

# Situation of Southeastern Anatolia in Thymus Surgery: To Whom, Why, and How Thymectomy Was Performed

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## ABSTRACT

**Objective:** We sought to obtain information on the number of thymic lesions, surgical method, histopathology. We also investigated the relationship between thymic lesions and myasthenia gravis.

**Methods:** We retrospectively examined patients who underwent thymectomy for different thymic pathologies in our clinic between February 1998 and April 2014 according to their demographic characteristics, symptoms, surgical method, resection width, and histopathological diagnosis.

**Results:** The proportion of men and women was similar. The average age was 40.6±14.7 years. The most common symptom was rapid fatigue and the most common surgical method was median sternotomy. During extended thymectomy, we resected and reconstructed the anatomical structures. We found a high degree of association between thymoma and myasthenia gravis. The average life expectancy of the patients was 171.8±8.8 months.

**Conclusion:** Although the indications of thymectomy are not well known, the surgical procedures vary. We would therefore continue developing ourselves as the center where these surgeries are most frequently performed in the Southeastern Anatolia Region.

**Keywords:** Thymoma, thymectomy, myasthenia gravis

## INTRODUCTION

Thymoma, seminoma, and lymphoma are primary malignant tumors occurring in the anterior mediastinum, making up the majority of malignant mediastinal tumors (1). Studies on anterior mediastinal tumors and those of the thymus correlate with those on myasthenia gravis (MG) (2). According to the literature, 30% of patients with thymoma develop MG, while approximately 10-15% of patients with MG develop thymoma (3, 4).

The most common indications for thymectomy are thymic neoplasia and MG (5). The main goal of surgery in thymic neoplasia is complete resection of the tumor, and tumoral invasion and metastasis when necessary (6); this is because complete surgical removal of thymomas is the most important long term prognostic marker of thymic malignancies (7). The main goal of surgery in MG is to eliminate the production of antibodies that cause autoimmune diseases. Currently, thymectomy is indicated in patients with common MG and ocular symptoms that cannot be controlled by anticholinesterase (ACE) (2, 8).

Thymectomy can be performed with median sternotomy (MS), and with less invasive methods such as partial sternotomy, transcervical approach, video-assisted thoracoscopic surgery (VATS), and transcervical-VATS combination (9). There are two schools of thought concerning the form of excision during thymectomy: those who advocate the method that protects the sternum and those who perform sternotomy with resection of the surrounding tissue and thymus to prevent local recurrence (10). The surgery indicated for MG depends on the width of the thymectomy required for complete remission. For this purpose, studies revealing the thymic tissue distribution and presence of ectopic thymic tissue in the anterior mediastinum have been conducted. Regardless of the approach used in MG patients, the aim is complete remission (11, 12).

In this study, we retrospectively examined patients who underwent thymectomy for various reasons according to their demographic data, symptoms, surgical methods, resection width, and histopathological diagnoses, and aimed to obtain information

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on thymic lesions in our region and the connection between the thymic lesions and MG.

## METHODS

### Cases

We included 80 patients who underwent thymectomy for different thymic pathologies between February 1998 and April 2014 in Gaziantep University, Faculty of Medicine, Şahinbey Research and Practice Hospital Thoracic Surgery Clinic. Gaziantep University Clinical Research Ethics Committee Presidency (ethics committee approval number: 167). All patients provided an informed consent.

The inclusion criteria were as follows:

- Patients with benign or malignant lesions on radiology
- Patients with MG who have thymic lesions or thymus residues in the anterior mediastinum on radiology
- Patients with unresectable thymomas or thymic carcinomas that became resectable after chemotherapy (CT), radiotherapy (RT), or chemoradiotherapy (CRT)

The exclusion criteria were as follows:

- Patients operated for an anterior mediastinal mass and whose pathological diagnosis was out of the thymus (such as lymphoma)
- Patients undergoing thymectomy but whose pathology reports were not available
- Patients aged  $\leq 16$  years

### Preoperative Evaluation

We obtained a detailed anamnesis from all patients and performed physical examinations. We performed routine biochemical tests, chest X-ray, electrocardiography, and chest computed tomography (CT) tests in all patients (Figure 1). In some patients, we performed a mediastinal magnetic resonance imaging to evaluate the relationship between the lesion and anatomical structures, and the resectability of the lesion (Figure 2). We performed CT scan and positron emission tomography (Figure 3) to screen for metastases in patients with thymomas or thymic carcinoma.

We evaluated MG patients in the neurology clinic and requested a surgery upon neurologist approval. While all of this group of patients used ACEs, some of them also used immunosuppressive drugs. Some patients required intravenous immunoglobulin and plasmapheresis.

#### Main Points:

- When a thymic mass is diagnosed, myasthenia gravis screening should be performed for each patient.
- Thorax computed tomography should be performed in every patient diagnosed with myasthenia gravis to investigate the presence of thymic lesion.
- Median sternotomy may be considered for wide resection in the presence of thymoma or thymic carcinoma.
- Minimally invasive surgery may be considered in patients with myasthenia gravis if thymoma is not suspected.

Figure 1. Axial CT image of a patient with thymic lesion



Figure 2. MRI image of a patient with suspected invasion

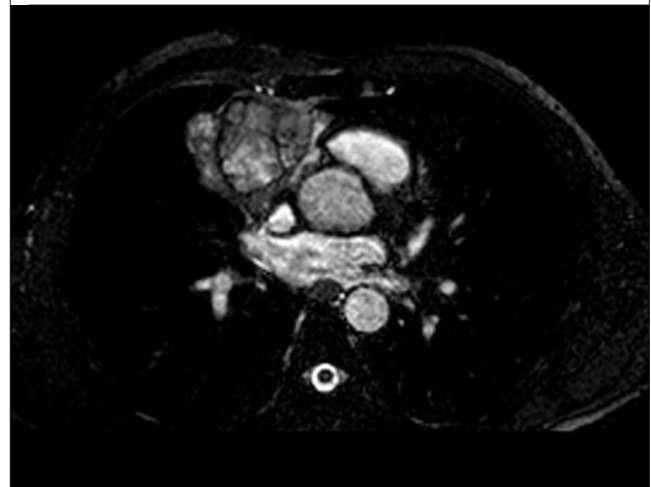
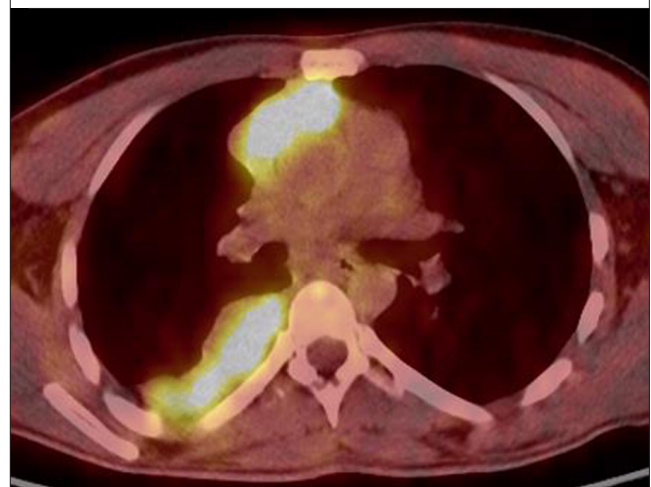


Figure 3. PET-CT image of a patient diagnosed with thymoma with metastasis



**Anesthesia Applications**

Although standard procedures for thoracic surgery are applied, muscle relaxants are either not used or used in selected patients, according to the anesthesiologist and neurologist.

**Surgical Methods**

Our basic rules in thymus surgery are: The mediastinum should be well explored, the cervical pole and mediastinal fat tissue should be resected, the phrenic nerve should be preserved, the tumor capsule should not be damaged, and the resection should be extended from the diaphragm to the neck. Therefore, MS has been used frequently. In patients with MG, right VATS was used from 2008 if there was no radiologic image of the thymoma.

Exploration also included the lungs and pleura to determine whether the thymic mass invaded the surrounding tissues and whether there is a metastasis (Figure 4). This was in accordance with the definition of extended thymectomy defined as “block resection of the thymus and adipose tissue in the anterior mediastinum via MS” (Figure 5). Due to invasion, various degrees of resection and reconstruction have been applied to anatomical structures like the pericardium, diaphragm, vascular structures, phrenic nerve, and lung.

Right VATS was done in patients with MG and no thymoma image (Figure 6). Left VATS was done to some patients with masses localized to the left and requiring exploration of the aorticopulmonary window. As a rule, complete thymectomy was performed in VATS (Figure 7). Some patients who started with VATS switched to thoracotomy or MS for various technical reasons, and these patients were not included in the VATS group.

**Postoperative Care**

All patients were taken to the intensive care unit, and most patients were taken to the service after a day of intensive care follow-up. All MG patients were evaluated by the postoperative neurologist, and ACE and immunosuppressive treatments were continued.

Histopathologically, all patients diagnosed with thymoma or thymic carcinoma presented to the tumor council and the need for an additional oncological treatment was decided. Patients with MG continued their neurological follow-up.

**Statistical Analysis**

Statistical analyses were conducted using IBM SPSS Statistics for Windows 22.0 (IBM SPSS Corp.; Armonk, NY, USA). Student’s t test (for normally distributed variables) and Mann Whitney u tests (for variables without normal distribution) were used to compare numerical variables in groups. Kaplan Meier method was used to calculate survival probabilities. P <0.05 was considered significant.

**RESULTS**

Regardless of the reasons for performing thymectomy, we examined the demographic data, symptoms, surgical approaches, resection width, and histopathological diagnosis of all patients. In addition, we obtained the survival analyses of all patients who underwent thymectomy. The invasion status of patients undergoing extended thymectomy and the resections and recon-

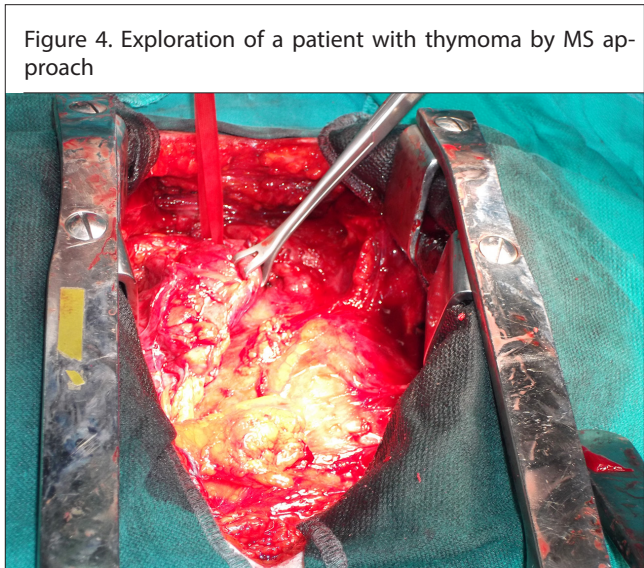


Figure 4. Exploration of a patient with thymoma by MS approach

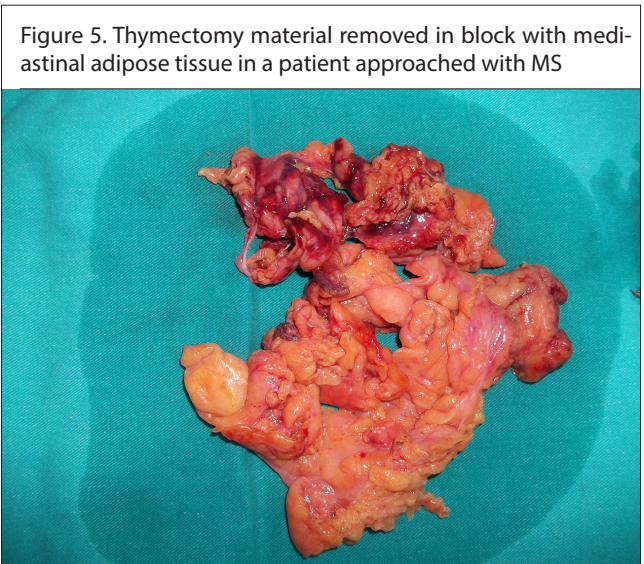


Figure 5. Thymectomy material removed in block with mediastinal adipose tissue in a patient approached with MS



Figure 6. Thoracoport incisions in right VATS approach

**Table 1.** Distribution of all patients undergoing thymectomy by age and gender

	Under 20	20–29 years	30–39 years	40–49 years	50–59 years	60 years and over	Total n (%)
Female n (%)	4 (5%)	11 (13,75%)	4 (5%)	6 (7,5%)	8 (10%)	5 (6,25%)	37 (46,25%)
Male n (%)	–	8 (10%)	10 (12,5%)	14 (17,5%)	6 (7,5%)	4 (5%)	43 (53,75%)
Total n (%)	4 (5%)	18 (22,5%)	14 (17,5%)	20 (25%)	14 (17,5%)	9 (11,25%)	80 (100%)

Figure 7. Thymic lesion and mediastinal adipose tissue in the patient approached with right VATS

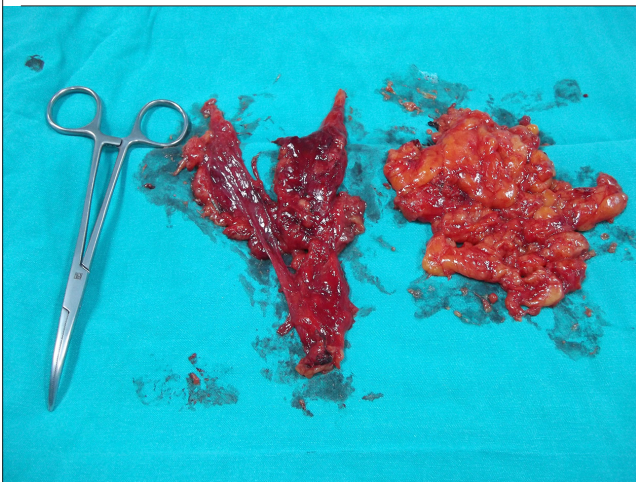
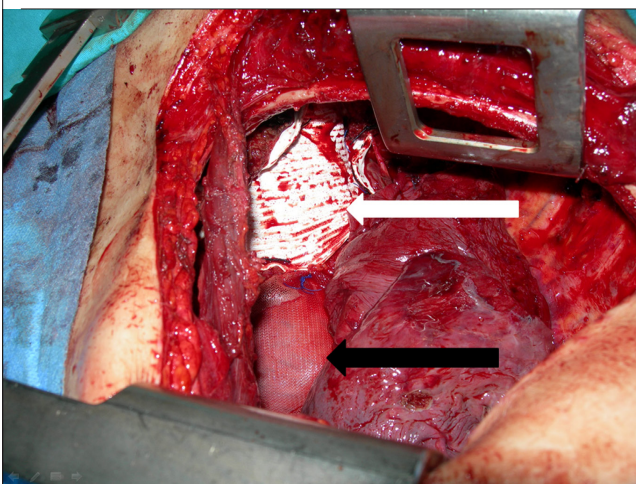


Figure 8. Diaphragmatic graft (white arrow) and pericardial graft (black arrow) after resection in a patient with diaphragm and pericardial invasion



structions applied to anatomical structures depending on this invasion are given in table 3. We delayed the analysis on the improvement in the clinical condition of MG patients because it is seen in the long term. However, we analyzed the connection between MG and histopathological diagnosis.

**Demographic Data**

Of the 80 patients included, 38 (47.5%) were women and 42 (52.5%) men. The age range of the patients was 17–74 years and

the mean age was 40.6±14.7 years. Concerning the age distribution by gender, the age range of women was 17–72 years (mean 39.1), and that of men was 20–74 years (mean 41.7) (Table 1).

**Symptoms**

Table 2 shows the distribution of the symptoms, which were mostly associated with MG. None of the 8 asymptomatic patients (10%) had MG.

**Surgical Method**

MS was most commonly used, followed by right VATS. Table 3 shows the number of malignancy and number of patients with MG according to the surgical approach used.

In our clinic, before 2008, thymectomies were performed by MS. Of the 20 patients who underwent right VATS, 11 (55%) were patients with non-thymomic MG. Only one (5%) of the 20 patients who underwent thymectomy through right VATS had a thymoma.

**The Rate Of Surrounding Organ Invasion In Extended Thymectomies**

Invasion into the surrounding anatomical structures was detected in 13 (16.25%) patients, 10 with thymoma, and 3 with thymic carcinoma. While 4 (5%) of these patients had macroscopic residues, 9 (11.25%) were completed with no residue (Table 4). Invasion of more than one anatomical structure was frequently seen in the same patient (Figure 8).

Eight (10%) patients had lung invasion in various degrees and localizations (Figure 9).

Six patients (7.5%) underwent various levels of resection and reconstruction of the vascular structures due to invasion (Figure 10).

One of three patients with phrenic nerve invasion had MG, and a residual tumor was left on the phrenic nerve. The phrenic nerve of the other two patients was resected.

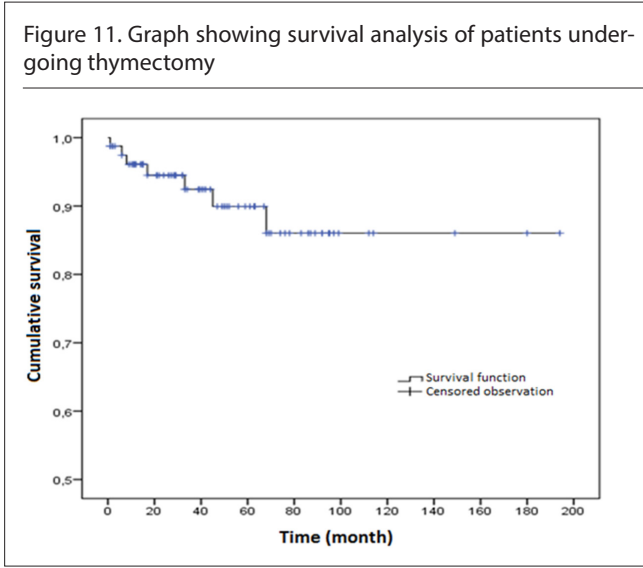
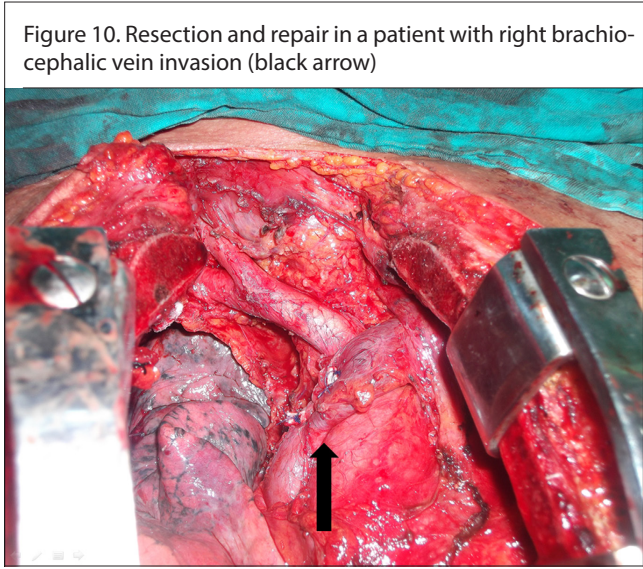
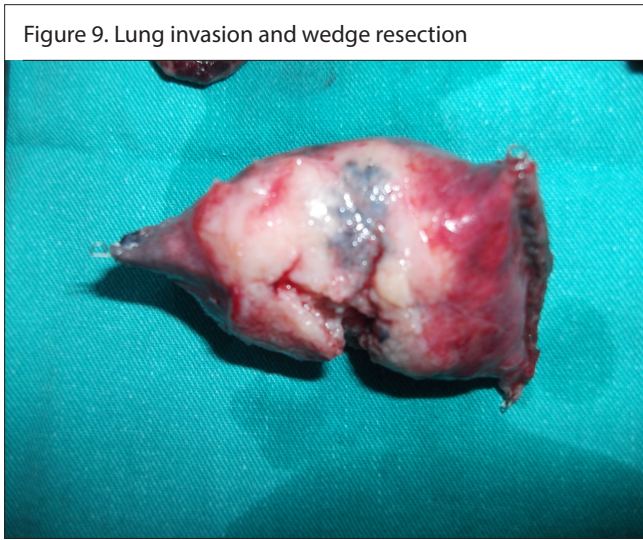
One patient with thymoma underwent pleurectomy for pleural invasion, and intracavitary hyperthermic perfusion chemotherapy (HIPEC) was performed after the operation.

**Histopathological Evaluation**

Histopathological results of the 80 patients who underwent thymectomy showed thymoma and thymic hyperplasia (Table 5).

**Survival**

Six of the 80 patients who underwent thymectomy died during follow-up, and one died early in the postoperative period. Figure



**Table 2.** Application symptoms of patients undergoing thymectomy

Symptoms	number	%
Rapid fatigue	37	46,3
Drooping of eyelides	26	32,5
Difficulty swallowing	19	23,8
Chest pain	17	21,3
Difficulty breathing	14	17,5
Difficulty speaking	7	8,8
Cough	2	2,5
Swelling of the face and neck	2	2,5
Hemoptysis	1	1,3
Frequent expectoration	1	1,3
Hoarseness	1	1,3
Arm pain	1	1,3
Backache	1	1,3
No symptoms	8	10

**Table 3.** Malignancy and MG rates according to the surgical approach

Surgical Approach	Number of		
	Cases	Malignant	MG
Median Sternotomy, n (%)	50	34 (68%)	30 (60%)
Right VATS, n (%)	20	1 (5%)	11 (55%)
Left VATS, n (%)	4	2 (50%)	0 (0%)
Right Thoracotomy, n (%)	4	3 (75%)	0 (0%)
Left Thoracotomy, n (%)	2	1 (50%)	1 (50%)

11 shows the survival analysis of patients undergoing thymectomy. The causes of death of patients are:

- Myocardial infraction on postoperative day 11 in 1 patient
- Heart failure in two patients, one at the 6<sup>th</sup> postoperative month and the other at the 68<sup>th</sup> postoperative month
- Myasthenic crisis in two patients, one at the 8<sup>th</sup> postoperative month and the other at the 17<sup>th</sup> postoperative month
- Thymoma in one patient at the 38<sup>th</sup> postoperative month
- Non-hodgkin lymphoma in one patient at the 45<sup>th</sup> postoperative month

The average life expectancy of the patients was 171.8±8.8 months.

**MG-Histopathology Relationship**  
 Histopathologically, 54% of patients diagnosed with thymoma had MG, while 47.6% of patients with MG had a thymoma. The number of non-MG and non-thymoma patients was 17 (21.25%).

**Table 4.** Invasive structures and resection rates in patients approached with MS

	Invasion n (%)	Resection n (%)	Grafting n (%)	Residue n (%)
Pericardium	10 (%12,5)	10 (%12,5)	5 (%6,25)	1 (%1,25)
Lung	8 (%10)	7 (%8,75)	–	1 (%1,25)
Vascular	6 (%7,5)	4 (%5)	3 (%6)	2 (%2,5)
Phrenic nerve	3 (%3,75)	2 (%2,5)	–	1 (%1,25)
Diaphragm	1 (%1,25)	1 (%1,25)	1 (%1)	0 (%0)
Pleura	1 (%1,25)	1 (%1,25)	–	0 (%0)
Atrium	1 (%1,25)	0 (%0)	–	1 (%1,25)

**Table 5.** Histopathological diagnoses after thymectomy

Histopathological diagnosis	Number	%
Thymoma	37	46,25
Thymic hyperplasia	29	36,25
Thymic carcinoma	4	5
Thymus tissue	4	5
Thymolipoma	4	5
Thymic cyst	2	2,5
Total	80	100

**Table 6.** The relationship between MG with histopathological diagnosis of patients undergoing thymectomy

Histopathological diagnosis	Patients with MG (n)	Patients without MG (n)	Total (n)
Thymoma	20	17	37
Timic hyperplasia	14	15	29
Timic carcinoma	–	4	4
Normal thymus tissue	4	–	4
Thymolipoma	4	–	4
Thymic cyst	–	2	2
TOTAL	42	38	80

Table 6 shows the relationship between MG and histopathological diagnosis.

**DISCUSSION**

Mediastinal masses arise from tissues normally located in the mediastinum or which migrated to the mediastinum during their development. The most common lesions in adults are thymomas, which are located in the anterior mediastinum (13, 14). Approximately 25% of all mediastinal tumors in adults and children are

malignant (15). We did not include patients aged ≤16 years. Thirty-seven (46.25%) of 80 patients who underwent thymectomy were diagnosed with different histopathological types of thymoma and 4 (5%) were diagnosed with thymic carcinoma (Table 7).

Most patients with thymoma (50–60%) were asymptomatic. Symptoms depend on the compression effect of the lesion on the surrounding tissues or systemic disease accompanied by the thymoma (6, 16, 17). According to our study, the most common symptoms in thymoma patients were those associated with MG.

While 30% of patients with thymomas have MG, approximately 10–15% of patients with MG had thymoma. In our study, 54% of patients diagnosed with thymoma had MG and 47.6% of patients with MG had thymoma. The coexistence of MG and thymoma in our study group was high, because all patients who apply to our clinic with thymic lesions were diagnosed with MG. This increased the number of patients with MG.

Literature on the form of excision had divided opinions some adopt sternotomy and others advocate the method that protects the sternum (11).

Most people advocate the transsternal thymectomy method because it extends out of the capsule (18). Stage I thymomas may relapse or metastasize although they are histologically mild in those who undergo transsternal thymectomy (19).

Advocates of the transcervical approach say that it is possible to see the anterior mediastinum directly with advanced imaging methods (20).

In a study in which minimally invasive thymectomy was recommended, VATS was considered safe and had a comparable resection rate when selectively used in MG and small thymic masses (21).

Minimally invasive approaches such as videothoroscopic, transcervical, and robotic surgery can be applied in early stage thymomas but no large series exist on this issue. Therefore, MS is still the most valuable approach for complete resection (22).

In our study, MS was used in patients with thymomas radiologically seen before surgery. However, if the tumor was encapsulated, there was no invasion into the surrounding tissue and the tumor could be removed with mediastinal fatty tissue using VATS or thoracotomy. Nevertheless, the results of multi-patient studies are needed to confirm that minimally invasive methods provide complete resection and complete remission.

Among patients with MS, 32% had benign thymic. This rate was 40.9% before the thoracoscopic approach, and decreased to 25% after its start. This may indicate that the minimally invasive approach is more rational in cases that we consider to be histopathologically benign.

Today, there is consensus on the application of surgery to ocular MG patients who cannot be controlled by ACE common MG and

patients (23, 24). Unfortunately, appropriate patient selection criteria for remission have not been defined. Likewise, the size required to perform surgery is not exactly defined (25). In the study by Toker, thymectomy was presented as a reliable surgery in MG patients (26). The current approach of our clinic was used MS only in MG patients who have radiologically thymoma images.

There is no standard treatment approach defined for thymic carcinoma, nor is there a universally accepted staging system. The most common approach is RT, CT, or both following surgical resection. Unfortunately, most tumors are not resectable and the effect of surgery is unclear. Most patients experience local and distant disease recurrence (6, 16).

In our study, there were four patients operated for thymic carcinoma. The symptoms of these patients were due to the lesion pressing on the surrounding tissue. There is no MG in our patients with thymic carcinoma. All patients were subjected to CRT before or after surgery according to the resectability condition.

Thymic benign lesions are thymic hyperplasia, thymic cysts, and thymolipoma. Surgical resection of benign thymic lesions can be performed by many methods depending on the size of the tumor, the body condition of the person, and the experience of the surgeon (27).

The histopathological results of 39 patients included in our study were benign. Among these patients, thymic hyperplasias accounted for 74.3% of benign thymic lesions. No recurrence was observed in the follow-up of patients with benign thymic lesions. Especially non-MG non-thymoma patients are excellent candidates for VATS.

## CONCLUSION

Thymectomies can be performed using various methods as curative treatment in malignant or benign thymic diseases and to contribute to the treatment of the disease in MG. Although there is not much discussion on the indication of thymectomy, there are differences in opinion regarding the method used. MG and thymic lesions have important health problems and change the comfort of patients. Because these patients may have a long hospital stay, it is very important for patients who will undergo thymus surgery, especially those with MG, to be treated in a hospital near their home. We would therefore continue developing ourselves as the center where these surgeries are most frequently performed in the Southeastern Anatolia Region.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Gaziantep University (05.05.2014 / 167).

**Informed Consent:** Informed consent was obtained from the patients who participated in this study.

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B.T., A.F.; Literature Search - B.E., B.T., M.Ş.; Writing Manuscript - B.E.; Critical Review - B.E., B.T., M.Ş., A.F.I.; Other - B.E., M.Ş.

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