Outcomes after Thymectomy in Patients with Thymomatous Myasthenia Gravis

Sani Rabiou¹,²,³ Moussa Toudou-Daouda⁴,⁵ Marwane Lakranbi³,⁶ Ibrahim Issoufou¹,³ Yassine Ouadnouni³,⁶ Mohamed Smahi³,⁶

¹ Department of Thoracic Surgery, General Referral Hospital of Niamey, Niamey, Niger
² Faculty of Medicine and Pharmacy, Abdou Moumouni University of Niamey, Niamey, Niger
³ Department of Thoracic Surgery, Hassan II University Teaching Hospital of Fez, Fez, Morocco
⁴ Department of Neurology, National Hospital of Niamey, Niamey, Niger
⁵ Department of Neurology, Hassan II University Teaching Hospital of Fez, Fez, Morocco
⁶ Faculty of Medicine and Pharmacy, Sidi Mohammed Ben Abdallah University of Fez, Fez, Morocco

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).
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 myasthenic 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 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 Bouchik et al.\(^13\) 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                    | IIIa            | 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            | Simple               | 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.

*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.*
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 Lin10 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.

#### Funding
None.

#### Conflict of Interest
None declared.

### References

1. Blalock A, Harvey AM, Ford FR, Lilienthal JL. The treatment of myasthenia gravis by removal of the thymus gland. JAMA 1941; 117:1529–1533
2. Wolfe GI, Kaminski HJ, Aban IB, et al; MGTX Study Group. Randomized trial of thymectomy in myasthenia gravis. N Engl J Med 2016;375(06):511–522
3. Cooper JD. History of thymectomy for myasthenia gravis. Thorac Surg Clin 2019;29(02):151–158
4. Bouchnik M, El Malik HO, Ouchen F, Achari A, Benosman A. Thymoma-associated myasthenia gravis: clinical features and surgical results [in French]. Rev Neurol (Paris) 2013;169(11):879–883
5. El Hammoumi M, Arsalane A, El Oueriachi F, Kabiri H. Surgery of myasthenia gravis associated or not with thymoma: a retrospective study of 43 cases. Heart Lung Circ 2013;22(09):738–741
6. Jaretzki A III, Barohn RJ, Ernstoff RM, et al; Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Myasthenia gravis: recommendations for clinical research standards. Ann Thorac Surg 2000;70(01):327–334

### Table 2 Outcomes at 3 years after surgery

| Patient no. | MGFA classa | 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.

aClass I corresponds to ocular muscle weakness with or no weakness of eye closure; Class IIa, mild weakness predominantly affecting limb and axial muscles.
7 Masaoka A, Monden Y, Nakahara K, Tanioka T. Follow-up study of thymomas with special reference to their clinical stages. Cancer 1981;48(11):2485–2492
8 Kondo K, Yoshizawa K, Tsuyuguchi M, et al. WHO histologic classification is a prognostic indicator in thymoma. Ann Thorac Surg 2004;77(04):1183–1188
9 Yu L, Zhang XJ, Ma S, Li F, Zhang YF. Thoracoscopic thymectomy for myasthenia gravis with and without thymoma: a single-center experience. Ann Thorac Surg 2012;93(01):240–244
10 Agasthian T, Lin SJ. Clinical outcome of video-assisted thymectomy for myasthenia gravis and thymoma. Asian Cardiovasc Thorac Ann 2010;18(03):234–239
11 Zheng Y, Cai YZ, Shi ZY, et al. Different neurologic outcomes of myasthenia gravis with thymic hyperplasia and thymoma after extended thymectomy: a single center experience. J Neurol Sci 2017;383:93–98
12 Nguyen TG, Nguyen NT, Nguyen VN, Nguyen TK, Vu DT, Le VA. Video-assisted thoracoscopic surgery for myasthenia gravis with thymoma: a six-year single-center experience. Asian J Surg 2021;44(01):369–373
13 Mao Z, Hu X, Lu Z, Hackett ML. Prognostic factors of remission in myasthenia gravis after thymectomy. Eur J Cardiothorac Surg 2015;48(01):18–24