ORIGINAL ARTICLE

UDC: 616.8:617.542
DOI: https://doi.org/10.2298/VSP190715133M

The neurological outcome in the patients with myasthenia gravis who underwent thymectomy via sternotomy and video-assisted thoracoscopic surgery (VATS)

Neurološki ishod lečenja bolesnika sa miastenijom gravis koji su timektomisani sternotomijom i video asistiranom torakoskopskom hirurgijom (VATH)

Vesna Martić*†, Nebojša Marić†‡, Vlado Cvijanović†‡

Military Medical Academy, *Clinic for Neurology, ‡Clinic for Thoracic Surgery, Belgrade, Serbia; †University of Defence, Faculty of Medicine of the Military Medical Academy, Belgrade, Serbia

Abstract

Background/Aim. Thymectomy is accepted in the surgical treatment of the patients with myasthenia gravis (MG). Earlier thymectomy via sternotomy has recently been replaced by video-assisted thoracoscopic surgery (VATS), which is less invasive. The aim of this study was to determine the effectiveness and reliability of the two methods of surgical removal of the thymus by comparing the neurological outcome in patients with MG. **Methods.** The study included 60 patients with MG who underwent thymectomy at the beginning of their treatment: 30 patients underwent thymectomy via sternotomy, and the remaining 30 patients via VATS. In order to evaluate the effects of these two operation techniques, we compared the data related directly to the operation – the number of postoperative hospital days, the incidence of postoperative complications, as well as the data related to the neurological monitoring of these patients: directly after the operation, one year after the surgery and up to three years after the surgery. **Results.** The data related to the immediate postoperative period indicate a significantly shorter hospitalization after the VATS thymectomy (p < 0.001), but the percentage of postoperative complications in both groups was the same (p = 0.381). Clinical deterioration in the first year after the operation showed a uniform distribution, regardless of the type of performed operation (p = 0.470). The number of performed rethymectomies in the group that underwent thymectomy via sternotomy vs. VATS was of borderline statistical significance (p = 0.054). Complete stable remission, as a confirmation that the thymic tissue was removed in its entirety, was observed in about 11% of the patients who underwent thymectomy. For other patients, clinical remission was maintained with anticholinesterase and immunosuppressive therapy. **Conclusion.** The shorter hospitalization time and faster postoperative recovery, with an equal clinical efficacy and aesthetic component, favors the VATS thymectomy compared to thymectomy via sternotomy as more acceptable in the surgical treatment of the patients with MG.

Key words:
myasthenia gravis; thymectomy; sternotomy; surgery, thoracic, video-assisted; surgery, thoracic, procedures; treatment, outcome.

Apstrakt

Uvod/Cilj. Timektomija je prihvaćena metoda hirurškog lečenja bolesnika sa miastenijom gravis (MG). Ranija timektomija putem sternotomije zamenjena je poslednjih godina video asistiranom torakoskopskom hirurgijom (VATH) kao manje invanzivnom metodom. Cilj rada bio je da se poređenjem neurološkog ishoda utvrde efikasnost i pouzdanost te dve metode hirurškog uklanjanja timusa kod bolesnika sa MG. **Metode.** Studijom je bilo obuhvaćeno 60 bolesnika sa MG koji su timektomisani na početku lečenja: 30 bolesnika je timektomisano sternotomijom, a preostalih 30 putem VATH. U cilju procene efekata te dve operativne tehnike poređeni su podaci koji su se odnosili direktno na operaciju – broj hospitalnih dana posle operacije, incidencija postoperativnih komplikacija, ali i podaci koji se tiču neurološkog praćenja tih bolesnika: neposredno posle operacije, godinu dana posle operacije i do 3 godine posle operacije. **Rezultati.** Podaci koji se odnose na neposredni postoperativni period ukazali su na signifikantno kraću hospitalizaciju posle timektomije putem VATH (p < 0,001), dok je procenat postoperativnih komplikacija u obe grube bio isti (p = 0,381). Utvrđena je uniformna distribucija kliničkog

Correspondence to: Vesna Martić, Military Medical Academy, Clinic of Neurology, Crnotravska 17, 11 000 Belgrade, Serbia.
E-mail: vesnamartic.bgd@gmail.com

pogoršanja prve godine posle operacije, nezavisno od načina operacije (p = 0,470). Broj učinjenih retimektomija u grupi bolesnika putem VATH bio je granično statistički značajan (p = 0,054). Kompletna stabilna remisija, kao potvrda da je timusno tkivo bilo uklonjeno u potpunosti ostvarena je kod oko 11% timektomisanih bolesnika. Kod ostalih bolesnika klinička remisija je održavana antiholinesteraznom i imunosupresivnom terapijom. **Zaključak.** Kraća hospitalizacija i brži postoperativni oporavak sa podjednakim kliničkim učinkom i estetskom komponentom favorizuju timektomiju VATH u odnosu na timektomiju putem sternotomije kao prihvatljivijom metodom hirurškog lečenja obolelih od MG.

Ključne reči:
miastenija gravis; timektomija; sternotomija; hirurgija, torakalna, video-asistirana; hirurgija, torakalna, procedure; lečenje, ishod.

Introduction

Myasthenia gravis (MG) is an autoimmune disease characterized by pathological weakness and fatigue of voluntary muscles. Besides a conservative treatment, thymectomy takes an important role in the treatment of patients with MG [1, 2]. Surgical removal of the thymus gland in the patients with MG allows a stable clinical course, the greater number of clinical remissions, and reduces the dose of a drug required in the conservative treatment of the disease [3].

It is believed that the thymus is responsible for the initiation of the immunological processes, which cause the occurrence of autoantibodies to the acetylcholine receptor (AChR) [4]. Although the association with the anti-MG acetylcholine receptor (AChR) antibodies was first noticed by Lindstrom et al. [5] in 1976, the benefit of thymectomy in patients suffering from MG was observed much earlier, at the beginning of the last century. So, the first thymectomy in patients with MG was performed in 1911 by Ferdinand Sauerbruch, in a transcervical way, after the X-ray recording of the chest showed an increased thymic shadow, and after the thymectomy a clinical recovery was recorded. Since transcervical thymectomy proved insufficient because of the low visibility and since it was accompanied by the large remnants of residual thymic tissue which required rethymectomy, it was quickly replaced by thymectomy via sternotomy [6].

Thymectomy via sternotomy was described for the first time in 1939 by Dr. Alfred Blalock in the case of a 21-year-old patient with MG, following her clinical remission for 3 years [2].

Some time after that, in 1941, thymectomy was performed on 7 MG patients without thymoma, also with a clinical postoperative recovery. Blalock published his results in the series of 20 patients in 1944 [2].

Thymectomy via sternotomy as the optimal method of surgical treatment was long in use, until 1993, when David Sugarbaker for the first time made a video-assisted thoracoscopy (VATS) with laparoscopic approach to the thymus from the auxiliary area, which was far less invasive and accompanied by smaller postoperative scars [7].

The goal of thymectomy is a complete removal of the thymus gland and mediastinal fat tissue that can be a source of ectopic thymic tissue, which is often not available using modern diagnostics.

Since thymectomy via sternotomy approach requires full and open access to the chest cavity, which leaves a big scar (Figure 1), VATS thymectomy has almost entirely taken its place in recent years (Figure 2).

Fig. 1 – The scar after thymectomy via sternotomy.

Fig. 2 – The scar after thymectomy via video-assisted thoracoscopy (VATS).

In our region, VATS thymectomy was first performed in 2012. By the end of 2018, at the Clinic of Thoracic Surgery, Military Medical Academy in Belgrde, 70 VATS thymectomy was performed using at first three, then two, and

now uniportal VATS thymectomy that is described as the standard [8].

This study compared the results of patients with MG who underwent thymectomy via sternotomy and VATS.

Methods

Among 60 patients with clinically, neuropsychologically, immunologically and pharmacologically verified MG treated at the Clinic for Neurology, Military Medical Academy in Belgrade from 2000 to 2018, 30 patients underwent thymectomy via sternotomy and the other 30 via VATS.

VATS thymectomy, as a newer surgical technique has been used at our institution since 2012, and after that all of our patients underwent thymectomy by VATS. In patients operated via VATS method, a unipolar technique by one-sided access to the right or left side was used, which was decided on by a thoracic surgeon with respect to the anatomical localization of the thymus, but the access to the right was more secure because of the relationship with the brachiocephalic vein.

Duo to the pathohistological (PH) findings in the operated thymus, we distinguish atrophic thymus, hyperplasia thymus and the thymoma.

In relation to the way of thymectomy, we compared the following parameters: age, gender, the length of hospitalization, the incidence of complications and lethal outcomes immediately after the thymectomy, the incidence and treatment of postoperative exacerbations, the frequency of rethymectomy, and the length of postoperative recovery.

As a stable and complete remission was the confirmation that the thymic tissue was completely removed, we followed the postoperative outcome immediately after thymectomy, then one year after the operation, as well as for a period longer than one year (up to 3 years). In doing so, the clinical status of the patients was assessed by Oserman and Genkins [9].

In order to evaluate the effect of these two operation techniques, we compared the data related directly to the operation (the number of postoperative hospital days, the incidence of postoperative complications), as well as the data related to the neurological monitoring of these patients in the form of postoperative recurrence and rethymectomies due to residual thymic tissue. The evaluation of the clinical disease achieved by comparing the severity of the disease was performed according to Osserman and Genkins [9] method pre- and postoperatively: immediate postoperatively, on the day of the discharge, one year after the surgery and up to three years after it.

With regard to the recommendation that a thymectomy should be done when the patient is stable, the patients achieved clinical remission with medicaments first, and following that the thymectomy was performed. With medications, the patients were held in a state of clinical remission during the postoperative recovery.

In the postoperative period, the dosages of corticosteroids were carefully reduced because any reduction of the dose of the drug carries a risk of relapse. Non-steroidal immunosuppressive drugs were added when a corticosteroid therapy was not enough or in order to avoid its adverse effects. According to the consensus of experts, among non-steroidal immunosuppressive drugs, azathioprine is the first choice for the treatment of MG, which was respected in our group of patients, who were very tolerant and without any side effects from the therapy with azathioprine. The deterioration of their condition most frequently occurred due to the abrupt reduction in therapy, due to an infection or due to residual thymic tissue. Therefore, clinical deterioration was the indication for the control scanner of the chest.

A complete statistical analysis of the data was done with the statistical software package, SPSS Statistics 18.

Most of the variables were presented as the frequency of certain categories, while the statistical significance of differences was tested with the χ^2 test.

In case of continuous data, variables were presented as mean value ± standard deviation (SD), minimal (min) and maximal (max) values. Kolmogorov-Smirnov test was used for the evaluation of normal data distribution. According to the results of this test, statistical significance between the groups was tested by *t*-test or alternatively by Mann-Whitney or Wilcoxon test.

All the analyses were estimated at $p < 0.05$ level of statistical significance.

Results

As in the total population of our patients (43 women and 17 men), and in both groups of patients operated by different techniques, women significantly dominated: 70.6% in the group with thymectomy via sternotomy and 76.9% in the group operated via VATS ($p < 0.001$); so there were no statistically significant differences in the distribution of the sexes in both groups.

The average age of our patients in the total population was 41.67 ± 13.90 years (min 28, max. 65 years) and there were no statistically significant differences in age among the sexes ($p = 0.236$) or between the groups of patients operated by different techniques ($p = 0.486$).

The average duration of hospitalization for the patients operated via sternotomy was 10.13 ± 2.604 days (the shortest 4 and the longest 16 days), while the average duration of hospitalization for the operated by VATS was 5.04 ± 1.661 (minimum of 2 and maximum of 9 days). Comparing the duration of the hospitalization in relation to the manner of thymectomy performed, statistically significantly longer hospitalization was after the thymectomy via sternotomy ($p < 0.001$).

Among the postoperative complications, all patients reported soft and transient paresthesia in the operated area, which withdrew in the first few postoperative months. Among the more serious complications, there was one death during the first week of operation due to myocardial infarction in the group operated via sternotomy, which proved to be statistically insignificant in terms of postoperative complications among the patients operated with different surgical techniques ($p = 0.381$). Pneumonia and myasthenic crisis,

which are often mentioned as possible postoperative complications, were not seen among our patients.

The average clinical condition score in patients before the operation via sternotomy was 2.65 ± 0.702 (min 2, max 4), and after the operation 1.20 ± 1.08 (min 0, max 3), which indicates a statistically significant recovery ($p = 0.002$). The average preoperative clinical condition score of patients operated via VATS method was 2.0 ± 0.75 (min 1, max 4) and after the operation 1.0 ± 1.0 (min 0, max 3), which indicates a statistically significant postoperative recovery, also ($p \leq 0.001$). In addition, there was no significant difference in the preoperative MG severity between the patients treated with different surgical techniques ($p = 0.062$). To conclude, there was a significant clinical improvement after the thymectomy via sternotomy and VATS method ($p = 0.01$). A comparison of the immediate postoperative outcomes demonstrated that both operational techniques are equally successful when it comes to the immediate postoperative recovery ($p = 0.762$).

Comfort scanner of the chest, performed in 3 of the patients, showed rest of thymic tissue, which was an indication for reoperation (Figure 3). All 3 reoperated patients had been operated via sternotomy previously. Among the reoperated patients, two underwent sternotomy again, but one patient underwent VATS. This difference in the number of reoperated patients treated with the different techniques, was of borderline statistical significance ($p = 0.054$). There were no complications in the reoperated patients.

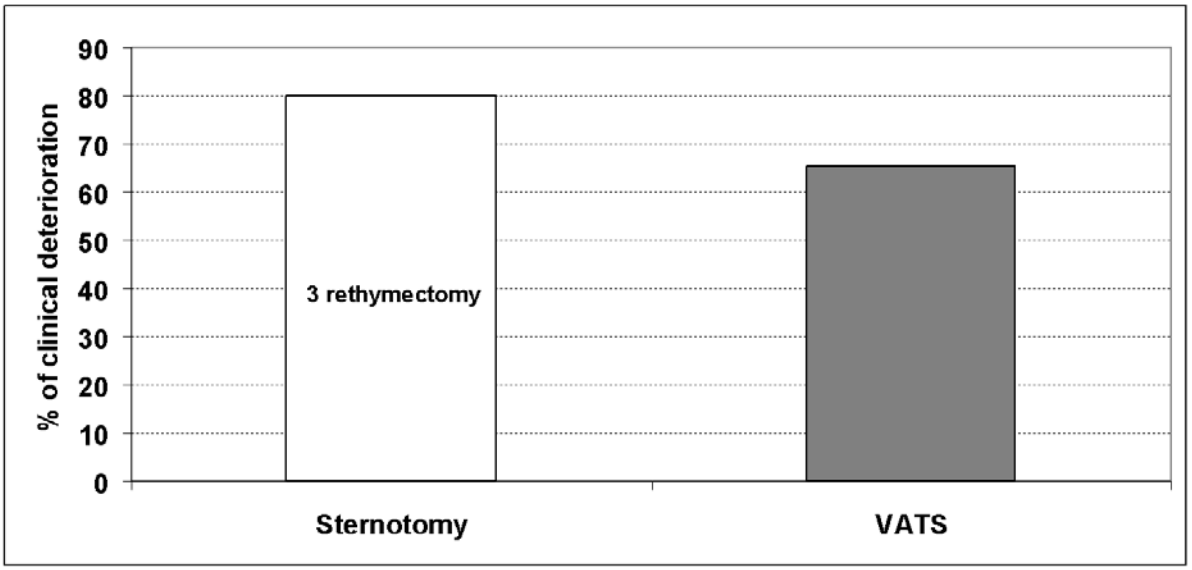

Fig. 3 – The number of rethymectomies during the first year after the thymectomy. VATS – video-assisted thoracoscopic surgery.

During the first year after the surgery, clinical deterioration occurred in 24 (80%) of the patients who underwent sternotomy and in the group operated on by VATS, deterioration was noted in 15 (65.2%) of the patients (Figure 3). This difference in percentage was not statistically significant, and there was a homogeneous distribution of deterioration regardless of the type of surgery ($p = 0.470$).

We observed a recorded patient, reoperated via sternotomy, in whom deterioration was provoked by an infectious syndrome during the first year after surgery.

In patients without the rest of thymic tissue, clinical deterioration was solved by raising the dose of the existing anticholinesterase and corticosteroid therapy (80% operated on via sternotomy and 56.5% operated on by VATS). The introduction of azathioprine (Imuran®) in the therapy was recorded in 20% of the patients operated on via sternotomy and in 34.8% of the patients operated on by VATS); therapeutic plasma exchange (PE) was used in none of the patients operated on via sternotomy and in 8.7% of those operated on by VATS (the PE is useful when other therapies are not sufficient, or when it is necessary to minimize the exacerbations). Using χ^2 test ($p = 0.325$), no statistically significant differences were found in the treatment of the deterioration in the patients operated on by various techniques.

The reliable data about our patients in the next two years were obtained only for 34 patients: for 12 operated on via sternotomy and 22 operated on via VATS. In the observation period of 3 years after the thymectomy, 2 patients from both operated groups were in a complete clinical remission – disease symptom-free and without a treatment for the period of one year.

The second group of patients was only on pyridostigmine (Mestinon®): 3 patients operated on via sternotomy and 1 patient operated on via VATS were included. The third group of patients was on Mestinon® and on corticosteroid therapy: 2 patients underwent sternotomy and 6 patients were operated on by VATS.

The fourth group was treated with Imuran®: 5 patients were operated on via sternotomy and 13 were operated on via VATS. None of the patients underwent PE a year after the thymectomy (Figure 4).

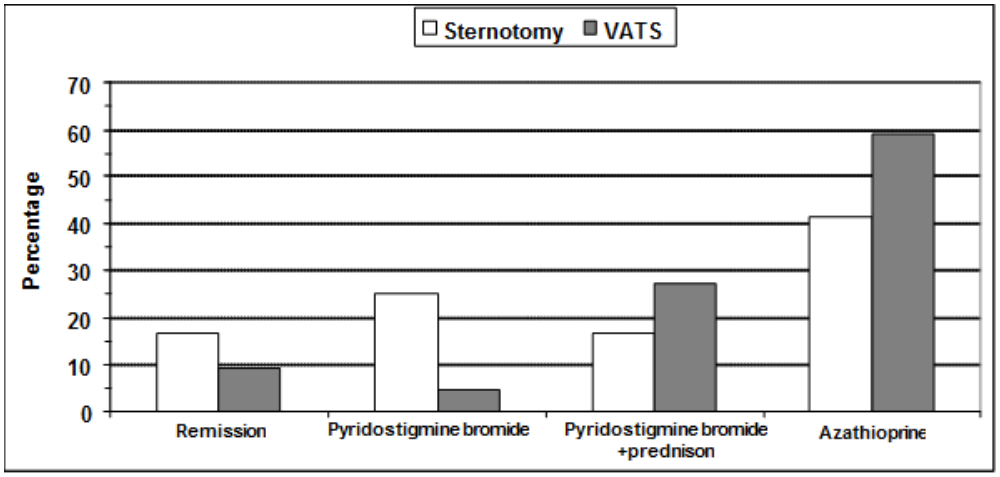

Fig. 4 – Clinical outcome and therapy 3 years after the surgery (% of patients)
VATS – video-assisted thoracoscopic surgery.

The χ^2 test showed that the kind of treatment did not significantly differ in patients operated on by a different techniques more than one year after the operation ($p = 0.358$).

In the group operated on by sternotomy, 2 patients had atrophic thymus, 1 had thymoma and 27 patients had thymic hyperplasia. In the group of patients operated on by VATS, 3 had atrophic thymus, one thymoma and 26 patients thymic hyperplasia.

Among our patients, one was seronegative; he was treated by VATS, and in this patient a thymic hyperplasia was seen.

PH type of thymus was almost uniform in the group of patients operated on by sternotomy and the patients operated on via VATS ($p = 0.896$).

A total of 5 patients were diagnosed with the atrophy of the thymus. The average age of these patients was 67.60 ± 6.986 years and it was a statistically significant difference compared to the patients with thymic hyperplasia and thymoma ($p < 0.001$).

Discussion

Thymectomy is an option which can minimize or even avoid immunosuppressive therapy in seropositive generalized myasthenia. It is suggested in younger than 45 years of age, with the advice to be done as soon as possible, because then the better the results of treatment can be achieved[10].

As MG is a heterogeneous disease, there is no single standard in the treatment of this disease that has been accepted as the best for everyone with MG [11]. Initial therapy dose of pyridostigmine should be adjusted to the symptoms of the disease. Corticosteroids and immunosuppressive therapy are introduced when pyridostigmine is not enough to achieve therapeutic goals [11, 13].

Younger patients, with a less severe and shorter duration of the disease, more likely have a complete remission after thymectomy [3].

Clinical remission refers to the situation in which a patient is disease-free and may have some weakness in the closing of the eyes, but without any other weakness of the muscles [11].

Also, thymectomy is done in seronegative generalized MG patients, when there is weak and uncertain response to immunosuppressive therapy [11].

If a patient does not respond or has insecure course to immunosuppressive therapy or if there are side-effects after its initiation, thymectomy is the method of choice in elderly patients, also [10]. As we followed this recommendation, the average age of our patients was 41.67 ± 13.902 years.

All MG patients with thymoma should be operated on [12].

Women were dominant in our group of the operated patients, corresponding to the data from the literature, where there is a higher incidence of women with the early-onset MG (before the age of 50), in which thymectomy is primarily indicated [1, 13].

Publications of sporadic positive effects of thymectomy on the clinical course of patients with MG have recently been replaced by the publications which compare the clinical course of patients treated surgically and conservatively [3, 8, 14].

One of them has shown a significantly more likely achieved clinical remission after thymectomy than without the operation (20% vs. 10%) [6].

In our group of a total of 60 patients, a significant improvement in the clinical picture of patients directly after thymectomy ($p = 0.01$) has been noted.

The effect of thymectomy in different decades in the period from 1940 to 2000 was followed by another large study [6], which observed that in all the decades the number of patients in complete clinical remission is about 10%. It corresponds to our results that about 11% of our patients were in complete clinical remission and without a treatment for a period longer than one year [6]. The number of patients who had postoperative recovery gradually grew from 30% to almost 60% at the closing decade of the year 2000. Clinical remission of our patients was achieved by combining differently anticholinesterase and immunosuppressive drugs but no patient required PE in the period after one year after thymectomy.

The percentage of subjects [3, 10] whose condition continued to deteriorate and those who died decreased from decade to decade, which perhaps explains the modern concepts of pharmacological treatment of this disease.

It is known that MG with early or late beginning has a different HLA gene and various autoimmune targets, but the same mechanism of development. The existence of different targets of autoimmunity confirms the differences in thymic pathology: follicular hyperplasia of the thymus is often seen in the early onset of a seropositive MG, whereas the atrophy of the thymus is the most common finding in late onset of MG (15–20%) [6, 13]. There is an equal distribution of different PH findings of thymus: thymoma, thymic atrophy and hyperplasia ($p = 0.896$) among our patients operated on by different techniques.

Atrophic thymus was found in five of our patients (16.7%). They were significantly older (67.60 ± 6.97 years) compared to the patients with hyperplasia and thymoma ($p < 0.001$) in the corresponding data from the literature.

Thymoma is seen in 10% to 15% of cases [15], usually between 45 and 55 years of age, which corresponds to our results because thymoma was found in one patient in both groups.

Following parameters directly related to the operation, such as the duration of the operation, intraoperative blood loss, the perception of pain, duration of hospitalization, the need for artificial respiration, postoperative complications resulting in death have been most commonly used in comparison effects of thymectomy via sternotomy and via VATS [15, 16]: It has been shown a certain advantage of VATS thymectomy in relation to thymectomy via sternotomy due to a shorter hospitalization, minor loss of blood and better cosmetic effect. A meta-analysis of 12 studies that dealt with this problem also gives the advantage to VATS thymectomy because fewer postoperative complications and low frequency of myasthenic crisis [17, 18]. Similar data were obtained in our group of patients: significantly longer hospitalization after sternotomy ($p < 0.001$), and one death in the group operated via sternotomy, which did not come out statistically significant, while myasthenic crisis and pneumonia, often referred to as postoperative complications in the literature, were not observed among our patients [17].

The incomplete removal of the thymus leads to an unstable postoperative course, while the criteria for a complete stable remission is that the thymic tissue was removed in its entirety [18]. Therefore, apart from the results related directly to the operation, we followed the clinical status of our patients immediately after the surgery, then one and 3 years after the operation.

Immediate postoperative recovery was statistically significant ($p = 0.002$), and both operational techniques were equally effective ($p = 0.762$).

The number of clinical deteriorations in the first year after the operation showed that there was a homogeneous distribution of deterioration, regardless of the type of surgery ($p = 0.470$). In 3 patients the cause of deterioration was the remnant of thymic tissue, which was an indication for rethymectomy.

All 3 patients who had a need for rethymectomy had previously been operated by sternotomy. This difference in the number of rethymectomies between patients treated by various techniques was of borderline statistical significance ($p = 0.054$).

Other exacerbations were solved by correcting anticholinesterase therapy and corticosteroids, the introduction of azathioprine and a series of PE.

It was concluded that there were no statistically significant differences ($p = 0.325$) in the treatment of deterioration in the patients operated on by various techniques.

Three years after the surgery, two (around 11%) of the patients in both operated groups were in complete clinical remission: symptom-free and without a treatment for a period longer than one year [8]. Other patients were on the combination of anticholinesterase therapy and immunosuppressives, and none of them had a need for PE. Types of treatment, 3 years after the operation, were not significantly different in patients operated on by different techniques ($p = 0.358$).

Conclusion

The sternotomy and VATS thymectomy achieve equal clinical results, but shorter hospitalizations and better cosmetic effects favor VATS, and it is now a more acceptable technique for thymectomy in the patients with MG.

REFERENCES

1. *Wilkins KB, Bulkley GB.* Thymectomy in the integrated management of myasthenia gravis. Adv Surg 1999; 32: 105–33.
2. *Kirschner PA.* Alfred Blalock and thymectomy for myasthenia gravis. Ann Thorac Surg 1987; 43(3): 348–9.
3. *Beghi E, Antozzi C, Batocchi AP, Cornelio F, Cosi V, Evoli A*, et al. Prognosis of myasthenia gravis: a multicenter follow-up study of 844 patients. 1991. J Neurol Sci J 1991; 106(2): 213–20.
4. *Grob D.* Course and management of myasthenia gravis. J Am Med Assoc 1953; 153(6): 529–32.
5. *Lindstrom JM, Seybold ME, Lennon VA, Whittingham S, Duane DD.* Antibody to acetylcholine receptor in myasthenia gravis. Prevalence, clinical correlates, and diagnostic value. Neurology 1976; 26(11): 1054–9.
6. *Kirschner PA.* The history of surgery of the thymus gland. Chest Surg Clin N Am 2000; 10(1): 153–65, x.
7. *Sugarbaker DJ.* Thoracoscopy in the management of anterior mediastinal masses. Ann Thorac Surg 1993; 56(3): 653–6.
8. *Caronia FP, Arrigo E, Trovato S, Lo Monte AI, Cottone S, Sgalambro F,* et al. Uniportal bilateral video-assisted sequential thoracoscopic extended thymectomy. J Vis Surg 2017; 3: 69.
9. *Osserman KE, Genkins G.* Studies in myasthenia gravis: review of a twenty-year experience in over 1200 patients. Mt Sinai J Med 1971; 38(6): 497–537.
10. *Fan L, Ma S, Yang Y, Yan Z, Li J, Li Z.* Clinical differences of early and late-onset myasthenia gravis in 985 patients. Neurol Res 2019; 41(1): 45–51.

11. *Sanders DB, Wolfe GI, Benatar M, Evoli A, Gilhus NE, Illa I,* et al. International consensus guidance for management of myasthenia gravis. Neurology 2016; 87(4): 419–25.
12. *Jaretzki A 3rd, Barohn RJ, Ernstoff RM, Kaminski HJ, Keesey JC, Penn AS*, et al. Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Neurology 2000; 55(1): 16–23.
13. *Sussman J, Farrugia ME, Maddison P, Hill M, Leite MI, Hilton Jones D*. Myasthenia gravis: Association of British Neurologist management guidelines. Prac Neurol 2015; 15(3): 199–206.
14. *Palace J, Newsom-Davis J, Lecky B*. A randomized double-blind trial of prednisolone alone or with azathioprine in myasthenia gravis. Myasthenia Gravis Study Group. Neurology 1998; 50(6): 1778–83.
15. *Lo CM, Lu HI, Hsieh MJ, Lee SS, Chang JP*. Thymectomy for myasthenia gravis: Video assisted versus transsternal. J Formos Med Assoc 2014; 113(10): 722–6.
16. *Chang PC, Chou SH, Kao EL, Cheng YJ, Chuang HY, Liu CK,* et al. Bilateral video-assisted thoracoscopic thymectomy vs extended transsternal thymectomy in myasthenia gravis: a prospective study. Eur Surg Res 2005; 37(4): 199–203.
17. *Zahid I, Sharif S, Routledge T, Scarci M*. Video-assisted thoracoscopic surgery or transsternal thymectomy in the treatment of myasthenia gravis? Interact Cardiovas Thorac Surg 2011; 12(1): 40–6.
18. *Qi K, Wang B, Wang B, Zhang LB, Chu XY*. Video-assisted thoracoscopic surgery thymectomy versus open thymectomy in patients with myasthenia gravis: a meta-analysis. Acta Chir Belg 2016; 116(5): 282–8.

Received on July 15, 2019
Revised on November 25, 2019
Accepted on November 25, 2019
Online First November, 2019