Outcomes after Thymectomy in Patients with Thymomatous Myasthenia Gravis

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Abstract

Objectives This article describes the clinical outcomes after thymectomy in patients with thymomatous myasthenia gravis (T-MG) managed in the department of thoracic surgery of Hassan II University Hospital of Fez, Fez, Morocco.

Materials and Methods We performed a retrospective analysis of medical records of 16 patients with T-MG between January 2009 and January 2017.

Results There were 11 women and 5 men with a median age of 40 years at the thymectomy time and a median time of onset of symptoms to thymectomy of 12 months. At the preoperative evaluation (Myasthenia Gravis Foundation of America [MGFA] clinical classification), 7 patients were class II, 7 class III, and 2 class IV. Nine patients were in Masaoka stage I, and the remaining 7 patients stage II. We recorded one case of postoperative myasthenic crisis. At 3 years of follow-up after thymectomy, 6 patients had complete stable remission and the other 10 patients improved. Of these patients with clinical improvement, 6 patients were in MGFA class I and the remaining 4 patients class II.

Conclusion The present study shows the beneficial effect of thymectomy in patients with T-MG. Postoperative clinical outcomes seem to be better when the preoperative severity of myasthenic symptoms is mild (MGFA class II).

Keywords
- myasthenia gravis
- thymoma
- thymectomy
- clinical improvement
- complete stable remission rate

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Introduction

The beneficial effect of thymectomy in myasthenia gravis (MG) management was first reported in 1941 by Blalock et al.[1] Thymectomy increases the rates of complete stable remission (CSR) in the patients with MG who underwent thymectomy compared with those managed medically alone.[2,3] In Morocco, few studies have been reported on thymectomy in MG management.[4,5] The present study aimed to describe the clinical outcomes after thymectomy in patients with thymomatous MG (T-MG) managed in the department of thoracic surgery of Hassan II University Hospital of Fez, Fez, Morocco.

Materials and Methods

Study Design and Patients

We performed a retrospective analysis of the medical records of 16 patients with T-MG who underwent thymectomy in the department of thoracic surgery of the Hassan II University Hospital of Fez between January 2009 and January 2017. The diagnosis of MG was made by the neurologists of the department of neurology of the Hassan II University Hospital of Fez. All patients were diagnosed with seropositive generalized MG and referred to the department of thoracic surgery for thymectomy. For each patient, a preoperative clinical evaluation was performed by a neurologist, and the Myasthenia Gravis Foundation of America (MGFA) clinical classification[6] was used for clinical staging. For each patient, the postoperative clinical evaluation data using quantitative myasthenia gravis score were collected up to 3 years after surgery, as well as the modification of medical treatment. MGFA postintervention status was used to assess the clinical status of patients after thymectomy.

Ethical Approval

Ethics approval for this study was not required because it was a retrospective study, and the patient management was not affected. The written informed consent has been waived by the Institutional Review Board of Hassan II University Teaching Hospital of Fez.

Results

There were 11 women and 5 men (sex ratio females to males at 2.2). ►**Table 1** details the baseline characteristics of the 16 patients. The median age of the patients was 40 years at the thymectomy time and the median time of onset of symptoms to thymectomy was 12 months. Before thymectomy, 7 patients were in MGFA class II, 7 patients class III, and 2 patients class IV. In 3 patients (patients 4, 6, and 9), a cure of intravenous immunoglobulins (2 g/kg administered over 5 days) was performed to improve myasthenic symptoms before thymectomy. Before surgery, 6 patients were under azathioprine (AZT) and pyridostigmine bromide (PB); 3 patients under AZT, PB, and prednisone (PN); and 3 patients under PB and PN. Four patients were under PB alone.

The surgical approach was a vertical total sternotomy in 15 patients and thoracoscopy in the other patient (patient 2). All patients had undergone a thymectomy enlarged to the adjacent fatty tissues. According to Masaoka's clinical staging,[7] 9 patients were classified as stage I and stage II for the other 7. The postoperative course was simple in 14 patients, while one patient (patient 10) had presented a postoperative myasthenic crisis and the other patient (patient 2) hemothorax.

According to the World Health Organization histologic classification,[8] the histologic analysis showed AB thymoma in 2 patients, B1 in 8 patients, B2 in 3 patients, B3 in 1 patient, and thymic carcinoma in 2 patients. Adjuvant therapy (chemotherapy or radiotherapy) was performed in the 2 patients with thymic carcinoma (patients 3 and 4), the patient with B3 thymoma (patient 5), and in the 3 patients with B2 thymoma (patients 6, 9, and 15).

At 3 years of follow-up after thymectomy (►**Table 2**), 6 patients had CSR and the other 10 patients improved with reduced doses of PB and/or AZT. Of these 10 patients who improved, 6 patients were in MGFA class I and the remaining 4 patients class II. There were no cases of disease exacerbation or myasthenic crisis during the 3 years of follow-up in the 10 patients who improved. Among the 6 patients with CSR, 4 patients (patients 2, 12, 14, and 15) were in MGFA class II and the other 2 patients (patients 7 and 11) class III at the preoperative evaluation. Five patients (patients 2, 7, 11, 12, and 14) among the 6 patients with CSR had the histologic type B1 thymoma while the other patient (patient 15) had a B2 thymoma. We recorded no cases of recurrence of MG in the 6 patients with CSR. We also did not record any deaths during the follow-up period in the 16 patients.

Discussion

The present study shows a rate of CSR of 37.5% and an improvement rate of 62.5% at 3 years of follow-up after thymectomy in patients with T-MG, aged 17 to 62 years (median age 40 years).

The T-MG forms are more severe, characterized not only by the predominance of bulbar and respiratory signs but also by the high frequency of postoperative myasthenic crises varying from 17 to 35.2%.[4,9] The frequency of postoperative myasthenic crisis was 6.3% in the present study. Findings inferior to ours have also been reported in patients with T-MG, ranging from 3 to 3.4%.[10,11] The rates of CSR after thymectomy in patients with T-MG are variable. Nguyen et al[12] reported a rate of CSR of 22.6% at 12 months of follow-up, whereas Bouchikh et al[4] and Agasthian and Lin[10] reported at 5 years of follow-up a rate of CSR of 7 and 28%, respectively. A study with a follow-up of 24 to 56 months after thymectomy (a follow-up period similar to ours which is 36 months) reports a rate of CSR of 14.9%,[9] a result lower than ours which is 37.5%. Studies have reported mild preoperative severity of myasthenic symptoms (MGFA class I–II) as an independent factor of postoperative CSR in patients with T-MG.[11,13] In the present study, 7 patients (43.8%) were in MGFA class II on the whole sample, and among the 6 patients

Table 1 Baseline characteristics of the 16 patients with seropositive generalized myasthenia gravis

Patient no.	Sex	Age at surgery (y)	Onset to surgery (mo)	MGFA class[a]	Acetylcholinesterase inhibitor	Corticosteroid or immunosuppression therapy	Chest CT
1	M	46	5	IIa	PB, 180 mg	PN, 50 mg	Thymoma
2	F	25	120	IIb	PB, 240 mg	AZT, 100 mg	No thymoma
3	M	35	48	IIb	PB, 240 mg	AZT, 150 mg	Thymoma
4	F	45	48	IIIb	PB, 300 mg	AZT, 150 mg	Thymoma
5	M	48	108	IIa	PB, 240 mg	AZT, 100 mg	Thymoma
6	M	48	12	IVa	PB, 240 mg	PN, 20 mg + AZT, 150 mg	Thymoma
7	M	40	3	IIIa	PB, 300 mg	–	Thymoma
8	F	36	12	IIIa	PB, 300 mg	PN, 20 mg + AZT, 150 mg	No thymoma
9	F	53	24	IVb	PB, 240 mg	AZT, 150 mg	Thymoma
10	F	52	6	IIIa	AMBC, 50 mg	PN, 40 mg	Thymoma
11	F	17	15	IIIa	PB, 240 mg	PN, 10 mg + AZT, 150 mg	Thymoma
12	F	29	36	IIa	PB, 240 mg	AZT, 100 mg	Thymoma
13	F	62	6	IIIa	PB, 300 mg	PN, 50 mg	Thymoma
14	F	35	2	IIa	PB, 240 mg	–	Thymoma
15	F	39	1	IIa	PB, 240 mg	–	Thymoma
16	F	40	3	IIIa	PB, 240 mg	–	Thymoma
Patient no.	**Preoperative preparation**	**Surgical approach**	**Surgical gesture**	**Postoperative course**	**WHO histologic classification**	**Masaoka clinical stage**	**Adjuvant therapy**
1	No	VTS	TEAFT	Simple	B1 thymoma	I	No
2	No	TS	TEAFT	Hemothorax	B1 thymoma	I	No
3	No	VTS	TEAFT	Simple	TC	II	CT
4	IVIG	VTS	TEAFT	Simple	TC	II	RT
5	No	VTS	TEAFT	Simple	B3 thymoma	I	RT
6	IVIG	VTS	TEAFT	Simple	B2 thymoma	II	RT
7	No	VTS	TEAFT	Simple	B1 thymoma	I	No
8	No	VTS	TEAFT	Simple	B1 thymoma	I	No
9	IVIG	VTS	TEAFT	Simple	AB thymoma	II	CT
10	No	VTS	TEAFT	MC	B2 thymoma	I	No
11	No	VTS	TEAFT	Simple	B1 thymoma	I	No
12	No	VTS	TEAFT	Simple	B1 thymoma	I	No
13	No	VTS	TEAFT	Simple	AB thymoma	II	No
14	No	VTS	TEAFT	Simple	B1 thymoma	II	No
15	No	VTS	TEAFT	Simple	B2 thymoma	II	RT
16	No	VTS	TEAFT	Simple	B1 thymoma	I	No

Abbreviations: AMBC, ambenonium chloride; AZT, azathioprine; CT, chemotherapy; CT, computed tomography; F, female; IVIG, intravenous immunoglobulins; M, male; MC, myasthenic crisis; MGFA, Myasthenia Gravis Foundation of America; PB, pyridostigmine bromide; PN, prednisone; RT, radiotherapy; TC, thymic carcinoma; TEAFT, thymectomy enlarged to the adjacent fatty tissues; TS, thoracoscopy; VTS, vertical total sternotomy; WHO, World Health Organization.

Note: Stage I corresponds to macroscopically completely encapsulated and microscopically no capsular invasion; Stage II, macroscopic invasion into surrounding fatty tissue or mediastinal pleura.

[a]Class II corresponds to mild weakness; class III, moderate weakness; class IV, severe weakness; a indicates predominantly limb and axial presentation; b, predominantly bulbar presentation.

Table 2 Outcomes at 3 years after surgery

Patient no.	MGFA class[a]	Acetylcholinesterase inhibitor	Immunosuppression therapy	MGFA postintervention status
1	I	PB, 120 mg	AZT, 100 mg	Improved
2	–	–	–	CSR
3	I	PB, 120 mg	AZT, 75 mg	Improved
4	IIa	PB, 180 mg	AZT, 100 mg	Improved
5	I	PB, 120 mg	AZT, 50 mg	Improved
6	IIa	PB, 120 mg	AZT, 100 mg	Improved
7	–	–	–	CSR
8	I	PB, 120 mg	AZT, 75 mg	Improved
9	I	PB, 120 mg	AZT, 100 mg	Improved
10	I	AMBC, 20 mg	AZT, 100 mg	Improved
11	–	–	–	CSR
12	–	–	–	CSR
13	IIa	PB, 120 mg	AZT, 100 mg	Improved
14	–	–	–	CSR
15	–	–	–	CSR
16	IIa	PB, 120 mg	AZT, 100 mg	Improved

Abbreviations: AMBC, ambenonium chloride; CSR, complete stable remission; MGFA, Myasthenia Gravis Foundation of America; PB, pyridostigmine bromide.

[a]Class I corresponds to ocular muscle weakness with or no weakness of eye closure; Class IIa, mild weakness predominantly affecting limb and axial muscles.

with CSR, 5 patients (5/6 = 83.3%) were in MGFA class II. The variability of the CSR rates between studies in patients with T-MG could be explained both by the degree of the preoperative severity of myasthenic symptoms and the duration of postoperative follow-up period, as demonstrated in the study by Nguyen et al.[12]

A study has shown that patients with thymoma had a higher rate of recurrence of MG than those without thymoma.[9] The rate of recurrence of MG ranges from 3 to 7.5% in patients with thymoma.[9,12] Agasthian and Lin[10] do not report a recurrence of MG in their patients. In the present study, we recorded no cases of disease exacerbation or myasthenic crisis in the patients who improved or of recurrence of MG in the patients with CSR during the 3-year follow-up period after thymectomy. In addition, we did not record any deaths during the follow-up period in the present study.

The main limitations of the present study were its retrospective nature, the small sample size, and the postoperative follow-up period relatively short (36 months).

Conclusion

The present study shows the beneficial effect of thymectomy in patients with T-MG. Postoperative clinical outcomes seem to be better when the preoperative severity of myasthenic symptoms is mild (MGFA class II). Although so modest due to the small sample size, the results of this study could help the neurologists of our institution choose the alright patients with T-MG to suggest for thymectomy.

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Conflict of Interest
None declared.

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