Mid-term results of thoracoscopic thymectomy for myasthenia gravis

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Abstract

Context: Video-assisted thoracic surgery (VATS) has been proposed as a less invasive technique for treatment of myasthenia gravis. **Materials and Methods:** A total of 31 patients underwent a right-sided VATS to remove all anterior mediastinal fat and thymic tissue during a 4-year period in our institution. None of the patients had associated thymoma. **Results:** All procedures were performed successfully with no conversion to sternotomy. The mean operating time was 190 minutes. The median intubation time and assisted ventilation were 24 and 18 hours, respectively. The median ICU and hospital stays were 3 and 7 days, respectively. The median time for post-operative chest drainage was 48 hours. There was no perioperative mortality. Eight significant complications occurred. One patient had atelectasis, 1 patient had aspiration pneumonia, and 3 patients had postoperative myasthenic crisis and required prolonged mechanical ventilation. Other complications were granuloma of the vocal cord, right recurrent laryngeal nerve palsy, and temporary brachial plexus injury due to poor intraoperative positioning. The mean length of follow-up was 20 months (range: 3-42 months). Overall, 27 patients (87%) had improved clinically and 11 patients (35%) had complete remission. The resulting scars were cosmetically acceptable for all patients. **Conclusion:** VATS provides an effective alternative approach to thymectomy and has several advantages over open techniques. VATS causes minimal postoperative complications, shortens hospital stay, and gives better cosmetic results.

Key words: *Myasthenia gravis, thoracoscopy, thymectomy, thymus gland, video-assisted thoracic surgery*

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Introduction

Thymectomy is a radical but effective treatment for generalized myasthenia gravis (MG).[1,2] The strongest evidence of its efficacy is a computer-matched series, which has shown a reduction in myasthenia-related mortality from 44 to 14% and an increase in the remission rate from 8 to 35%.[3] A meta-analysis suggested that patients are twice as likely to achieve medication-free remission after thymectomy.[4] The aim of the operation is to remove all thymic tissue from the neck to the diaphragm in the anterior mediastinum.[2]

However, surgery, with its associated co-morbidities, long-lasting pain, and lifelong scar on the neck or chest, is not particularly suitable for the predominantly young female clinical population, and there is no guarantee of remission.[2]

Video assisted thoracic surgery (VATS) was introduced in 1992 as a minimally invasive tool for thymectomy in patients with MG. It was hoped that the less invasive thoracoscopic approach would be associated with less morbidity, equal effectiveness, and greater patient acceptance leading to earlier thymectomy in more patients with the disease.[5]

The purpose of this report is to provide the results for a group of 31 patients who underwent thoracoscopic thymectomy (TT) for MG in a single institution so that a more firm assessment of the approach can be made.

Materials and Methods

Informed consent was obtained for a VATS from 31 consecutive patients with generalized MG who were referred to the Department of Minimal Invasive Surgery from the Department of Neurology between January 2004 and December 2007. A single surgical team performed all of the operations in cooperation with an experienced neurologist and anesthesiologist for handling of perioperative cares.

Under general anesthesia, either a left-sided double-lumen endotracheal tube (DLT) for selective lung ventilation or a single-lumen endotracheal tube (SLT) in conjunction with CO_2 insufflation (up to maximum pressure of 8 mmHg) were applied.[6] The patient was turned 45° to the left and skin preparation and draping allowed access for sternotomy or thoracotomy, should either be required. The operating surgeon stayed on the right side of the patient in a cephalad position to the camera man.

Operations were performed through the right-sided approach with four thoracoscopic ports (two 10 mm and two 5 mm). A clear view of the entire mediastinum allowed a complete en bloc removal of all mediastinal fat and the thymus gland with its cervical horns. With the use of standard endoscopic instruments including graspers and scissors, the dissection began at the inferior portion of the thymic gland just anterior to the phrenic nerve. By a combination of blunt and sharp dissection, all anterior mediastinal tissue was teased off the pericardium. Next, the gland was dissected off the retrosternal area and contralateral pleura with blunt dissection. After visualization of the innominate vein, the thymic vein(s) were double-clipped. Then, dissection was carried cephalad to the innominate vein until the superior horns of the thymus were identified. The fascial attachments of the thymus to the inferior part of the thyroid gland were divided. The specimen was placed into an endoscopic bag and removed through one of the port incisions. One chest tube was left in place of one port and the remaining incisions were closed. Patients were routinely sent to the intensive care unit (ICU).

Preoperative data (age, gender, Myasthenia Gravis Foundation of America (MGFA) clinical staging,[5] duration of disease, medications, associated diseases), operative data (need for conversion, operation time, operative complications), postoperative data (duration of assisted ventilation and intubation, duration of chest tube drainage, duration of ICU and hospital stay, post-operative complications and hospital cost), pathology result, and follow-up data were collected prospectively. Data were collected from the medical records and supplemented with telephone surveys.

Results

The study population consisted of 25 females (81%) and 6 males (19%) with a mean age of 25 years old (range: 14-45 years old). By preoperative staging by the MGFA clinical classification, no patient was in Class I, 20 patients (65%) were in Class II, 5 patients (16%) were in Class III, 2 patients (6%) were in Class IV, and 4 patients (13%) were in Class V. The mean duration of disease was 18 months (range: 1-72 months). Associated disorders included 2 patients with hypothyroidism, 2 patients with hyperthyroidism, and 1 patient with Cushing Syndrome. All patients were on pyridostigmine preoperatively with a mean daily dose of 235.4 ± 86.2 mg. Prednisolone had been administered as a second drug to 9 patients. A total of 4 patients underwent preoperative plasma exchange and 15 patients received preoperative intravenous immunoglobulin.

All procedures were performed successfully, with no conversion to sternotomy. The mean operating time was 190 minutes (range: 120-300 minutes). Five patients were extubated at the end of the operation. The median intubation time of others was 24 hours (range: 3-264 hours) with a median assisted ventilation of 18 hours (range: 0-72). The median ICU and hospital stays were 3 days (range: 1-15) and 7 days (range: 2-27 days), respectively. We did not employ an aggressive early discharge policy. The median time for post-o perative chest drainage was 48 hours (range: 10-120 hours). The median hospital cost was $1038 (range: $356-3014); about 90% of the hospital cost of each patient was paid by insurance companies.

There was no perioperative mortality. Eight significant complications occurred. One patient had atelectasis, 1 patient had aspiration pneumonia, and 3 patients had postoperative myasthenic crisis, required prolonged intubation, and assisted ventilation. Two patients developed post operative hoarseness. One patient had granuloma of the vocal cord, which was excised 2 months later. The other had right recurrent laryngeal nerve (RLN) palsy. The other significant morbidity was temporary right upper extremity weakness subsequent to brachial plexus injury due to poor intraoperative positioning. Complete morbidity and mortality according to the MGFA classification is summarized in Table 1.

We believed that a complete thymectomy was achieved in all cases by examination of the thymic bed and resected specimen. Histologic examination revealed normal or atrophic and hyperplastic thymus in 10 and 21 patients, respectively. None of the patients had associated thymoma.

The mean length of follow-up was 20 months (range: 3-42 months). A total of 11 patients (35%) had complete

Table 1: Myasthenia Gravis Foundation of America (MGFA) operative/postoperative morbidity and mortality

Length of surgery	190 (120-300) minutes
Intraoperative complications	1: Vocal cord injury after intubation with double lumen tube 1: Recurrent laryngeal nerve injury 1: Brachial plexus injury due to poor positioning
Hospital stay	7 (2-27) days
Intensive care days	3 (1-15) days
Ventilatory support	18 (0-72) hours
Infection	1: Aspiration pneumonia
Transfusions	0
Nerve injury	1: Recurrent laryngeal nerve
Persistent pain	0
Chylothorax	0
Death	0

remission (complete freedom of symptoms without medications). Improvement (improved symptoms or less medication requirement) was seen in 16 patients (52%). There was no response to surgical therapy in 2 patients (6.5%). Two patients (6.5%) had progression of disease postoperatively. Overall, the benefits of TT were observed in 87% of the patients. The resulting scars were cosmetically acceptable for all patients.

Discussion

No prospective randomized clinical trials (RCTs) comparing open thymectomy with VATS have been conducted. At present, such trials are unlikely to be held for a variety of reasons. Randomization is difficult with procedures that are still evolving. Another important reason is that most centers prefer a single approach. The lack of well-defined objective categories of MG severity and response to therapy often made the investigation of improvement results weak.[7]

Large case series and nonrandomized comparative studies, however, have consistently reported less postoperative complications and pain, better cosmetic results, and at least the same outcomes from VATS than from open thymectomy.[2,5,7-11]

In comparison with the early postoperative results of thymectomy after partial sternotomy and VATS approaches, significant differences were noted for the duration of chest tube drainage, the amount of drainage, the length of hospital stay, and the visual analogue scale pain score.[8] In another study, operative bleeding was significantly less in the VATS group than in the sternotomy group.[9]

In a matched pair comparison of three groups who underwent thymectomy through anterolateral thoracotomy, sternotomy and VATS, there was no difference in complete remission of MG. The overall postoperative morbidities were significantly lower in VATS than in open thymectomy techniques. The best cosmetic results were achieved after TT.[7]

One comparative study showed no statistically significant difference in the postoperative improvement between open thymectomy and TT. However, ICU and hospital stays were shorter after thoracoscopic surgery.[10]

Recently, Bachmann, *et al*. reported long-term outcome and quality of life after open and TT in 131 patients with a median follow-up time of 8 years. Minimally invasive surgery was found to be superior in terms of improvement in MG-associated symptoms. Additionally, the hospital stay was shorter and the patients felt less disturbed by direct effects of the operation.[11]

The incidence of postoperative myasthenic crisis is about 20-30%.[12,13] We encountered an incidence of about 10% in our cases, which was required prolonged mechanical ventilation. In the study conducted by Liu, *et al*. preoperative bulbar symptoms, history of preoperative myasthenic crisis, history of preoperative infection, and large preoperative dose of pyridostigmine were all independent risk factors of postoperative myasthenic crisis. Good preoperative care may prevent postoperative myasthenic crisis in the patients with such factors.[13]

We had five other post-operative complications. Only one of them (RLN palsy) was related to the surgical technique. The lower frequency of nerve palsy with our patients can be explained by the absence of infiltrating thymomas. Several studies indicated a lower procedural morbidity as opposed to transternal thymectomy. Our 16% overall morbidity rate mirrors that of other minimally invasive approaches and compares favorably to the 25-33% reported for open thymectomy.[7,14] In one comparative study, the overall postoperative morbidity rate was 25% for the sternotomy approach as compared with 15% for the thoracotomy approach and 5% for the VATS approach.[7]

One patient developed vocal cord granuloma subsequent to vocal cord injury after intubation with a DLT. In another report, we showed that one lung ventilation with a DLT is not necessary for TT. The use of a SLT with CO_2 insufflation is a safe method of intubation for TT and provides good surgical exposure. It avoids the risk, time, and cost of DLTs.[6] The lesser degree of chest wall trauma associated with VATS has resulted in better preservation of lung function postoperatively.[15] This may play an important role toward earlier extubation and reducing the incidence of postoperative pulmonary infections in patients with severe MG.[16]

Hypertrophic scar or keloid formation is a possible complication of any skin incision, more so for upper

chest incisions. It is therefore understandable that a predominantly young and female patient population would defer or reject the offer of surgery. In addition, the disability of a sternotomy prevents or impairs sport and employment for 6 to 12 weeks, even without complications such as sternal infection, instability, and wire breakage or protrusion.[2] The VATS approach eliminates these problems.

A meta-analysis of outcomes of surgery in MG by various techniques revealed complete remission rates range from 17 to 52% and clinical improvement ranges from 57 to 97%.[17] In 31 patients at a mean follow-up time of 20 months, our clinical improvement rate was 87%. It is comparable with published series of other approaches.[2,5,7,10,11,16-19] Several studies showed at least similar outcomes of open thymectomy and TT.[7,10,11]

The major limitations of this study are small sample size studied in a single center with a relatively short follow-up period. Obviously, a larger sample size with a longer follow-up time could better clarify the effectiveness of this minimally invasive approach.

We concluded that minimally invasive approach for thymectomy is technically feasible and safe. TT is associated with minimal postoperative morbidities and favorable outcomes. Further validation of this approach for thymectomy, however, awaits RCTs with long-term follow-ups and accurate comparison with outcomes of the more traditional approaches.

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