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Video-Assisted Thoracoscopic Thymectomy as an Optimal Treatment in Myasthenia Gravis

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ABSTRACT

Background: Myasthenia gravis is a neurological disorder characterized by muscle weakness. The role of thoracoscopic thymectomy in the treatment of this disease is controversial, but has some advantages that include less pain, shorter hospital stays, and better cosmetic results.
Objectives: After the introduction of video-assisted thoracoscopic surgery (VATS) thymectomy, there has been increased interest in the use of this technique for myasthenia gravis. We conducted a retrospective study to assess the safety and efficacy of VATS thymectomy in treatment of myasthenia gravis.
Patients and Methods: The medical records of 50 patients who underwent VATS thymectomy for the treatment of myasthenia gravis between May 2005 and June 2010 in Afzalipour Hospital, (affiliated to Kerman Medical University of Sciences, Iran) were reviewed. The patients were examined for response to treatment; for patients who were not available for examination, data was obtained through telephone conversations.
Results: Forty-three of 50 patients were accessible. Of these, 34 were female and 16 were male, with a mean age of 34.8 years. The treatment responses were remission, 6 (16%); improvement, 30 (70%); and without change, 7 (16%). The total positive response to treatment was 84 percent.
Conclusions: VATS thymectomy has been considered as a safe and effective treatment in myasthenia gravis and was associated with low mortality and morbidity. VATS thymectomy is recommended for the treatment of myasthenia gravis.

▸ *Implication for health policy/practice/research/medical education:*
This article is a study that can show the role of minimal invasive thymectomy in patient with myasthenia gravis. This article could be useful for researchers and students who are interested in the fields of neurology, immunology and thoracic surgery.

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1. Background

Myasthenia gravis is a chronic disease that affects postsynaptic cholinergic receptors and presents with intermittent fatigue and weakness in striated muscle (1, 2). It occurs at a rate of 2 cases per 100,000 people annually. Most presented classifications of myasthenia gravis are alterations of Osserman's, sorting out patients with only ocular involvement from with generalized weakness, and additional separating with mild, moderate, or severe generalized weakness. Osserman classifications have included grouping based on the course of disease, such as "acute fulminating" and "late severe", and also included categories for muscle atrophy and childhood beginning (3). The role of surgery and the most effective surgical techniques for the treatment of this disease are controversial among surgeons and neurologists (4). Thymectomy may be useful for many patients, but some neurologists may not refer patients for surgery because of their concern regarding complications and their doubts about the role of surgery in the treatment regime (1).

2. Objectives

There are various surgical techniques for the treatment of myasthenia gravis, including transcervical thymectomy, transsternal thymectomy, and video-assisted thoracoscopic surgery (VATS) thymectomy (5, 6). The efficacy of VATS thymectomy is controversial, but its potential advantages include shorter hospital stays, less postsurgical pain, and better cosmetic results (7). To show our experience with this technique, we conducted a retrospective study to assess the safety and efficacy of VATS thymectomy in myasthenia gravis.

3. Patients and Methods

The medical records of patients who underwent VATS thymectomy for myasthenia gravis from August 2005 to August 2010 were reviewed. The data that was collected included age and sex, severity of the disease based on Osserman's criteria, duration of surgery, conversion to open surgery, complications and mortality of surgery, stay duration in intensive care unit (ICU), stay duration in hospital, and histopathological assessment of the thymus. The patients were examined for response to treatment as well. For patients who were not accessible for examination, data was obtained through telephone conversations. The response to treatment was evaluated on the basis of remission, improvement, lack of change, and progress of the disease. The surgery was performed by two thoracic surgeons: one had expertise in using a left-sided approach and the other in using a right-sided approach. Our surgical procedure involved the following steps. Under general anesthesia administered using a double lumen endotracheal tube, the patient was positioned in a left or right semi lateral position depending on the intended left or right VATS approach. The skin preparation was performed in such a way that conversion to sternotomy or thoracotomy was possible, if necessary. The intercostal ports were made in the second and fourth intercostal spaces along the maxillary line and in the fifth space along the anterior axillary line. The clear view of the mediastinum allowed dissection of the entire pericardial fat and thymus, which was performed by using routine devices, such as a grasper, scissors, and ligature. Dissection of the thymus from its inferior border anterior to the phrenic nerve was performed. The thymic vein clipped and cut in early cases and incised with Ligature in later cases. The dissection was performed to the upper corners of the thymus, and the thyrothymic adhesions were cut. The specimen was removed through the anterior axillary port, and after insertion of a chest tube via the posterior axillary port, the other ports were closed in a routine manner. All of the patients were routinely transferred to the ICU following surgery. Results were presented as means ± standard deviations for continuous data and absolute or relative frequency for categorical data. The chi-square was used to determine the association between response to treatment and histopathology with assistance of SPSS version 16 (SPSS Inc, Chicago, IL, USA).

4. Results

There were 50 patients, including 34 (68%) females and 16 (32%) males. The patients ranged in age from17 to 77 years, with a mean age of 34.8 years. Contact to 7 patients was not possible therefore the evaluation of the response to surgery was performed among 43 patients. The mean duration of disease prior to surgery was 17.6 months, with a range of 15 days to 96 months. The most severe

Table 1. Characteristics of Patients Who Underwent VATS Thymectomy

	Value, No. (%)
Disease severity [a]	
Class 1	4 (7.8)
Class 2	15 (36)
Class 3	25 (51)
Class 4	5 (10.2)
Side of operation	
Right	28 (56)
Left	22 (46)
Reason of conversion to open surgery	
Adhesion	
Bleeding	4
Lack of innominate vein exposure	3
Complications	1
Prolonged ventilation support	6 (11.9)

[a] Disease severity is based on Osserman's grading and in one patient was unknown.

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grade of myasthenia gravis was class 3, which was detected in 51% of the patients *(Table 1)*. A slightly higher number of patients were treated with the right-sided procedure *(Table 1)*. The duration of surgery was 228.64 ± 64.22 minutes, with a range of 120 to 480 minutes. The length of the hospital stay was 4.8 ± 3.1 days and the length of the ICU stay was 3.4 ± 2.7 days. The most common cause of conversion to open surgery, which occurred in 8 patients, was adhesion of the thymus to adjacent organs *(Table 1)*. The sole postsurgical complication was prolonged respiratory support *(Table 1)*, and no mortality occurred. The duration of follow-up for response to treatment following surgery was 3.2 ± 1 years. Remission occurred in 6 (14%) patients, improvement was observed in 30 (70%) patients, and no change in the disease state was detected in 7 (16%) patients. The histopathological analysis of the thymus showed thymoma in 8 (16%) patients, follicular hyperplasia in 17 (34%) patients, and normal thymus in 25 (50%) of patients. There was no relationship between the histopathological results and response to treatment ($P = 0.422$), but there was relationship between these results and conversion to open surgery and patients with thymoma was more common ($P = 0.00$) *(Tables 2* and *3)*

5. Discussion

VATS thymectomy was introduced in 1992 as a minimally invasive procedure (8). Since the thymus is located mainly in the anterior mediastinum, VATS can provide an extensive view with appropriate contrast and magnification of view, and these factors are essential for dissection in thymectomy (1). Because thymectomy via sternotomy has disadvantages such as increased pain, prolonged postsurgical remission time, and respiratory problems like respiratory distress, many physicians and patients might not choose this method of treatment (9). The transcervical approach to thymectomy may leave behind a part of the thymus, and for the reason that lack of good exposure, this technique is not recommended by many surgeons (9, 10). Since the introduction of VATS thymectomy, many studies have been conducted to compare the costs of treatment, length of hospital stay, and cosmetic aspects of this technique to those of open procedures (11). However, there have been few randomized clinical trials due to prolonged period of treatment for myasthenia gravis and the heterogeneity and fluctuation in severity of this disease (1). Various studies have been conducted on the length of hospital stay and mortality of VATS thymectomy, and some are listed in *Table 4*. In the present study, the length of hospital stay and ICU admission period were 4.8 and 3.4 days, respectively, and complications were detected in 11.9% of patients, which are similar to those observed in former studies. Prolonged respiratory support was assessed as a complication in our study, but there were no other types of postsurgical complications observed *(Table 4)*. Similar to the results from other studies, no mortalities occurred in our series of patients, which strongly suggests that VATS thymectomy is a safe procedure (9).

Table 2. Correlation Between Histopathology and Response to VATS Thymectomy

	Response to VATS Thymectomy [a], No. (%)		
Histopathology of the Thymus	Remission	Improvement	No Change
Thymoma	2 (33.3)	4 (66.7)	0 (0.0)
Normal Thymus	2 (9.5)	14 (66.7)	5 (23.8)
Follicular Hyperplasia	2 (12.5)	12 (75)	2 (12.5)

[a] *P* value = 0.422

Table 3. Correlation Between Histopathology and Conversion to Open Surgery

Histopathology	Complete VATS, No. (%)	Conversion to Open Surgery [a], No. (%)
Thymoma	3 (37.5)	5 (62.5)
Normal thymus	24 (96)	1 (4)
Follicular hyperplasia	15 (88.2)	2 (11.2)

[a] ***P* value** = 0.00

Table 4. Length of Hospital Stay and Morbidity Rates for Video-Assisted Thoracoscopic Surgery Thymectomy Performed in Former Studies

	Sample size	Morbidity, %	Hospital Stay, d
Sarvcenko *et al.* (2002) (12)	36	5	1.6
Wright *et al.* (2002) (13)	26	4	4
Manlulu *et al.* (2005) (1)	36	11	3
Tumulescu *et al.* (2009) (14)	107	9	2.3
Lin *et al.* (2010) (15)	38	5	5.6

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Table 5. Comparison in Improvement and Remission for video-assisted thoracoscopic surgery (VATS) and Transthoracic Open Thymectomy (TT) Between Present and Former Studies

	Sample Size	Type of Procedure	Remission, %	Improvement, %
Sarvcenko *et al.* (2002) (12)	36	VATS	14	83
Wright *et al.* (2002) (13)	26	VATS	27	81
Manlulu *et al.* (2005) (1)	36	VATS	22.2	92
Tumulescu *et al.* (2009) (14)	107	VATS	59.3	97.2
Meyer *et al.* (2009) (16)	48	VATS	34.9	95.4
Lashkarizade *et al.*	43	VATS	14	84
Calhoum *et al.* (1999) (17)	100	TT	35	85
Shrager *et al.* (2002) (18)	78	TT	39.7	---
Shrager *et al.* (2003)	120	TT	41	---
de Perrot *et al.* (2003) (19)				
Shrager *et al.* (2006) (20)	151	TT	37.1	79.5

The rates of remission and improvement in myasthenia gravis in our patient were 14% and 84%, respectively. The responses to treatment after VATS and transthoracic thymectomy are presented in *Table 5*. Meta-analysis studies have shown that remission after VATS thymectomy is achieved in 17% to 52% of patients and improvement in 56% to 97% of patients (8). The improvement rate of our patients folowing VATS thymectomy was similar to that reported in other studies for VATS thymectomy, but the remission rate appeared to be slightly lower, which is probably related to the mid-term follow-up of our patients. The response to VATS thymectomy was similar to or better than that shown by transthoracic thymectomy *(Table 5)* however VATS thymectomy is preferred because it results in fewer postsurgical pain and better cosmetic results (21). In the present study, half of the patients had normal histopathology of the thymus, and no relationship was detected between the pathology of the thymus and response to treatment. In 2003, Mantegazza and colleagues reported that the response to treatment after VATS thymectomy in patients with follicular hyperplasia was better. In the study of Magtegazza, follicular hyperplasia occurred in half of the patients, but in our study, normal histopathology of the thymus was observed in half of the patients (22). Conversion to open surgery occurred in 4 of our patients with thymoma, and a relationship was detected between thymoma and conversion to open surgery. This seems logical because adhesion or invasion to adjacent organs may be more prevalent and exposure more limited in patients with thymoma than in patients without. In myasthenia gravis patients with thymoma, open thymectomy has been suggested and VATS thymectomy may be performed by surgeons who have sufficient experience with the procedure (23). On the other hand, limitation of our study was the mid-term follow-up, i.e., there was no follow-up on some of the patients. Similar to the conclusions reached by other researchers, we believe that VATS thymectomy is the suggestible procedure for patients with myasthenia gravis since it provides an excellent surgical field, is less invasive and quicker than the alternatives, shows improved patient recovery, and has better aesthetic outcomes (9). VATS thymectomy is suggested for patients with myasthenia gravis because of its fewer complication rate and satisfactory patient responses. In myasthenia gravis patients with thymoma that shows no adhesion to adjacent organs, VATS thymectomy can be performed, but patients should be advised that there may be a somewhat higher risk for conversion to open surgery.

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Authors' Contribution

Study concept and design: Lashkarizadeh, Ajami, Baghai Wadji. Analysis and interpretation of data: Ajami, Baghai Wadji. Drafting of the manuscript: Vahedian, Pourseyedi. Critical revision of the manuscript for important intellectual content: Zeynali, Samareh Fekri, Baghai Wadji. Statistical analysis: Lashkarizadeh.

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None declared.

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