

Clinical Outcomes Following Extended Thymectomy for Myasthenia Gravis: Report of 17 Cases

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Purpose: This retrospective study was undertaken to assess the changes in the clinical status of patients with generalized myasthenia gravis (MG) treated with extended thymectomy and to identify prognostic variables that may be of significance in optimizing patient selection.

Patients and Methods: We reviewed the clinical outcomes of 17 patients who underwent extended thymectomy for MG. Main factors influencing the outcome are changes in clinical stage and medication requirement before and after thymectomy, age, sex, duration of disease, stage of disease, antibody status, histological characteristics of the thymus, and duration of follow-up.

Results: There was remission in 4 patients (23.5%), improvement in 9 patients (53%), and no change in 4 patients (23.5%). Patients in Osserman stage IIB and with a higher rate of decrease in acetylcholine receptor (AChR) antibody ratio showed a greater degree of postoperative improvement. Age of the patient, sex, presence or absence of thymoma, and time elapsed between diagnosis and operations were not found to be significant prognostic factors.

Conclusion: The present study demonstrated that extended thymectomy for MG is an effective therapy with no great morbidity or mortality. Patients in preoperative stage IIB and with higher rate of change in the AChR antibody titer showed the greatest degree of postoperative improvement. (*Ann Thorac Cardiovasc Surg* 2006; 12: 203–6)

Key words: myasthenia gravis, thymectomy, thymoma, antiacetylcholine receptor antibody

Introduction

Myasthenia gravis (MG) is an organ-specific autoimmune disorder characterized by weakness and fatigue of the voluntary muscles. It is believed to be caused by an antibody-mediated attack against the skeletal muscle nicotinic acetylcholine receptor (AChR) at the neuromuscular junction. The weakness tends to increase with re-

peated activity and improves with rest. Ptosis and diplopia occur early in a majority of patients. The disease may affect the limb muscles as well as the diaphragm and the neck extensors. A patient requiring mechanical ventilation due to severe respiratory weakness is said to be in crisis.¹⁾ MG is extremely rare, with a prevalence of 50 to 125 cases per million population. The condition may affect individuals in any age group, with a peak incidence in females in their thirties and forties and in males aged between 60 and 70 years.²⁾

Medical treatment involves the use of anticholinesterase agents, immunosuppressive drugs, plasmapheresis, and gammaglobulin; this has been reported to provide low complete clinical remission. Currently, thymectomy is recognized as a standard effective therapy complementing the medical management of patients with MG. The extent of thymic resection and the operative approach have become subjects of increasing controversy. With the ad-

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vent of minimally invasive video-assisted thoracoscopic thymectomy, traditional transsternal and transcervical thymectomy are rarely performed.

Factors that influence the response to thymectomy still remain controversial. A number of factors influencing the success of thymectomy for MG have been reported.

The purpose of the present study was to assess the results obtained by extended thymectomy for MG in a series of 17 patients as well as to determine the major prognostic factors influencing the postoperative outcome.

Patients and Methods

We reviewed the clinical outcomes of 17 patients who had undergone extended thymectomy for MG at Hakodate Ishikai Hospital between 1987 and 2001. Patient data covering a time period of 6 months to 14 years was available for our review. Osserman classification was used for staging; patients' clinical stage distribution was as follows: grade I, ocular involvement; grade IIA, mild generalized ocular myasthenia; grade IIB, moderate generalized myasthenia involving bulbar musculature; grade III, acute fulminant form; and grade IV, severe late myasthenia. All the patients had undergone extended thymectomy that includes complete en-bloc extirpation of thymic and adjacent tissue including fatty tissue through median sternotomy. Postoperatively, all patients received medical treatment with one or more therapies that include anticholinesterase agents and corticosteroids. The responses to thymectomy were classified as remission, improvement, no change, worse, or death (Table 1). The rates of remission and improvement were calculated. In our study, the factors that presumably influence the prognosis after

extended thymectomy are as follows: age of the patient, sex, presence or absence of thymoma, clinical status according to Osserman classification, the AchR antibody decrease ratio (the serum titer at 1 month after operation/preoperative titer), and time elapsed between diagnosis and operation.

Mann-Whitney's U test and Paired t-test were used to assess the significance between groups and a probability of less than 0.05 was considered significant.

Results

The clinical outcome of all patients is summarized in Table 2. After extended thymectomy, 4 patients (23.5%) showed remission and 9 patients (53%) showed improvement. The mean age of patients was 42+19 years, with a range of 18 to 77 years; 13 (76%) patients were females and 4 (24%) were males.

Preoperatively, the duration of symptoms ranged from 1 month to 6 years (mean, 15 months).

Osserman classification yielded the following results: grade I, 4 patients; grade IIA, 7 patients; grade IIB, 6 patients. No patients met the criteria for grades III and IV.

Postoperative pathologic study of the thymus revealed thymoma in 7 cases (41%), hyperplasia in 6 cases (35%), thymus in 3 cases (18%), and fat tissue in 1 case (6%).

No postoperative morbidity or mortality was seen.

One patient (6%) died of acute myocardial infarction within 5 years of operation.

AchR antibody fold titer, this difference was statistically significant (Fig. 1).

Patients in Osserman grade IIB were most likely to reach remission and show improvement; this difference was statistically significant ($p=0.03$).

Discussion

MG remains a potentially debilitating and life-threatening illness despite progress in therapy. The benefit of thymectomy as a part of the treatment of MG has been repeatedly demonstrated since the initial observations of Blalock et al. in 1939.³⁾ The specific clinical features that are considered as indications for operation remain ill-defined and controversial. Most clinicians reserve the procedure for selected patients with generalized disease, with consideration given to factors such as age, severity of symptoms, response to medication, and duration of disease.⁴⁾

The need for complete removal of thymic tissue is based on the current understanding of thymic embryol-

Table 1. Classification of postoperative response

Response	Symptom/medication
Remission	None/none
Improvement	Improve/decrease
	Improve/unchange
	Improve/increase
	Unchange/decrease
No change	Unchange/unchange
Worse	Worse/increase
	Worse/unchange
	Unchange/increase
Death remission rate	
= numbers of remission/total (%)	
Improvement rate	
= number of remission and improvement/total (%)	

Table 2. Summary of clinical course of 17 patients in this study

Patient no.	Age (y)	Sex	Duration of symptoms (day)	Osserman classification	Pathologic study	Outcome
1	59	M	148	I	Thymoma	Remission
2	68	M	71	I	Thymoma	Improvement
3	64	M	316	I	Thymoma	No change
4	77	F	26	I	Thymoma	No change
5	58	F	1,300	IIA	Fat tissue	Improvement
6	69	F	250	IIA	Thymus	Improvement
7	23	F	137	IIA	Thymus	Improvement
8	23	F	83	IIA	Hyperplasia	No change
9	33	F	86	IIA	Thymoma	Improvement
10	32	F	75	IIA	Thymoma	Improvement
11	60	F	2,204	IIA	Thymoma	No change
12	42	F	339	IIB	Hyperplasia	Remission
13	18	F	138	IIB	Hyperplasia	Remission
14	36	M	1,897	IIB	Hyperplasia	Remission
15	26	F	240	IIB	Hyperplasia	Improvement
16	22	F	335	IIB	Hyperplasia	Improvement
17	54	F	204	IIB	Thymus	Improvement

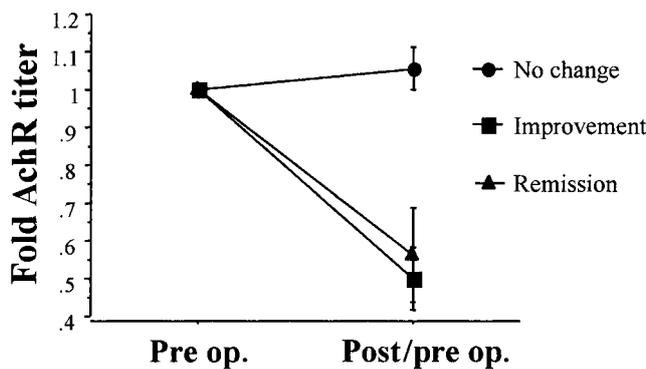


Fig. 1. Preoperative and postoperative AchR antibody fold titer was found to be statistically significant.

*p=0.0247, §p=0.0054 (Mann-Whitney’s U test).
 †p=0.0397, #p=0.0002 (Paired t-test).

ogy and the immunologic basis of MG. The thymus arises from the third and fourth branchial arches and migrates caudally. Fusion of the gland results in the traditionally described four-lobed structure. The lower lobes of the thymus tend to leave thymic corpuscles scattered throughout the mediastinal fat.⁵⁾ The symptoms of MG are the result of the destruction of AchR. This appears to be a consequence of both T cell and humorally mediated components of the immune system.⁶⁾ The exact mechanism by which the thymus affects the course of MG is unclear. It is likely, however, that thymectomy removes a source of auto sensitization and depletes the specific T-suppressor cell population responsible for the AchR breakdown.⁷⁾

In this study, 53% patients who underwent extended thymectomy showed improvement, and 23.5% of all the patients achieved remission. The clinical condition of 4 patients remained unchanged, and deterioration was not observed in any patient. Furthermore, 9 of the 17 patients in this study experienced clinical improvement following extended thymectomy indicated by a lower Osserman stage, decreased medication, or both. These results are consistent with other reported data.⁸⁻¹¹⁾

Clinical factors positively influencing the outcome of MG following thymectomy have been reported to include age, sex, preoperative stage, duration of symptoms, and the presence or absence of thymoma.^{2,12,13)}

Evaluation of a variety of prognostic factors yielded mixed results. Although a greater improvement has been described in female patients¹⁴⁾ and in younger patients,^{9,15)} most other studies have shown no age or sex related bias,^{10,11)} our results agree with the results of these studies.

A potentially important observation in this study is that preoperative duration of symptoms has no independent influence on the postoperative outcome. Most clinicians have noted that shorter duration of symptoms is associated with more favorable results after thymectomy.

Remission and improvement following thymectomy are occasionally delayed. Maggi⁹⁾ et al. found the best remission rate in patients is seen during the 5-10-year postoperative period and not prior to this period; this may be the result of immunologic “memory” or the disease process itself.

A better outcome after thymectomy for MG has been reported in the preoperative Osserman stages I and III,^{2,10} whereas we found a better remission and improvement rate in stage IIB.

There was no significant difference in the improvement between various histologic findings. Thymomas are known to be present in 9% to 16% of patients with MG and are associated with greater severity of MG.¹⁶ With few exceptions, thymectomy is undertaken in virtually all the patients having MG with thymoma. Previous studies^{10,17} have demonstrated that thymectomy in patients with thymoma is associated with a poorer outcome as compared to that in patients without thymoma.

Eighty-five percent of the patients have been found to be positive for anti-AchR antibodies; however, this titer does not correlate with the severity of symptoms.^{2,7} This finding suggests that the antibodies may vary in their capacity to produce myasthenic weakness. The functional activities of the antibodies in accelerating degradation or blocking AchRs have been shown to correspond closely to the severity of myasthenic weakness. This study suggested that the patients with a higher rate AchR antibody decrease ratio have optimal results.

There is a general consensus that patients with MG should be treated by thymectomy; the surgical approach to be used, i.e., transsternal, transcervical, or video-assisted remains controversial. The rationale for transsternal thymectomy is based on the fact that the thymus arises from several sites, and there may be ectopic nests of thymic tissue scattered throughout the anterior mediastinum and even in the retrothyroid space. For complete removal of the thymic tissue, a transsternal approach with anterior mediastinal dissection⁷ or a combined cervicothoracic approach¹⁸ has been suggested.

The present study demonstrated that extended thymectomy is an effective therapy for MG, with no great morbidity or mortality. Age of the patient, sex, presence or absence of thymoma, and time elapsed between the diagnosis and operation were not found to be significant predictors. Patients classified as Osserman stage IIB and higher rate of AchR antibody fold titer showed a greater degree of postoperative improvement.

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