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Original Article

Early Outcomes of Thoracoscopic versus Open Extended Thymectomy in Myasthenia Gravis Patients

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Abstract

Background: The debate concerning the impact of surgical approaches for thymectomy on the outcomes of myasthenia gravis continues. This study aimed to present the preliminary outcomes of thoracoscopic versus transsternal thymectomy for patients with myasthenia gravis.

Methods: A total of 60 patients participated in this cohort study. Twenty-seven of these patients underwent thymectomy via video-assisted thoracoscopic surgery (VATS) with one (n= 7) or two ports (n= 20) (Group I). Thirty-three patients underwent thymectomy via the transsternal approach (Group II). The study was conducted over one year, and the patients were followed for three months postoperatively.

Results: The duration of the operation (88±9 vs. 131±6 min, P<0.001) and volume of blood loss (109±12 vs. 434± 54 ml; P<0.001) were significantly lower in the VATS patients. Additionally, early extubation was significantly more common in Group I than in Group II (100% vs. 48%; P <0.001). Compared with Group II patients, Group I patients had a significantly lower need for blood transfusions (0 vs. 6 (18%); P<0.001) and postoperative intensive care units (0 vs. 28 (85%); P <0.001). Compared with Group II, Group I had a lower VAS pain score after 24 h (4 (3-5) vs. 6 (6-7); P<0.001). Patient mobilization occurred significantly earlier in Group I than in Group II (5.89 ± 1.45 vs. 19.09 ± 6.38; P <0.001). No cases of video-assisted thoracoscopic surgery were converted to open surgery, and no cases of operative mortality were reported in either group.

Conclusions: Compared with open thymectomy, thoracoscopic thymectomy might yield superior results. Thoracoscopic thymectomy is associated with a shorter duration of operation, less blood loss, less need for blood transfusion, less need for the ICU, a lower pain score, and an earlier timing of patient mobilization. Therefore, thoracoscopic thymectomy could be preferable to open thymectomy for the surgical treatment of myasthenia gravis.

KEYWORDS

Thoracoscopic thrombectomy; Myasthenia gravis; Video-assisted thoracoscopic surgery; Trans-Sternal and open thymectomy

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Introduction

Autoimmune myasthenia gravis (MG) is characterized by the gradual weakening of muscles caused by the body's production of antibodies directed against acetylcholine receptors. This weakness initially affects the eye muscles and then spreads to other skeletal muscles, eventually causing respiratory failure [1].

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Thymic B lymphocytes are the most important producers of these antibodies [2]. The medical management of MG includes the administration of anticholinesterase agents, immunosuppressive drugs, plasmapheresis, and corticosteroids. Clinical remission rates in patients treated with these methods have reached 15% [3]. Moreover, surgical removal of the thymus gland is an accepted modality for treating MG that achieves marked clinical improvement in the symptoms of myasthenia gravis [4].

As a means of reducing the probability of MG recurrence, complete thymectomy is recommended. This procedure involves the removal of all thymic and perithymic tissue. Several studies have demonstrated that patients can benefit from this procedure in controlling symptoms and preventing recurrence [5]. Thymectomy can be performed via various surgical techniques, including transcervical, transsternal, subxiphoid, robotic, and video-assisted thoracoscopic surgery (VATS) [6]. According to a recent report, the minimally invasive technique and the most frequently used technique for thymectomy operations was VATS, which had a frequency of 68% [7].

Concerning the treatment of MG, a comparison between VATS and median sternotomy revealed that VATS is generally associated with reduced blood loss, a shorter duration of time consumed during the operation, and a shorter length of stay in the hospital. Additionally, VATS lessens the likelihood of postoperative complications by reducing the amount of tissue damage, postoperative pain, and the possibility of infection [8, 9]. The impact of surgical approaches on the recurrence rate continues to be debated. This study aimed to present the preliminary outcomes of thoracoscopic versus transsternal thymectomy surgery performed on patients who had been diagnosed with MG.

Patients and Methods

Design and patients

A total of 60 patients participated in this prospective cohort study. Twenty-seven of these patients underwent thymectomy via VATS, while the remaining 33 patients underwent thymectomy via the conventional complete transsternal approach over one year. A preoperative diagnosis of myasthenia gravis was made according to clinical symptoms and electrophysiological tests, such as the repetitive nerve stimulation test (RNS) and single-fiber electromyography (SFEMG), which were already performed on patients by neurologists before referral to surgery. These patients included both male and female participants. In addition, a serological investigation was carried out to detect the presence of antibodies against the acetylcholine receptor (AChR), and the results of this investigation were positive for every patient. In addition, a routine clinical history was taken, a neurological examination was carried out, and the patients were classified into four classes according to Osserman's classification [10]: Class I: ocular involvement only; Class IIA: mild generalized weakness with slow progression and gradual involvement of the bulbar and skeletal muscles; Class IIB: moderate generalized weakness with gradual progression to a more severe form; Class III: acute fulminant form with rapid disease progression and acute involvement of respiratory muscle; and Class IV: late severe form with acute progressive symptoms starting two years after the onset of myasthenia.

Settings:

The research was carried out at Tanta University Hospitals in Tanta, Egypt, after the approval of the local ethical committee (Approval: 35921/10/22). All the patients provided written consent after being fully informed. The study included both sexes with a preoperative diagnosis of MG on the basis of clinical symptoms, electrophysiological tests, and serological tests. Patients with a thymoma with a maximal diameter greater than 6 cm, a thymoma with radiological evidence of invasion into surrounding organs, patients who had received neoadjuvant therapy in the past, or patients whose body mass index (BMI) was greater than 30 kg/m2 were excluded.

Data and outcomes:

All the patients in the study underwent a comprehensive assessment, including a medical history and radiological and laboratory tests, including a complete blood count (CBC), liver and renal function tests, and an acetylcholine receptor (AChR) antibody test. Additionally, radiological investigations, including chest radiography and high-resolution chest CT with intravenous contrast, were performed. Following each plasmapheresis session, CBC and tests were conducted for sodium, potassium, calcium, and magnesium levels; prothrombin time; and the international normalized ratio (INR).

Plasmapheresis sessions were conducted before and after surgery according to the severity of the case, guided mainly by an assessment from the Neurology Department to eliminate proteins with autoimmune biological activity, particularly antibodies targeting acetylcholine receptors. The number of sessions depended on the severity of the case. The final session should be performed within a timeframe of 24–48 hours before the operation to reduce antibody levels and the risk of postoperative myasthenic crisis.

Thoracoscopic thymectomy

It was performed mainly through the right side of the patient but also through the left side, where the thymus gland was easily accessed while the patient was under general anesthesia. A double-lumen endotracheal tube was used to deflate the lung on the side, which was previously indicated. The patients were supine, with the roll placed under the ipsilateral chest and their arms moving away from their body over a cushioned support. This was performed to improve access to the axilla for the insertion of the thoracoscopy port. The bilateral chest, including the sternum, is prepped and draped. In twenty patients in the VATS group, two ports ranging from 2–3 cm in size were utilized. The first port was positioned below the nipple in the fourth or fifth intercostal space in the midclavicular line (submammary fold). This location was where the 5–10 mm thoracoscope with a 30-degree camera was inserted to visualize the thymus. Using a second port in the fifth intercostal space along the mid-axillary line, dissecting instruments, sponge-holding forceps, clip appliers, long blade diathermy pens, and harmonic scalpels were used. For seven patients in the VATS group, only one port was utilized. Dissection was performed through the lower horn of the thymus first until it reached the upper horn to be easily removed. The pericardial and diaphragmatic fat were subsequently removed to decrease the release of antibodies stored in the fat, limiting the recurrence of symptoms. There was no need to add more ports, use CO2 insufflation, or open the other side of the pleura. Finally, one chest tube was inserted through the incision of the port to drain any residual material. (Figure 1)

Figure 1: A) Vertical size of the thymus gland after thoracoscopic thymectomy; B) Size of the wound in bicortal thoracoscopic thymectomy

Transternal Thymectomy

Under general anesthesia, while the patient was lying in the supine position, intubation and ventilation were carried out with the assistance of an endotracheal tube with a single lumen. A midline sternotomy incision was made. There was complete removal of the thymus gland and the pericardial fat that extended from the lower neck level down to the diaphragm on both sides of the right and left phrenic nerves. Following the completion of the procedure, two chest tubes were used: one was inserted in the pleural space, and the other was inserted in the retrosternal space. Sternal wires were then used to secure the sternum.

Postoperative data

Immediate extubation, need for admission to the ICU, amount of blood loss, length of hospital stay, time of removal of chest tubes, postoperative complications, and results of histopathological examination. Postoperative chest radiography was performed as a standard procedure to identify the presence of pneumothorax, retain pleural collection, and

Table 1: Comparison of the demographic, preoperative, and operative data between patients who underwent thoracoscopic thymectomy (Group I) and those who underwent conventional thymectomy (Group II). The data are presented as the means ± SDs, frequencies (%) or means and SDs.

		Group I (n=27)	Group II (n=33)	P value
Age (years)		31.3 ± 9.48	36.3 ± 10.17	0.055
Sex	Male	9 (33.33%)	17 (51.52%)	0.157
	Female	18 (66.67%)	16 (48.48%)	
BMI (kg/m^2)		26.78 ± 2.23	26.91 ± 2.45	0.827
Comorbidities		3 (11.11%)	8 (24.24%)	0.191
Complaint	Ptosis	15 (55.56%)	26 (78.79%)	0.054
	Dysphagia	9 (33.33%)	12 (36.36%)	0.807
	Diplopia	8 (29.63%)	4 (12.12%)	0.092
	Dyspnea	4 (14.81%)	3 (9.09%)	0.492
Preoperative				
Plasmapheresis	One session	4 (14.81%)	2 (6.06%)	0.146
	Two sessions	7 (25.93%)	4 (12.12%)	
	Three sessions	6 (22.22%)	8 (24.24%)	
	Four sessions	4 (14.29%)	9 (27.27%)	
	Five sessions	1 (3.7%)	7 (21.21%)	
	No	5 (18.52%)	3 (9.09%)	
CT-chest findings	Thymic hyperplasia	12(44.44%)	17 (51.52%)	0.190
	Thymoma	1 (3.7%)	5 (15.15%)	
	Normal thymus	14 (51.85%)	11 (33.33%)	
Intraoperative				
Duration of operation (min)		87.96±8.58	130.91±6.05	<0.001
Blood loss (ml)		109.26±12.07	434.85±53.74	<0.001

CT: computed tomography

prevent abnormal diaphragm elevation. After surgery, the patient consistently received pyridostigmine bromide and corticosteroids, with doses comparable to those taken before the operation. The doses were subsequently modified on the basis of symptomatic improvement postsurgery. Patients are generally advised to continue their follow-up with neurology outpatient clinics. Plasmapheresis has been employed in the management of imminent myasthenic crises and as a periodic treatment for certain individuals suffering from severe MG.

Statistical analysis

Statistical analysis was carried out via SPSS v26 software (IBM Inc., Chicago, Illinois, USA). Histograms and the Shapiro–Wilks test were utilized to determine whether the data distribution was normal. With the help of an unpaired Student's t test, the means and standard deviations (SDs) of quantitative parametric variables were calculated, and comparisons were made between the two groups. The median and interquartile range (IQR) were used to report the quantitative nonparametric data, and the Mann–Whitney test was used for analysis. The chi-square test was used to analyze the qualitative variables, which are expressed as frequencies and percentages (%). To be considered statistically significant, a two-tailed P value that was lower than 0.05 was used.

Results

Demographic, preoperative, and operative data

Comorbidities and presenting symptoms (ptosis, dysphagia, diplopia, and dyspnea) were not significantly different between the two groups. Preoperative findings (plasmapheresis and CT-chest findings) were not significantly different between the two groups. The duration of

Table 2: Comparison of surgical and postoperative data between patients who underwent thoracoscopic thymectomy (Group I) and those who underwent conventional thymectomy (Group II). Data are presented as the median (IQR), mean, standard deviation (SD), number, and percentage

		Group I (n= 27)	Group II (n= 33)	P
Surgical resection (Extended thymectomy)		27 (100%)	33 (100%)	---
Need for blood transfusion		0 (0%)	6 (18.18%)	<0.001
Immediate extubation		27(100%)	16(48.48%)	<0.001
Need for ICU postoperative		0(0%)	28(84.85%)	<0.001
NRS score	2 h	6 (5 - 6)	8 (7 - 9)	<0.001
	24 h	4 (3 - 5)	6 (6 - 7)	<0.001
	48 h	2 (2 - 2)	6 (6 - 6)	<0.001
Number of chest drains	1	27 (100%)	0	<0.001
	2	0	33 (100%)	
Hospital stay (days)		1.67± 0.48	7.82± 1.42	<0.001

NRS: Numerical rating scale; ICU: intensive care unit

the operation and amount of blood loss were significantly lower in Group I than in Group II (P <0.001) (Table 1).

Surgery and postoperative data

Surgical resection was extended to thymectomy in all patients in the two groups. The need for blood transfusion, numerical rating scale (NRS) score, and postoperative intensive care unit (ICU) score were significantly lower in Group I than in Group II (P <0.001). No cases of VATS conversion to open surgery occurred. The incidence of immediate extubation was significantly greater in Group I than in Group II (P <0.001) (Table 2).

The number of chest drains and length of hospital stay were significantly greater in Group II than in Group I (P <0.001). The timing of patient mobilization was significantly lower in Group I than in Group II (P <0.001). The need for plasmapheresis postoperatively was not significantly different between the two groups, wound infection was significantly different between the two groups at the 3-month postoperative follow-up, and the dose of steroids was significantly lower in Group I than in Group II (Table 3).

Table 3: Timing of patient mobilization, need for plasmapheresis, postoperative follow-up, and dose of steroids in the studied group. The data are presented as the means ± SDs or frequencies (%).

		Group I (n=27)	Group II (n=33)	P
Timing of patient mobilization (h)		5.89 ± 1.45	19.09 ± 6.38	<0.001
Need for plasmapheresis postoperatively	One session	4 (14.81%)	2 (6.06%)	0.403
	Two sessions	10 (37.04%)	6 (18.18%)	
	Three sessions	9 (33.33%)	9 (27.27%)	
	Four sessions	4 (14.81%)	8 (24.24%)	
Postoperative follow-up				
Phrenic nerve injury		0 (0%)	0 (0%)	---
Wound infection		1 (3.5%)	5 (15%)	0.032
Myasthenic crisis		0 (0%)	8 (24.24%)	0.773
Residual muscle weakness		6 (22.22%)	10 (30.3%)	0.481
Decreased steroid dose		19 (70.3%)	11 (33.3%)	0.007

Discussion

Several treatment strategies are available for managing myasthenia gravis, including anticholinesterase medicines, steroids, immunosuppressive medications, and plasmapheresis, to reduce the serum antibody concentration [11,12]. A complete clinical remission rate as low as 18% after medical treatment has been reported in several studies. [13-15] Surgical treatment has grown in popularity, with clinical remission rates as high as 42% and clinical improvement rates as high as 94% [16,17]. Since the introduction of VATS for thymectomy in 1992, several studies have shown that the VATS approach reduces intraoperative blood loss, injury to surrounding tissues, postoperative pain, and postoperative complications [17]. The majority of research findings indicate the effectiveness of thymectomy in treating patients with myasthenia gravis [18,19].

This study revealed that the operative time was significantly shorter in the VATS group than in the open thymectomy group. This could be explained by the use of a minimally invasive technique, which allows small incisions. Toker and colleagues [12] reported that the average duration of VATS was 100 min, which is different from our findings in the VATS group (90 min). In contrast, Muhammad [20] reported a significantly longer operative time in the VATS group. The author explained this finding by the low level of experience in VATS at the time of the study. With respect to blood loss, there was less blood loss in the VATS group than in the open thymectomy group. This could be explained by the fact that open surgery results in more blood loss secondary to the associated sternotomy incision and closure. Confirming our data, Xie and associates [21] reported that, compared with the open thymectomy group, the VATS group experienced a significantly lower amount of blood loss. Our data disagreed with those of Erşen and colleagues [22] and revealed no significant difference in the amount of blood loss between the open group (n=22) and the VATS group (n=19). Thus, the need for blood transfusion was significantly lower in the VATS group than in the open thymectomy group because the VATS group experienced less blood loss. In support of our data, Ye and associates [23] reported that blood transfusion was needed for only one patient in the VATS group.

All patients in this study underwent extended thymectomy with no residual thymic tissue in either group. This finding indicates that thoracoscopic thymectomy provides effective surgical excision, similar to open thymectomy, with fewer complications. In agreement with these findings, Fiorelli and colleagues [24] reported that VATS thymectomy was an effective approach for removing the thymus and surrounding tissue. However, this procedure offers the advantages of a minimally invasive approach that results in less pain and faster recovery. Our study revealed that the need for postoperative ICU admission was significantly lower in the VATS group than in the open thymectomy group. Similarly, Lo and collaborators [25] reported that the need for postoperative intensive care unit (ICU) care was significantly lower in the VATS group than in the open thymectomy group [25]. The NRS score for postoperative pain was significantly lower at 2 h, 24 h, and 48 h in the VATS group than in the open thymectomy group. The most likely reasons for the decrease in pain were the limitations in skin and chest wall incisions and the difference in the number of inserted chest tubes between the two techniques. A small incision could also be considered the major contributor to decreased postoperative pain. Muhammad [20] reported that the VATS group had significantly lower analgesic requirements than did the open thymectomy group. In support of our data, Fiorelli and collaborators [24] reported a significant decrease in pain scores following VATS compared with the open approach. Minimal postoperative pain permits early postoperative physiotherapy and accelerates the recovery of respiratory function and early resumption of daily activities. These consequences are especially crucial for MG patients who are relatively young, employed, and physically active. The postoperative number of chest drains was significantly different between the 2 groups. One chest tube in the VATS group was associated with decreased postoperative pain. Conversely, Yuan and associates [26] reported that the number of chest drains was not significantly different between the VATS and open thymectomy groups.

The length of hospital stay and time of removal of chest tubes were significantly shorter in the VATS group than in the open thymectomy group. Additionally, Toker and colleagues [12] reported that the length of hospital stay was 1–6 days, which was close to our findings. In agreement with our data, Xie and associates [21] reported that the duration of chest drainage and length of hospital stay were significantly shorter in the VATS group than in the open thymectomy group. In terms of postoperative complications, the group that underwent VATS had a significantly lower wound infection rate than did the group that underwent open thymectomy. In agreement with our results, Muhammad [20] reported that the wound infection rate was significantly lower in the VATS group than in the open thymectomy group. Erşen and collaborators [22] agreed with our findings, as there was no difference in the incidence of wound infection between the VATS group and the open group. However, the incidence of myasthenic crisis was not significantly different between the VATS group and the conventional thymectomy group. Kakhaki and colleagues [27] reported that postoperative complications and myasthenic crises occurred in 26.5% of patients. Our data are supported by those of Siwachat and associates [28], who reported insignificant differences in myasthenic crisis between the thoracoscopic and open groups. Moreover, there was no discernible difference in the level of residual muscle weakness between the group that underwent open thymectomy and the group that underwent VATS. These results are in agreement with those of Kauppi and colleagues [29]. Notably, three patients in the VATS group experienced transient worsening of muscle weakness, which was close to our results (7.41%). In agreement with our data, Gung and associates [30] conducted a meta-analysis of 23 studies comparing thoracoscopic surgery and sternotomy for MG patients and reported that there was no significant difference between the groups in that study. Muscular weakness presented in the form of upper and lower limb and bulbar manifestations. It was evaluated by neurological examination and was found to have improved or not improved, and the dosage of the medications was reduced or not.

After three months of follow-up, there was a significant difference between the VATS and open groups. The dose of steroids decreased in most VATS groups until they stopped but remained at the preoperative dose in most open groups. The pathological findings of the resected specimen affect postoperative treatment, and the cure rate of myasthenic symptoms is high for thymoma patients.

Study Limitation:

Our study limitations include that it was a single-center study, and the generalizability of the results to other centers may not be applicable. The sample size was relatively small, and the study power could have been affected by the small number of patients in each group. The follow-up period was short, and long-term outcomes were not evaluated.

Conclusion

Compared with open thymectomy, thoracoscopic thymectomy might yield superior results. Thoracoscopic thymectomy was associated with a shorter duration of operation, less blood loss, a smaller wound size, less need for blood transfusion, less need for the ICU, a lower pain score, an earlier timing of patient mobilization, a shorter postoperative hospital stay, and a lower incidence of wound infection. Therefore, thoracoscopic thymectomy could be preferable to open thymectomy for the surgical treatment of MG.

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