

Long-Term Outcomes after Thymectomy for Myasthenia Gravis: “VATS” Vs Open Surgery

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| Received: 25.01.2019 | Accepted: 04.02.2019 | Published: 15.02.2019

DOI: [10.21276/sjams.2019.7.2.20](https://doi.org/10.21276/sjams.2019.7.2.20)

Abstract

Original Research Article

Myasthenia gravis is an autoimmune disease with a great impact on quality of life. Thymectomy is a frequently used treatment for myasthenia gravis (MG) and is virtually always indicated in MG patients who have a thymoma. Throughout history, Thymectomy for nonthymomatous myasthenia gravis improved clinical outcomes, that supported by a randomised controlled trial. The surgical approach almost performed for the past decade has been a mini-invasive surgery (MIS). **Methods:** We retrospectively reviewed 48 patients with myasthenia gravis undergoing thymectomy between January 2008 and December 2015. The aim of this study was to determine the outcome of the long-time results after thymectomy for all the patients paying special attention to postoperative disease-related outcomes, quality of life, and differences regarding the operative approach. **Results:** 48 patients with myasthenia gravis were followed up after thymectomy for a median time of 4.58 years (range, 1–8 years). Our results indicated that the hospital stay was significantly shorter with minimally invasive procedures, overall, perioperative complications were found in 25 patients (52.08%). Three patients developed post-operative myasthenic crisis but generally the procedure was well tolerated and the perioperative mortality rate was 6.25%. A thymoma was identified on histology in 50 %, whereas 50 % had hyperplastic, atrophic and normal thymic histology. Perioperative complications statistical analysis showed no significant differences between open surgery and minimally invasive surgery (MIS), Outcome was favourable for the majority of patients, with 8.33 % achieving complete stable remission (CSR) and an additional 64.58 % achieving pharmacological remission. Anti-cholinesterase reduce was significant for patients who underwent MIS. **Conclusion:** Thymectomy for MG is generally safe and well tolerated; open or minimally invasive thymectomy both contribute to an improvement in myasthenia gravis symptoms and a significant reduction in the mean doses of anti-cholinesterase. Moreover, the hospital stay is shorter, and the aesthetic result is better with MIS procedure.

Keyword: myasthenia gravis, thymectomy, open surgery, mini-invasive surgery (MIS).

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INTRODUCTION

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder of the post-synaptic acetylcholine receptors resulting in striated muscle weakness and fatigue.

The thymus is known to play an important role in T lymphocyte education and self-tolerance. Therefore, thymus pathology is thought to be an important mediator in the development of myasthenia gravis. This relationship between the thymus and myasthenia gravis was demonstrated in 1901 by Weigert [2]. The first thymectomy was performed by Sauerbruch in 1911-on a 20-year-old woman with hyperthyroidism and myasthenia gravis [1].

In 1936, Alfred Blalock performed a transsternal total thymectomy during a remission period from severe myasthenia [20]. By 1944, he had accumulated experience in 20 cases, firmly establishing the role of thymectomy in the treatment of these patients. During the following years, thymectomy gained widespread acceptance in the treatment of myasthenia. Different surgical approaches were presented: transsternal or transcervical treatment. In the 1990s, Landreneau *et al.* reported the thoracoscopic resection of a stage I thymoma with a satisfactory outcome [21], and in recent years, minimally invasive thoracoscopic performed an extracapsular resection of the thymus including the mediastinal fatty tissue, with sharp dissection from the pericardium. Moreover a randomized, medication controlled, rater-blinded trial

showed a benefit of thymectomy in patients with myasthenia gravis over a period of 3 years with respect to clinical outcomes[22].

PATIENTS AND METHODS

This study describes a series of 48 patients with generalized myasthenia gravis who underwent thymectomy surgery in the department of thoracic Surgery between January 2008 and December 2015.

The clinical course data during the hospitalization and consultation in our outpatient clinic were reviewed, and survival data was generated. Disease severity was classified according to the Myasthenia Gravis Association of America (MGFA) clinical classification.

The MGFA post intervention status was used to describe outcome at the latest clinical review for each patient. Additionally, neuroclinical signs were assessed using a modified Osserman classification as follows: 0 (no symptoms), 1 (ocular signs and symptoms), 2 (mild generalized weakness), 3 (moderate weakness), and 4 (severe generalized weakness and/or respiratory dysfunction).

Patients were placed in 2 groups: open surgery (open group) and VATS thymectomy (MIT group). The SPSS 20. Software was used for statistical analysis.

RESULTS

48 Patients with myasthenia gravis undergoing surgery were followed up for a median time of 4.58 years (range, 1–8 years).

The median age of the patients was 34.16 years (range, 12–80 years) at the time of the operation. 17 (35.41%) were male and 31 (64.58%) were female.

The preoperative diagnosis was based on clinical features, electromyography, and detection of anti-acetylcholine receptor antibodies (AChRAb).

The whole of patients had mild–moderate myasthenia (MGFA Grade II). The preoperative modified Osserman classification was 2 for 40 patients and 3 for 8 patients. Anti-acetylcholine-receptor antibodies (AChRAb) were found to be positive for 46 patients (95.83%) (Table 1).

Table-1: Patients characteristics

	Overall	Thymoma	Normal or atrophic	Thymic hyperplasia
Overall	48	24	19	5
Male	18	12	5	1
Female	30	12	14	4
Disease duration(years)		1.44	2.68	3
Average age at thymectomy (years)	34.16 10-63	42.54 10-60	30 10-63	23.4 3-37
Anti-AChR antibody	97.91%	96%	100%	100%
Osserman score (Average)	73.33%	87.70%	83.42%	79%
MGFA II	100%	100%	100%	100%
Followed duration(years)	4.58 (average) 1-8			
treatment				
-anticholinesterasic(pill)	6.49	6.08	7	6.4
-Prednisolone	6.25%	1.2%	0.5%	0%
-Steroid sparing agents		0%	1%	0%
-Plasmapheresis		0%	1%	0%

Prior to thymectomy, 6.25% of patients were treated with prednisolone; one patient was also treated with alternative steroid sparing agents.

The clinicopathologic data showed no difference between the patients who underwent open surgery (n = 34) and those who had minimally invasive surgery (MIS) (n = 18) (Table 2).

Table-2: Comparative clinicopathological characteristics

	Overall		Open surgery		MIS		P value
	n	%	n	%	n	%	
Sex							0.215
Male	17	35.41	12	35.29	5	35.71	
Female	31	64.58	22	64.70	9	64.28	
Onset age							0.102
≤45 years	32	66.66	21	61.76	11	78.57	
> 45 years	16	33.33	13	38.23	3	21.42	
Histology							0.007
-Thymoma	24	50	13	38	01	7	
-Nonthymoma	24	50	21	61	13	92	
Osserman score	2		2		2		-

MIS: minimally invasive surgery

Complete surgical resection was performed for all the patients. There were 32 open thymectomies and 16 minimally invasive thymectomies. Of the MIS cases there were 2 conversions to an open procedure and all

were admitted to the intensive care unit (ICU) post operatively (Table3).

The average ICU stay was 2.25 days for 45 patients and was 5, 53, and 42 days for 3 patients respectively.

Table-3: Operative method

Overall	Open surgery				MIS
	Sternotomy	Manubriotomy	VATS conversion	Trans-sternal with cervical incision	VATS
48	18	13	2	1	14
100%	37.5%	27.08%	4.16%	2.08%	29.16%

MIS: minimally invasive surgery

A thymoma was identified on histology in 50 %, whereas 50 % had hyperplastic, atrophic and normal thymic histology.

The perioperative mortality rate was 6.25% (3 patients). Overall, perioperative complications were

found in 25 patients (52.08%). 5 patients (10.41%) needed re-intubation because of respiratory failure, one patient(2.08%) had a pneumothorax and three patients(6.25%) had a post thymectomy myasthenic crisis who needed plasmapheresis, but generally the procedure was well tolerated (Table 4).

Table-4: Complications of open surgery versus minimally invasive surgery

Complications	Overall		Open surgery n=34		MIS n=14		P value
	N	%	N	%	N	%	
Death	3	6.25	1	4.16	2	8.33	-
Arrhythmia	2	4.16	1	4.16	1	4.16	-
Myasthenic crisis	3	6.25	2	8.33	1	4.16	-
Needed intubation	5	10.41	3	12.5	2	8.33	-
Tracheostomy	2	4.16	2	8.33	0	0	-
Pneumonia	4	8.3	3	12.5	1	4.16	-
Atelectasia	1	2.08	1	4.16	0	0	-
Pneumothorax	1	2.08	1	4.16	0	0	-
Patients	48	100	24	50	24	50	0.11

Perioperative complications statistical analysis showed no significant differences between open surgery and MIS. Overall, 8.33% of the patients were in complete remission (open surgery5.88 % vs MIS, 14.28 %). And a great significant reduction in the mean doses of mestinon/mythelase (64.58%) open surgery58.8 % vs MIS, 78.57 %).

However, there is a great significant difference between open surgery and MIS on the anti-

cholinesterase reduce, (p = 0,018 < 0.05) with a high anti-cholinesterase reduce for patients who underwent MIS.

The last follow-up visit showed despite a significant improvement, one patient worsened, and four remained unchanged in terms of myasthenia gravis-associated symptoms (Table5).

The lengths of hospital stay were significantly different between the transsternal thymectomy and VATS thymectomy groups (12.1 days vs 7.6 days).

DISCUSSION

MG has an incidence of 3 to 30 per million per year [3], and thymectomy is typically restricted to patients under the age of 60 [4]. Therefore, only a small number of individuals are expected to undergo thymectomy for MG. Different approaches for open surgery have been used with comparable outcomes and complications, with remission rates between 30% and 50% [5-9].

In recent years, minimally invasive thymectomy has been established [10-12], there advantages of a minimally invasive approach are obvious with less postoperative pain and smaller scars as important factors. Furthermore, an excellent visualization of the mediastinum is provided, and the hospital stays was significantly shorter.

It was shown that minimally invasive thymectomy is a safe procedure with results as equal to

better as for open surgery. Myasthenia associated complications are shown to occur for 40% of the patients [13] and postoperative complications for 27.5% to 70% [13, 14], and 5 to 15% of death [15]. These results are mostly comparable with our findings of 52.08% with no significant differences found between the two surgical approaches.

Three (6.25%) patients developed a post-operative myasthenic crisis (MC) but, previous studies have noted a higher proportion of patients up to 19 % developing MC after thymectomy [16]. We attribute the low rate of MC in our cohort to adequate post-operative care in a specialist neurointensive care facility.

In a long-term followup study, a continuous increase in the remission rate was observed [17]. In our trial after surgery to the last follow-up visit, we were able to confirm the tendency of late improvements after thymectomy [18]. Doses of anti-cholinesterase also could be reduced, (table 5). After minimally invasive procedures, the hospital stay was shorter, with best aesthetic results.

Table-5: the long-term evolution

	Open surgery n = 34		Mini invasive Surgery; n = 14		Overall		P value
	N	%	N	%	N	%	
Complete remission, no medications	2	5,88	2	14,28	4	8,33	0.115
Asymptomatic (decreased medications)	20	58,8	11	78,57	31	64,58	0.018
No change	4	11,76	0	0	4	8,33	-
Worsening symptoms	1	2,94	0	0	1	2,08	-
Lost sight	5	14,70	0	0	5	10,41	-
Death	2	5,88	1	7,14	3	6,25	0.218
Overall	34	70,83	14	29,16	48	100	0.098

The patient with thymoma did not show a poor response to Thymectomy and Medication requirement in patients of myasthenia gravis decreases significantly after thymectomy [19]. Our study fully agrees with these findings.

CONCLUSION

Based on our results we conclude that minimally invasive thymectomy is a beneficial approach and was found to be a safe procedure over all for myasthenia gravis, the procedure is associated with a great rate of CSR and a significant reduction in the mean doses of anti-cholinesterase. The hospital stay is shorter, and the aesthetic result is better. There are no significant complication difference between open surgery and minimally invasive surgery due to the disease.

Abbreviations

CSR = complete stable remission; MG = myasthenia gravis; MGFA = Myasthenia Gravis Foundation of

America; VATS = video-assisted thoracic surgery; MIS = mini-invasive surgery

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