery (VATS); robotic surgery; thymic tumor

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## Introduction

Minimally invasive surgery (MIS) is increasing to become the preferred surgical approach for anterior mediastinal tumors. Recently, instead of conventional approach (CA) such as median sternotomy and thoracotomy, video-assisted thoracoscopic surgery (VATS) is performed for anterior mediastinal tumor. Some authors reported the advantages of VATS, such as lower blood loss, shorter postoperative pleural drainage duration and length of hospital stay (1-5). However, lack of perspective sensation by two-dimensional view and restricted movements of surgical instruments lead to difficulty of handling the tissues and longer learning curve. Robot-assisted thoracoscopic surgery (RATS) has been adopted to alleviate the shortcoming of VATS recently and some thoracic surgeons reported favorable results of RATS for anterior mediastinal tumors (6,7), and Rückert *et al.* report that the complete remission rate of MG for RATS is better than that for VATS (8). In this study, the authors reported our experience with MIS including RATS for thymic epithelial tumors and compared the surgical results of MIS with those of CAs.

## Methods

Between March 2001 and December 2014, 129 patients underwent surgical treatment for thymic epithelial tumors at Tokyo Women's Medical University. Of these, 59 patients underwent MIS including VATS and RATS (MIS group) and 70 patients were CA (CA group). The clinical outcomes of matched groups were compared. The study was approved by the Human Research Ethics Board of Tokyo Women's Medical University (no. 2307 and no. 150801). Informed consent was obtained from all patients.

### *Surgical procedure of CA and VATS*

Endotracheal intubation using a double-lumen endotracheal tube was performed in all cases. There were no patients in CA group underwent operation under general anesthesia with single-lung ventilation. In VATS cases, all procedures were performed via three or four ports under complete thoracoscopic view. Surgical procedures were extended thymectomy, total thymectomy, and hemi-thymectomy. Extended thymectomy was performed in patients with myasthenia gravis (MG). Excepting hemi-thymectomy, both an extended thymectomy and a total thymectomy were performed by bilateral sides approach. Extubation in

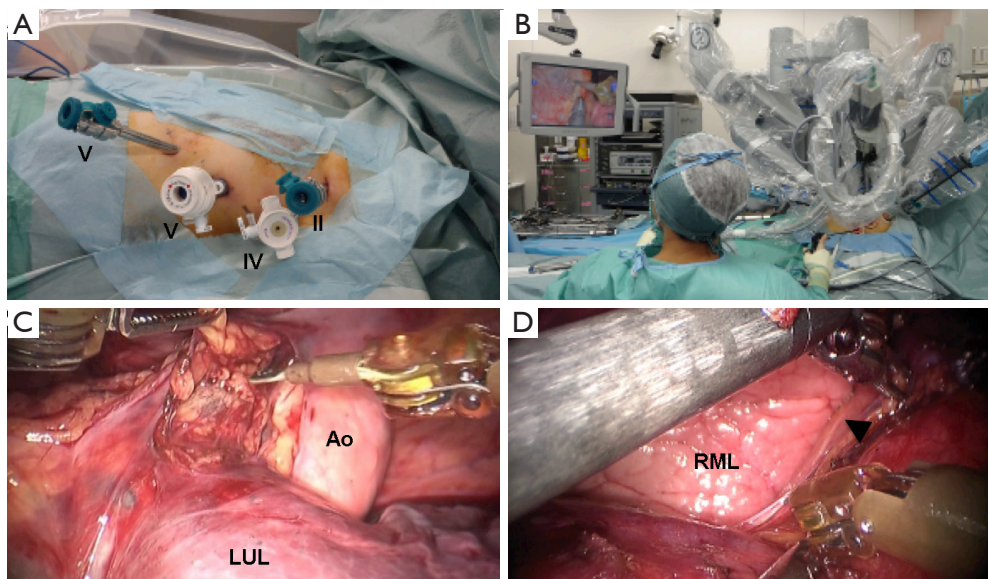
the operating room was attempted in all patients. Patient with MG was managed in the intensive care unit for post-operative observation overnight.

### *Surgical procedure of RATS*

A robotic system (da Vinci S, Intuitive Surgical, Inc., Sunnyvale, CA, USA) was used. Robotic procedures are usually performed by three surgeons, the surgeon at the console and the two tableside surgeons, who place the trocars and connects them with the robotic arms, changes the robotic instruments, and manipulates additional endoscopic instruments through the auxiliary ports.

The surgical procedures were performed under general anesthesia with single-lung ventilation using a double-lumen endotracheal tube. Patients were placed in supine position with elevation of the left side (side up at a 30-degree angle) and the ipsilateral arm was placed low. Approach was performed via left side. Total four incisions for camera, instruments, and assist were made (*Figure 1A*). The camera trocar was first inserted at the fifth intercostal space (ICS), along the anterior axillary line. Pleural adhesion presence was observed by thoracoscopy, which was used only for intrathoracic observation through the first port. The robotic arms were placed in the second (8 mm) and fifth (12 mm) ICS along the anterior-axillary line, and fifth (8 mm) ICS along the midclavicular line. An assist port was placed in the fourth ICS (12 mm) along the mid-axillary line. The patient cart was docked from the right side of the patient. A three-dimensional high definition scope was inserted through the fifth ICS. Both 8 mm ports, in principle, EndoWrist Monopolar Cautery Instrument (Permanent Cautery Spatula, Intuitive Surgical, Inc.) were used as the right arm and EndoWrist Bipolar Cautery Instrument (Fenestrated Bipolar Forceps, Intuitive Surgical, Inc.) was used as the left arm. During the operation, the device of right arm and left arm was replaced. Table surgeons cleaned the lens for securing of the operative field of vision and used ultrasonically activated device for transecting vessels, and were responsible for suction, through the assist port (*Figure 1B*). Accessory thymic tissue is resected if patient with MG (*Figure 1C*). Left sided approach allows extensive removal of fat sited in aortopulmonary window and left pericardiophrenic angle (9). Thymic tissue is completely resected along the right phrenic nerve under good visualization (*Figure 1D*).

The medical records were reviewed for information relating to age, gender, tumor histology, Masaoka stage,



**Figure 1** Settings of robotic system and intraoperative findings. (A) Trocar placement in robotic procedure. The robotic arms were placed in the second and fifth intercostal space (ICS) along the anterior-axillary line, and fifth ICS along the midclavicular line. An assist port was placed in the fourth ICS along the mid-axillary line; (B) table surgeon assists operation through the assist port; (C) accessory thymic tissue in the aortic-pulmonary window is resected patient with myasthenia gravis; (D) the thymic gland was resected along with the right phrenic nerve (black arrow head). Ao, aorta; LUL, left upper lobe; RML, right middle lobe.

Myasthenia Gravis Foundation of America (MGFA) clinical classification, WHO classification, TNM classification, operative details, duration of chest drainage, duration of postoperative hospital stay, and postoperative complications.

Continuous variables were expressed as mean, standard deviation, and categorical variables were expressed as number and percentage. The categorical variables were analyzed by the Chi-square test, and continuous variables were analyzed by the Wilcoxon's signed rank test.  $P < 0.05$  was considered statistically significant. All statistical analyses were performed with JMP software (version 11.2.1, SAS Institute Inc., Cary, NC, USA).

## Results

There were 129 consecutive surgical treatments for thymic epithelial tumors at authors' institution during the study period. The clinical characteristics of the 129 patients are presented in *Table 1*. Of these, 59 patients (35 males and 24 females) underwent MIS including VATS and RATS, the mean age was  $56.5 \pm 13.2$  years. 70 patients (42 males and 28 females) underwent CA, the mean age was  $58.7 \pm 13.2$  years. The surgical procedures in MIS group included extended thymectomy in 8, total thymectomy in 4, right hemi-

thymectomy in 24, and a left hemi-thymectomy in 23 patients. The surgical procedures in CA group included extended thymectomy in 11, total thymectomy in 56, right hemi-thymectomy in 2, and a left hemi-thymectomy in 1 patient.

The mean tumor size was 35.6 mm in MIS group and 49.2 mm in CA group. Tumor size in MIS group was significantly smaller than those in CA group ( $P = 0.0011$ ). The number of patients with MG was 9 (15.3%) in VATS group and 11 (15.7%) in CA group, with no significant difference.

The operating time, blood loss, duration of drainage, and length of postoperative hospital stay in MIS group were significantly less than those in CA group ( $P < 0.0001$ ). There were no perioperative complications in MIS group. Perioperative complications occurred in 5 patients in CA group: pleural effusion in two patients, right heart injury, postoperative myasthenic crisis, postoperative bleeding, in one patient each. The operative mortality rate was 0% in MIS group, 1.4% in CA group.

The tumor histology in MIS group was thymoma in 22 (WHO classification type AB in 3, type B1 in 10, type B2 in 7, type B3 in 2 patients), thymic cancer in 5 (TNM classification stage I in 4 and II in 1 patient), thymic cyst

**Table 1** Characteristic of the patients in MIS and CA group

Variables	MIS group (n=59)	CA group (n=70)	P value
Gender (%)			
Male/Female	35 (59.3)/24 (40.7)	42 (60.0)/28 (40.0)	0.938
Age	56.5±13.2	58.7±13.2	0.33
Tumor size (mm)	35.6±21.7	49.2±26.0	0.001
Myasthenia gravis (%)			0.943
+/-	9 (15.3)/50 (84.7)	11 (15.7)/59 (84.3)	
MGFA class			0.198
I	0	4	
IIa	6	5	
IIb	2	2	
IIIb	1	0	
Surgical procedure (%)			<0.0001
Extended thymectomy	8 (13.6)	11 (15.7)	
Total thymectomy	4 (6.8)	56 (80.0)	
Hemi-thymectomy	47 (79.6)	3 (4.3)	
Operating time (min)	164.2±82.1	240.9±128.9	<0.0001
Blood loss (mL)	50.6±77.2	389.6±446.6	<0.0001
Duration of drainage (days)	2.3±1.6	4.0±2.1	<0.0001
Length of stay (days)	6.6±4.4	10.9±5.6	<0.0001
Perioperative complications (%)	0 (0)	5 (7.1)	0.062
Mortality (%)	0 (0)	1 (1.4)	0.357
Pathology (%)			<0.0001
Thymoma	22 (37.3)	57 (81.4)	
Thymic cancer	5 (8.5)	8 (11.4)	
Thymic cyst	29 (49.1)	4 (5.7)	
Thymic lipoma	3 (5.1)	1 (1.5)	
Thymoma WHO classification (%)			0.854
A	0	2 (3.5)	
AB	3 (13.6)	9 (15.8)	
B1	10 (45.5)	24 (42.1)	
B2	7 (31.8)	13 (22.8)	
B3	2 (9.1)	9 (15.8)	
Thymic cancer TNM classification (%)			0.061
Stage I	4 (80.0)	1 (12.5)	
Stage II	1 (20.0)	2 (25.0)	
Stage III	0	4 (50.0)	
Stage IV	0	1 (12.5)	

Continuous variables are expressed as mean ± standard deviation, and categorical variables are expressed as numbers and percentages (%). P values were calculated by Fisher's exact test or the Chi-square test for categorical data, or Mann-Whitney's U test for continuous data. MIS, minimally invasive surgery; CA, conventional approach; MGFA, Myasthenia Gravis Foundation of America.

**Table 2** Characteristic of the patients in robot-assisted thoracoscopic surgery

Variables	n (%) or mean $\pm$ SD
Number of patients	9
Gender (%)	
Male/Female	5 (55.6)/4 (44.4)
Age (years)	48.8 $\pm$ 9.2
Tumor size (mm)	32.8 $\pm$ 18.3
Myasthenia gravis+ (%)	
+/-	3 (33.3)/6 (66.7)
MGFA class	
IIa	2
IIIb	1
Surgical procedure	
Extended thymectomy	3 (33.3)
Total thymectomy	4 (44.4)
Hemi-thymectomy	2 (22.2)
Operating time (min)	204.3 $\pm$ 55.4
Blood loss (mL)	44.1 $\pm$ 71.9
Duration of drainage (days)	1.6 $\pm$ 0.5
Length of postoperative stay (days)	7.0 $\pm$ 0.9
Perioperative complications	0
Mortality	0
Pathology (%)	
Thymoma	5 (55.6)
Thymic cyst	4 (44.4)
Thymoma WHO classification (%)	
AB	1 (20.0)
B1	1 (20.0)
B2	3 (60.0)

Continuous variables are expressed as mean  $\pm$  SD, and categorical variables are expressed as numbers and percentages (%). SD, standard deviation; MGFA, Myasthenia Gravis Foundation of America.

in 29, and thymic lipoma in 3 patients. In CA group, the tumor histology was thymoma in 57 (WHO classification type A in 2, type AB in 9, type B1 in 24, type B2 in 13, type B3 in 9 patients), thymic cancer in 8 (TNM classification stage I in 1, II in 2, III in 4, IV in 1 patient), thymic cyst in

4, and thymic lipoma in 1 patient. Pathological examination confirmed complete resection of the tumor in all patients.

No recurrence was observed in MIS group but 5 patients in CA group had recurrence. The site of recurrence was pleural cavity in 2 patients occurred in 34 and 6 months after surgery, and the local recurrence at the surgical margin in 3 patients occurred in 10, 32, and 24 months after surgery.

In MIS group, 9 patients (5 males and 4 females) underwent RATS (*Table 2*). The mean age was 48.8 years. There were extended thymectomy in 3, total thymectomy in 4, and hemi-thymectomy in 2 patients. The mean operative time, blood loss, duration of drainage, and length of postoperative stay were 204.3 $\pm$ 55.4 min, 44.1 $\pm$ 71.9 mL, 1.6 $\pm$ 0.5 days, and 7.0 $\pm$ 0.9 days, respectively. The tumor histology was thymoma in 5 (WHO classification type AB in 1, type B1 in 1, type B2 in 3 patients) and thymic cyst in 4 patients. The mean tumor size was 32.8 $\pm$ 18.3 mm (range, 16–70 mm) in RATS. Patients with MG were 3 (33.3%). Conversion to VATS or open surgery occurred in no cases. There were no perioperative complications including postoperative myasthenic crisis.

## Discussion

Various tumors, cysts, and other abnormalities relate to the thymus is located in the anterior portion of the mediastinum. Although median sternotomy is accepted as a gold standard for thymic epithelial tumors, due to the technical improvements including new endoscopic instruments in VATS, VATS resection has been gaining in popularity for mediastinal tumor.

In this study, extended thymectomy and total thymectomy were performed mainly in the CA group. On the other hand, the extended thymectomy and total thymectomy by MIS was low with approximately 20%. The recurrence rate of the CA group was high. As a reason, it was that there were a lot of thymoma and thymic cancer and large tumor cases. However, for a resection of small size solid tumor and cystic lesion, MIS is good adaptation. According to previous reports, VATS has become an efficient procedure that results in lower blood loss, shorter drainage duration and postoperative hospital stay compared with those of CA in previous reports (1-5). In this study, the operating time, estimated blood loss, drainage duration, and length of hospital stay in MIS group were all significantly less than those of CA group, these results indicated less invasiveness, similar to previous reports (1-5).



Oncological outcomes are important issues when performing MIS for malignant tumors of thymus. Past reports show that thoroscopic thymectomy for early stage thymoma presented comparable oncological outcomes to the transsternal approach (2,5,10). The extent of resection (i.e., hemi-thymectomy, total thymectomy, extended thymectomy) is still controversial. There is no evidence to perform total thymectomy for a thymoma without MG. A recent report suggests that the efficacy of partial or subtotal thymectomy for early stage thymoma, such as Masaoka stage I and II thymoma (11). Although further investigation is still required to select the patient, early stage thymoma localized in the left or right side is resected by hemi-thymectomy, resulted in favorable prognosis at the authors' institute.

Approach side is also under debate, it includes bilateral and unilateral, right or left sided. To date, there is no report comparing these approaches. Schneider *et al.* reported that they had changed the surgical access to the left-sided approach by two reasons (12). First, coming through the left thoracic cavity, the right phrenic nerve is protected by the superior vena cava in the delicate region of the right upper thymic horn. Due to a more ventral localization, the left phrenic nerve is easier to identify and preserve. Second, accessory thymic tissue in the aortic-pulmonary window is accessible only from the left side. Mineo *et al.* reported left sided VATS thymectomy, they prefer this approach because it allows extensive removal of fat sited in aortopulmonary window and left pericardiophrenic angle (9). The authors prefer left-sided approach when performing RATS for these reasons.

The authors have been performing RATS since 2012. Past reports show that the RATS for thymic disease is safe and feasible (6,7,12). RATS has been adopted to alleviate the shortcoming of VATS: it provides a 3-dimensional view, it increases the comfort of the surgeon via the use of EndoWrist instruments (Intuitive Surgical, Inc.), and it enables technically demanding operations with increased freedom for intrathoracic movement. These advantages allow to perform total thymectomy and extended thymectomy by one-sided approach more comfortable and safe. The authors consider that it may lead to less invasive surgery.

As Kumar *et al.* mentioned, RATS' limitations should also be borne in mind, which include loss of haptic feedback, limited platform availability, high initial and recurring cost and requirement of special trained team (13). The cost of RATS is a very important issue, Deen *et al.* reported that RATS costs significantly higher than VATS (14). In Japan,

RATS has not been covered by insurance, therefore, RATS is the very expensive surgical approach. Other reasons for the delay in the spread of RATS are proposed by Nakamura *et al.* (15).

This study has some important limitations. This study was a retrospective single institutional study and included small sample size with various diseases. The results of this study need to be confirmed in a multicenter study with a larger number of patients.

The authors reported in this study reveal that MIS is feasible and safe for both thymic epithelial tumors. MIS including RATS can be standard surgical treatment of anterior mediastinal tumors.

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## Footnote

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/vats.2017.08.07>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Human Research Ethics Board of Tokyo Women's Medical University (no. 2307 and no. 150801). Informed consent was obtained from all patients.

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