

Long-Term Outcome after Thymectomy for Myasthenia Gravis

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Background: Myasthenia gravis (MG) is an autoimmune disorder that affects the neuromuscular junction of skeletal muscles. Main treatments consist of pharmacologic and surgical treatments, such as a thymectomy. Even when patients receive recommended therapy, many still suffer from weaknesses. There is very limited data available regarding clinical responses to treatment and long-term outcomes of MG.

Objective: To study the long-term outcomes of clinical responses after thymectomies in patients with MG, as well as compare dosages of medication use before and after thymectomy and associating factors.

Materials and Methods: Retrospectively reviewed 123 MG patients treated by pharmacological treatment and thymectomy between 1997 and 2011 in Srinagarind Hospital, Khon Kaen University. Endpoints included improvement of clinical symptoms during follow-up time and the response to therapy-defined categories such as complete stable remission (CSR), pharmacologic remission (PR), improved, stabilized or worsened. The average dosage of pharmacological treatment before and after the procedure and factors associated with satisfactory outcomes are also studied.

Results: Among 123 patients, 94(75.8%) are females with a median age of 49.82 years (IQR 41.76 to 58.36) and average age of diagnosis of 37.45 years (27.51 to 45.33). The average period for thymectomy after diagnosis was 8.12 months (1.87 to 23.21). The surgical method of thymectomy is divided into transsternal and video-assisted thoracoscopic thymectomy, each with 115 and 8 patients respectively. The duration of follow-up was 36.18 months (19.82 to 76.9). Histological examination showed thymoma and non-thymoma were 20.32% and 79.68% respectively. In terms of overall response, 95.12% had a good response (CSR, PR, improved), while 4.88% had a poor response (stable, worse). 28 patients (22.76%) had CSR, 70 patients (56.91%) had PR and 19 patients (15.45%) had improvement of clinical symptoms. The disease had stabilized in 5 patients (4.07%), and 1 patient (0.81%) had worsening symptoms. Most of the patients required lower doses of pyridostigmine and prednisolone after surgery. Multivariate Cox regression analysis revealed that those with an age of diagnosis before 40 years old and lower dose of pyridostigmine use at 12 months after thymectomy showed significantly higher rates of CSR.

Conclusion: Thymectomy along with pharmacologic therapy for MG patients showed satisfactory results in achieving remission and improving clinical response rates. Favorable factors for satisfactory outcome were age of diagnosis before 40 years old and lower dose of pyridostigmine use at 12 months after thymectomy.

Keywords: Myasthenia gravis, Thymectomy, Outcome

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Myasthenia gravis (MG) is an autoimmune disorder that affects the neuromuscular junction (NMJ) of skeletal muscles. Many patients have an acetylcholine receptor antibody (AChR Ab) attached to the acetylcholine receptor⁽¹⁾ at the NMJ of the skeletal muscle which leads to abnormalities in neurotransmission. The weaknesses usually fluctuate, as they worsen after repeated use of muscles and improve with rest. Weakness may affect any skeletal muscle including the ocular muscles, the extraocular muscles (EOM), eyelids and

respiratory muscles. Therefore, Myasthenia gravis has a variety of presentations that include mild ptosis, difficulty in swallowing, weakness of skeletal muscles, and weakness of respiratory muscles that cause respiratory failure. Diagnosis is made by taking a patient's history and analyzing typical examination findings. The definite diagnosis is confirmed by testing for Acetylcholine receptor antibody (AChR-Ab), muscle specific receptor tyrosine kinase (MuSK), etc.

MG treatment can be divided in 2 groups:

Ocular MG: starts treatment with acetylcholinesterase inhibitors such as pyridostigmine-may add Prednisolone if the symptoms not improved. Performing thymectomy in patients with non-thymomatous ocular MG has remained controversial^(2,3).

Generalized MG: treatments include medical

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treatment (pyridostigmine, steroid, immunosuppressive drugs) and thymectomy which is recommended for MG patients with thymoma and generalized MG.

The goals of treatment are to maintain an asymptomatic state while not receiving any therapy for MG during this period (complete stable remission; CSR). Gronseth et al, reported that MG patients who underwent thymectomies achieved better remission rates compared with those who did not undergo thymectomy, especially in patients with generalized MG who had the AChR antibody. However, due to confounding differences between surgical and non-surgical treatment for MG, the role of thymectomy remains controversial⁽⁴⁾.

Many studies from various countries that researched the long-term outcomes of MG patients after thymectomy showed that remission rates were between 21 to 50 percent^(2,5-11). There were few reports after thymectomies in Thailand, although Witoonpanich R, et al retrospectively reviewed 128 patients during 1981 to 1987, and reported that remission rate after thymectomy along with medication treatment was 41.2 percent⁽¹²⁾. Glinjongol C, et al (2004) retrospectively reviewed 32 patients between 1990 to 2004, and showed that remission rate was 40 percent⁽¹³⁾.

Prognostic factors associated with a high remission rate were younger age of onset (less than 40 years old^(2,3) and shorter duration of symptoms prior to surgery (performing thymectomy within 18 months after diagnosis). Older patients and patients with thymoma had a lower remission rate⁽²⁾. Despite receiving medications and standard treatments, many patients still suffered from MG-related symptoms which reduced quality of life⁽¹⁴⁾.

Most of the previous studies were retrospective case series or retrospective cohort-type studies with no comparison with controlled groups, no standardized methods for assessing patients' status before and after thymectomy, and varying definitions of remission and improvement criteria. Furthermore, some of the studies with positive results after thymectomy did not provide data about pharmacological treatment⁽¹⁵⁾. In consequence, comparing of the outcomes of thymectomy and pharmacological treatment remains difficult. In Thailand, there are still limited studies available regarding clinical responses and long-term outcomes of MG patients after thymectomy. The main objective of this research is to study the long-term outcomes of clinical responses after thymectomy in patients with MG, compare dosage of medication use before and after thymectomy and associating factors. The data from the study population was retrospectively reviewed with a focus on general characteristics, types and doses of medication treatment, and disease severity before and after thymectomy.

Objective

Primary objective

To study treatment outcomes after thymectomies, assessed from signs and symptoms of patients at OPD visits for follow-up by using MGFA Classification.

Secondary objective

1) To evaluate long-term outcomes after thymectomies, by categorizing the response into 5 groups, including

Complete stable remission (CSR) is defined as patient had no symptoms of MG for at least 12 months and did not receive any medications for MG during this period.

Pharmacologic remission (PR) is defined as patient had no symptoms of MG for at least 1 year but had to take medications in order to control symptoms.

Improve is defined as substantial improvement in symptoms or clinical manifestations compared to pre-operative period and had to take medication to control symptoms.

Stable is defined as no substantial decrease in symptoms or clinical manifestations compared to preoperative period and had to take medication to control symptoms.

Worse is defined as worsening of symptoms or clinical manifestations compared to pre-operative period and had to take medication to control symptoms.

2) To evaluate average dosages of pharmacologic treatment before and after the procedure (6, 12 months and last OPD visit).

3) To evaluate factors associated with satisfactory outcome and disease remission after thymectomy.

Materials and Methods

Retrospective, non-randomized study, by collecting data from patients' record in OPD and IPD charts of all patients who are diagnosed with MG, in Srinagarind Hospital, Khon Kaen, Thailand, during 1997 to 2011, by using data collection forms. The data include:

Gender

Age of onset, age of diagnosis

Associated underlying diseases

Disease severity prior to surgery, 6 and 12 months after surgery, and last follow-up visit. Assessed by using MGFA classification.

Medication treatment before surgery, including cholinesterase inhibitors, immunosuppressive drugs. Dosage of medication use at 3, 6, 12 months after surgery and last follow-up visit.

Thymectomy technique used.

Pathology result of thymus gland

Duration from diagnosis to surgery

Duration of follow-up period.

Response to treatment and outcome

Patients' status (alive, dead, lost to follow-up, refer to other hospital).

The study protocol was approved from the Khon Kaen University Ethics Committee in Human Research (HE551206).

Study population

Inclusion criteria

Myasthenia gravis patients, diagnosed by neurologists, have been treated in Srinagarind Hospital,

Khon Kaen, Thailand, during 1997 to 2011.

Aged >15 years

Received both medication treatment and thymectomy.

Follow-up duration at least 1 year after thymectomy.

Exclusion criteria

Patients with follow-up duration less than 1 year after thymectomy.

Incomplete data.

Statistical analysis

Descriptive statistics were used for categorical and continuous variables and were analyzed in percentage and median, respectively. Categorical variables were compared by the χ^2 and Fisher's exact tests. Student's t-test was used for comparison of continuous variables. Kaplan-Meier survival curves and Cox proportional hazard model was used for multivariate analyses of prognostic factors.

Results

During the study period, there were 231 patients with Myasthenia gravis who had thymectomies. Only 123 cases were appropriate for the present study (72 cases had follow-up period less than 12 months and 36 cases had incomplete medical records).

There were 93 females and 30 males (75.6% and 24.4% respectively) with an average age of 49.82 years old (IQR 41.76 to 58.36). Average age at diagnosis is 37.42 years. There were 70 cases (56.9%) which were diagnosed before age 40 years and 53 cases (34.1%) which were diagnosed after age 40 years. Most of the patients, 93 cases (75.6%), had no other diseases. The other 30 cases (24.4%) suffered from diseases with 15 cases of hyperthyroid/Graves' disease, 2 cases of multinodular goiter, 2 cases of rheumatoid arthritis, 1 case of diabetes mellitus, and 1 case of SLE. The average duration from diagnosis to the operation was 8.12 months (IQR 1.87 to 23.21). Most cases (115 cases, 93.5%) had undergone transsternal thymectomy, while 8 cases (6.5%) underwent Video Assisted Thoracoscopic Thymectomy (VATS). Biopsy results from surgical specimens (thymic histology) show 71 cases of thymus hyperplasia (57.72%), 23 cases of thymoma (18.69%), 12 cases of normal thymus tissue (9.75%), 6 cases of thymus involution (4.88%), 3 cases of atrophic change (2.44%) 3 cases of lymphoid hyperplasia (2.44%), 2 cases of thymic carcinoma (1.63%), 1 case of other multilocular thymic cyst, 1 case of calcified thymus with granuloma, and 1 case loss of pathologic data (Figure 1). The average duration of follow-up after surgery was 36.18 months. (IQR 19.82 to 76.9)

The responses to treatment in individual cases were evaluated by neurologists using signs and symptoms of follow-up patients and were then classified in severity using MGFA classification. Prior to surgery, most of the patients' severity was classified in Class IIB (56.92%), followed by Class V (Respiratory muscle weakness leading to respiratory

failure) 28.45%.

There was improvement in patients' symptoms in most of the cases after the procedure. It is interesting to note that most of these patients (79.67%) were in normal conditions when they came to the latest follow up.

To study the dosage of pyridostigmine:

The average dose of pyridostigmine 3 months before the thymectomy was 360mg/day.

The average dose of pyridostigmine 6 months after the thymectomy was 240 mg/day.

The average dose of pyridostigmine 12 months after the thymectomy was 180 mg/day.

The average dose of pyridostigmine during the last period of follow-up was 180 mg/day.

Comparing the drug dosage before surgery and the last follow-up period, there are 85 patients (68.55%) who could reduce the dosage of pyridostigmine.

Most patients receive azathioprine and prednisolone, immunosuppressive drugs that are used to control the disease. There was only one patient who received methotrexate with prednisolone, and one patient who received mycophenolate mofetil with prednisolone.

The average dose of prednisolone 3 months before the thymectomy was 15 mg/day.

The average dose of prednisolone 6 months after the thymectomy was 10 mg/day.

The average dose of prednisolone 12 months after the thymectomy was 12.5 mg/day.

The average dose of prednisolone during the last period of follow-up was 10 mg/day.

Comparing the drug dosage before surgery and the last follow-up period, 75.86% of patients could reduce dosage of prednisolone.

For azathioprine:

The average dose of azathioprine 3 months before the thymectomy was 100 mg/day.

The average dose of azathioprine 6 months after the thymectomy was 100 mg/day.

The average dose of azathioprine 12 months after the thymectomy was 100 mg/day.

The average dose of azathioprine during the last

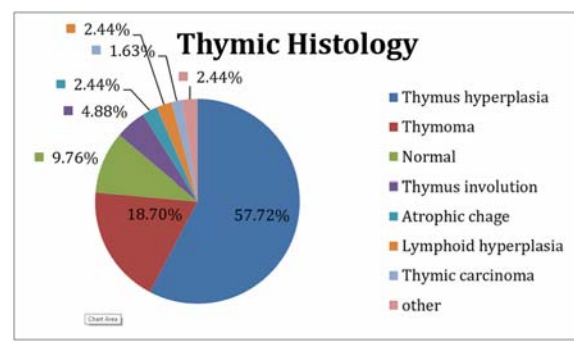


Figure 1. Pathological results of thymic tissue.

Table 1. Compare severity of symptoms before and after surgery

| MGFA Clinical Classification | 3 months before surgery | 6 months after surgery | 12 months after surgery | Latest follow-up |
|------------------------------|-------------------------|------------------------|-------------------------|------------------|
| Class I | 1 (0.81%) | 21 (17.07%) | 25 (20.32%) | 18 (14.63%) |
| Class IIA | 14 (11.38%) | 7 (5.69%) | 4 (3.25%) | 2 (1.63%) |
| Class IIB | 70 (56.92%) | 18 (14.63%) | 12 (9.76%) | 4 (3.25%) |
| Class IIIA | 0 | 0 | 0 | 1 (0.81%) |
| Class IIIB | 1 (0.81%) | 1 (0.81%) | 0 | 0 |
| Class IVA | 0 | 0 | 0 | 0 |
| Class IVB | 2 (1.63%) | 0 | 0 | 1 (0.81%) |
| Class V | 35 (28.45%) | 2 (1.6%) | 0 | 0 |
| Normal | 0 | 74 (60.16%) | 82 (66.67%) | 98 (79.67%) |

Table 2. Average dosage of drugs used during the study (mg/day)

| | Before thymectomy | 6 months after thymectomy | 12 months after thymectomy | During the last follow-up period |
|----------------|-------------------|---------------------------|----------------------------|----------------------------------|
| Pyridostigmine | 360 | 240 | 180 | 180 |
| Prednisolone | 15 | 10 | 12.5 | 10 |
| Azathioprine | 100 | 100 | 100 | 100 |

Table 3. Demographic data and clinical characteristics of patients

| | (n = 123) |
|--|--------------------------|
| Gender (female: male) | 93:30 |
| Age | 49.82 (41.76 to 58.36)* |
| Age when diagnosed | 37.45 (27.51 to 45.33)* |
| Duration from diagnosis to thymectomy (months) | 8.12 (1.87 to 23.21)* |
| Presence of respiratory failure from respiratory muscle weakness before thymectomy | 35 (28.45%) |
| Associated disease | |
| Absent | 30 |
| Present | 93 |
| Thyroid diseases | 55% |
| Diabetes | 35% |
| Rheumatoid arthritis | 6% |
| SLE | 4% |
| Thymectomy techniques | |
| Trans-sternal thymectomy | 115 |
| VATS thymectomy | 8 |
| Duration of follow up (months) | 36.18 (19.82 to 76.9)* |
| Average dosage of medications used during 3 months before thymectomy | |
| Pyridostigmine | 360 mg/day (240 to 480)* |
| Prednisolone | 15 mg/day (10 to 30)* |
| Azathioprine | 100 mg/day (50 to 100)* |
| Number of patients that can reduce medication dosage | |
| Pyridostigmine | 68.55% |
| Prednisolone | 75.86% |
| Azathioprine | 28% |

* Median (interquartile range)

period of follow-up was 100 mg/day.

Comparing the drug dosage before surgery and the last follow-up period, 28% of patients could reduce dosage of azathioprine. From Table 2 The average dose of

pyridostigmine in the last follow-up period had been reduced, compared to before thymectomy and 6 months after thymectomy

To evaluate long-term treatment after thymectomy,

Table 4. Relation between age of diagnosis and treatment results

| Age when diagnosed | Complete stable remission (cases, %) | | Number of cases |
|--------------------|--------------------------------------|------------|-----------------|
| | Yes | No | |
| ≤40 years old | 21 (30) | 49 (70) | 70 |
| >40 years old | 7 (13.21) | 46 (86.79) | 53 |

Table 5. Factors associated with remission of disease after thymectomy

| | Person-time | Incidence rate/ 1,000 patient-month | Hazard ratio (95% CI) | p-value |
|--|-------------|--|-----------------------|---------|
| Gender | | | | |
| Male | 1,613.90 | 3.10 | 1 | |
| Female | 4,464.03 | 5.15 | 1.51 (0.57 to 3.99) | 0.40 |
| Age when diagnosed | | | | |
| ≤40 years old | 3,408.23 | 4.01 | 1 | |
| >40 years old | 2,669.70 | 1.25 | 0.41 (0.18 to 0.98) | 0.04 |
| Associated disease | | | | |
| Present | 1,802.52 | 3.32 | 1 | |
| Absent | 4,275.41 | 5.15 | 1.36 (0.55 to 3.36) | 0.50 |
| Thymectomy technique | | | | |
| Transsternal thymectomy | 5,771.51 | 4.68 | 1 | |
| VATs | 306.43 | 3.26 | 0.49 (0.07 to 3.61) | 0.48 |
| Tissue pathology | | | | |
| Thymic hyperplasia | 2,827.11 | 7.07 | 1 | |
| Thymoma | 1,340.46 | 2.23 | 0.38 (0.11 to 1.28) | 0.12 |
| Thymus involution | 398.07 | 2.51 | 0.36 (0.04 to 2.72) | 0.32 |
| Other | 1,512.30 | 2.64 | 0.43 (0.14 to 1.27) | 0.13 |
| Tissue pathology | | | | |
| Non thymoma | 4,737.48 | 5.28 | 1 | |
| Thymoma | 1,340.46 | 2.23 | 0.48 (0.14 to 1.60) | 0.234 |
| Disease severity before surgery | | | | |
| No respiratory failure | 4,326.07 | 5.54 | 1 | |
| Respiratory failure | 1,751.87 | 2.28 | 0.48 (0.14 to 1.60) | 0.091 |
| Receiving pyridostigmine 6 months after surgery | | | | |
| Yes | 5,743.86 | 4.18 | 1 | |
| No | 334.07 | 11.97 | 3.59 (1.20 to 10.75) | 0.022 |
| Receiving pyridostigmine 12 months after surgery | | | | |
| Yes | 5,386.23 | 3.71 | 1 | |
| No | 691.70 | 11.57 | 3.53 (1.54 to 8.09) | 0.003 |
| Receiving prednisolone 6 months after surgery | | | | |
| Yes | 2,003.34 | 1.99 | 1 | |
| No | 4,074.59 | 5.89 | 3.07 (1.64 to 9.04) | 0.042 |
| Receiving prednisolone 12 months after surgery | | | | |
| Yes | 2,043.80 | 2.44 | 1 | |
| No | 4,034.13 | 5.70 | 2.44 (0.91 to 6.55) | 0.076 |

there were 28 cases (22.76%) that had no symptoms and no need to take medication (complete stable remission; CSR). There were 70 cases (56.91%) that had no symptoms but were still taking medications (pharmacological remission; PR). There were 19 cases (15.45%) that had improvement of

symptoms compared to before thymectomy. There were 5 cases (4.07%) that remained the same as before thymectomy. There was 1 case (0.81%) that had a worsening of symptoms.

Subgroup analysis showed that amongst those diagnosed before 40 years of age, 21 cases (30%) were in

Table 6. Multivariate analysis of factors associated with remission of disease after thymectomy

| Variable | Number of patients | Hazard ratio (95% CI) | p-value |
|--|--------------------|-----------------------|---------|
| Age when diagnosed | | | |
| ≤40 years old | 70 | 1 | |
| >40 years old | 53 | 0.22 (0.09 to 0.55) | 0.001 |
| Dosage of pyridostigmine use 12 months after surgery (every 100 mg of dose increasing) | | 0.42 | <0.001 |

CSR. As for those diagnosed after 40 years of age, 7 (13.21%) were in CSR. Dividing patients into 2 groups good response (including CSR, PR, improved) and poor response (including stable and worsening of symptoms) 117 cases (95.12%) were in good response group and 6 (4.88%) were in the poor response group. Continuous follow-up with the CSR group showed that 35.71% had a recurrence of symptoms. 7 cases (5.7%) that had undergone a thymectomy and received medication treatment had a recurrence of respiratory failure. During the study, 1 case (0.8%) died due to severe pneumonia with septic shock. At the conclusion of the present study, 52.4% of patients remained in regular follow-up, 37.9% were referred to a local hospital, and 9.7% did not follow-up.

Univariate analysis showed that factors associated with the reduction of the CSR rate were an age of diagnosis greater than 40 years old and using pyridostigmine after 6 and 12 months after surgery. The association was statistically significant. Gender, associated diseases, surgical techniques, tissue pathologic results, immunosuppressive drug, dosage of medication received before and after surgery, the occurrence of respiratory failure were not significantly associated with CSR rate.

Multivariate analysis after adjusting confounding factors showed that patients who were diagnosed before 40 years of age were associated with higher CSR rate, 4.55-fold compared to patients who were diagnosed after 40 years of age. The association was statistically significant (hazard ratio 0.22, p -value = 0.001, 95% CI 0.09 to 0.55). For patients who received pyridostigmine at 12 months after surgery, every 100 mg dose increase correlated with a lower rate of CSR at 59%. The association was statistically significant (hazard ratio 0.42, p -value <0.005, 95% CI 0.27 to 0.65).

Discussion

The main treatment of MG consists of pharmacologic therapy including anticholinesterase agents, plasmapheresis, immunosuppressive agents and surgical treatment, and thymectomies. Despite receiving recommended therapy, many patients still suffer from weaknesses.

Previous studies reported improvement rates of 23.2 to 81%^(12,16,17) and remission rates of 25.7 to 40%^(2,5-8,12,13,16) following a thymectomy. Similarly, our study found an overall remission/improvement rate of 95.12% and a clinical unchanged/worsened rate of 12.5%. The results showed that 28 patients (22.76%) were in (complete stable remission (CSR). 70 patients (56.91%) were in pharmacological

remission (PR). 19 patients (15.45%) showed improvement of symptoms but were not in remission. 5 of them (4.07%) were stable. 1 patient (0.81%) was in worse condition.

The factors affecting the disease remission were the higher dosage of pyridostigmine used 12 months after surgery that lead to a statistically significant lower remission rate, and age of diagnosis at 40 years old or below was significantly associated with the higher remission rate. Similar results to previous studies that younger aged patients had better result of treatment^(5,9,18).

Gender, duration of disease before surgery, and occurrence of respiratory failure prior to surgery, had no statistical significance associated with CSR. The present study showed that the occurrence of respiratory failure prior to surgery caused delayed remission, but it was not statistically significant, similar to the study results from Lin, et al⁽³⁾ and Witoonpanich R, et al⁽¹²⁾. In contrast, results from Sonett J⁽¹⁵⁾ showed that the less severe diseases were associated with a higher remission rate.

Two surgical thymectomy techniques had no statistically significant results in disease outcome, comparable with previous study from Yu, et al⁽¹⁶⁾ and Mantegazza R, et al⁽¹⁰⁾. Furthermore, tissue pathology results had no effects on remission rate, similar to Huang CS, et al⁽¹¹⁾, Kim HK, et al⁽¹⁹⁾ and Donaldson DH, et al⁽²⁰⁾. However, in contrast to Yu, et al⁽¹⁶⁾ and Cosi V, et al⁽²¹⁾ stated that non-thymoma results were significantly associated with higher remission rate, especially thymic hyperplasia which is associated with a better treatment outcome^(8,10). There were some previous studies that showed that the tissue pathologic result of thymoma is significantly associated with poorer outcome^(2,5,20,22).

The present study has several limitations. First, Myasthenia gravis is a rare disease and the inclusion criteria population has to have undergone a thymectomy, so the sample size is small. Second, the study is a retrospective study that might be biased due to missing data and the heterogeneity of medical records on the symptoms and severity of the patients, both pre- and post-operatively.

However, the present study is superior in number of sample size compared to previous studies, as the study was held at a medical school in a tertiary care hospital with patients that were referred from other hospitals in North Eastern Thailand. There were well-documented medical records that could be reviewed.

Conclusion

Thymectomies along with medical treatment seems to be an effective treatment for Myasthenia gravis patients that lead to remission and good responses. Factors that were significantly associated with higher remission rate were age when diagnosed before 40 years and the dosage of pyridostigmine of less than 100 mg 12 months after surgery. There are several ways to improve the power of this study. First, to reduce recall bias, a prospective study may improve the study. Second, other factors that may affect outcome of treatment such as AChR antibody and Anti-MuSK should be obtained. Third, for standard medical records and to reduce heterogeneity, systematic pattern of records should be obtained, including disease severity, symptoms, dosage of each medication. Finally, there should be a more effective follow-up system.

What is already known on this topic?

Myasthenia gravis (MG) is an autoimmune disorder that affects the neuromuscular junction of skeletal muscles. Main treatments consist of pharmacologic and surgical treatments, such as a thymectomy.

What this study adds?

Thymectomies along with medical treatment seems to be an effective treatment for Myasthenia gravis patients that lead to remission and good responses.

Potential conflicts of interest

The authors declare no conflicts of interest.

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ผลการรักษาระยะยาวด้วยการผ่าตัดต่อมไทมัสและปัจจัยที่มีผลต่อการดำเนินของโรคกล้ามเนื้ออ่อนแรงมิยแอสทีเนียกราวิส

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ภูมิหลัง: โรคกล้ามเนื้ออ่อนแรงมิยแอสทีเนียกราวิส (myasthenia gravis; MG) เป็นโรคภูมิคุ้มกันต่อต้านตนเองชนิดหนึ่ง ส่งผลต่อการส่งกระแสประสาทบริเวณ neuromuscular junction การรักษาหลักเป็นการรักษาด้วยยา และการผ่าตัดต่อมไทมัสเมื่อมีข้อบ่งชี้ มีผู้ป่วยเป็นจำนวนมากที่ได้รับการรักษาตามข้อบ่งชี้ แต่อาการอ่อนแรงยังไม่ดีขึ้น ข้อมูลเกี่ยวกับการตอบสนองต่อการรักษาและผลระยะยาวหลังจากการผ่าตัดต่อมไทมัสยังมีจำนวนน้อย

วัตถุประสงค์: เพื่อศึกษาการตอบสนองต่อการรักษาหลังการผ่าตัดต่อมไทมัส และศึกษาผลระยะยาวหลังจากการผ่าตัดต่อมไทมัส ปริมาณยาที่ใช้เทียบก่อนและหลังผ่าตัด และปัจจัยที่มีผลต่อการสงบของโรคหลังการผ่าตัดต่อมไทมัส

วัสดุและวิธีการ: เป็นการศึกษาวิจัยแบบย้อนหลัง ในผู้ป่วยโรคกล้ามเนื้ออ่อนแรงมิยแอสทีเนียกราวิส จำนวน 123 ราย ที่ได้รับการรักษาด้วยยาและการผ่าตัดต่อมไทมัส ระหว่าง ปี พ.ศ. 2540 ถึง พ.ศ. 2554 ซึ่งมารักษาที่โรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น

ผลการศึกษา: ผู้ป่วย 123 ราย มีผู้ป่วยเพศหญิง 94 ราย (ร้อยละ 75.8) มีค่ามัธยฐานของอายุ 49.82 ปี (พิสัยควอไทล์ 41.76 ถึง 58.36) อายุที่วินิจฉัย 37.45 ปี (27.51 ถึง 45.33) ค่าเฉลี่ยของระยะเวลาดังแต่วินิจฉัยถึงการผ่าตัดต่อมไทมัสเท่ากับ 8.12 เดือน (1.87 ถึง 23.21) วิธีการผ่าตัดที่ใช้ประกอบด้วย การผ่าตัดผ่านกระดูกหน้าอก จำนวน 115 ราย และการผ่าตัดโดยการส่องกล้อง 8 ราย ระยะเวลาดิตตามการรักษาหลังผ่าตัดเฉลี่ย 36.18 เดือน (19.82 ถึง 76.90) ผลขึ้นเนื่องจากการผ่าตัดเป็นเนื้องอกต่อมไทมัสร้อยละ 20.32 และไม่ใช่เนื้องอกต่อมไทมัสร้อยละ 79.68 เมื่อศึกษาการตอบสนองต่อการรักษามีผู้ป่วยที่โรคสงบโดยปราศจากการใช้ยาและสามารถหยุดยาทั้งหมดได้ (complete stable remission; CSR) 28 ราย (ร้อยละ 22.76) มีผู้ป่วยที่โรคสงบแต่ยังต้องใช้ยา (pharmacologic remission; PR) 70 ราย (ร้อยละ 56.91) มีผู้ป่วยอาการดีขึ้น แต่ยังต้องใช้ยา 19 ราย (ร้อยละ 15.45) มีผู้ป่วยอาการคงที่ 5 ราย (ร้อยละ 4.07) และมีผู้ป่วยที่อาการแย่ลง 1 ราย (ร้อยละ 0.81) ซึ่งเมื่อเทียบอาการระหว่างก่อนเข้ารับการรักษา ด้วยการผ่าตัดต่อมไทมัสและการติดตามการรักษาแล้วสุดท้ายที่แผนกผู้ป่วยนอก พบว่ามีผู้ป่วยที่ตอบสนองดี (CSR, PR และอาการดีขึ้น) ร้อยละ 95.12 และมีผู้ป่วยที่ตอบสนองไม่ดี (อาการคงที่และแย่ลง) คิดเป็นร้อยละ 4.88 หลังการผ่าตัดผู้ป่วยส่วนมากสามารถลดปริมาณยาที่ใช้ลงได้ อายุที่วินิจฉัยโรคน้อยกว่า 40 ปี และการใช้ยา pyridostigmine ในขนาดที่น้อยกว่า 100 มิลลิกรัมในช่วง 12 เดือนหลังผ่าตัดเป็นปัจจัยที่มีผลต่อการสงบของโรคอย่างมีนัยสำคัญทางสถิติ

สรุป: การผ่าตัดต่อมไทมัสร่วมกับการรักษาด้วยยาสำหรับผู้ป่วยโรคกล้ามเนื้ออ่อนแรงมิยแอสทีเนียกราวิส ผู้ป่วยส่วนมากเกิดโรคสงบและอาการดีขึ้น ปัจจัยที่มีผลต่อการสงบของโรคคือ อายุขณะวินิจฉัยที่น้อยกว่า 40 ปี และการใช้ยา pyridostigmine ในขนาดที่น้อยกว่า 100 มิลลิกรัมในช่วง 12 เดือนหลังผ่าตัด
