Role of VATS in thymectomy for non-thymomatous myasthenia gravis

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ABSTRACT

Background: There are different surgical techniques used for thymectomy. Each technique has its own advantages and disadvantages. However, using a less invasive approach would provide a better outcome.

Methods: From June 2015 to February 2017, a prospective study included a total number of 50 patients of non-thymomatous myasthenia gravis (MG) who were randomly divided into two groups: group A (25 patients who underwent VATS thymectomy), and group B (25 patients who underwent thymectomy via ministernotomy). Efficacy and outcome of both procedures were compared. Patients were followed-up for at least one year postoperatively.

Results: Both procedures were safe and effective in the management of MG. There was no significant difference between both groups regarding preoperative data. In VATS group, there were significant decreased operative times (p value = 0.00), significant decreased blood loss (p value = 0.039), significant decreased postoperative respiratory and cardiac complications (p value = 0.025 and 0.018 respectively) and significant shorter length of ICU and hospital stays (p value = 0.039 and 0.007 respectively) when compared to ministernotomy group. There was no statistically significant difference between both groups regarding complete stable remissions and clinical improvement. No mortality was recorded in both groups.

Conclusions: Thoracoscopic thymectomy should be the technique of choice in the management of MG. It has better intraoperative and short-term results than that of thymectomy via ministernotomy. However, longer periods of follow-up is needed to evaluate long-term results properly.

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1. Introduction

Myasthenia gravis (MG) is a systemic autoimmune disorder in which there are antibodies against acetylcholine receptors of the neuromuscular junction [1]. The clinical picture of MG is due to these antibodies which decrease the number of acetylcholine receptors resulting in progressive weakness and easy fatigability of the voluntary muscles. This condition worsens after repetitive movements and improves after rest [2]. Ocular weakness symptoms are the first complaint in nearly
half of the patients who usually develop ptosis or diplopia. Muscular weakness is always symmetrical involving both sides to the same extent. Generalized weakness is seen in most of the patients in up to 85%. However, MG clinical course might be totally unexpected with an abrupt or a gradual onset of development of symptoms. Moreover, there might be an aggravation of symptoms or spontaneous remissions [3].

The thymus gland has a substantial role in the pathogenesis of MG. So, thymectomy is done to improve the muscular weakness associated with MG and to excise any thymoma that may be present in nearly in 10% of patients with MG. Most of the thymomas are benign tumors that grow very slowly but sometimes thymomas may be malignant. Thymectomy is recommended for all cases of thymoma. It is also recommended for MG patients with moderate to severe weakness. It is also recommended for cases of MG with mild weakness that is associated with dyspnea or dysphagia which are due to the weakness of the respiratory and oropharyngeal muscles respectively [4].

There are many surgical approaches for thymectomy that may depend upon the experience and the preference of the surgeon. The full sternotomy approach provides very excellent direct visualization and allows extension of resection if necessary. However, new less invasive approaches might be implemented: partial sternotomy and VATS. Thymectomy includes excision of all the thymus and perithymic tissues including all visible mediastinal fat. The excision boundaries are extended superiorly to the thyroid gland, laterally to both phrenic nerves and inferiorly to the pericardial sac and mediastinal pleura [5].

2. Patients and methods

From June 2015 till February 2017, a prospective study was conducted after approval from the institutional Ethical Committee. Informed consents were taken from all patients. This prospective study included a total number of 50 patients of non-thymomatous MG who were randomly divided into two groups (group A and group B). Randomization was done by a computer program (Random Number Generator) which generates random numbers in a random number table. Group A consists of 25 patients who underwent VATS thymectomy while group B consists of 25 patients who underwent thymectomy via ministernotomy. This study was designed to compare efficacy and outcome of both procedures.

Preoperative patients’ data including age, sex, body mass index, symptoms of MG, history of receiving medical treatment for MG, past history of mechanical ventilation and the class of the American Society of Anaesthesiologists ASA (ASA) were studied.

Intraoperative and postoperative data including operative time, total blood loss, chest drain duration, duration of ICU stay, respiratory and cardiac complications, development of wound infection, the total length of hospital stay, clinical improvement and development of complete stable remission were also studied. Complete stable remission was noted when there were no manifestations of MG for at least 1 year and the patient was not receiving any medications for MG throughout that time and when there was no detected muscular weakness at all on careful neurological examination [6].

Exclusion criteria include

1. Patients with MG and thymoma (i.e. thymomatous MG) because of the increased rate of possible conversion from VATS to open thymectomy.
2. Patients under the age of 12 years because thymus has still an important role in the development of immune system.
3. Patients in the early stage of MG (usually in the first year of presentation onset) where spontaneous remission within the first year is still possible.

Preoperative preparation varied markedly according to the clinical status of the patients. Patients without any bulbar symptoms and presenting with only motor symptoms, anticholinesterase drugs were given. Meanwhile, patients with respiratory failure were primarily treated in ICU where mechanical ventilation was started together with anticholinesterase drugs, immunosuppressors, and corticosteroids. Plasmapheresis might be needed in some patients. When plasmapheresis was done, the operation was postponed for 48 h after the last plasmapheresis to minimize the risk of bleeding and infection. When plasmapheresis due to the removal of clotting factors and immunoglobulins during plasmapheresis.

2.1. VATS thymectomy

Right VATS thymectomy was routinely used in this study. The patient was in the supine position. After standard double lumen intubation and right lung isolation, three thoracic ports were used: one 10 mm port was made in the 7th intercostal space at the anterior axillary line and used as a camera port, a 2nd 5 mm port was made in 3rd intercostal space at the anterior axillary line and a 3rd 5 mm port was made in 5 t h intercostal space at the midaxillary line. A 30° camera was used together with a Harmonic scalpel to dissect the thymus successfully and safely by avoiding phrenic nerves and left brachiocephalic vein injuries. Dissection usually started at the lowermost part of the thymus just in front of the right phrenic nerve. The thymus was dissected anteriorly from the retrosternal area. The arterial blood supply to the thymus arising from the internal mammary artery was identified and ligated by endoscopic hemoclips. The left brachiocephalic vein could be identified at this point where dissection could continue along it till identifying and ligating the thymic veins at their entry to the left brachiocephalic vein by endoscopic hemoclips. Blunt dissection was then used to dissect the thymus from the contralateral mammary artery was identified and ligated by endoscopic hemoclips.
pleura. Special care was taken to avoid injury of the left phrenic nerve at this point. Then a fan retractor was introduced to retract the thymus and to allow dissection above the left brachiocephalic vein till identification and dissection of the superior horns of the thymus. The fascial attachments between the thymus and lowermost part of the thyroid gland were finally divided. An endobag was used to retrieve the thymus without fragmentation. Hemostasis was then ensured and a single 30 F chest tube was routinely placed after lung reinflation (Figs. 1–3).

2.2. Ministernotomy

Ministernotomy differs from total median sternotomy in that the sternum was not totally divided but only the manubrium and upper part of the body of the sternum down to the level of the fourth intercostal space. A Finochietto retractor was used to expose the upper part of the mediastinum where the thymus was totally removed together with the surrounding fat. The phrenic nerves were used as the lateral limits of the dissection which usually started from the base of the thyroid gland upwards till the pericardium downwards. Both phrenic nerves should be well identified to avoid their injury which might
cause diaphragmatic palsy. This diaphragmatic palsy might seriously impair the postoperative clinical outcome if happened. After complete resection, good haemostasis and intact both pleural spaces were ensured. A suction drain was finally placed near the suprasternal notch. Sternum, muscles, subcutaneous tissue and skin were closed in layers after haemostasis to conclude this procedure.

2.3. Postoperative care

It included early patient extubation in the operation room, adequate analgesia and postoperative chest x-ray in the sitting position. The chest drain was removed when there was no air leak nor bleeding. Moreover, postoperative care included decreasing the anticholinesterase medications to the half dose with gradual tapering of the dose of corticosteroids from the 3rd postoperative week onwards. Immunosuppressive drugs with cytotoxic therapy and plasmapheresis were only used in patients with persistence of symptoms and corticosteroids resistance.

Patients were followed-up for at least one year postoperatively. Follow-up was achieved by clinical visits and by telephone contact. Patient assessment was done by applying the postintervention classification of Myasthenia Gravis Foundation of America (MGFA) [6].

2.4. Statistical analysis

SPSS version 20 was used for the statistical analysis of the collected data. All the continuous values were shown as mean ± standard deviations and percentage. Significance between the two groups was determined by independent t-test if data were quantitative and chi-square test if data were categorical. Fisher’s exact test was used if there were expected cell frequencies less than 5. A p value of less than 0.05 was considered significant. Patients’ data, pre-operative, operative and postoperative findings and complications were compared.

3. Results

In VATS group, there were 14 males and 11 females with mean age of 34.6 ± 6.75 years and a body mass index of 22.6 ± 1.55 kg/m² while in the ministernotomy group, there were 13 males and 12 females with mean age of 40.2 ± 7.04 years and a body mass index of 23.1 ± 1.82 kg/m². There were 9 patients (36%) who had a previous history of mechanical ventilation in VATS group while there were 11 patients (44%) in the ministernotomy group. The ASA class was 2.37 ± 0.65 in VATS group while it was 2.44 ± 0.58 in the ministernotomy group. There was no significant difference between both groups regarding age, sex, body mass index, preoperative clinical symptoms, previous history of mechanical ventilation and ASA class. These data are summarized in Table 1.
The mean operative time in VATS group was 61.6 ± 8.77 min while it was 94.68 ± 2.86 min in the ministernotomy group. There was a significantly shorter operative time (p = 0.000) in VATS group. The mean total blood loss in VATS group was 65.6 ± 17.33 ml while it was 197.8 ± 27.23 ml in the ministernotomy group. There was a significantly less blood loss (p = 0.039) in VATS group. There was no significant difference between both groups regarding the duration of the chest drain (p = 0.587) where it was 2.4 ± 0.50 days in VATS group and 3.56 ± 0.50 days in the ministernotomy group.

Respiratory complications in the form of postoperative dyspnea that mandated mechanical ventilation were noted in 3 patients (12%) in VATS group and in 10 patients (40%) in the ministernotomy group with a significant statistical difference between both groups (p = 0.024). Cardiac complications in the form of arrhythmia were noted in 2 patients (8%) in VATS group and 9 patients (36%) in the ministernotomy group with a significant statistical difference between both groups (p = 0.017). Only 1 patient (4%) in VATS group developed wound infection while 6 patients (24%) in ministernotomy group developed mild superficial wound infection with no significant statistical difference between both groups (p = 0.098). Only 2 patients (8%) in VATS group required postoperative plasmapheresis while it was required in 3 patients (12%) in the ministernotomy group with no significant statistical difference between both groups (p = 1.000).

The mean duration of ICU stay in VATS group was 1.28 ± 0.45 days while it was 2.44 ± 0.51 days in the ministernotomy group. There was a significantly shorter ICU stay (p = 0.039) in VATS group. The mean duration of total length of hospital stay in VATS group was 5.48 ± 0.51 days while it was 7.92 ± 0.86 days in the ministernotomy group. There was a significantly shorter total length of hospital stay (p = 0.007) in VATS group.

11 patients (44%) in VATS group had a complete stable remission which occurred in 9 patients (36%) in the ministernotomy group with no significant statistical difference between both groups (p = 0.773). Clinical improvement was noted in 22 patients (88%) in VATS group while it was noted in 20 patients (80%) in the ministernotomy group with no significant statistical difference between both groups (p = 0.702). No mortality was reported in both groups. The comparison between intraoperative and postoperative data in both groups is summarized in Table 2.

4. Discussion

VATS thymectomy approaches are variable and depend on the surgeons’ preference and experience. It includes unilateral (right or left) or bilateral VATS approaches. There is still a controversy over the best approach to be used. In this study, right VATS thymectomy was routinely used in all patients of the VATS group. Mineo et al. recommended left VATS as a safer manoeuvre because superior vena cava becomes outside the surgical field and thus decreasing the risk of its injury. Moreover, they suggested that left VATS thymectomy could provide an easier and safer dissection of the perithymic fat at the left pericardiophrenic angle [7].

On the other hand, surgeons favoring right VATS thymectomy approach have suggested that the superior vena cava could be easily identified from the right-side approach and could be used as a landmark to find out the left brachiocephalic vein. Moreover, right side approach is more comfortable and convenient for right-handed surgeons especially when they start at the right lower pole by providing better instrument handling in the wider pleural cavity on the right side. Furthermore, they recommended right VATS approach for any patient with cardiomegaly because this cardiomegaly decreases the available space in the already smaller left pleural cavity which makes instrument handling more difficult [8].

Bilateral VATS approach provides better visualization of the important key structures and hence, makes complete excision easier [9].

However, there is no sufficient large and recent prospective studies that could show whether one approach is superior to another [10–12].

Despite these controversies, the superiority of VATS thymectomy over sternotomy approach had been demonstrated by several studies. This may be due to the smaller wound away from the midline which would provide better cosmeses, faster

Table 1

Comparison between preoperative patients' data in both groups.

<table>
<thead>
<tr>
<th></th>
<th>VATS</th>
<th>Ministernotomy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agerowhead</td>
<td>34.6 ± 6.75</td>
<td>40.2 ± 7.04</td>
<td>0.727</td>
</tr>
<tr>
<td>Sex: Male/female</td>
<td>14/11</td>
<td>13/12</td>
<td>1.000*</td>
</tr>
<tr>
<td>BMI: Kg/m²</td>
<td>22.6 ± 1.55</td>
<td>23.1 ± 1.82</td>
<td>0.494</td>
</tr>
<tr>
<td>Symptomsa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ptosis</td>
<td>12 (48%)</td>
<td>11 (44%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Double vision</td>
<td>6 (24%)</td>
<td>12 (48%)</td>
<td>0.077</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>18 (72%)</td>
<td>18 (72%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>8 (32%)</td>
<td>6 (24%)</td>
<td>0.754*</td>
</tr>
<tr>
<td>Generalized weakness</td>
<td>21 (84%)</td>
<td>22 (88%)</td>
<td>1.000*</td>
</tr>
<tr>
<td>Previous mechanical ventilation</td>
<td>9 (36%)</td>
<td>11 (44%)</td>
<td>0.773*</td>
</tr>
<tr>
<td>ASA class</td>
<td>2.37 ± 0.65</td>
<td>2.44 ± 0.58</td>
<td>0.738</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation or numbers of patients (with the percentage in parenthesis).

BMI: body mass index, ASA: American Society of Anaesthesiologists.

* Fisher's exact test is used if there are expected cell frequencies less than 5.
and better healing, decreased the postoperative length of ICU and hospital stays, and earlier return to work and daily activities without a difference in outcome when compared with sternotomy approach [13–15]. There is a clear perception that sternotomy provides good visualization but it is much more invasive and carries greater morbidity. On the other hand, VATS provides better illumination and magnification which is obtained by the advanced cameras which offers a better exposure of the operative field [16].

Jurado et al. reported that VATS approach for thymectomy provides less intraoperative blood loss, decreased needs for blood products and earlier removal of chest drain [11]. These results coincide with the data obtained by this study. There are decreased risk and incidence of cardiac and pulmonary complications (e.g., arrhythmia, pleural effusion, and pneumonia) with VATS approach when compared to sternotomy approach. These complications delay patients’ recovery and prolong the duration of their ICU and hospital stays [17,18]. These data support the results obtained by this study.

Deep sternal wound infection may complicate the sternal approach and may lead to prolonged morbidity and hence increases the long-term mortality. This risk increases with old age, diabetes, obesity, smoking and steroid administration. Many MG patients receive steroids which increases the probability of developing a sternal wound infection and wound dehiscence [19].

Sympathetic stimulation associated with sternotomy might cause arrhythmia which may result in hemodynamic instability which necessitates close monitoring and further management. Other complications of sternotomy include increased incidence of keloid formation and bad cosmes, brachial plexus injury following sternal retraction, neuropathic pain for a long time and pseudoarthrosis [19]. Of these reported complications of sternotomy approach for thymectomy, only arrhythmia and superficial wound infection had occurred in this study.

This study demonstrated that VATS approach was superior to ministernotomy approach in the early postoperative results and short-term outcomes. These results matched with the data published by several recent studies [19–25]. However, this study needs a longer period of follow-up to evaluate long-term results properly. Other studies demonstrated the absence of any significant statistical differences between VATS approach and sternotomy approach for thymectomy in mid-term and long-term complication rates and survival [18,26].

9. Conclusions

Thoracoscopic thymectomy should be the technique of choice in the management of MG. It has better intraoperative and short-term results than that of thymectomy via ministernotomy. However, long-term results need additional follow-up to be properly evaluated.

Conflicts of interest

The author has no conflict of interest to declare.

Acknowledgments

None.

References


Table 2
Comparison between intraoperative and postoperative data in both groups.

<table>
<thead>
<tr>
<th></th>
<th>VAT</th>
<th>Ministernotomy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative time in minutes</td>
<td>61.6 ± 8.77</td>
<td>94.8 ± 2.8</td>
<td>0.000</td>
</tr>
<tr>
<td>Total blood loss in ml</td>
<td>65.6 ± 17.33</td>
<td>197.8 ± 27.23</td>
<td>0.039</td>
</tr>
<tr>
<td>Chest drain duration in days</td>
<td>2.4 ± 0.50</td>
<td>3.56 ± 0.50</td>
<td>0.587</td>
</tr>
<tr>
<td>Respiratory complications</td>
<td>3 (12%)</td>
<td>10 (40%)</td>
<td>0.024</td>
</tr>
<tr>
<td>Cardiac complications</td>
<td>2 (8%)</td>
<td>9 (36%)</td>
<td>0.017</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1 (4%)</td>
<td>6 (24%)</td>
<td>0.098</td>
</tr>
<tr>
<td>Postoperative plasmapharesis</td>
<td>2 (8%)</td>
<td>3 (12%)</td>
<td>1.000</td>
</tr>
<tr>
<td>ICU stay in days</td>
<td>1.28 ± 0.45</td>
<td>2.44 ± 0.51</td>
<td>0.039</td>
</tr>
<tr>
<td>Total length of hospital stay in days</td>
<td>5.48 ± 0.51</td>
<td>7.92 ± 0.86</td>
<td>0.007</td>
</tr>
<tr>
<td>Complete stable remission</td>
<td>11 (44%)</td>
<td>9 (36%)</td>
<td>0.773</td>
</tr>
<tr>
<td>Clinical improvement</td>
<td>22 (88%)</td>
<td>20 (80%)</td>
<td>0.702</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation or numbers of patients (with the percentage in parenthesis).

* Fisher’s exact test is used if there are expected cell frequencies less than 5.