Transsternal versus video-assisted thoracoscopic thymectomy in correlation to clinical improvement evaluated by the Myasthenia Gravis Foundation of America score in myasthenic patients

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Background
Surgical management of myasthenia gravis is well established and has proven high efficacy in addition to clinical management for improving clinical outcome. Different surgical approaches for thymectomy are feasible including cervicotomy, median sternotomy, manubriotomy (ministernotomy), and video-assisted thoracoscopic surgery (VATS). Each approach has its pros and cons in terms of wound healing, operative time, the amount of blood lost during the operation, and the level of expertise necessary. Depending on the size of the excised thymus and its attachment to the surrounding structures, the best treatment for thymectomy varies from patient to patient.

Objectives
This study aimed to compare the clinical outcomes of traditional transsternal and video-assisted thoracoscopic methods in thymomatous and nonthymomatous myasthenic patients as measured by the Myasthenia Gravis Foundation of America score in thymomatous and nonthymomatous myasthenic patients.

Patients and methods
Clinical follow-up of two equal groups of myasthenic patients undergoing thymectomy by transsternal (median sternotomy and manubriotomy) and VATS approaches was performed.

Result
Transsternal thymectomy still have superior outcome to VATS in terms of clinical improvement of myasthenic symptoms, which may be attributed to better access, wider field, and ability to perform extended radical thymectomy involving removal of the whole thymic tissue and surrounding fat.

Conclusion
Selecting the surgical approach for thymectomy plays a crucial role in postoperative clinical improvement. Thymectomy through open transsternal access is still favored in large thymic masses for complete stable clinical remission.

Keywords:
thymectomy, transsternal, video-assisted thoracoscopic surgery

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Introduction

Surgical treatment is strongly recommended for patients with myasthenia gravis, whether thymomatous or nonthymomatus. The benefit of thymectomy develops over time, and the anticipated progress may take months to years to manifest clinically. Low-dose glucocorticoids and IVIg are often used to prepare patients for surgery. Most experts believe that thymectomy is a viable treatment choice for anti-acetyl choline receptor antibody-positive MG that develops before the age of 50 [1].

Transsternal thymectomy

Technique

In a supine state, the patient's arms are secured at his or her sides. A simple endotracheal intubation will suffice. Starting just below the sternal notch and running to the tip of the xyphoid process, the skin incision is median and vertical. Depending on the surgeon's choice, the skin incision can be minimized for esthetic purposes [2]. Electrocautery is used to cut the pectoral fascia and mark the periosteum. The interclavicular ligament must be incised before the sternum can be divided with the saw, and the anesthetist should stop ventilation to prevent opening the pleura and developing pneumothorax. Vertical and strict median osteotomies may be performed from the top down or from the bottom up. After the sternum has been divided, diathermy can be used to stop periosteal

bleeding, while bone wax can be used to control bone marrow bleeding [3]. A small retractor can be initially used to gradually open the sternum and then a larger retractor can be used later to gain a wider field and better visualization of the anterior mediastinum. In most cases, a slight retraction is enough to perform an extended thymectomy in a relaxed manner. The fat of the inferior mediastinum is resected first. Beginning at the diaphragm and moving upward, the anterior mediastinal fat is incised. The thymus and surrounding fat are then raised toward the brachiocephalic trunk, and the draining veins together with internal mammary artery branches to the thymus gland are clipped or ligated [4]. Finally, a blunt dissection is used to remove the cervical horns of each lobe as well as all surrounding fat tissue. One mediastinal drainage (24 F or less) is placed into an epigastrium incision at the completion of the operation (Fig. 1) [5].

Video-assisted thoracoscopic thymectomy

Advantages of the video-assisted thoracoscopic surgery (VATS) technique include better esthetic outcomes, less requirement of postoperative analgesics, shorter hospital stay, earlier return to work, and lower risk of bleeding [6].

Indication

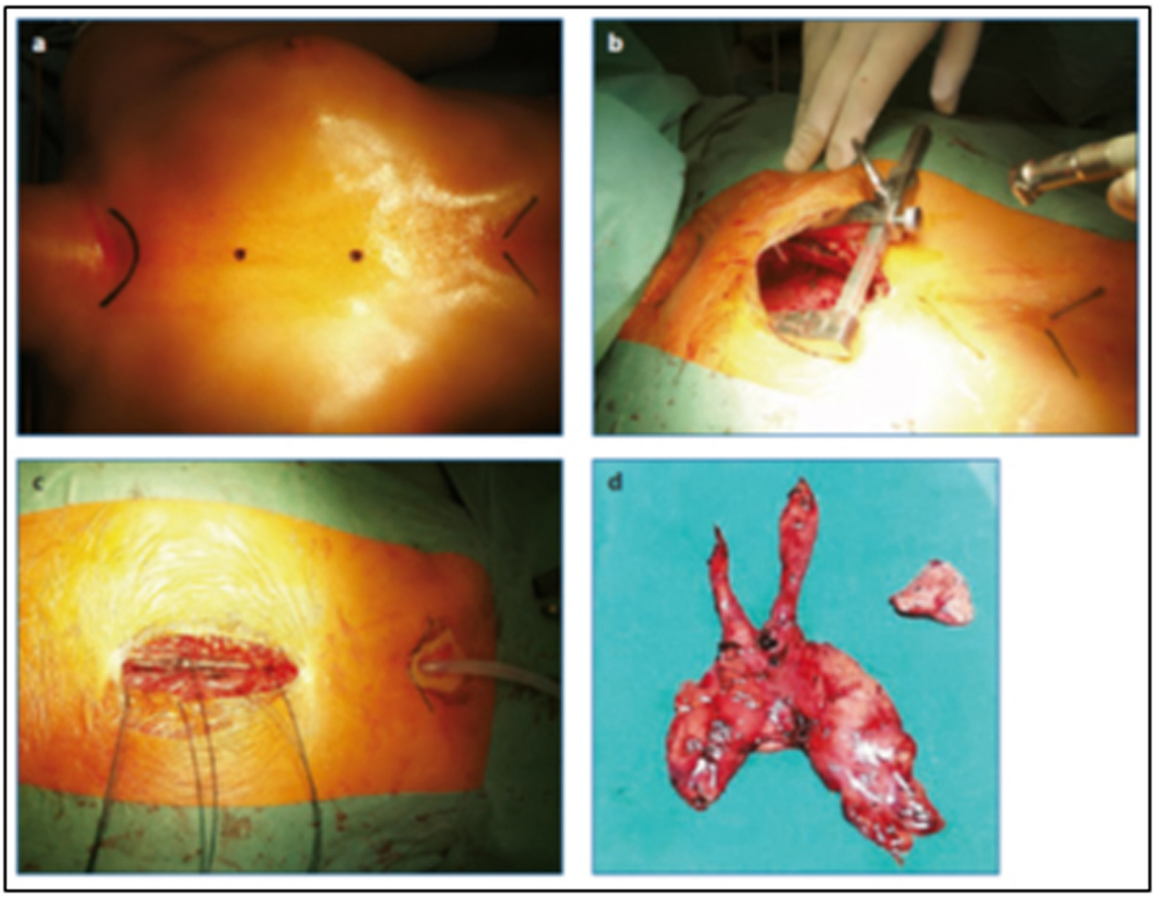
Patients with nonmalignant hyperplasia of the thymus gland should be considered for VATS thymectomy. Encapsulated thymomas with a maximum diameter of about 5 cm show no invasion to the surrounding structures. There is an indication for an open procedure in patients who have a presumption of malignancy or who have larger thymomas [7].

Positioning

The operation is carried out under general anesthesia, with the patient being monitored through an arterial line, and double-lumen endotracheal intubation and contralateral one-lung ventilation are used. The patient is positioned in a 30° retroverted supine position (Fig. 2) [8].

The ipsilateral arm is placed over the head of the patient in a holder. Care should be taken to not overextend the shoulder, and thus avoid brachial plexus injury (Fig. 3) [8].

Figure 1



(a) Skin-sparing incision for a vertical median sternotomy. (b) Operative view. (c) Sternotomy closure. (d) Surgical specimen [5].

The surgeon and the assistant stand on the ipsilateral side of the patient while the scrub nurse stands on the opposite site. A sternotomy tray is always ready in the operating theater for a potential conversion (Fig. 4) [8].

Port placement

Three 5-mm ports are placed at the lateral edge of the breast gland (Fig. 5). A 5-mm skin incision is used to establish the first port. To induce a pneumothorax, a dissector is inserted using blunt dissection along the upper edge of the fourth intercostal space in the mid-axillary plane.

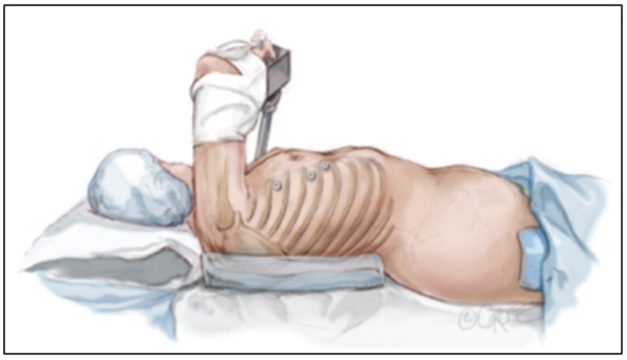
A 5-mm port with a trocar is then inserted into the same incision, and a 5-mm, 30° thoracoscope is used to search for adhesions and pathology in the thoracic cavity. The average pressure for carbon dioxide insufflation is 6–8 mmHg.

A second 5-mm port is bluntly inserted using a trocar into the anterior axillary line in the third intercostal space under thoracoscopic guidance, and a third 5-mm port is bluntly introduced into the midclavicular line in the fifth or sixth intercostal space. This incision is then extended to 1–3 cm depending on the size of the specimen to be resected at the end of the procedure [10].

Procedure

According to the International Thymic Malignancy Interest Group's guidelines, the entire thymic gland,

Figure 2

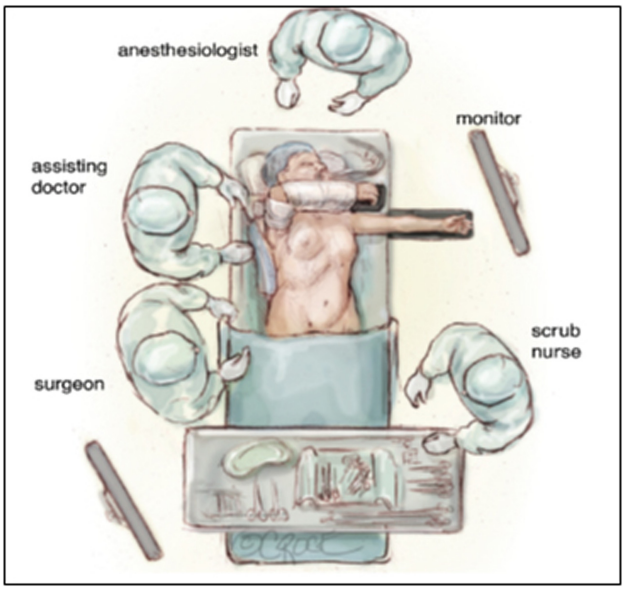


Positioning for a right-sided video-assisted thoracoscopic thymectomy [8].

Figure 3

Positioning of the ipsilateral arm in a hanger [8].

Figure 4



Theater setup for a right-sided video-assisted thoracoscopic thymectomy [8].

Figure 5

Arrangement of trocars for left-sided thoracoscopic thymectomy [9].

including the two upper and two lower horns, as well as all fatty tissue in the anterior mediastinum, are excised 'en bloc' using a bipolar energy unit (LigaSure) for dissection [10].

Patients and methods

Sixty myasthenic patients with variable Myasthenia Gravis Foundation of America (MGFA) scores (Table 1), with grades 1, 2, 3, and 4 in 20% (12 patients), 40% (24 patients), 30% (18 patients), and 10% (six patients), respectively (Fig. 6), were distributed into two equal groups with similar proportions of clinical severity in each group. This research was performed at the Department of Cardiothoracic Surgery, Ain Shams University Hospitals. Ethical Committee approval and written, informed consent were obtained from all participants. The first group underwent transsternal thymectomy, while the second group underwent video-assisted thoracoscopic thymectomy. Both groups were followed up for 2 years postthymectomy and assessed based on clinical improvement estimated by the MGFA score in relation to the preoperative score and surgical approach.

Each surgically treated group (transsternal and VATS) was then followed up clinically for 2 year duration and subdivided into four groups based on the MGFA score into complete stable remission (CSR), clinical improvement, same clinical state, and deterioration that required either mechanical ventilation on top of myasthenic crisis or repeated sessions of plasmapheresis to reduce the antibody load causing skeletal muscle weakness.

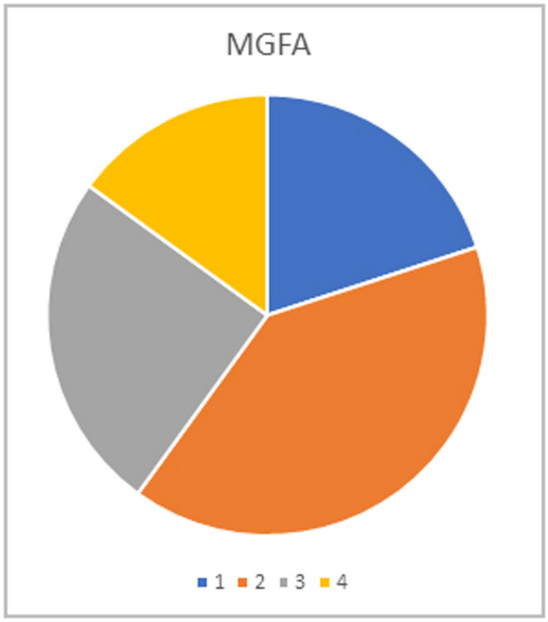
Patients' demographic and other characteristic clinical data were as follows (Table 2).

Results

Among the first group managed by the transsternal approach, 16 patients showed CSR defined by complete resolution of symptoms and cessation of pharmacological therapy, eight patients showed clinical improvement, four patients showed no change in clinical outcome, and only two patients deteriorated clinically and required postoperative plasmapheresis.

In terms of the second group managed by the VATS approach, 12 patients showed CSR, six patients showed clinical improvement, eight patients showed no change in clinical outcome, and four patients deteriorated clinically (two of them required

Figure 6



Baseline clinical grade of the studied cases.

Table 1 Myasthenia Gravis Foundation of America clinical classification and score for evaluation and grading the clinical severity of myasthenia gravis

MGFA clinical classification	
Class I	Any ocular muscle weakness
Class II: mild weakness affecting muscles other than ocular muscles may also have ocular muscle weakness of any severity	A-predominantly affecting limb, axial muscles, or both
	B-predominantly affecting oropharyngeal, respiratory muscles, or both
Class III: mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity	A-predominantly affecting limb, axial muscles, or both
	B-predominantly affecting oropharyngeal, respiratory muscles, or both
Class IV: mild weakness affecting muscles other than ocular muscles; may also have ocular muscle weakness of any severity	A-predominantly affecting limb, axial muscles, or both
	B-predominantly affecting oropharyngeal, respiratory muscles, or both
Class V	Intubation with mechanical ventilation

MGFA, Myasthenia Gravis Foundation of America.

Table 2 Demographic and clinical patient variables

Variables	Transsternal (*N*=30)	VATS (*N*=30)
Mean age (years)	28.3	31.8 years
Male : female	1 : 2	1 : 1
Preoperative immunosuppressants	24 cases	26 cases
Associated autoimmune diseases (e.g. SLE and RA)	17 cases	21 cases
Extended radical thymectomy	27 cases	19 cases
Mean excised thymus size (cm)	5.4	4.7
WHO histology (T-MG only)		
A, AB, B1	12 cases	14 cases
B2, B3	5 cases	7 cases

RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; T-MG, thymoma-associated myasthenia gravis; VATS, video-assisted thoracoscopic surgery.

Table 3 Comparison between the clinical outcomes of the two groups

	Trans-sternal	VATS
Complete clinical remission	16	12
Clinical improvement	8	6
No clinical improvement	4	8
Clinical deterioration	2	4

VATS, video-assisted thoracoscopic surgery.

mechanical ventilation for myasthenic crisis) (Table 3 and Fig. 7).

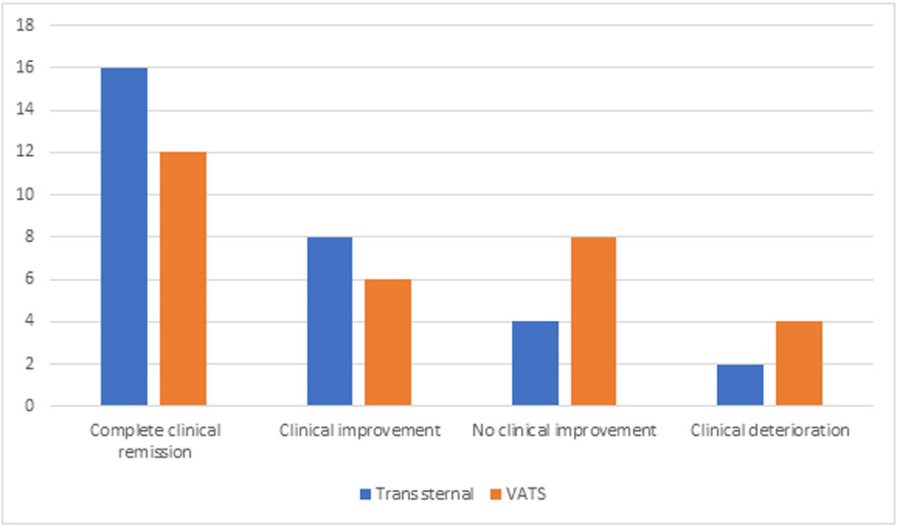
Discussion

Alfred Blalock was the first to perform a thymectomy for MG in 1941 [11]. Thymectomy is commonly recognized as a conventional surgical treatment for MG in addition to medical therapy. The findings of the most recent randomized trial showed that extended transsternal thymectomy plus alternate-day prednisone in contrast to alternate-day prednisone alone improved clinical outcomes over a 3-year span [12]. Transsternal, transcervical, unilateral thoracoscopic, bilateral thoracoscopic, and subxyphoid single-portal thymectomy are all techniques with comparable outcomes. Trans-sternal thymectomy was once the most widely accepted procedure as a standard technique, but with the introduction of thoracoscopic thymectomy, a surgical debate evolved on which approach achieves better long-term clinical improvement for MG. In our institution, both open and thoracoscopic surgeries are performed, and there was a significant long-term clinical improvement of thymectomized myasthenic patients through the transsternal approach over thoracoscopy during follow-up in the outpatient clinic after discharge from the hospital. Despite the greater intraoperative blood loss due to larger incision and longer postoperative hospital stay for the transsternal approach, it is still a safe and effective approach, especially in cases with large thymoma and thymic malignancy invading surrounding structures. VATS thymectomy (either right or left sided) can be rationalized in patients with nonenlarged thymus as in nonthymomatous myasthenic patients and patients with thymic nodules for histopathology for surgeons with thoracoscopic expertise and high number of operated cases to achieve more thymic tissue clearance through the thoracoscopic approach.

There has been previous research contrasting the VATS and transsternal approaches to thymectomy in patients with thymoma. Agatsuma and colleagues tested the clinical efficacy of VATS and compared the oncologic results of VATS to those of sternotomy. The clinical results of 2835 patients with thymic epithelial tumors treated in 32 Japanese institutions between 1991 and 2010 were gathered retrospectively. The researchers compared postoperative complications, positive surgical margins, recurrence place, and survival in 140 of 142 VATS-treated patients (VATS group) to 140 of 1294 sternotomy-treated patients (sternotomy group) using propensity scores. In the VATS group, eight patients experienced postoperative complications. The morbidity rate of the VATS group was not markedly different from that of the sternotomy group (P=0.25). In four patients, surgical margins were found to be positive (three in the VATS group; one in the sternotomy group). The recurrence rate between groups did not vary statistically significantly (median follow-up period: 3.7 years in the VATS group and 5.2 years in the ST group). The most common site of recurrence was the pareital pleura. In terms of morbidity, incomplete resection rate, and prognosis, VATS thymectomy was feasible and equivalent to sternotomy for the treatment of patients with thymoma. However, further follow-up is required to determine long-term results [13].

Zahid and colleagues carried out another meta-analysis to observe how VATS compares to median sternotomy

Figure 7



Bar graph of the clinical outcome of transsternal and VATS approaches. VATS, video-assisted thoracoscopic surgery.

in the surgical treatment of myasthenia gravis patients (MG). Seventy-four papers were found, 15 of which provided the best evidence to address the clinical query. VATS was found to achieve comparable postoperative mortality and full stable remission (CSR) rates, with superior results in terms of hospital stay, operative blood loss, and patient satisfaction at the cost of doubling of operative time. VATS had lower operative blood loss (73.870.7 vs. 155.391.7 ml; $P<0.05$) and a shorter overall hospital stay (5.62.2 vs. 8.13.0 days; $P=0.008$) in nonthymomatous myasthenia gravis patients, according to six reports. At a 6-year follow-up study comparing video-assisted thoracoscopic extended thymectomy to transsternal thymectomy in only thymoma-associated myasthenia gravis, patients had comparable CSR (11.3 vs. 8.7%, $P=0.1090$). The recurrence rate of thymoma (9.64%) was not markedly different between the two groups ($P=0.1523$). In eight trials comparing VATS and the transsternal method in mixed thymoma-associated myasthenia gravis and nonthymomatous myasthenia gravis patients, researchers discovered a shorter hospital stay (1.92.6 vs. 4.64.2 days, $P=0.001$) and less postoperative treatment (76.5 vs. 35.7%, $P=0.022$). For VATS, there was a shorter stay in the ICU (1.5 vs. 3.2 days, $P=0.018$) and improved cosmetic satisfaction (100 vs. 83, $P=0.042$). VATS and transsternal approaches had similar complication rates (23 vs. 19%, $P=0.765$), with no mortalities in both groups [14].

Conclusions

Agatsuma *et al.* [13], stated that 'It is uncertain if VATS thymectomy for MG has the same surgical outcomes as median sternotomy due to a lack of randomized prospective clinical trials.' However, from our study, it became evident that the transsternal approach still did not lose ground in the clinical outcome of MG compared with VATS.

Conventional transsternal thymectomy either by manubriotomy (ministernotomy) or by full median sternotomy still has superior clinical outcome when compared to the VATS approach for myasthenic patients in terms of achievement of CSR or clinical improvement estimated by the MGFA score. Transsternal thymectomy warrants better accessibility for removal of the whole thymus and surrounding fat when performing total radical thymectomy particularly for large thymomas and thymic carcinomas invading surrounding structures (e.g. left innominate vein and phrenic nerve). VATS thymectomy is a viable option for treating early-stage small-sized thymoma. However, concerns about incomplete surgical resection keep VATS for thymectomy from being widely accepted as a standard approach, especially in malignant cases.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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