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ORIGINAL ARTICLE

Thoracoscopic versus Classic Trans-Sternal Thymectomy for Myasthenia Gravis: Single-Center Experience.

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ABSTRACT

Background: Myasthenia gravis (MG) is a neuromuscular junction autoimmune disease that has a great impact on quality of life. Thymectomy can be approached by classic trans-sternal or thoracoscopic thymectomy. This study aimed to evaluate the surgical outcomes of video assisted thoracoscopic thymectomy (VATS) as compared to the classic trans-sternal thymectomy in Sultan Qaboos University hospital (SQUH) and also to compare its outcomes to the international standards.

Methods: MG patients had undergone either VATS or classic trans-sternal thymectomy. Only patients with complete data were included. Medical records were examined for patient demographics, preoperative conditions, co-morbidities, perioperative and postoperative outcomes.

Results: A total of 56 thymectomies were performed. Among them, 22 were done by VATS and 34 were done by classic trans-sternal thymectomy. Total hospital stays, postoperative wound infection, visual analogue scale (VAS) for pain score and postoperative medications (antibiotics and analgesics) were significantly less in VATS group.

Conclusions: VATS thymectomy achieved superior results compared to the classic trans-sternal approach in terms of fewer postoperative complications such as wound infection and VAS for pain score, fewer postoperative medications and shorter hospital stay. Future prospective studies with longer follow-up periods are required to confirm these results.

Keywords
Myasthenia gravis; Thoracoscopy; Thymectomy; Sternotomy

INTRODUCTION

Myasthenia gravis (MG) is a neuromuscular junction autoimmune disorder that affects the impulse transmission between the motor neuron and the innervated muscle causing its weakness. It is triggered by antibody-mediated loss of acetylcholine receptors which are assumed to be produced by the thymus. Thymic changes commonly seen in MG include thymic follicular hyperplasia (thymitis), thymic atrophy, thymoma, and thymolipoma [1].

The treatment of MG mainly aims at a complete stable remission, and the modalities that are used nowadays include symptomatic treatments – mostly Acetyl cholinesterase inhibitors, short-term immune therapy, and long-term immune therapy including thymectomy [2].

Surgical treatment with thymectomy is an effective choice for management of MG [3]. Thymectomy is advised in all MG patients with thymoma. In non-thymomatous MG, there is evidence supporting thymectomy as a therapeutic modality especially in patients with generalized, acetylcholine receptor (AChR)- associated MG as it helps to avoid or minimize the dose or duration of immunotherapy [4].

As a general rule, MG patient, scheduled for thymectomy, should be managed by a team work of the thoracic surgeons and MG-specialized neurologists to determine indication, time of surgery and pre- and post-operative management.
cervical trans-sternal approach and video assisted thoracoscopic thymectomy (VATS). The classic trans-sternal and VATS are the two main approaches used for thymectomy in the treatment of patients with MG [5].
The objective of this study was to evaluate the perioperative characteristics and the efficacy of VATS in comparison to the classic trans-sternal thymectomy in myasthenia gravis patients in Sultan Qaboos University hospital (SQUH) and also to compare the postoperative outcomes of both techniques.

METHODS

Study Design and Population

The list of MG patients who had undergone either VATS or classic trans-sternal thymectomy from January 2008 to December 2018 was obtained from the Operation Room registry at Sultan Qaboos University hospital, Muscat, Oman. Then the hospital information system (Track-Care) was used to check the medical records of those patients. The total number of patients with MG patients was 56; of which 34 patients had undergone classic trans-sternal thymectomy and 22 had undergone VATS. The VATS thymectomy service started in 2012 in our hospital and since this time, all cases requiring thymectomy surgery have been performed by VATS. From this time until 2018, only 4 cases were performed using a trans-sternal technique. Only those patients with complete data have been included. Patients with incomplete data were excluded from the study. The privacy of the patient has been maintained; the name or identification number of the patient has been used so that the numbers 1-56 could be identified.
Written informed consent was obtained from all participants. The study was approved by the Medical Research Committee and Ethics Committee, College of Medicine and Health Sciences, Sultan Qaboos university, and was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. The design of the study is shown in Figure 1.

Data Collection

There are many operative approaches for thymectomy: classical median sternotomy approach (full median sternotomy), partial sternotomy approach, trans-cervical approach, combined trans-

The collected data included age, sex weight, height, co-morbidities (diabetes, epilepsy, sickle cell anemia, hypertension, thyroid diseases and systemic lupus erythematosus), findings of preoperative CT, preoperative steroids and plasmapheresis. All patients underwent serum testing for AChR antibodies. Results of antibody levels >0.02 nmol/L were considered as seropositive [6]. Perioperative findings in both groups included operative time and blood loss. Also, post-operative data were recorded e.g. complications, medications [Intravenous Patient controlled analgesia (IV PCA) with Fentanyl], visual analogue scale (VAS) for pain score, duration of ICU and hospital stay and follow-up outcomes.
The previous parameters have been set to compare the two procedures. Medical records were reviewed for demographics, co-morbidity, perioperative and postoperative patient data. Myasthenia Gravis Foundation of America (MGFA) classification was added as follow; class I: any ocular muscle weakness, and all other muscle strength is normal, class II: mild generalized weakness, class III: moderate generalized weakness, class IV: severe generalized weakness and class V: defined by intubation, with or without mechanical ventilation [7]. Patients have also been followed-up postoperatively for about one year. Follow-ups have been achieved through both clinical visits and telephone contact. The outcomes of surgery were assessed according to De Filippi postoperative classification [8].

Surgical procedures

The ultimate selection of VATS or trans-sternal thymectomy was determined by the thoracic surgeon's experience and the patient's preference considering limitation of VATS. In both procedures, maximal thymectomy has been performed. All thymic tissues with adjacent fatty tissues in the anterior mediastinum have been removed to ensure the removal of any ectopic thymic tissue.

Classic trans-sternal thymectomy

Through sternotomy, sternal retractor was placed to clearly visualize the thymus, and the thymus was dissected from the pericardium and surrounding structures. En block resection of the thymus was done with all fatty tissues from the diaphragm caudally and the thyroid gland cephalically extending

laterally to the right and left phrenic nerves. Main structures such as innominate vein and artery, trachea, superior vena cava, azygos vein and right bronchus were protected.

Thoracoscopic thymectomy

The thymus was approached either from the right, the left or bilaterally. Depending on the side approached, the lung on that side was collapsed with a double lumen endotracheal tube. In addition, CO2 insufflation has been used to provide more workspace. If the approach was bilateral, the lungs would be insufflated one at a time. The patient was placed in a semi-supine position and his arm situated abducted over a padded screen. This was done to get better access to the axilla in order to insert the ports, which were usually 3-4 ports of 10mm and 5mm size. The thoracoscope has been inserted through the 10mm port to visualize the thymus. Dissection was done with dissecting instruments via the 5mm ports. Finally, the thymus and all adjacent fatty tissues were dissected and removed with an endo-bag. All patients were approached from the right side except one who was approached bilaterally as the left phrenic nerve could not be viewed from the right side.

Statistical analysis

Statistical Package for the Social Sciences SPSS software version 23 was applied for the analysis of the results. We used Mann-Whitney test for abnormally distributed variables and Student's t-test for normally distributed variables to test the significance of difference between the two groups. The Chi-square Test was used for the categorical variables. Statistically significant results were considered when the probability values (p-value) were less than 0.05. Categorized variables included procedure used (1=VATS, 2= classic trans-sternal thymectomy), sex (1=male, 2=female), co-morbidities (1= yes, 2=no), complications (1=yes, 2=no). They were presented by frequency (%) and analyzed by Chi-square and fisher exact tests. Continuous variables were presented as mean ± standard deviation. Normality test was done for each continuous variable to determine which test to use.

RESULTS

Patient Demographics

The results showed that 75 % of the 56 patients included in the study were female and 25% were male. The youngest patient was 18 years old and the oldest was 47 years old. Demographic data was summarized in (Table 1).

Patient Comorbidities, Preoperative Data

Patients in both groups were assessed preoperatively according to Myasthenia Gravis Foundation of America (MGFA) classification and there was no significant difference between the two groups identified (Table 1). There were no significant differences regarding the duration of the illness, co-morbidities such as diabetes, epilepsy, sickle cell anemia, hypertension, thyroid disorders, systemic lupus erythematosus. Findings of preoperative CT, preoperative steroids, plasmapheresis and acetylcholine receptor antibody-positive patients. The data was summarized in (**Table 1**).

Perioperative and Post-operative outcomes

There were significant differences between the two groups regarding VAS for pain score, wound infection, post-operative analgesics and length of hospital stay. Patients with VATS had lower pain score, fewer wound infections and less analgesics dosage. VATS exhibited significantly shorter hospital stays. Results showed that there were no significant differences between the two procedures when it came to duration of operation, amount of blood loss, postoperative complications e.g. extubation, atelectasis, myasthenic crisis, re-intubation and pneumonia after the operation and the duration of ICU stay. In 56 patients at a mean follow-up time of 12 months, the outcomes of surgery by both techniques were assessed according to De Filippi postoperative classification which revealed complete remission rates (complete freedom of symptoms without medications) 40.9% in VATS, 35.3 % in classic trans-sternal thymectomy, clinical improvement (asymptomatic patients with decreased medication 27.3 % in VATS, 29.4 % in classic trans-sternal thymectomy, improved, decreased symptoms or decreased medication 18.2 % in VATS, 17.6 % in classic trans-sternal thymectomy). There was no change in 9.1 % in VATS, 11.8% in classic trans-sternal thymectomy. Patient had worsening symptoms 4.5 % in VATS, 5.9 % in classic trans-sternal thymectomy. There were no significant differences between the two procedures. No mortality was recorded in both groups. The data were listed in (**Table 2 & 3**).

Table 1: Patients demographics and preoperative data

Variable	VATS Thymectomy (n = 22)	Classic Trans-sternal Thymectomy (n = 34)	P-value
Sex Female, n (%)	16 (73%)	26 (76%)	0.75
Age, y mean ± SD (range)	 32 ± 12 (24 – 47)	 27 ± 13 (18 – 39)	 0.15
BMI, Mean ± SD Range	 31.1 ± 6 (26.3 – 33.9)	 28.6 ± 8 (24.4 – 33.3)	 0.19
ASA Class	2.42 ± 0.81	2.39 ± 0.76	0.89
MGFA class, n (%) I II III IV V	 1 (4.5%) 6 (27.3%) 10 (45.5%) 2 (9.1%) 3 (13.6%)	 2 (5.9%) 10 (29.4%) 14 (41.2%) 3 (8.8%) 5 (14.7%)	 0.87 0.93 0.25 0.66 0.75
Duration of disease, y Median Range	 1.16 0.2 – 4.1	 1.09 0.25 – 4.2	
AChR antibody Positive Negative	 16 (72.7%) 6 (27.3%)	 24 (70.6%) 10 (29.4%)	
Comorbidities G6PD Diabetes SLE Epilepsy HTN Sickle cell anemia Hyperthyroidism	 2 (9.1%) 1 (4.5%) 0 0.0%) 1 (4.5%) 1 (4.5%) 1 (4.5%) 1 (4.5%)	 0 (0.0%) 2 (5.9%) 1 (2.9%) 1 (2.9%) 3 (8.8%) 0 (0.0%) 1 (2.9%)	 0.15 0.66 0.61 0.85 0.48 0.39 0.85
Preoperative prednisolone (mg) plasmapheresis	25.1 ± 11.85 5 (22.7%)	29.7 ± 11.94 10 (29.4%)	0.21 0.76
Preoperative CT finding Normal Thymus Thymic hyperplasia Thymoma Thymic cyst	 11 (50%) 9 (41%) 2 (9%) 0 (0.0%)	 15 (44%) 13 (38%) 4 (12%) 2 (6%)	 0.67 0.84 0.58 0.36

Continuous variables are presented as mean ± SD and categorical variables as number and percent. AChR = Acetylcholine receptor; ASA = American Society of Anesthesiologists class; BMI = Body Mass Index; G6PD = glucose six phosphate dehydrogenase deficiency; HTN = hypertension; MGFA class = Myasthenia Gravis Foundation of America (MGFA); SLE = systemic lupus erythematosus.

Table 2: Perioperative findings and postoperative conditions in both groups

	VATS Thymectomy (n = 22)	Classic Trans-sternal Thymectomy (n = 34)	P-value
Perioperative findings Operative time, min Blood loss, ml	 148.2 ± 39.1 130.2 ± 55.6	 122.8 ± 32.8 127.2 ± 44.4	 0.23 0.83

	VATS Thymectomy (n = 22)	Classic Trans-sternal Thymectomy (n = 34)	P-value
Postoperative VAS score			
Day 1	3.07 ± 1.03	4.47 ± 1.30	0.003#
Day 2	2.8 ± 1.0	4.0 ± 1.1	<0.001#
Day 3	1.6 ± 0.8	2.9 ± 0.9	<0.001#
Postoperative condition & Complications			
No complications	19 (86%)	28 (82%)	0.69
Immediate extubation	18 (82%)	27 (79%)	0.82
Atelectasis	1 (4.5%)	2 (5.9%)	0.66
Myasthenic crisis	1 (4.5%)	2 (5.9%)	0.66
Reintubation	0 (0.0%)	1 (2.9%)	0.62
Pneumonia	1 (4.5%)	1 (2.9%)	0.85
Wound infection	0 (0%)	6 (17.6%)	0.04#
ICU stay, hours	23.73 ± 3.75	25.47 ± 3.56	0.2
Length of hospital stay, days	3.5 ± 0.72	7.8 ± 1.02	<0.001#
Analgesics doses, mg (PCA with fentanyl)	6.80 ± 3.15	14.22 ± 2.55	<0.01#

Continuous variables are presented as mean ± SD and categorical variables as number and percent. PCA= patient-controlled analgesia; VAS = Visual analogue scale; # significant difference between groups.

Table 3: De Filippi Classification after one-year Follow-up

De Filippi Class	VATS Thymectomy (n = 22)	Classic Trans-sternal Thymectomy (n = 34)	P-value
Class 1 (*Complete remission)*	9 (40.9%)	12 (35.3%)	0.67
Class 2 (*asymptomatic, decreased medication)*	6 (27.3%)	10 (29.4%)	0.55
Class 3 (*improved, decreased symptoms or decreased medication)*	4 (18.2%)	6 (17.6%)	0.66
Class 4 (*no change)*	2 (9.1%)	4 (11.8%)	0.56
Class 5 (*worsening symptoms)*	1(4.5%)	2 (5.9%)	0.66

Categorical variables are presented as number and percent.

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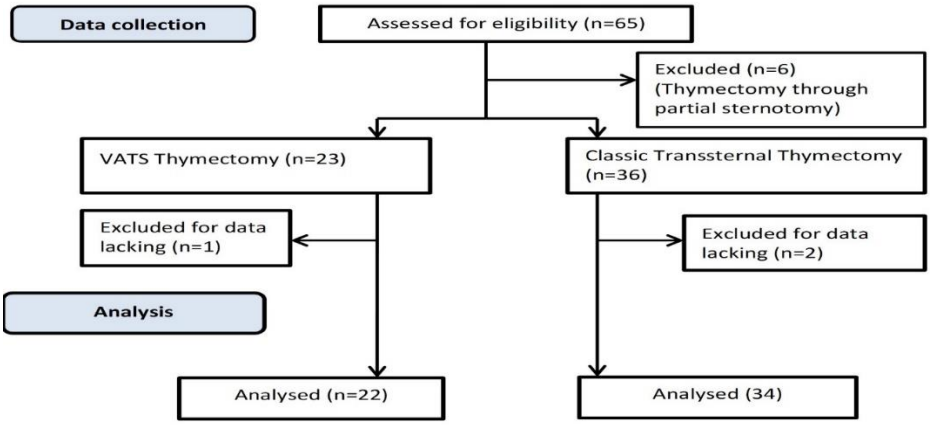

Fig. 1: Flow chart of the study

DISCUSSION

Surgical approaches to thymus vary considerably across the world. Trans sternal thymectomy is the most recommended approach in Europe and North America, as it facilitates easy access and control of major vascular structures in the anterior mediastinum. On the other hand, a lateral thoracotomy is also used. About, 10% of thymectomies are done by minimally invasive procedures. In Asia, about 35% of the resections are currently carried out by VATS [9].

Various technical approaches to VATS thymectomy have been reported, including bilateral or single-sided approaches from either the left or right hemi-thorax, subxiphoid and trans-cervical approaches [10-12]. The technique chosen varies depending on the skills and preferences of the individual surgeon.

Maximal thymectomy (complete excision of the thymic tissues and all mediastinal fat from neck to diaphragm and from right phrenic to left phrenic nerve) is required for removal of any ectopic thymic tissue. In more than 20% of the patients, tiny islets of functional thymic tissue are found throughout the anterior mediastinal fat [13].

This retrospective study used a number of parameters in order to evaluate the safety, and efficacy of VATS thymectomy as compared to the classic trans-sternal approach in cardiothoracic division, Sultan Qaboos University Hospital.

When comparing the two groups in our study, demographic data showed a predominance of female sex in both groups, but the difference was not statistically significant in both groups. There was also no statistically significant difference in age, BMI, American Society of Anesthesiologists Classification (ASA), Myasthenia Gravis Foundation of America (MGFA) classification, comorbidity and CT findings in both groups.

In our study, VATS was superior to the classical trans-sternal thymectomy. There was a significant difference between the two groups in the incidence of wound infection and the number of doses of antibiotics, with the VATS group having fewer wound infections and therefore fewer antibiotics. In the same respect, measurements of VAS for pain score revealed significant differences between the two groups. VATS patients had less pain score. This explained the fewer number of doses of analgesics in VATS group. Our results were comparable to those of other researchers [14]. This could be related to minimal surgical incision and therefore less tissue injury that would render the patient less susceptible to infection and pain. Previous studies have shown that minimally invasive thymectomy procedures, such as VATS, tend to reduce the use of narcotic analgesics compared to open thymectomy two weeks after the procedure [15].

Our findings also showed that the duration of hospital stay in the VATS group was significantly shorter. This may be explained by small surgical wounds and lower incidence of wound infection in VATS group compared to sternotomy group.

Our results compared perioperative conditions and the postoperative complications of VATS versus classic trans-sternal thymectomy. There were no significant differences between the two procedures in terms of duration of operation (P-value 0.23), amount of blood loss (P-value 0.83), postoperative complications e.g. extubation (P-value 0.82), atelectasis (P-value 0.66), myasthenic crisis (P-value

0.66), re-intubation (P-value 0.62) and pneumonia after the operation (P-value 0.85) and the duration of ICU stay (P-value 0.2).

Regarding follow-up time for about 12 months, both techniques were assessed according to the De Filippi postoperative classification. The results of surgery revealed a non-significant difference between the two procedures in terms of complete remission rates (P-value 0.67), clinical improvement (P-value 0.55), improved, decreased symptoms or decreased medication (P-value 0.66), no change (P-value 0.56), worsening symptoms (P-value 0.66). Our results are consistent with Toolabi et al., Bachmann et al. and Lin et al. [16-18].

Several studies compared the peri-operative and post-operative outcomes of VATS and classic trans-sternal thymectomy in MG and in other conditions as well, such as in thymoma or in anterior mediastinal tumors [11]. In agreement with other studies [19], we found that VATS was effective for treating MG with decreased hospital stay, postoperative complications such as wound infection and VAS for pain score compared to classic trans-sternal thymectomy. In addition, VATS thymectomy resulted in a decrease in the dosage of analgesics. Christison-Lagay et al. reported that VATS was a safe and a minimally morbid operation that could achieve comparable results to classic trans-sternal thymectomy in the amount of medication, duration of hospital stays and admission-related hospital expenses, and a reduced or comparable operating time matched with that reported for a historical series of open thymectomies [20]. Raza and Woo also concluded that the VATS approach to thymectomy in compared to the open approach (median sternotomy) is a safe and an effective technique. It has the benefit of fewer complications, is minimally invasive and allows for faster recovery [21].

CONCLUSION

VATS thymectomy achieved superior results compared to the classic trans-sternal approach in terms of fewer postoperative complications such as wound infection and VAS for pain score, fewer postoperative medications and shorter hospital stay. Additional randomized prospective studies with longer follow-up periods are recommended to confirm our results.

Conflict of Interest: Nothing to declare.

Financial Disclosures: Nothing to declare

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