ORIGINAL ARTICLE

RESULTS OF MINIMALLY INVASIVE VATS THYMECTOMY IN MIASTENIA GRAVIS PATIENTS COMPARED WITH MORE INVASIVE APPROACHES – 10-YEAR EXPERIENCE IN A SINGLE CENTER

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Abstract

Introduction: *Myasthenia gravis (MG) is an autoimmune, neurologic disease that causes a wide range of symptoms. While the transsternal, transcervical and thoracotomy approaches are accepted as effective, there is still debate regarding the VATS approach.*

Materials and Methods: *We analyzed our center's surgical experience with thymectomy for myasthenia gravis, comparing the results of patients operated on using VATS and more invasive approaches, over a period of 10 years.*

A search of the department's surgical database for myasthenia gravis cases between January 2010 and January 2021, revealed a total of 40 cases. Twenty-four patients were included in the final analysis and were distributed into two groups: the VATS procedure group (group A) and the open procedure group (group B). The latter included sternotomy, thoracotomy, transcervical and hemiclamshell approaches. Only radical thymectomies were included.

The established outcomes were clinical improvement defined as asymptomatic remission, reduction, or discontinuation of the medication necessary to achieve optimal symptom control.

Results: *The median follow-up time was 27 months (ranging from 4 to 75 months). Videothoracoscopy radical thymectomy was performed on 12 patients. Complete remission with no medication was achieved in 1 case (8.3%), while 2 patients (16.7%) became asymptomatic with reduced medication. An improvement (reduced symptoms or decreased medication) was observed in 8 cases (66.6%). No change in clinical outcome was noted in 1 patient (8.3%). None of the patients reported worsening symptoms.*

Open thymectomy was performed on 12 patients. Complete remission with no medication was achieved in 1 case (8.3%), while 2 patients (16.7%) became asymptomatic with reduced medication. An improvement was noted in 6 cases (50%). No change in clinical outcome was observed in 3 patients (25%) whereas 2 of them (16.7%) experienced slightly better symptom control but with a significant increase in medication. One patient (8.3%) described the clinical results as without any significant change. None of the patients reported worsening symptoms.

Conclusion: *The videotoracoscopic approach in the treatment of myasthenia gravis is non-inferior compared to the open approach and effective in a long-term follow-up, offering all the additional benefits of less invasive surgery.*

Keywords: *Myasthenia gravis, thymectomy, minimally- invasive surgery, open surgery, thymoma*

INTRODUCTION

Myasthenia gravis is an autoimmune neurological disease [1,3,6,8] with an annual incidence of 1 to 2 per 100,000, while the prevalence can be as high as 20 to more than 50 per 100,000.[3] The disorder has two sex-related peaks: the first one in the second and third decades of life, affecting more women, and the second peak in the sixth and seventh decades, affecting mostly men[3]. The disease is characterized by various symptoms that can vary from ocular to bulbar and generalized symptoms[1,3,6,8].

There are two mechanisms of MG. The prevalent autoimmune mechanism is caused by antibodies against the acetylcholine receptors in the neuromuscular junction[1,3,6,8], which, in combination with local complement deposition, decrease the number of available postsynaptic nicotinic acetylcholine receptors (AChR), thus impairing neuromuscular transmission. In the second variant, the antibodies target the muscle-specific serine kinase (MuSK), interrupting the cytoskeleton at the endplate region[3]. When compared to the AChR variant, MuSK-positive patients tend to have a bulbar distribution with more frequent atrophy of the respective muscles[10]. In MuSK-positive cases, exemplary thymic anomalies are missing or less prominent, making the standard treatment modalities less successful [3,11]

Myasthenia gravis has been reported to be associated with other thymic diseases. One of the most common associations is with thymoma. These patients may suffer from a variety of autoimmune diseases in over 50% of the cases, the most common of which are MG, erythroid aplasia and hypogammaglobinemia. Up to 25% of thymoma patients will have clinically apparent MG and an in additional 25% of clinically asymptomatic thymoma patients, circulating anti-acetylcholinesterase receptor (anti-Ach-R) autoantibodies will be detected. Conversely, in 5–15% of the patients with MG, preoperative tests eventually demonstrate an unsuspected thymoma[4].

The thymic gland plays a key role in the development of the disease, and the total removal of thymic tissue – radical thymectomy (removal of the thymus gland and anterior mediastinal fat from the neck to the diaphragm and phrenic-to-phrenic nerve) (Fig.2) is believed to be the crucial approach in its treatment[1,2,3,4,5,7,8]. While transsternal, transcervical, or thoracotomy with transcervical thymectomy are widely accepted options5, there are still many doubts surrounding the videotoracoscopic approach3,[4,6,7,8,9]. These reservations result from the belief that a minimally invasive approach is not effective in removing all thymic tissue foci widely spread in the mediastinum and the neck.[1,4,9]

The recognition of the significance of radical thymectomy dates back to 1977 when preliminary surgical-anatomic studies revealed that not only is the thymic tissue widely spread in the cervical region and anterior mediastinum, but it is also present in multiple microscopic thymus foci distributed within the mediastinal fat tissue[1]. At that time, the Jaretzki team conducted a study involving 95 patients and advocated that only 'combined transcervical-transsternal en bloc resection comes as close to the complete removal of thymic tissue as is surgically possible' [1].

Since its introduction in 1990, the video-assisted thoracoscopic approach has become a viable option for various thoracic diseases, demonstrating benefits in short-term follow-up[12]. However, certain thoracic disorders such as myasthenia gravis require a longer follow-up period to illustrate the results of surgical excision due to their variable course and the fact that the benefits are not typically immediate.[2]

Initially, thoracic surgeons expressed skepticism about using the VATS approach for procedures like thymectomy or lobectomy, despite accepting it for minor surgeries, due to concerns about its limitations in fully removing the intended tissue and its inability to ensure adequate oncologic or myasthenic disease management[12]. Nevertheless, a gradual increase in its rate of utilization prompted further studies that demonstrated the non-inferiority of the VATS approach compared to the open approach.

Our objective was to compare the outcomes of VATS and open procedures to establish the non-inferiority of the minimally invasive approach

MATERIAL AND METHODS

Our analysis is a retrospective study conducted at a single center, based on the 10-year experience within our department. We conducted a search in our database for cases of Myasthenia gravis between January 2010 and January 2021, resulting in a total of 40 cases. After excluding patients for whom follow-up data was unavailable or who could not be contacted to confirm the clinical outcomes, 24 patients were ultimately included in the final analysis. The inclusion criteria were as follows: a confirmed diagnosis of Myasthenia gravis, surgical excision performed between January 2010 and January 2021, and access to follow-up data.

We analyzed both the baseline and post-operative clinical characteristics related to the incidence of Myasthenia gravis. Additionally, we examined patient-specific parameters such as age at diagnosis, gender, duration of the disease prior to surgery, symptoms (ocular or generalized), histopathology, and the surgical approach employed. Our investigation focused on the clinical outcomes of radical thymectomy, specifically considering the cessation or improvement of the symptoms, the ability to decrease or discontinue medication, and the timing of symptom improvement based on the DeFilippi postoperative classification (Table I).

The final analysis included 24 patients, who were divided into two groups: those who underwent VATS procedures (group A) and those who underwent open procedures (group B). The latter group encompassed sternotomy, thoracotomy, transcervical, and hemiclamshell approaches.

Given the relatively small size of our patient cohort, conducting a statistical analysis was not feasible. Therefore, we opted to analyze the results using descriptive analysis techniques.

RESULTS

GROUP A - Videothoracoscopy thymectomy was performed on 12 patients. All of them underwent a 3 port VATS left-side procedure with CO2 insufflation (Fig. 1). The patient characteristics are presented in Table II. One patient had an exceptionally long disease duration of 240 months; this patient, evacuated from Guinee-Bissau in an advanced disease stage, is noteworthy as many authors believe that early intervention (<2 years) yields more favorable outcomes[1,3,6,7]. This outlier patient´s extremely prolonged disease duration

Table 1 DeFilippi postoperative classification

Class	Description
1	Complete remission, no medications
2	Symptomatic, decreased medications
3	Improved, decreased symptoms or decreased medications
4	No change
5	**Worsening symptoms**

Table 2 Patients caracteristics - group A

	n = 12 (%)
Gender	
Women	10 (83%)
Men	2 (17%)
Mean age of surgery	48.9 years old (range 32-69)
Sympthoms prior to surgery	
Ocular (diplopy + ptosis)	12 (100%)
Generalises myasthenia	11 (91.7%)
Mean duration of the disease prior to surgery	33 months (range 1 week to 20 years)
Pathologic results	
thymoma	5 (42%)
hyperplasia	4 (33%)
normal thymic tissue	3 (25%)
The mean length of hospital stay	3.8 days (range 3-6 days)
The mean follow-up	27 months

could potentially influence the overall results of the sample.

The mean hospitalization time was 3.75 days (ranging from 3 to 6 days), with one patient (8.3%) experiencing delayed discharge (defined as exceeding the median of 4 days).

The average follow-up period was 27 months, calculated from the surgery date until March 2021 when patient contact was established. All 12 included patients were alive at the time of follow-up.

Results were evaluated based on the DeFilippi postoperative classification (Fig.3) and can be reviewed in Table III. Among the 11 cases (91.7%) showing clinical improvement, positive outcomes were predominantly achieved during the first postoperative year, with most patients noting immediate improvement following thymectomy.

GROUP B – Open thymectomy was conducted on 12 patients. Patient characteristics are detailed in Table II. The average follow-up duration was 90 months, calculated from

Table 3 Results - group A

	n = 12 (%)
Complete remission with no medication	1 (8.3%)
Asymptomatic with decreased medication	2 (16.7%)
An improvement (decreased symptoms or decreased medications)	8 (66.6%)
No clinical improvement with prednisolone doses reduction	1 (8.3%),
No change in clinical outcome	1 (8.3%)
Slightly better symptoms but with a significant increase in medication doses	
Worsening symptoms	0 (0%)
Positive results on 1st post-op year	11 (91.7%)

the surgery date till March 2021 when patient contact was established. All 12 patients included in this group were alive at the time of follow-up.

The average hospitalization time was 6.25 days (ranging from 3 to 8 days), with 7 patients (58.3%) experiencing delayed discharge (defined as exceeding the median of 6 days).

Similar to group A, results for group B were assessed using the DeFilippi postoperative classification (Fig.3) and can be found in Table III. Among the 9 cases (75%) showing clinical improvement, the majority experienced positive results during the first postoperative year, with most noting immediate improvement following thymectomy.

DISCUSSION

It is generally believed that the success of thymectomy can be gauged by achieving complete and persistent remission[1]. In our study, we observed a higher rate of positive outcomes in the VATS procedure group (91.7% vs. 75% in the non-VATS group). The thoracoscopic approach appears to offer better technical efficacy for removing thymic foci compared to transsternal, transcervical, or other invasive strategies[5,6,8,9]. It allows excellent visualization of the thymic gland and a safe angle for the thymic horn removal[2,4,5,6].

While many authors believe that early intervention (<2 years) leads to better outcomes[1,3,6,7], we were unable to establish such an association.

As anticipated, patients undergoing open surgery experienced notably longer hospital stays compared to videotoracoscopic surgery (3.75 vs. 6.25 days). A comparison of hospitalization and reasons for delayed discharge are presented in Table V. Clearly, in terms of patient benefits and cost-effectiveness, videotoracoscopic surgery proves superior to open approaches.

Table 4 **Patients caracteristics - group B**

	n = 12 (%)
Gender	
Women	10 (83%)
Men	2 (17%)
Mean age of surgery	48.8 years old (range 16-71).
Sympthoms prior to surgery	
Ocular (diplopy + ptosis)	9 (75%)
Generalises myasthenia	10 (83%)
Mean duration of the disease prior to surgery	14 months (range 2 to 24 moths)
Pathologic results	
thymoma	8 (67%)
hyperplasia	1 (8.3%)
normal thymic tissue	1 (8.3%)
thyroid tissue	1 (8.3%)
pavimentocellular carcinoma	1 (8.3%)
The mean length of hospital stay	6.3 days (range 3-8 days).
The mean follow-up	90 months
Surgical approach	
median sternotomy	7 (58.3%)
antero-lateral thoracotomy	2 (16.7%)
conversion from VATS procedure	1 (8.3%)
transcervical + thoracoscopy	2 (16.7%)
posterior reoperation by sternotomy caused by residual thymic tissue	1 (8.3%)
hemiclamshell	1 (8.3%)

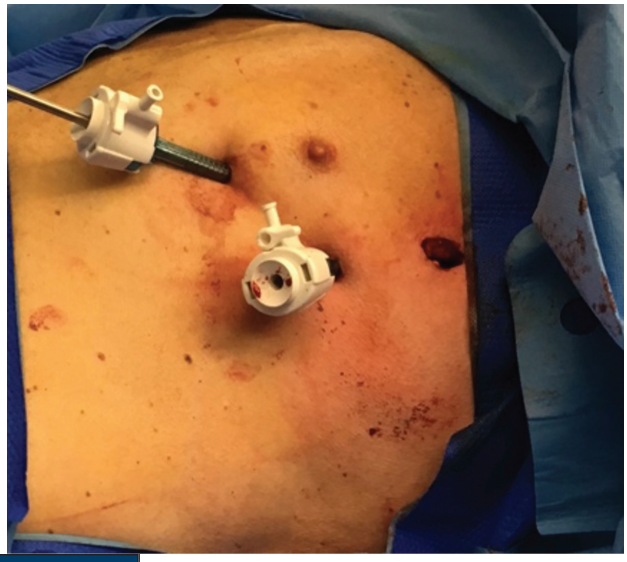

Figure 1 *Surginal incisions - 3 ports*

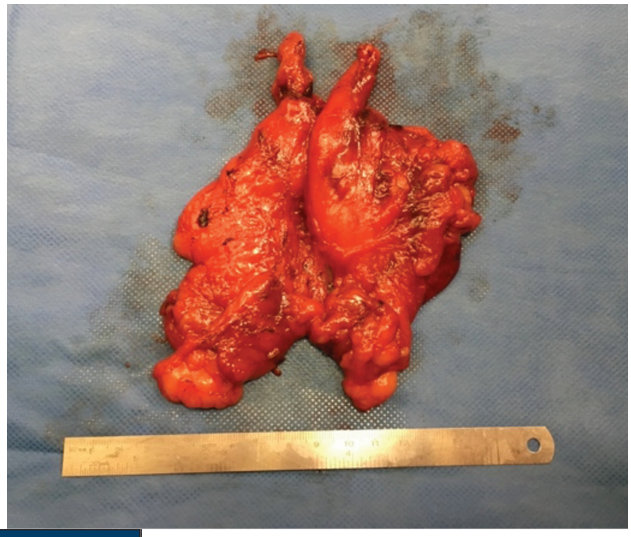

Figure 2 *Ressected thymic gland*

Table 5 **Results - group B**

	n = 12 (%)
Complete remission with no medication	1 (8.3%),
Asymptomatic with decreased medication	2 (16.7%)
An improvement (decreased symptoms or decreased medications)	6 (50%)
No clinical improvement with prednisolone doses reduction	1 (8.3%),
No change in clinical outcome	3 (25%)
Slightly better symptoms but with a significant increase in medication doses	2 (16.7%)
No significant change while taking the same therapeutic doses	1 (8.3%),
Worsening symptoms	0 (0%)
Positive results on 1st post-op year	9 (75%)

Table 6 **Comparison of results**

VATS surgery	Clinical improvement	Clinical remision
Thymoma (n = 5)	4 (80%)	1 (20%)
Non- thymoma (n =7)	7 (100%)	0

Open surgery	Clinical improvement	Clinical remision
Thymoma (n = 8)	6 (75%)	1 (12.5%)
Non- thymoma (n =4)	3 (75%)	0

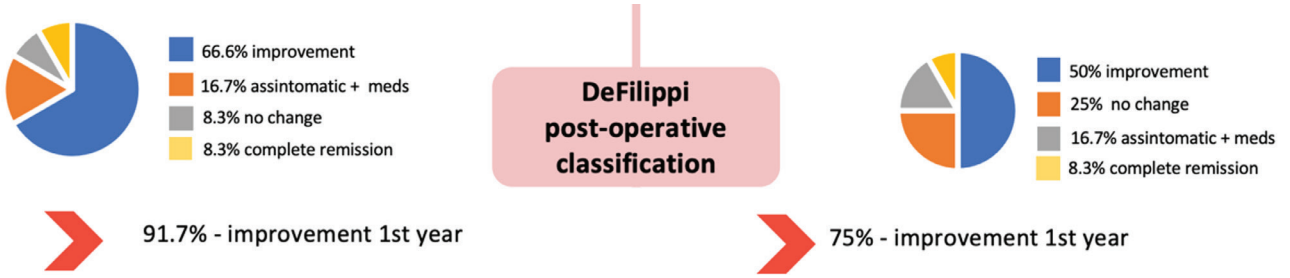

Figure 3 *DeFilippi post-operative classification*

Figure 4 *Pathological results*

Although it has long been recognized that thymectomy response is worse in patients with thymoma due to symptom severity, many thymoma patients respond symptomatically to radical thymectomy, justifying its application in these cases[1,8]. Our results do not entirely align with this. In group A (VATS), 4 out of 5 patients with thymoma improved (80%) with 1 case achieving total remission (20%). Among non-thymoma VATS patients, all patients demonstrated clinical improvement (2 were asymptomatic with medication, and 5 significantly improved) but none achieved complete remission. This suggests that thymoma and non-thymoma outcomes in group A are quite comparable.

Group B (open surgery) exhibited a different trend, with patients having thymoma showing better disease control. Among 8 thymoma cases 6, (75%) experienced clinical improvement - 1 (12.5%) achieved total remission, 1 (12.5%) became asymptomatic with medication, 4 (50%) improved clinically, while 2 (25%) couldn't reduce medication or improve symptoms. In the non-thymoma subgroup, 3 out of 4 patients (75%) showed improvement - 1 (25%) was asymptomatic with medication and 2 (50%) improved clinically. No patient achieved total remission, and 1 (25%) was unable to reduce medication or improve symptoms.

Despite a significantly higher remission rate during the first post-operative year, as we observed in the majority of our patients, Myasthenia gravis can exhibit a variable course, with improvement possible even years after surgery.

Comparing VATS and open approach results, the open approach had a significantly lower percentage of clinical improvement or total remission, both in thymoma and non-thymoma subgroups (Table IV).

We couldn't establish a correlation between age, sex, or disease duration and results[1,6].

CONCLUSIONS

The findings of our review should be approached with caution due to the retrospective nature of the study, the limitations of our small cohort, and its susceptibility to statistical errors, which make it challenging to draw robust conclusions.

Our results, despite these limitations, suggest that based on our center's experience, the videotoracoscopic approach demonstrates non-inferiority in treating Myasthenia gravis during long-term follow-up, offering all additional benefits of less invasive surgery such as reduced hospital stay duration (3.75 vs. 6.25 days), improved cosmetic outcomes, and greater overall patient satisfaction compared to open surgery.

As we continue to analyze larger patient cohorts operated in our department or via an interhospital database, we hope to validate these findings and demonstrate the non-inferiority of videotoracoscopic resections.

Hopefully, in the coming years, as we analyze a larger cohort of patients operated at our department or with an interhospital database, and as so we will be able to verify the presented data and demonstrate the non-inferiority of videotoracoscopic resections.

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