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TECHNIQUE

# Improved procedures and comparative results for video-assisted thoracoscopic extended thymectomy for myasthenia gravis

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**Abstract**
*Introduction* We previously introduced video-assisted thoracoscopic ET (VATS-ET) as a therapeutic option for MG with acceptable results. We have conducted further investigations to improve the procedure without deterioration of operative results, including myasthenia gravis (MG) remission rate and palliation rate. Here, we report the details of our current procedure, as well as surgical results and patient outcomes as compared with the original VATS-ET procedure.
*Material and methods* From January 2002 to September 2013, we performed a VATS-ET procedure with an anterior chest wall lifting method for 77 patients who had MG with or without a thymoma. During that period, we investigated the appropriate indications and improved the procedure.
*Results* Our current indication for this procedure is MG with the anti-acetylcholine receptor antibody or sero-negative type, or MG with a thymoma <5 cm in diameter without invasion to adjacent organs. With our procedure, the thymus and surrounding tissue are sufficiently resected using a bilateral thoracoscopic surgical method without neck incision. Remission and palliation rates were found to be equivalent to those obtained with the original VATS-ET procedure.
*Conclusion* VATS-ET is suitable for select patients with MG with or without a thymoma. In addition, our current method has shown to be effective while also offering cosmetic advantages as compared with the original, neck incision needed, VATS-ET method.

**Keywords** Video-assisted thoracoscopic extended thymectomy (VATS-ET) · Myasthenia gravis (MG) · Thymoma · Indications · Minimal invasive surgery · Anti-acetylcholine receptor

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In a previous report, we noted our use of an extended thymectomy (ET) as a therapeutic option for myasthenia gravis (MG) [1]. In addition, we previously introduced video-assisted thoracoscopic ET (VATS-ET) as a therapeutic option for MG with acceptable results [2, 3]. VTAS-ET is performed as an optimal surgical approach for MG patients in many institutes, though the procedures utilized are not standardized [3–6]. As one of the leading hospitals for treatment of MG, we have conducted further investigations to improve the procedure without deterioration of operative results, including MG remission rate and palliation rate. Here, we report the details of our current procedure, as well as surgical results and patient outcomes as compared with the original VATS-ET procedure.

## Materials and methods

From 2002 to December 2013, a total of 77 MG patients with or without a thymoma underwent VATS-ET at our institute and were included in this study. This period was separated into three sub-periods. Period 1, in which we performed this procedure with an open direct approach for a neck incision to dissect the upper poles of the thymus [7], was from 2002 to 2007. Period 2, which represented a transitional period with increasing sophistication of the procedure, was from 2008 to 2010. Also during this period, we investigated the necessity of an open direct approach, resection of the internal thoracic vein, and indications for VATS-ET for thymoma treatment. The third period (Current Period) started from 2011 and is ongoing. During this time, we have been performing the current procedure, which we describe in detail below. To analyze the effects of alterations to the procedure, this study compared results between Period 1 and the Current Period.

### Period 1

A total of 33 patients were treated during Period 1 (Table 1) and details of the operation procedure have been described elsewhere [3]. Briefly, the patient was placed in a supine position under general anesthesia with selective one-lung ventilation. Three trocars were introduced to the anterior axillary space, each through a 2-cm chest wall incision. The chest wall was lifted using costal hooks (Sonne Medical Instruments; Tokyo, Japan), catching the bilateral third ribs with a power of 10 kgf. The mediastinal pleura was subsequently incised bilaterally just anterior to the phrenic nerves, and then the thymic veins were dissected out. The entirety of the thymus and mediastinal fat were removed from the pericardium above the diaphragm. A 4-cm-low collar incision was made and the upper poles of the thymus were mobilized from the thyroid using a direct approach. Chest drains were placed bilaterally and removed the next day. Patients were normally extubated immediately after the operation.

**Table 1** Patient characteristics

| | Period 1 ($n = 33$)[a] | Period 2 ($n = 27$) | Current period ($n = 16$)[a] |
|---|---|---|---|
| Sex ratio, female: male | 26:7 | 16:9 | 11:5 |
| Age at onset median (range), years | 34 (13–73) | 39 (4–72) | 40.5 (16–72) |
| Age at thymectomy median (range), years | 41 (15–73) | 39 (20–76) | 40.5 (17–72) |
| Steroid treatment before operation, Cases (%) | 9 (27.3) | 13(48.1) | 5 (31.3) |
| MGFA clinical classification[a, b] cases (%) | | | |
| No symptoms | 0 | 2 (7.4) | 1 (6.3) |
| Class Iq | 3 (9.1) | 3 (11.1) | 2 (12.5) |
| Class IIa | 4 (12.1) | 12 (44.4) | 5 (31.3) |
| IIb | 4 (12.1) | 7 (25.9) | 0 |
| Class IIIa | 7 (21.2) | 0 | 4 (25) |
| IIIb | 7 (21.2) | 3 (11.1) | 3 (18.7) |
| Class IVa | 4 (12.1) | 0 | 0 |
| IVb | 0 | 0 | 0 |
| Class V | 4 (12.1) | 0 | 1 (6.3) |

[a] Including cases with conversion to median sternotomy. No patients showed anti-muscle-specific kinase (MuSK) autoantibodies

[a, b] Myasthenia Gravis Foundation of America

### Period 2

In Period 2, during which we investigated various alternatives to improve the operation method, 27 patients were treated (Table 1). First, we investigated the indications for VATS-ET for a thymoma. Second, to improve the safety of the operation, we investigated the procedure, locations of incisions, and positioning of the costal hooks. Third, the optimal area for resection of tissue surrounding the thymus was investigated. Fourth, to improve the cosmetic impact of the operation, we considered a collar incision for the upper poles of the thymus. In addition, we investigated patient position, the optimal site of the incision to allow the VATS forceps to reach the upper poles of the thymus, and verification of navigation through a neck incision or with ultrasonography guidance.

### Current period

We have been performing the current procedure for VATS-ET since 2011. The indications are MG with the anti-acetylcholine receptor antibody or sero-negative type, or MG with a thymoma <5 cm in diameter without invasion to adjacent organs. Sixteen patients have been treated during this period at the time of writing (Table 1). Details of the current procedure are described below, with time indications in parentheses showing the corresponding time points in the supplemental video.

Under general anesthesia, the patient is placed in a supine position, with the arms at the side of but not touching the body, a pillow under the back, and the neck pulled to the chest (flexed-neck position; Fig. 1A). For women, the breasts are gathered using draping tape (Fig. 1B).

First, a right-side operation is performed. A camera port is made at the 4th intercostal space (ICS) on the lateral mammary line alongside the mammary glands. Next, a 3-cm diameter working port is made with a wound around the mammary gland line using a Wound Retractor XS

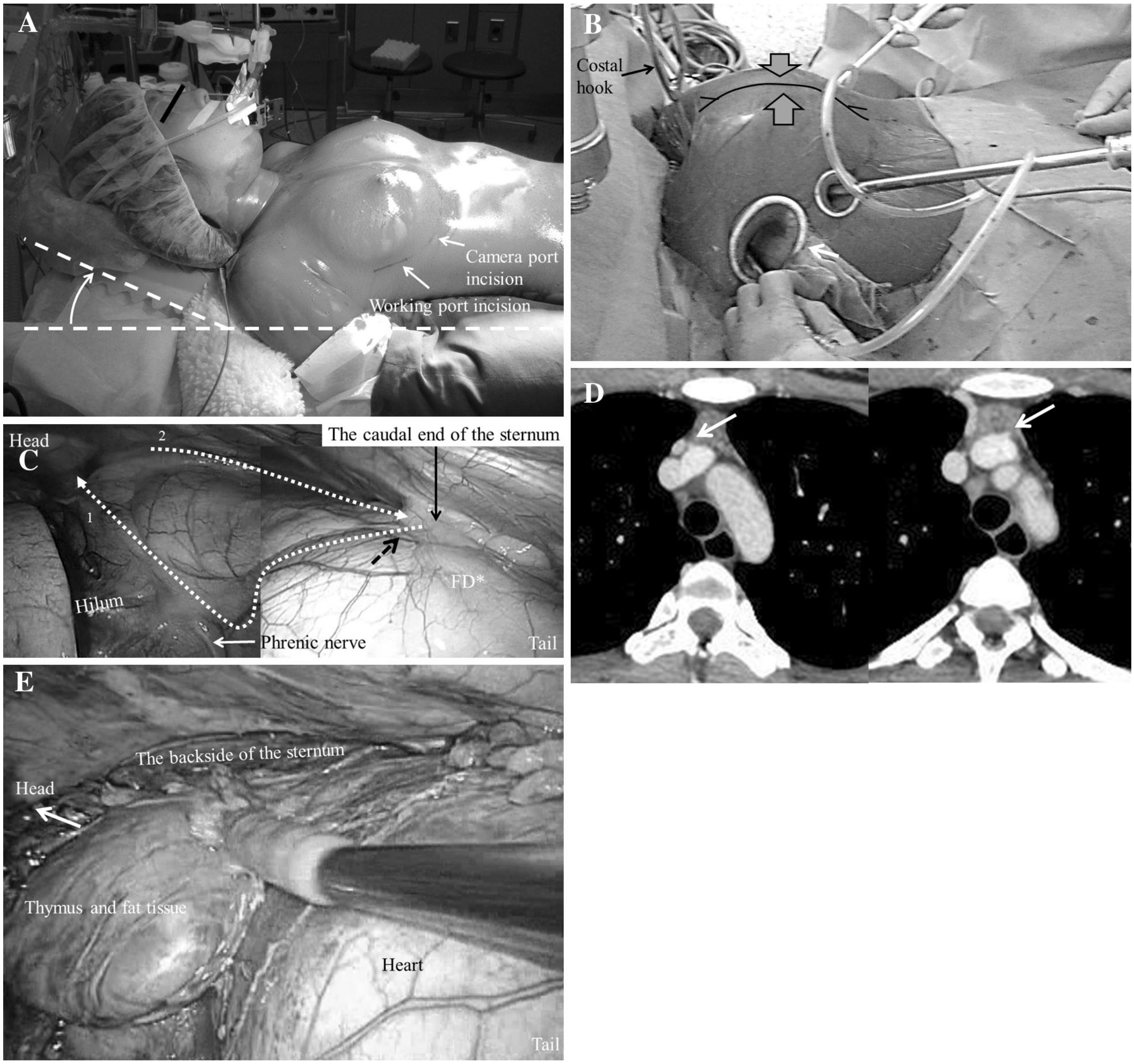


**Fig. 1** **A** Patient position and port design for video-assisted thoracoscopic extended thymectomy (VATS-ET). **B** For women, the breasts are gathered using draping tape, and the port wounds are made along the plane between the serratus anterior muscle and chest wall. After resection of the internal thoracic vein, a hook is placed at the 2nd rib. **C** Resection area and procedure. *Dotted lines* represent incision lines in the pleura. The procedure is performed along Line 1 (along the phrenic nerve), followed by Line 2 (incision line of the mediastinal pleura behind the sternum) (FD: fat tissue of diaphragm). **D** Representative preoperative contrast computed tomography of thymic veins. Two veins were detected using preoperative thin-slice contrast-enhanced computed tomography (*arrows*). **E** Dissection of thymus and surrounding fat tissue from right thoracic cavity. When the pleura behind the sternum is incised, the thymus and surrounding fat tissue hang and block the operative field, as shown here

(Applied Medical Japan; Tokyo, Japan) through the 3rd ICS on the anterior axillary line under thoracoscopy (Fig. 1A, B). The caudal end of the resection area is set at the end of the area of thymic fat, which represents the rostral end of fat tissue continuing from the diaphragm (Fig. 1C, dotted arrow) (00:00–00:07). The mediastinal pleura is first incised to the dorsum (00:10–00:26), and then just anterior to and along the phrenic nerve (Fig. 1C, dotted line 1) (00:27–00:42). While incising the pleura, the phrenic nerve is taped to mark and preserve this important structure (00:27). On the superior vena cava (SVC), the internal thoracic vein is identified and encircled (00:43–00:53), and the vein is ligated on the SVC side and divided using an ultrasonic energy device (00:54–01:08). For dissection of the internal thoracic vein, ligation is performed on the SVC side, because this part might be rubbed during the following procedure. In addition, dissection can avoid hooking and injuring the vein during the procedure from the other side. Subsequent to dissection of the vein, a costal hook is inserted to catch the 2nd rib in an extra-pleural manner after probe puncture (01:09–01:18). The anterior chest wall is lifted about 3 cm with a power of 10 kgf, the same as in the original method [3]. Dissection of the internal thoracic vein before lifting of the thoracic wall is performed to avoid extension stress on the vein. From the right side, the dissection around the left innominate vein from the anterior chest wall behind the sternum is extended deeply to the left-side pleura (01:19–01:23). Preoperatively, the thymic veins are carefully identified using thin-slice contrast-enhanced computed tomography (Fig. 1D, arrows), and then dissected using an ultrasonic energy device (01:24–01:29). Next, the rostral side of the left innominate vein is dissected, including the inferior thyroid vein (03:43–03:48, vein dissected from left side in video). The dissection between the thymus and heart is extended from the caudal to rostral side and deep to the left-side pleura (01:30–01:42). Finally, the pleura behind the sternum is incised in a rostral to caudal direction and the space behind the sternum is completely dissected to the left side (Fig. 1C, dotted line 2; Fig. 1E) (01:43–01:56). The procedure in the right thoracic cavity is then finished and the operation area moves to the left side.

While the surgeons are moving and making incisions on the left thoracic skin and thoracic wall, similar to the right side, the patient requires sufficient ventilation of both lungs, because an immediate change of one-lung ventilation from the left to right cannot maintain a satisfactory level of oxygenation. After resuming one-lung ventilation, the thoracoscope is carefully inserted into the left thoracic cavity, as the heart occupies the thoracic cavity at the level of the camera port (01:58–02:03). The mediastinal pleura is dissected with air from the right thoracic cavity (Fig. 2A) (02:30–02:06), and the caudal end of thymic fat is dissected under direct visualization through the camera port (02:10–02:17), because the mediastinal wall at this level is too near to the chest wall. A costal hook is then inserted to catch the 2nd rib after a probe puncture, similar to the right side (02:18–02:26), but prior to identification of the left internal thoracic vein. The pleura is incised just anterior to the phrenic nerve (Fig. 2A, dotted line 1), with the phrenic nerve taped while making that incision. After sufficiently extending the incision to the level of the left innominate vein, the isolated left innominate vein is visually identified (02:27–02:41). The left internal thoracic vein can then be dissected, when the left internal thoracic vein appears (Fig. 2B) (02:42–02:55). The pleura behind the sternum is incised from the rostral to caudal side (Fig. 2A, dotted line 2) (02:56–03:02). In cases of MG without a thymoma, the thymus is divided at the level of the innominate vein for handling (03:16–03:34) and the caudal thymus is removed

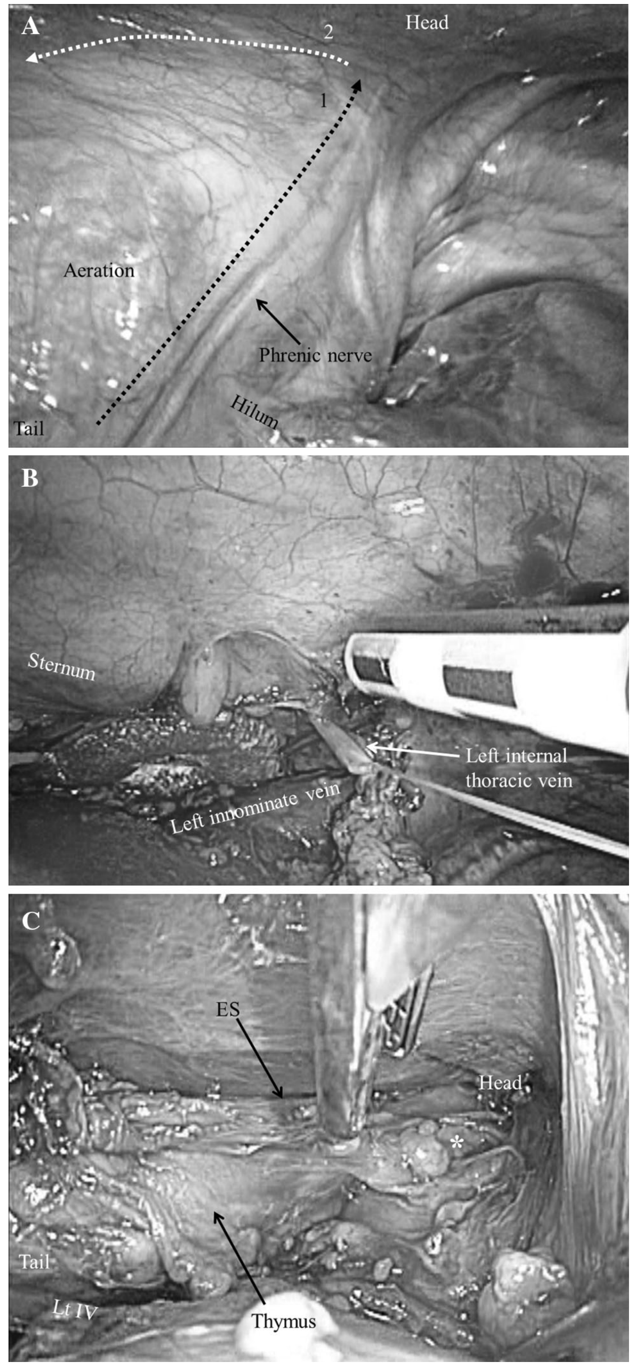


**Fig. 2** (**A**) Procedure in left thoracic cavity. Aeration by air from the right thoracic cavity dissects along the plane under the mediastinal pleura. The caudal end of the thymus is dissected, and the thymus and surrounding fat are easily released from the mediastinum. The pleura is incised along the phrenic nerve (No. 1), followed by behind the sternum (No. 2) for the same reason as the right side. (**B**) Dissection of left internal thoracic vein. Resection area from left side. The thymus is retracted in a caudal direction (ES: upper edge of sternum). The upper resectable edge of the thymus from the left thoracic cavity is marked with a surgical clip (clipping point "*"), which can be seen from the right thoracic cavity. Additional upper tissue is resectable from the right side

(03:35–03:39). Dissection of the thymus is then expanded in a rostral direction (03:40–03:42). The upper edge of the sternum is identified by pushing at the corresponding point from the outside (03:49–03:57). Rigid connective tissues are dissected using an ultrasonic energy device to expand the dissection in a rostral direction (03:58–04:07). When the thymus tissue becomes narrow, the tissue is divided using an ultrasonic energy device (04:08–04:15). The remaining left upper pole is then marked with a surgical clip (Fig. 2C) (04:16–04:22). Similarly, the upper narrow part of the right-side thymus, as with the right upper pole, is identified and dissected. The left-side procedure is then finished. Hemostasis is checked and a chest drain inserted.

The operation field is again moved to the right thoracic cavity. Cervical dissection of the thymus is expanded (04:26–04:53) and the left upper thymus is visualized. Normally, the marked left upper pole can be seen (04:54), and the narrow part at the more rostral side of the marking is identified as the left upper pole of the thymus and resected (04:55–05:00). A chest drain is retained in the right thoracic cavity. Patients are normally extubated immediately after the operation, with the drains removed on postoperative day 1, similar to Period 1.

### Statistics

Operative time and blood loss were recorded as median values and ranges, and compared between Period 1 and the Current Period using *t* tests. Values of $p < 0.05$ were considered significant.

## Results

Median age at the time of disease onset and operation, and disease severity according to the Myasthenia Gravis Foundation of America (MGFA) clinical classification are shown in Table 1. No significant differences were seen for these characteristics between Period 1 and the Current Period. Two female patients in Period 1 underwent conversion to a sternotomy, while 1 female in the Current Period underwent conversion to a sternotomy ($p = 0.98$, compared with Period 1), due to bleeding from the left innominate vein. In the Current Period, no patients required postoperative re-intubation ($p = 0.13$, compared with Period 1). All patients in both groups were alive at the time of writing. Although 1 patient in the Current Period suffered from left phrenic nerve paralysis, there were no significant differences identified as compared with Period 1 ($p = 0.16$).

The median operation time was significantly longer in the Current Period (including conversion cases, $p = 0.003$) (Fig. 3A), while blood loss was not significantly different

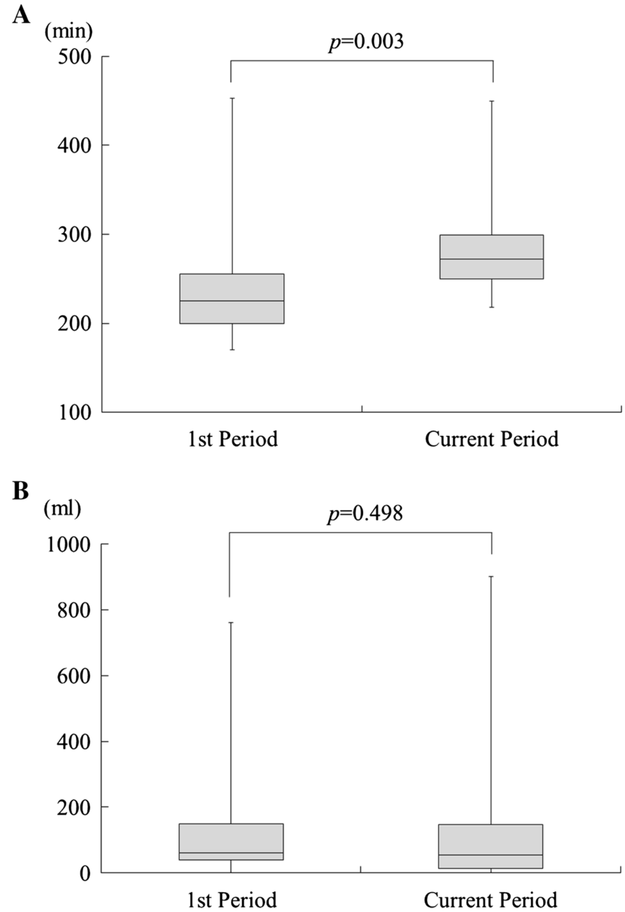


**Fig. 3** **A** Operation time and **B** blood loss. Both groups included patients who underwent conversion to a median sternotomy. Values are shown as the median (*horizontal bars*), with interquartile ranges (*boxes*) and 5th to 95 percentiles (*error bars*)

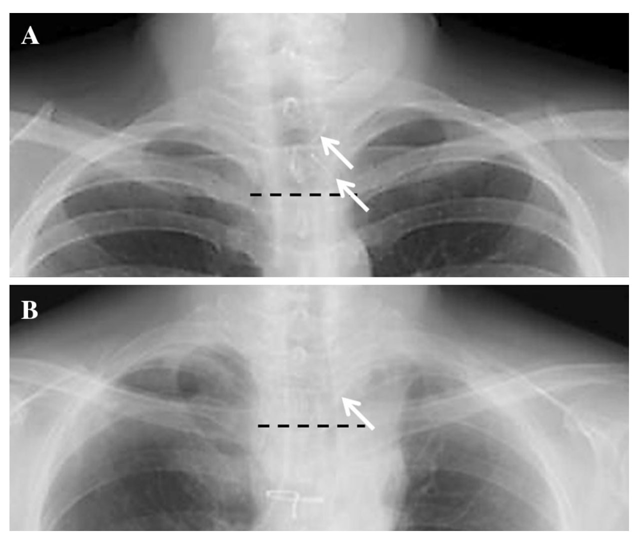


**Fig. 4** Chest X-ray images obtained after **A** a video-assisted thoracoscopic extended thymectomy and **B** an extended thymectomy through a median sternotomy

between the periods ($p = 0.498$) (Fig. 3B). The resected area reached the neck over the sternum, similar to ET through a mediastinal incision (Fig. 4A, B).

## Discussion

VATS-ET was established for patients with MG to decrease the invasiveness of surgical intervention as compared to conventional ET [2, 3, 7]. In addition, thoracoscopic operations offer efficacy for MG while remaining safe. We previously reported the effectiveness of our VATS-ET procedure in a study that compared results of conventional procedure performed via a median sternotomy (Open ET) [3]. In addition, in regard to the original procedure, our previous study found that the area of resected thymus was insufficient when using only the flexed-neck position and a 4-cm neck incision was needed to resect the poles under direct vision [7]. However, with VATS-ET, improvement of the cosmetic appearance after the operation represents an important advantage for patients, especially females, because most MG patients without a thymoma are young women. Some of our patients who underwent the original VATS-ET later complained of the appearance of the neck incision scar. Therefore, we sought to make improvements to the procedure to reduce the neck incision without narrowing the area of resection for the thymus and surrounding fat tissue, as well as to maintain or improve safety.

The reasons for procedure changes are partly described in the Methods section. In addition, our previous study reported that the resection area of the thymus was insufficient with the flexed-neck position and a 4-cm neck incision was needed to resect the poles under direct vision [7]. That inadequate resection was overcome by resection of the internal thoracic vein and upper pole from the contralateral side. As for the reasoning for the placement and length of the working port, we found that when the thymus is dissected from the left innominate vein, the most dangerous point of this procedure, the forceps can be used in a position parallel to the innominate vein from the rostral side of the wound, thus avoiding blurring of the forceps from impressing the wound edge. In addition, when the forceps are impressed into the caudal end of the wound, the caudal end of thymic fat can be easily accessed (Fig. 1A). For cosmetic reasons, the wounds should be placed around the breasts. However, to safely reach the left innominate vein, the thoracotomy should be placed in the 3rd intercostal space. For women, the breasts are gathered using draping tape, and the port wounds are made in the plane between the serratus anterior muscle and chest wall. After resection of the internal thoracic vein, the hook is placed at the 2nd rib. The reason for catching the 2nd rather than the 3rd rib is to make space in front of the innominate vein. The hook is inserted to catch the rib in an extra-pleural manner, because breaching of the pleura can result in blood oozing, possibly blocking the operation field (Fig. 1B). The caudal end of the resection area is decided (Fig. 1C: arrow) as compared with an open procedure. When ET was performed with a median sternotomy, we could not visualize diaphragmatic fat and recognize the caudal end of thymic fat as the level of the diaphragm, because of the level of the caudal end of the sternum. The procedure is performed along Line 1 (along the phrenic nerve), followed by Line 2 (incision line of the mediastinal pleura behind the sternum) in Fig. 1C, because if Line 2 is incised before the other procedures, the thymus hangs loosely and blocks the operation field. Finally, the pleura behind the sternum is incised from the rostral to caudal side, and the space behind the sternum is dissected sufficiently to the left side, because aeration of the left mediastinal pleura from the right thoracic cavity can help with dissection and the left thoracic cavity. When the pleura behind the sternum is incised, the thymus and surrounding fat tissue hang and block the operative field, as shown in Fig. 1D. The left internal thoracic vein is not routinely dissected, because it normally diverges in a rostral direction enough to safely lift the thoracic wall. However, the vein should be resected when identified to avoid accidental hooking and injury from the contralateral approach (Fig. 2A).

Indications for thymoma surgery have been investigated by Kimura et al. of our institute [8], resulting in our criteria for VATS-ET. There were no cases of mortality or significant differences in morbidity seen between Period 1 and the Current Period.

Blood loss and sternotomy conversion rate were investigated as indicators of operation safety, with no significant differences found between Period 1 and the Current Period. The reason for conversion to a median sternotomy was mainly because of bleeding from the left innominate vein after being accidentally pulled off the thymic vein. Variations in the number of thymic veins and anatomical features are common, and we now routinely perform thin-slice contrast-enhanced computed tomography preoperatively to detect any thymic veins (Fig. 1D). The longer operation time in the Current Period as compared to Period 1 may represent the learning curve for the operation. In Period 1, nearly all of the operations were performed entirely by a single surgeon [3]. In contrast, the procedures in the Current Period are performed by three staff surgeons. However, there are fewer steps as compared to Period 1, thus it is anticipated that operation time will be shortened in the future.

A previous report compared amounts of removed thymic tissue amounts to show non-inferiority [3]. However, that amount includes the thymoma, thus the samples are heterogeneous and unable to be compared. Therefore, we no longer measure removed tissues. However, chest X-ray examinations after performing VATS-ET revealed an upper resection limit similar to open ET. We consider that our current VATS-ET method can be used to sufficiently resect thymic tissue including surrounding fat tissue, even as compared with a conventional open ET operation.

As one of the leading institutions in Japan treating patients with MG, we consider it vital to continue improving our operative methods. VATS-ET is suitable for select patients with MG with or without a thymoma. In addition, our current method has shown to be effective while also offering cosmetic advantages as compared with the original VATS-ET method.

**Disclosures** Tomoyuki Nakagiri, Masayoshi Inoue, Yasushi Shintani, Soichiro Funaki, Tomohiro Kawamura, Masato Minami, Mitsunori Ohta, Yoshihisa Kadota, Hiroyuki Shiono and Meinoshin Okumura have no conflicts of interest or financial ties to disclose.

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