Lateral versus Subxiphoid Thoracoscopic Thymectomy For Non-Thymomatous Myasthenia Gravis

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Background: VATS thymectomy, performed using the intercostal approach (LVATS), is the most widely used minimally invasive surgical treatment for thymus surgery worldwide. Subxiphoid single-port thoracoscopic thymectomy (SVATS) is a recent alternative approach to LVATS.

Methods: Between May 2019 and February 2023, 60 patients with non-thymomatous myasthenia gravis were enrolled in this prospective study. Patients were randomly divided into two groups: (The LVATS group and the SVATS group); each group contained 30 patients. The mean operative time, blood loss, conversion to open thymectomy, duration of postoperative pleural drain, total length of hospital stay, and postoperative complications were evaluated.

Results: The mean age was 37.3±5.61 in the LVATS group, while it was 39.7±6.39 in the SVATS group. The mean operating times were 94.66±14.31 minutes in the LVATS group and 90.56±10.80 minutes in the SVATS group, with no significant difference observed (P=0.227). The LVATS group had a significant drop in hemoglobin level (1.86±0.77 gm%) compared to the SVATS group (1.31±0.46 gm%) (P=0.014). The mean duration of chest drains was significantly longer in the LVATS group (2.03±0.18 days) compared to the SVATS group (1.70±0.46 days)(p=0.001). The mean duration of postoperative pain was significantly longer in the LVATS group (8.36±0.80 days) compared to the SVATS group (6.16±1.14 days)(p=0.018). The mean total length of hospital stay was significantly longer in the LVATS group (12.46±0.73days) compared to the SVATS group (11.06±0.58 days) (P=0.003).

Conclusion: Both LVATS and SVATS are safe and effective procedures for treatment of non-thymomatous myasthenia gravis. SVATS provides less intraoperative blood loss and a shorter duration of pleural drain, hospital stay, and postoperative pain.

Keywords: Thoracoscopy, thymectomy, Myasthenia Gravis.

Introduction

Myasthenia gravis (MG) is an autoimmune disorder where antibodies target acetylcholine receptors at the neuromuscular junction, leading to muscular weakness and fatigue. This condition increases with repeated movements but improves with rest. Nearly half of individuals develop ptosis or diplopia as their first complaint. Muscular weakness is symmetrical, affecting both sides to the same extent. Approximately 85% of patients exhibit generalized weakness. However, the MG clinical course could be totally unexpected, with symptoms appearing suddenly or gradually.

Additionally, symptoms may worsen or resolve on their own.[1] The thymus gland plays a significant role in the development of MG. Thymectomy is performed to alleviate muscle weakness and remove any thymoma, which is present in approximately 10% of MG patients. So, thymectomy is an important step in the management of patients with myasthenia gravis (MG). In recent years, techniques for thymectomy for myasthenia gravis have become significantly less invasive than the traditional median sternotomy.

VATS thymectomy, performed using the intercostal technique (LVATS), is the most widely used minimally invasive surgical treatment for thymus surgery worldwide.[2-5] Advances in surgical techniques have accelerated the development of new thymectomy approaches. Subxiphoid thoracoscopic thymectomy (SVATS) is a recent alternative approach to LVATS.

Whether to use LVATS or SVATS for thymectomy is still debated. Thymectomy involves the removal of the entire thymus and perithymic tissues, including any visible mediastinal fat. The excision borders extend superiorly to the thyroid gland, laterally to both phrenic nerves and inferiorly to the pericardial sac and mediastinal pleura.[3] The study aimed to evaluate the role of SVATS thymectomy in improving surgical and postoperative outcomes and to compare this approach with the traditional LVATS.

Methods

Between May 2019 and February 2023, 60 patients with non-thymomatous myasthenia gravis were enrolled in this prospective study. Patients were randomly divided into two groups: (the LVATS group and the SVATS group); each group contained 30 patients. Informed consent was obtained from every patient after approval of this study from the local Ethical Committee for Human Research. The study examined preoperative patient characteristics such as age, gender, body mass index, MG symptoms, history of medical treatment, and mechanical ventilation. The study examined intraoperative and postoperative data such as operative time, total blood loss, chest drain duration, respiratory and cardiac complications, wound infection, hospital stay length, clinical improvement, and complete stable remission. A patient was considered to have a completely stable remission if there had been no symptoms of MG for at least one year, the patient had not been using any MG drugs, and the patient had no visible muscular weakness after a thorough neurological examination.

Preoperative preparation

Preoperative preparation differed markedly depending on the patient's clinical status. Anticholinesterase medications were administered to patients with motor symptoms and no bulbar symptoms. Patients experiencing respiratory failure were treated in the intensive care unit (ICU) with mechanical ventilation, anticholinesterase medications, immunosuppressants, and corticosteroids. Plasmapheresis may be necessary in some cases. When plasmapheresis was performed, the operation was delayed for forty-eight hours following the completion of the last plasmapheresis to reduce the risk of bleeding and infection that could occur as a result of the removal of clotting factors and immunoglobulins during plasmapheresis.

Every patient was given 60 milligrams of oral loxoprofen three times a day beginning on the first postoperative day, and this treatment was continued for as long as requested.

Surgical techniques

1. **Lateral video-assisted thoracoscopic (LVATS) thymectomy:**

In lateral VATS thymectomy, patients were positioned in a supine position. Three one-centimeter skin incisions were made on the anterior axillary line of the third intercostal space and the midaxillary line of the third and sixth intercostal spaces. In all patients with myasthenia gravis, the lateral intercostal technique was used on both sides to remove all the adipose tissue anterior to both phrenic nerves.

2. **Subxiphoid video-assisted thoracoscopic (SVATS) thymectomy:**

SVATS thymectomy was performed in a supine position with legs extended apart. Generally, most patients did not require single lung ventilation. The surgeon stood between the patient's legs while the assistant was on the patient's right side and handling the camera. A 3-cm transverse incision was made 1 cm distal from the inferior end of the xiphoid process. We detach the thymus blindly from the back of the sternum using a finger dissection. We make a 1-cm incision on the fascia of the rectus abdominis to get enough space that could allow us to insert the port for this single-port surgery. Three mini-ports were inserted into the main port, one of which was assigned for a camera scope. In this study, the most commonly utilized camera scope was a rigid 30°/5-mm scope. A CO2 insufflation was carried out at a pressure of 8 mmHg. This CO2 insufflation helps the thymus to be detached from the back of the sternum, and the positive pressure applied during the CO2 insufflation procedure provides good space for the operation. Mediastinal pleura incisions were done bilaterally to establish a connection between the two thoracic cavities. When confirming the identification of the left and right phrenic nerves, an En-bloc resection of the thymus was performed.

Postoperative care:

Postoperative care involved early extubation in the operating room, giving sufficient analgesia, and requesting postoperative chest x-rays in the sitting position. The chest drain was removed when there was no air leak or bleeding. Postoperative treatment involved reducing anticholinesterase drugs to half dose and gradually lowering corticosteroid doses starting in the third postoperative week. Patients with persistent symptoms and corticosteroid resistance required immunosuppressive medications, cytotoxic therapy, and plasmapheresis. Patients were followed up for at least a year after surgery. Follow-up was achieved through clinical visits and phone contact.

Statistical analysis

SPSS version 26 was used to conduct statistical analysis of the collected data. Continuous values were presented as mean ± standard deviation and percentages. The two groups were compared using independent t-tests for quantitative data and chi-square tests for categorical data. Fisher's exact test was utilized when expected cell frequencies were less than 5. A p-value of <0.05 was considered significant.

Results

The mean age was 37.3±5.61 in the LVATS group, while it was 39.7±6.39 in the SVATS group. There were 16 (53.3%) males in the LVATS group, while there were 17(56.7%) males in the SVATS group.BMI was 21.3±2.31 in the LVATS group and 22.1±0.96 in the SVATS group. There were no significant differences between both groups regarding the clinical presentation and symptoms (ptosis, double vision, dyspnea, dysphagia, and generalized weakness). 10 (33.3%) patients in the LVATS group and 13 (43.3%) patients in the SVATS group had a past history of connection to mechanical ventilation. One (3.3%) patient in the LVATS group was receiving azathioprine tablets as a nonsteroidal immunosuppressant therapy. Preoperative plasmapheresis was used in 5 (16.7%) patients in the LVATS group and 7 (23.3%) patients in the SVATS group. The preoperative patients' data were summarized in **(Table 1).**

The mean operating times were 94.66±14.31 minutes in the LVATS group and 90.56±10.80 minutes in the SVATS group, with no significant difference observed (P=0.227). The mean total blood loss was measured by calculating the amount of hemoglobin drop between preoperative and discharge times. The LVATS group had a significant drop in hemoglobin level (Mean:1.86±0.77 gm%) compared to the SVATS group (Mean: 1.31±0.46 gm%) (P=0.014). The mean duration of chest drains was significantly longer in the LVATS group (Mean: 2.03±0.18 days) compared to the SVATS group (Mean: 1.70±0.46 days)(P=0.001). The mean duration of postoperative pain was significantly longer in the LVATS group (Mean: 8.36±0.80 days) compared to the SVATS group (Mean: 6.16±1.14 days)(p=0.018). The LVATS group received a significantly higher number of postoperative analgesic tablets (Loxoprofen 60 mg tablets) (26.31±2.45 tablets) compared to the SVATS group (21.86±1.63 tablets) (P=0.003). The mean total length of hospital stay was significantly longer in the LVATS group (Mean: 12.46±0.73days) compared to the SVATS group (Mean: 11.06±0.58 days)(p=0.003). There was no significant difference between both groups regarding the mean durations of ICU stay (P=0.121).

There were no significant differences between both groups regarding postoperative complications, including cardiac and pulmonary complications, phrenic nerve palsy, and wound infections. Postoperative plasmapheresis was indicated in 4(13.3%) patients in the LVATS group and 3(10%) patients in the SVATS group, with no statistical significance between both groups. Complete stable remission was observed in 9 (30%) patients in the LVATS group and 12(40%) patients in the SVATS group, with no statistical significance between both groups (P=0.589). Clinical improvement was seen in 21 (70%) patients in the LVATS group and 23(76.7%) patients in the SVATS group, with no statistical significance between the two groups (P=0.771). Intraoperative and postoperative data were summarized in **(Table 2).**

Table 1: Preoperative patients' data in both groups

	LVATS (n=30)	SVATS (n=30)	P value
Age	37.3±5.61	39.7±6.39	0.685
Sex (Male/Female)	16 (53.3%)/14 (46.7%)	17 (56.7%)/13 (43.3%)	1.000[a]
BMI	21.3±2.31	22.1±0.96	0.753
symptoms			
Ptosis	14 (46.7%)	17 (56.7%)	0.606[a]
Double vision	8 (26.7%)	11 (36.7%)	0.580[a]
Dyspnea	20 (66.7%)	24 (80%)	0.382[a]
Dysphagia	11 (36.7%)	8 (26.7%)	0.580[a]
Generalized weakness	24 (80%)	25 (83.3%)	1.000[a]
Previous mechanical ventilation	10 (33.3%)	13 (43.3%)	0.596[a]
Diabetes mellitus	2 (6.7%)	3 (10%)	1.000[a]
Corticosteroid therapy	8 (26.7%)	5 (16.7%)	0.532[a]
Cytotoxic drugs	1 (3.3%)	0 (0%)	1.000[a]
Preoperative plasmapheresis	5 (16.7%)	7 (23.3%)	0.748[a]

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

a: Fisher's exact test is used if there are expected cell frequencies less than 5

BMI: body mass index.

Table 2: Intraoperative and postoperative data in both groups

	LVATS (n=30)	SVATS (n=30)	P value
Operating times in minutes	94.66±14.31	90.56±10.80	0.227
Total blood loss (Hemoglobin drop in grams)	1.86±0.77	1.31±0.46	0.014
Chest drain durations in days	2.03±0.18	1.70±0.46	0.001
Cardiac complications	6 (20%)	4 (13.3%)	0.731 [a]
Pulmonary complications	10 (33.3%)	7 (23.3%)	0.567 [a]
Postoperative plasmapheresis	4 (13.3%)	3 (10%)	1.000 [a]
ICU stay in days	1.86±0.34	1.70±0.46	0.121
Phrenic nerve palsy	2 (6.7%)	1 (3.3%)	1.000 [a]
Wound infection	1 (3.3%)	1 (3.3%)	1.000 [a]
Duration of postoperative pain	8.36±0.80	6.16±1.14	0.018
Amount of postoperative analgesics[b]	26.31±2.45	21.86±1.63	0.003
Total length of hospital stay	12.46±0.73	11.06±0.58	0.003
Complete stable remission	9 (30%)	12 (40%)	0.589 [a]
Clinical improvement	21 (70%)	23 (76.7%)	0.771[a]

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

a: Fisher's exact test is used if there are expected cell frequencies less than 5

b: number of loxoprofen 60 mg tablets

Discussion

VATS thymectomy via a lateral intercostal approach has become the most commonly performed thoracoscopic procedure worldwide, replacing median sternotomy for thymoma or myasthenia gravis.[6] LVATS thymectomy incisions are small and lateral, making them less visible. In patients with myasthenia gravis, all adipose tissue anterior to both phrenic nerves is always removed. When approaching from only one side of the chest, ensuring an adequate operative field in the neck region might be difficult, and identifying the contralateral phrenic nerve might be challenging. Thus, the lateral method might be applied bilaterally. Furthermore, because the approach goes through the intercostal area, patients frequently experience intercostal post-thoracotomy pain syndrome, which is characterized by nerve paralysis or neuralgia that lasts months or even a lifetime and can occur at several port insertion incision sites.[7]

Moreover, post-thoracotomy pain syndrome rates are similar across open and thoracoscopic operations.[8,9] The study found that LVATS thymectomy patients required more postoperative analgesia due to intercostal nerve impairment caused by forceps and camera scope insertion, compared to SVATS, which does not need any intercostal incisions and avoids intercostal nerve injury. The SVATS group experienced shorter hospital stays. The LVATS thymectomy group experienced delayed hospital discharge due to pain, while the SVATS group reported reduced postoperative pain.

When comparing LVATS to SVATS, it has been found that SVATS offers better surgical views in the upper pole of the thymus and bilateral phrenic nerves.[10-12] This can potentially decrease the risk of unintended injury, which is crucial for proper and complete dissection of bilateral mediastinal fatty tissue. While the bilateral method effectively exposes the anterior mediastinum, it requires a greater number of incisions, potentially leading to increased surgical trauma.[13]

Moreover, using the subxiphoid incision has another benefit for instrument handling. The length of the incision gives the instruments room for gliding, which then substantially increases the technical feasibility. Using the subxiphoid incision, however, makes extensive thymectomy still feasible. Under direct thoracoscopic view, all the probable thymic-bearing mediastinal fat tissues can be eliminated; this could then convert into improved results.

Furthermore, the SVATS method eliminates the risk of sternal osteomyelitis. Patients have reduced pain and improved wound healing. This is especially crucial for treating young female patients with myasthenia. The subxiphoid wounds have healed adequately, and no incisional hernias have formed.

The study found no significant difference in surgery duration between SVATS and LVATS thymectomy. We think that surgeons should learn SVATS procedures for better patient outcomes, including reduced discomfort and improved wound results. Total blood loss and chest drain duration were less in the SVATS group. These results coincide with results obtained by Suda et al.[14]

In this study, two patients (6.7%) in the LVATS group and one patient (3.3%) in the SVATS group experienced phrenic nerve palsy. The phrenic nerve was injured due to problems detecting it when the mediastinal pleura was not opened. Endoscopic surgery requires frequent verification of the phrenic nerve's position to avoid injury due to the narrow operative field. No vascular injuries occurred in this study, but vascular injury prevention strategies are necessary. To treat hemorrhage during surgery, compress the bleeding spot using thymus tissue or a cotton finger. After compression, a fibrin sheet is applied to the bleeding spot in order to stop the bleeding. If bleeding cannot be managed, a median sternotomy is performed while patients remain supine.

Surgical outcomes showed that 9 patients (30%) in the LVATS group and 12 patients in the SVATS group achieved complete remission following surgery. We feel that the relatively lower complete remission rate in the present study is mainly due to a short follow-up period.

Conclusion

Our experience shows that both LVATS and SVATS techniques are effective for performing thymectomy in non-thymomatous myasthenic individuals. Both approaches are feasible and show good short-term results. The SVATS technique offers a clearer view of the bilateral pleural cavities and mediastinal structures. Patients with SVATS experienced less pain, less blood loss, and shorter hospital stays. SVATS is easy to learn, safe, and has good cosmetic results.

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