

## **SURGICAL OUTCOME OF THYMECTOMY IN MYAESTHENIA GRAVIS – A CASE SERIES REVIEW**

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### **ABSTRACT**

**Background:** Myasthenia gravis is a rare autoimmune disease caused by antibodies that probably originate from the thymus glands. In recent years, thymectomy has become a widespread procedure in the treatment of myasthenia gravis (MG). Transsternal approach with thymectomy is the accepted standard surgical approach for many years.

**Aim:** To evaluate the outcomes of 60 patients who underwent thymectomy for myasthenia gravis, quantify the degree of clinical improvement after thymectomy by evaluating changes in stage and medication requirement, and identify prognostic factors that may be helpful in determining the best patient selection.

**Materials and Methods:** The study group consists of 60 myasthenic gravis patients who were admitted to Gandhi Hospital's Cardiothoracic Surgery Department and received a transsternal complete thymectomy between February 2014 and December 2022.

**Results:** 34 (56.7%) were males and 26 (43.3%) were females in the study. Females were aged between 9 to 60 years and mean age was 33.8 years. Before thymectomy, 21 patients were on anticholinesterase agents (Pyridostigmine). Post-operative pathologic study of thymus findings were reported as follows, hyperplasia of thymus was observed in 22 patients (36.6%), thymoma in 13 patients (21.6%), thymic carcinoma, atrophy in 5 patients (8.4%) and normal thymus in 20 patients (33.4%). 16 days was the mean hospital stay with 4 patients having prolonged hospital stay due to complications. Follow up ranged from 7 months to 10 years. Mean follow up is 2.5 years. Complete remission was observed in patients in Osserman stage I, IIA and IIB.

**Conclusion:** Thymectomy is recommended for patients younger than 60 years with non-thymomatous, generalized AChR antibody-associated myasthenia gravis. The early-onset, severe myasthenia gravis, female, thymic hyperplasia, benefit the most. Patients classified as Osserman Class IIA and IIB benefit most from this procedure.

**Keywords:** Thymectomy, myasthenia gravis.

### **Introduction:**

Myasthenia gravis is an autoimmune condition that weakens and exhausts the affected muscle group by affecting the postsynaptic acetylcholine receptors of voluntary muscle.<sup>1,2</sup> Anticholinesterase medications, immunosuppressive medications, plasmapheresis, and gammaglobulin are used in medical treatment, with documented complete clinical remission rates (CCRRs) of just 15%. Myasthenia gravis and the thymus have been linked since 1901, but Blalock et al<sup>3</sup> were the first to show that thymectomy is advantageous for the condition in 1939<sup>4</sup>. Since then, thymectomy has gained popularity as a therapeutic option for myasthenia gravis due to the fact that most studies published in the literature indicate that it can produce complete clinical remission rates as high as 80%. However, there is still debate over the best surgical technique, how much mediastinal dissection is necessary, and how to choose the right patients. The goal of the current study was to evaluate the outcomes of 60 patients who underwent thymectomy for myasthenia gravis, quantify the degree of clinical improvement after thymectomy by evaluating changes in stage and medication requirement, and identify prognostic factors that may be helpful in determining the best patient selection.

**Materials and Methods:** The study group consists of 60 myasthenic gravis patients who were admitted to Gandhi Hospital's Cardiothoracic Surgery Department and received a trans-sternal complete thymectomy between February 2014 and December 2021. The neurologist reviewed each patient before to surgery and made a diagnosis based on clinical signs and symptoms, a positive edrophonium chloride test result, and an electromyography test. Based on the modified Osserman classification, clinical staging was performed on all cases. Persistent generalised myasthenia gravis while on a medicinal regimen, persistent ocular myasthenia gravis while receiving the proper medicine, and the presence of a thymoma as determined by computed tomography are all indications for surgical surgery. Each patient had a standard chest x-ray and a chest computed tomography prior to surgery. The radioimmunoassay for acetylcholine receptor antibody level, immunoglobulin level, serum complement test, thyroid function test, and serum studies for antithyroid antibodies were among the laboratory tests that were performed. All 60 patients had trans-sternal thymectomy and median sternotomy. From the lower limit of the pericardium inferiorly to the cervical thymic extension superiorly and from one phrenic nerve to the other, all thymic tissue and anterior mediastinal fat were excised. In the cases of individuals with invasive thymomas, attempts were made to remove all affected tissue. General anaesthesia was used during surgical procedures. All of the patients were kept on mechanical ventilation in an intensive care unit following surgery. One hour prior to extubation, all patients who had received anticholinesterase inhibitors (AChEI) before surgery did so again. Age, sex, Osserman stage, medication needed, test results, length of disease, and coexisting medical conditions were all recorded prior to surgery. Time to extubation, thymic abnormalities, complications, and length of hospital stay were all noted after surgery. Patients were followed up after being released at various intervals; the average follow-up was 2.5 years. A neurologist conducted interviews with each patient, and specific information of work tolerance, Osserman stage, and

exercise tolerance pharmaceutical needs, side effects, and follow-up length was noted. According to Milichat and Dodge's follow-up criteria, the patients' responses to their thymectomy were rated. Complete clinical symptom remission and more than 90 days without using an anticholinesterase inhibitor Clinically significant improvement with reduced medication. medication-induced moderate clinical improvement. No progress or a stable clinical status that hasn't changed. Clinical deterioration with the same or higher dosages of medication. The Fisher exact test and analysis of variance were used to statistically analyse the data, with p 0.05 being considered significant.

**Results:** 60 myasthenic gravis patients were selected and were admitted to Gandhi Hospital's Cardiothoracic Surgery Department and received a trans-sternal complete thymectomy between February 2014 and December 2021.

Table 1: Classification of patients into grades based on Ossermans classification.

Class/Grades	Number of patients	Percentage
I	10	16.7%
IIA	28	46.7%
IIB	15	25%
III	4	6.6%
IV	3	5%

Table 1 shows that application of Ossermans classification yielded grade I-10 patients; grade IIA-28 patients; grade IIB – 15 patients, grade III-4 patients and grade IV- 3 patients.

Table 2: Sex distribution, time elapsed from diagnosis to operation.

Sex	Number of patients	Percentage
Males	34	56.7%
Females	26	43.3%
Time elapsed	Number of patients	Percentage
2 years	45	75%
>2 years	15	25%

Table 2 shows that 34 (56.7%) were males and 26 (43.3%) were females and time elapsed from diagnosis to operation in 45 patients (75%) was 2 years and more than 2 years in 15 patients (25%).

Females were aged between 9 to 60 years and mean age was 33.8 years.

Table 3: Medication requirement.

Drugs	Before Surgery	After Surgery
Pyridostigmine	21	9
Pyridostigmine+Azathioprin	16	9
Combination+pheresis	15	10
Steroids	3	--
Pyridostigmine+steroids	5	--
None	--	32

Table 3 shows that before thymectomy, 21 patients were on anticholinestrase agents (Pyridostigmine), 3 were on corticosteroids, 5 were on anticholinestrase (Pyridostigmine)+steroids, 16 were on anticholinestrase (Pyridostigmine)+immunosuppresants (Azathioprin), 15 patients were on combined regimen of the drugs and had undergone plasmapheresis.

Table 4: Complications.

Type of Complications	Complications	Number of patients
Post-operative complication	Right sided pneumothorax	2
	Left lower lobe pneumonia	1
	Surgical wound infection	1
	Severe Myasthenic crisis	11
Late complication (3 months after surgery)	Thymoma recurrence	2
	Sinus over sternal region	1

Table 4 shows that 4 patients had post-operative complications out of which 2 patients had right sided pneumothorax, 1 patient had left lower lobe pneumonia and 1 patient had surgical wound infection, late complication i.e. 3 months after surgery were observed in 3 patients, out of which 2 patients had thymoma recurrence, 1 patient had sinus over sternal region. 11 patients had severe myasthenic crisis post-operatively, who were ventilated, intubated, treated with multiple plasmapheresis cycles, prednisolone and anticholinesterase agents. Out of 11 patients, 5 were in remission, 3 patients had improvement and 3 patients expired. 3 patients (5%) had mortality in hospital, out of which, 3 patients belonged to Ossermans grade IIB and had myasthenic crisis. In two patients, disseminated intravascular coagulation was observed, followed by septicemia and expired on 6<sup>th</sup> post-operative day. One patient required tracheostomy and prolonged ventilation with multiple plasmapheresis cycles and steroids but the patient expired on 100<sup>th</sup> post-operative day. On follow up, there is no postoperative death.

Table 5: Post-operative pathologic study of thymus.

Post-operative pathologic study of thymus	Number of patients	Percentage
Hyperplasia of thymus	22	36.6%
Thymoma	13	21.6%
Thymic carcinoma, atrophy	5	8.4%
Normal thymus	20	33.4%

Table 5 shows that post-operative pathologic study of thymus findings were reported as follows, hyperplasia of thymus was observed in 22 patients (36.6%), thymoma in 13 patients (21.6%), thymic carcinoma, atrophy in 5 patients (8.4%) and normal thymus in 20 patients (33.4%).

Table 6: Comorbidities.

Comorbidities	Number of patients
Myasthenis gravis+comorbid disease (15)	
Coexisting autoimmune disease (6)	
Thyrotoxicosis	3
Systemic Lupus erythematosus+ Chroloquine induced keratopathy	2
Antiphospholipid antibody syndrome	1
Steroid induced Cushings disease	6
Steroid induced diabetes mellitus	1
Hypertension	1
Pulmonary tuberculosis	1

Table 6 shows that 15 (25%) had myasthenis gravis with associated comorbid disease, 6 patients had coexisting autoimmune disease, out of which (3 patients had Thyrotoxicosis, 2 patients had Systemic Lupus erythematosus+ Chroloquine induced keratopathy, 1 patient had Antiphospholipid antibody syndrome), 6 patients had Steroid induced Cushings disease, 1 patient had Steroid induced diabetes mellitus, 1 patient had Hypertension and 1 patient had Pulmonary tuberculosis.

16 days was the mean hospital stay with 4 patients having prolonged hospital stay due to complications. Follow up ranged from 7 months to 10 years. Mean follow up is 2.5 years.

Table 7: Surgical outcome based on Ossermann stages.

Class/Grades	Number of patients	Remission Improvement	No improvement	Worse	Death
I	10	7	3	--	--
IIA	28	22	2	2	--
IIB	15	5	5	3	3
III	4	5	2	--	--
IV	3	--	1	--	--

Table 7 shows that complete remission was observed in patients in Osserman stage I, IIA and IIB.

### Discussion:

The first thymectomy for myasthenia gravis was performed in 1939 by Alfred Blalock<sup>3</sup> and colleagues, who successfully removed the thymus and thymic cyst from a 26-year-old women patient. Due to antibodies' attachment to acetylcholine receptors, myasthenia gravis is an autoimmune disorder that impairs neuromuscular transmission. The disorder can affect people of any age, although it most commonly affects women in their thirties and forties and men in their sixties and seventies. The eye is typically the first location affected, and roughly 80% of patients experience generalised muscle weakness. Anticholinesterase drugs, steroids, immunosuppressive drugs, and plasmapheresis are used as medical treatments for myasthenia gravis to lower serum antibody concentration. After receiving medical care, there have been

reports of a complete clinical remission rate as low as 18% as reported in Nieto IP et al<sup>2</sup>, Rubin JW et al<sup>5</sup> and Papatestas AE et al<sup>6</sup> study. Surgery has become a more widely accepted practice, with clinical improvement occurring in up to 95% of cases and complete clinical remission occurring in as many as 45% of cases as reported in Faulkner SL et al<sup>7</sup>, Olanow LW et al<sup>8</sup>, First WH et al<sup>9</sup> and Hatton PD et al<sup>10</sup> studies. Since there is thymic tissue present outside the capsule of the proper thymus, we used the transsternal approach, which is the recommended technique, to remove all thymic tissue, including the adipose tissue in the anterior mediastinum as reported in Masaoka A et al<sup>11</sup> studies. Studies conducted by Faulkner SL et al<sup>7</sup>, Hatton PD et al<sup>10</sup>, Cohn HE et al<sup>12</sup>, Jaretzki A et al<sup>13</sup> and Mulder DG et al<sup>14</sup> have reported similar results when compared to the present study that greater improvement was observed in female patients. For myasthenia gravis, the success of thymectomy has been influenced by a number of factors. In the present study, age did not correlate with the outcome although, studies conducted by Clark RE et al<sup>15</sup>, Venuta F<sup>16</sup> and Budde JM et al<sup>17</sup> reported that young adults have higher complete clinical remission rate. In the present study, a greater post-operative degree of clinical improvement was observed in patients in Osserman stage I, IIA and IIB than stage III and IV. Several authors have observed mixed results while evaluating the influence of Osserman's stage on degree of clinical post-operative improvement. 51% remission rate in IIA disease & 40% in IIB in Maggie et al<sup>19</sup> study. Greater improvement in patient with mild generalized symptoms in Papatestas et al study<sup>6</sup>. Roberts PF et al<sup>18</sup> study reported that for thymectomy, myasthenia gravis with ocular involvement remains uncertain. Untreated patients tend to develop generalized myasthenia gravis. Papatestas<sup>6</sup> and Masaoka et al<sup>11</sup> showed similar results as the present study in advocating thymectomy for ocular myasthenia gravis. After thymectomy, pathologic study of thymus was closely related to outcome when compared to the present study has shown similar results. Hyperplastic thymus was associated with higher complete clinical rate as in Rubin JW et al<sup>5</sup>, Hatton PD et al<sup>10</sup> and Buckingham JM et al<sup>20</sup> studies. In the present study, the patients with thymoma did not show a poor response to thymectomy than those with non-neoplastic thymus gland which had shown similar results with the findings of Olanow et al<sup>8</sup>. After thymectomy, medication requirement in patients of myasthenia gravis decreases significantly. In present study, there is strong relation between thymectomy and reduced post-operative medication requirement.

### **Conclusion:**

Thymectomy is recommended for patients younger than 60 years with non-thymomatous, generalized AChR antibody-associated myasthenia gravis. The early-onset, severe myasthenia gravis, female, thymic hyperplasia, benefit the most. Patients classified as Osserman Class IIA and IIB benefit most from this procedure. Thymectomy can reduce patient's need for medication and reduce the severity of myasthenia gravis regardless of age, sex, severity, or length of sickness, or thymic masses. Regardless of myasthenia gravis condition, all cases with thymoma should be operated by resection if possible. The goal of thymectomy is to remove as much thymic tissue as possible. If complete excision of thymoma is not possible, radiotherapy and chemotherapy should be given both to control myasthenic symptoms and to prevent local invasions. The role of thymectomy in ocular MG

is controversial. Plasmapheresis or intravenous immunoglobulin is recommended before thymectomy in patients with preoperative respiratory or bulbar symptoms.

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