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Research Article

Extended Videothoracoscopy Thymectomy in Patient with Myasthenia Gravis without Thymoma

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Abstract

Introduction: Thymectomy is the surgical treatment for patients with myasthenia gravis (MG). Recently, thymectomy is being performed using less invasive surgical techniques with the aim of minimizing surgical damage and the appearance of perioperative myasthenic attacks. Our objective is to analyze the safety of this procedure in patients with MG and in its follow-up.

Methods: This is a prospective follow-up study where we analyzed 42 patients collected from January 1, 2010 to January 1, 2017. Patients underwent extended thymectomy with the previous clinical diagnosis of MG without thymoma using videothoracoscopy (VATS).

Results: Patients presented an average age of 42 years and predominance of females (29 women). Surgical approach was a right video-assisted thoracoscopy and CO2 insufflation with a pressure of 8 mmHg. All patients underwent an extended thymectomy. The average surgical time was 111 minutes. Median length of hospital stay was 2 days (1 - 7). Two patients (4.7%) had a myasthenic crisis that required admission to the ICU and plasmapheresis. 3 patients (7.1%) presented infection of surgical wound and were treated with oral antibiotic. There were no perioperative deaths. With a median follow-up of 29 months, 33 (78.6%) patients are without treatment or with a decrease in the amounts of treatment prior to surgery.

Conclusion: Video-assisted thoracoscopy thymectomy for MG is a safe and effective procedure for the treatment of MG.

Keywords: *Myasthenia Gravis; Thymectomy; Videothoracoscopy; Myasthenia Gravis; Thymectomy; Video-Assisted Thoracoscopy; Myasthenic Crisis*

Abbreviations

VATS: Videothoracoscopy; MG: Myasthenia Gravis; TAC: Computed Tomography

Introduction

MG is a pathology of autoimmune etiology. The basis of its pathophysiology involves a blockage of the motor plate by binding of serum antibodies by binding to acetylcholine receptors of muscular membrane of motor plate [1].

Its clinical forms vary from ocular manifestations (43%) to presentation in a generalized form (47%) and myasthenic crises (10%). Thymus seems to play a definitive role in etiopathogenesis of this disease given that up to 85% of patients have thymic hyperplasia with active germinal centers [2-4].

First thymectomy was described in 1912 [5]. In 1941, Blalock published his surgical experience and demonstrated an improvement in symptoms after the removal of the thymus in patients with MG [6]. Since then, several studies have shown thymectomy improves symptoms in these patients and in most of them, reduces medication to control symptoms.

In 2016, a prospective, randomized, multicenter study comparing 2 groups of patients was published. One group treated with prednisone and a transsternal thymectomy and another group that was treated with prednisone only. The authors demonstrated that the group with thymectomy was statistically superior in the improvement of symptoms, reducing the need for medical treatment (54 versus 32 patients, 95% CI estimated 22) as well as the number of readmissions due to exacerbation of myasthenia (37 in front of 9 patients, $P < 0.001$) [7].

Historically, most used approach to perform thymectomy was transesternal approach for excellent visualization of the anterior mediastinum that allows a complete resection of the mediastinal fat with all the ectopic thymic tissue.

However, in the last 20 years, the introduction of VATS in surgical practice has made possible to perform a wide range of thoracic operations, including thymectomy [8].

Objective of this Study

The objective of this study is to present VATS thymectomy as a safe technique and an adequate alternative to improve clinical symptoms of patients with MG.

Methods

Scope of the study

Study conducted in 2 hospitals. Hospital of the Princess of Madrid and MD Anderson Cancer Center of Madrid. It is a prospective follow-up study in which 42 patients were included with the diagnosis of MG who underwent an extended thymectomy by VATS from January 1st 2010 to January 1st, 2018.

The study was communicated to Ethics Committees of both medical institutions giving their approval for its development. Patients were informed that were going to be part of the study and an informed consent was fulfilled.

Procedures

For the diagnosis of patients with MG, the clinical criteria of Osserman and Genkins were followed [9]. A computed tomography (TAC) was performed for mediastinal evaluation. Neurophysiological criteria were obtained from a repetitive stimulation test and positive single-fiber electromyography. The pharmacological test used was the Tensilon test.

An extended thymectomy was performed by right VATS with 1 incision of 10mm and 2 of 5 mm. We use CO2 insufflation with an average pressure between 6 and 8 mmHg, according to the hemodynamic tolerance of the patient. With patient in the supine position and selective intubation, thymus was resected together with the peritimic fatty tissue with identification of both phrenic nerves (Figure 1).

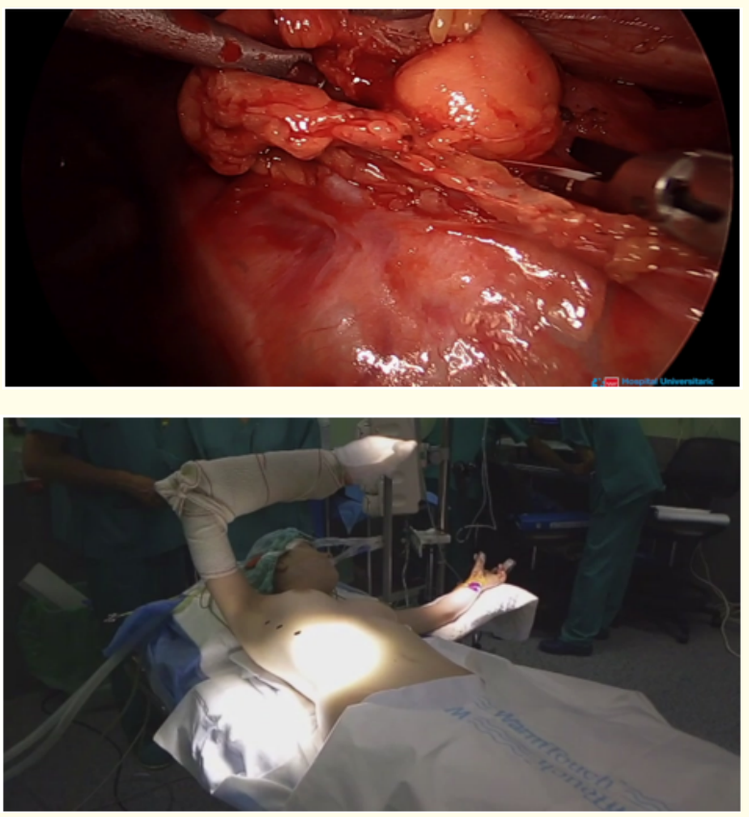

Figure 1: *Extended thymectomy by VATS.*

Those adult patients with moderate or severe generalized symptoms were candidates for surgery, regardless of the duration of the symptoms or their age. Patients with respiratory or oro-pharyngeal symptoms, regardless of their severity, were also included [3]. Patient's clinical condition must be adequate for the surgical intervention. Immunoglobulins were administered in 7 patients (400 mg/kg of weight/day, 3 doses) due to presenting bulbar symptoms before surgery. Rest of them continued with their usual medication.

Variables

Epidemiological variables were collected, such as age, sex, surgical risk classification ASA (American Society of Anesthesiologists) and the Osserman´s classification. Surgical variables were duration of surgery, hospital stay, intraoperative bleeding, perioperative myasthenic attacks, respiratory infection/pneumonia and surgical wound infection.

For the analysis of patient follow-up, four variables were used: treatment increase, equal treatment, reduction of treatment doses, suppression of treatment. They were evaluated in 1 month, 1 year and 2 years after surgery.

Statistic analysis

IBM SPSS version 20.0 program (IBM Corp., Armonk, NY, USA) was used for all statistical analysis. Descriptive statistics used for the variables included in the study: the quantitative variables were expressed as mean ± standard deviation. The qualitative variables were expressed as absolute value and percentage.

Results

Patients had a mean age of 34 years (range 18 - 67 years) with an ASA 2 (range 1 - 4). A preoperative classification was performed the week before surgery according to the Osserman criteria (Table 1). Considering its clinical characteristics 16 (38.1%) patients were in stage I, 9 (21.4%) in stage IIA, 10 in stage IIB (23.8%), in stage IIIA there were 5 (11.9%), 2 patient (4.76%) in phase IVB; as described in table 2.

Stage 0	Without
Stage I	Ocular muscle weakness
Stage II	Mild weakness of another muscle group other than the ocular IIA Affects extremities and/or axial muscles IIB Affects oro-pharyngeal or respiratory muscles
Stage III	Moderate muscle weakness other than ocular IIIA Affects extremities and/or axial muscles IIIB Affects oro-pharyngeal or respiratory muscles
Stage IV	Severe muscle weakness other than ocular IVA Affects extremities and/or axial muscles IVB Affects oro-pharyngeal or respiratory muscles
Stage V	Precise intubation

Table 1: *Osserman classification [9].*

	N	%
I	16	38.1%
IA	9	21.4%
IIB	10	23.8%
IIIA	5	11.9%
IIIB	0	0%
IVA	0	0%
IVB	2	4.7%
V	0	0%

Table 2: *Osserman [9] classification of patients according to their clinical characteristics.*

Table 3 describes distribution by gender (13 men, 29 women) and previous medical treatment to which the patients were subjected. All patients were treated with pyridostigmine, 26 (61.9%) received prednisone, 9 (21.4%) patients were treated with thiopurines and 8 (19%) patients required treatment with immunoglobulins preoperatively.

	N	%
Sex		
Male	13	31
Female	29	69
Previous treatment		
Pyridostigmine	42	100
Prednisoma	26	61.9
Thiopurines	9	21.4
Immunoglobulins	8	19
Thymic hyperplasia	37	88.1
Atrophic Thymus	5	11.9
Surgical complications		
Myasthenic crisis	2	4.7
Pneumonia	0	0
Wound infection	3	7.1
Mortality	0	0

Table 3: *Medical treatment and complications.*

Regarding perioperative complications, most frequent was surgical wound infection in 3 patients (7.1%). Two patients suffered a myasthenic crisis at 36 hours after surgery; they were treated in Intensive Care Unit (ICU) with immunoglobulins 400 mg/kg of weight/day diluted in 500 mL dextrose 5% and intensification of steroid treatment. The exacerbation of muscle weakness was defined as myasthenic crisis, compromising respiratory mechanics, swallowing, or one of the two and requiring respiratory and/or nutritional support.

The pathological anatomy of thymectomy showed an atrophic thymus without alterations in 5 patients and in 37 (88.1%) a thymic hyperplasia.

Table 4 shows intraoperative variables and hospital stay. Surgical procedure had an average duration of 111 minutes (range of 45 - 220). All patients were extubated in the operating room and maintained 24 hours with intensive monitoring. Intraoperative bleeding was 50 ml (20 - 150). Median hospital stay was 2 days (1 - 7).

	Average Interval	
Time of surgical procedure (minutes)	111	50 - 220
Bleeding (ml)	50	20 - 150
Hospital stay (days)	2	1 - 7

Table 4: *Operative variables and hospital stay.*

All patients were followed up in outpatient clinics of the Thoracic Surgery Service and the Neurology Service (Table 5). One month after hospital discharge, 7 (16.6%) had dropped their usual doses of drugs and 4 (9.5%) required an increase in the doses prior to surgery. One year after the surgical procedure, 20 (47.6%) patients had decreased the doses of the drugs and 8 (19%) were without treatment. At 2 years 25 (59.5%) needed less doses of drugs to control their disease and 10 (23.8%) did not need treatment.

	1 month		1 year		2 years	
	N	%	N	%	N	%
Drug drop	7	16.6	20	47.6	25	59.5
Same treatment	31	73.8	10	23.8	7	16.6
Increase drugs	4	9.5	0	0	0	0
No treatment	0	0	8	19	10	23.8

Table 5: *Monitoring of patients and variation of treatment.*

Discussion and Conclusion

Patients with MG often have a deterioration of symptoms when they are exposed to certain medications and stressors such as infections, pregnancy and surgical procedures [6].

MG exacerbation or seizures may arise from the stress of surgery or as a result of general anesthesia since the neuromuscular blocking drugs (NMBs) commonly used in general anesthesia also suppress neuromuscular transmission, which is already altered in MG. On the other hand, there is the possibility of drug interactions between drugs commonly used in patients with MG (pyridostigmine and azathioprine), and certain anesthetics and NMB [7].

The preoperative preparation for elective surgery in patients with myasthenia gravis (MG) should be coordinated with the patient's neurologist. Elective surgery should be performed during a stable phase of the disease, when the patient requires minimal immunomodulatory medication or glucocorticoids, to minimize the possibility of a postoperative myasthenic crisis. In addition to the routine preoperative evaluation, the evaluation of patients with MG should focus on bulbar and respiratory symptoms, as well as on the history of exacerbations or myasthenic attacks [8]. The role of preventive treatment in the preoperative period is not clear in order to avoid myasthenic attacks. Some authors, such as Vázquez-Roque, describe the administration of immunoglobulins (Intacglobin 400 mg/kg) 3 doses before surgery 2 doses later [10]. This author publishes his series of 23 patients with a trans-sternal thymectomy without postoperative myasthenic crisis. In our series, 1 patient suffered a myasthenic crisis with predominantly bulbar clinical symptoms resolved with immunoglobulins and intensification of the steroid treatment.

Surgical approach for extended thymectomy can be carried out through different approaches. So Bulkey [11] or Shrager [12] publish their series on thymectomy by cervicotomy. The latter author published a conversion rate of 7.9% at median sternotomy and a total complication rate of 7.3%, with 6.7% of these classified as mild (wound infections, seromas, atrial fibrillation, pneumothorax). One patient presented a paralysis of unilateral recurrent laryngeal nerve.

Our reconversion rate to sternotomy is 0. With a unilateral approach by VATS, CO2 insufflation facilitated dissection and allowed us to resect perithymic fat comprised between both phrenics next to the thymic gland. Use of bipolar energy and ultrasound has expedited the surgical times in our series with respect to that published in others, such as the most recent, by the author Numanami [13], where mean operative time is 180 minutes (94 - 446) with a VATS-subxiphoid approach, compared to our mean time of 111 minutes (45 - 220).

Regarding the follow-up, at 2 years 83.3% of patients had decreased or suspended medical treatment needed to control their neurological symptoms. These figures coincide with what was reviewed in the literature. In this way Cheng [14] communicates a 91% decrease or cessation of treatment in his series. Hess [15] in his review provides similar results.

Although our study has several limitations, including small sample size and brief follow-up, we describe our initial experience regarding extended thymectomy for CVT, a minimally invasive approach with a low complication rate. Future investigations with more patients and longer follow-up will be required to confirm the results of the procedure.

In conclusion, thymectomy by VATS with insufflation of CO2 could be a safe and useful approach to perform an extended thymectomy in patients with MG.

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