DOI: 10.7860/IJARS/2020/44127:2551

Original Article

Surgery Section

Video Assisted Thymectomy- A New Frontier in Myasthenia Gravis

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ABSTRACT

Introduction: Thymoma comprises 20% of all mediastinal neoplasms and 50% of all primary tumours in the anterior compartment. Thymic surgery has undergone a paradigm shift in approach from being transcervical to video assisted. Video assisted thymectomies in selected patients can decrease the inherent morbidities of a trans-sternal approach, while achieving similar therapeutic benefits.

Aim: To analyse the technical key points, morbidity and outcomes associated with video assisted thymectomy in early stage thymoma (Modified Masoaka stage I or II) with myasthenia gravis.

Materials and Methods: The present study was a retrospective observational analysis of 24 patients with thymoma and Myasthenia Gravis Foundation of America (MGFA) class II to IV myasthenia gravis who underwent video assisted thoracoscopic thymectomy in institution from May 2013 to May 2018. All patients with thymomas which on Contrast Enhanced Computed Tomography (CECT) did not show infiltration of the surrounding structures and were <5 cm were included. All patients were operated under General Anaesthesia (GA) with a single lumen tube with controlled CO_2 pneumothorax with right or left thoracoscopic approach. Primary outcomes studied were immediate and delayed complications, completeness of resection and rate of conversion to open. Secondary outcome included intensity of treatment required for myasthenia gravis after two years of follow-up.

Results: In present study, 83.3% of the patients were male and 63% belonged to 20-40 years of age. Only 8% of the patients belonged to <20 years of age. Mean operative time was 164±10 minutes in Video-Assisted Thoracoscopic Surgery (VATS). Blood loss in VATS was 178±47 mL. Mean chest tube duration was only 3.2±0.67 days. Duration of stay in the hospital was on an average 3.4±1.45 days. Mean VAS pain scale for VATS patients was 3.5±1.08. Postoperative complication occurred in 8.3% of the patients. About 50% of the patients achieved complete remission of myasthenia gravis symptoms and were free of any treatment.

Conclusion: Management of thymoma with myasthenia gravis remains an evolving clinical undertaking which requires multidisciplinary approach. In carefully selected patients, minimally invasive techniques such as video assisted thymectomies have very low immediate or long term morbidity with excellent remission rates for myasthenia gravis.

Keywords: Minimally invasive thymectomy, Thoracoscopic, Thymoma

INTRODUCTION

Thymomas are the most common anterior mediastinal mass, accounting for almost half of them [1]. They originate from epithelial thymic cells and contain epithelial, lymphocytic and mixed population. Young women and older men (40-60 years) are usually affected [2]. They are slow growing tumours with definite malignant potential including local invasion, systemic metastases but surprisingly without overt cytological features of malignancy on histopathology. Recently WHO classification has dropped "Type C' for thymic carcinomas and given A, AB, B1, B2, B3 and rare others [3]. Almost 50% are asymptomatic and are usually diagnosed on chest X-ray or autopsy, however 30% present with pressure or invasion symptoms like superior vena cava syndrome (dilated neck veins or facial oedema), cough, chest pain, dysphonia or dysphagia. Nearly, 20-70% of thymomas are associated with autoimmune disorders including myasthenia gravis, pure red cell aplasia and hypogammagolbulinemia [4].

Von Haberer H, in 1917 introduced transcervical thymectomy for thymic hyperplasia often found in thyrotoxicosis [5]. Blalock A et al., introduced upper sternotomy for thymectomies and introduced neostigmine for control of myasthenia gravis symptoms [6]. Crile G redescribed transcervical thymectomy for myasthenia gravis in an attempt to decrease the morbidity of a trans-sternal thymectomy [7]. Other incisions include lateral and anterior thoracotomies [8].

However, trans-sternal extended thymectomy remains gold standard [9]. In 1990s, a major drive in endoscopic surgeries resulted in the development of VATS thymectomy for early stage disease. Currently, European and North American countries prefer the trans-sternal approach (nearly 75%), whereas, Asian countries have adopted the minimally invasive technique more enthusiastically (almost 35%) [10]. In this study, an attempt was made to assess the technical key points, morbidity and surgical outcomes of VATS thymectomy in early stage.

MATERIALS AND METHODS

A retrospective observational analysis of 24 patients was carried out at Army hospital (R&R), a tertiary care centre that receives patients from all over the country who underwent video assisted thymectomy. All patients received standard of care as per standard guidelines. Approval from Institutional Ethical Committee (IEC) and scientific committee was obtained (IEC # 29/2020).

Inclusion criteria: Patients with clinical and biochemically proven myasthenia gravis belonging to MGFA class II, III and IV with an anterior mediastinal mass <5 cm in size with no infiltration into surrounding structures and have completed two years of follow-up post video assisted thymectomy were included.

Exclusion criteria: Any patient with prior thoracic surgery, known pulmonary tuberculosis or previous chest infection requiring surgical intervention or admission. MGFA class I (ocular MG) and class V (very severe) MG were also excluded.

A total 24 cases giving consent and satisfying inclusion and exclusion criteria who underwent video assisted thymectomy from May 2013 to May 2018 were selected for the study. Patients were evaluated clinically and subjected to imaging and relevant investigations. The clinical staging system proposed by WHO classification and modified Masoaka staging system were used

[11,12]. All postoperative specimens were fixed with 10% neutral formalin solution and subjected to histopathological examination.

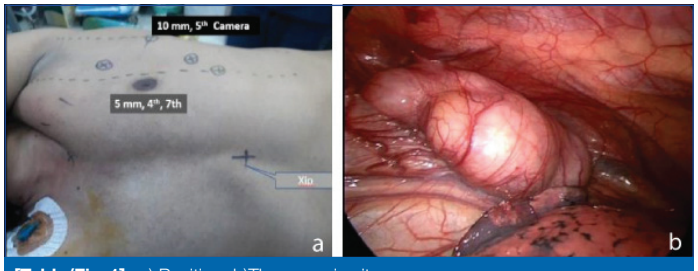
Patients with suspected myasthenia gravis underwent Acetylcholine Receptor (AChR) antibody and Repetitive Nerve Stimulation (RNST) to establish myasthenia gravis and classified according to MGFA classification. Contrast-Enhanced Computed Tomography (CECT) thorax was the modality of choice to confirm anterior mediational mass, assess mediastinal and thoracic organs and infiltration to surrounding structures like great vessels. All patients fulfilling the inclusion and exclusion criteria were discussed in a multidisciplinary team consisting of oncologists and neurologists. A neurologist was closely involved in optimisation of symptoms before anaesthesia. A pretested proforma was used to collect relevant information (patient data, clinical findings, preoperative investigations, surgical details, histopathological examination etc.,) from all the selected patients. Outcomes studied included complications of thymectomy, operative outcomes, conversion rates, intensity of treatment required for myasthenia gravis after two years of follow-up. Conversion rate was defined as the number of cases which needed to be converted to open trans-sternal thymectomy in view of bleeding, adherence to surrounding structures or injury to vital structures like lung. Intensity of treatment for myasthenia gravis was defined as the number of drug used in combination or any intervention (e.g., plasmapheresis/ intravenous immunoglobulins) needed to keep the individual asymptomatic post-thymectomy.

Procedure

Surgical procedure was performed by consultant oncosurgeons. For tumour in the midline or to the left, a left sided approach was used. This provided a better visualisation of the innonimate veins in its entirety and a better way of accessing the cervical horns.

The patient was placed in semi recumbent position with left side slightly elevated using soft gel pad. The left arm was stretched posteriorly to fully expose the left side chest wall. However, tumours which were located on the right side were approached via right hemithorax and positioned accordingly.

A 10 mm camera port was placed on the 5th intercostal space along the midaxillary line. Two 5 mm working ports were used, one at 4th intercostal space along anterior axillary line and an anterior port at 7th intercostal space in the inframammary region. Single lumen tube and CO_2 insufflation to about 6-8 mm Hg was used throughout to maintain the intrathoracic space for surgery. No case required single lung ventilation. A 5 mm accessory port, rarely necessary for larger tumours or with dense adhesions was made in the 8th or 9th intercostal space in the anterior axillary line. The procedure included removal of the thymoma along with all fibro fatty tissues anterior to the pericardium from thoracic inlet to the diaphragm lying between the right and left phrenic nerves. Specimen was delivered via the 10 mm port [Table/Fig-1a,b]. After completion of the procedure, a 20F chest drain was placed via the lowest 5 mm port to remove fluids.



[Table/Fig-1]: a) Position, b)Thymoma in situ.

Postoperatively, all patients were shifted to intensive care unit after extubation and kept under observation and neurologist care overnight. If uneventful, the patient was shifted to ward in the morning and drain output was monitored and removed when less than 100 mL.

After discharge from the hospital, patients were kept under regular follow-up with both the neurologist and oncosurgeon. Initial review was done at 10 days for wound and histopathology. If no adjuvant therapy was needed, then two-weekly follow-up was done until three months and then three monthly for two years. Data collection included all patients who completed two years of follow-up.

STATISTICAL ANALYSIS

MS excel was used to calculate Mean and Standard deviation.

RESULTS

The mean size of tumour was 40.8 mm (25-55 mm). About 15 patients belonged to 20-40 years of age. Only two were <20 years of age [Table/Fig-2]. Operative time was 164±10 min and average blood loss was 178±47 mL. Mean duration of chest tube drainage was 3.2±0.67 days [Table/Fig-3]. One case of pneumonia and phrenic nerve palsy each was noted. No patient had to be reintubated due to myasthenia crisis in the postoperative period. There was no perioperative mortality [Table/Fig-4]. About 12 (50%) had complete remission of symptoms of myasthenia gravis. None of the patients who were earlier on steroids required steroids postoperatively. Only two patients remained on a two-drug regime post thymectomy out of five. None required rescue intravenous immunoglobulins (IVIG) or steroid treatment [Table/Fig-5].

Age (in years)	Male (n=20)	Female (n=4)
<20	2	0
20-40	13	2
>40	5	2

[Table/Fig-2]: Demographic characteristics.

Parameter1	VATS (Mean±SD)
Mean operative time (min)	164.1±10
Blood loss (ml)	178±47
Mean chest tube duration (days)	3.2±0.67
Mean length of ICU stay (hours)	20.2±4.66
Mean length of hospital stay (days)	3.4±1.45
Mean VAS pain scale	3.5±1.08
Postoperative complication (%)	8.3

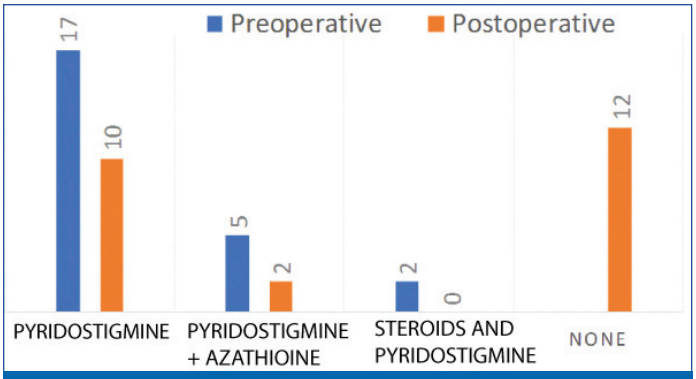
[Table/Fig-3]: Immediate postoperative outcomes.
VATS- Video-assisted thoracoscopic surgery; VAS- Visual analog scale; SD- Standard deviation

Parameter 1	VATS N(%)
Nosocomial pneumonia	1 (4.16%)
Phrenic palsy	1 (4.16%)
Myasthenia crisis-reintubation	0
Pneumothorax	0
Chylothorax	0
Perioperative mortality	0
Conversion to open	0
R1 resection[1]	2 (8.3%)

[Table/Fig-4]: Complications.
Resections where tumour was completely removed both grossly and microscopically were R0 resection, resections where tumour cells are microscopically seen on the margins were R1 resection and termed R2 resection if gross tumour was left behind; VATS- Video-assisted thoracoscopic surgery

DISCUSSION

The global experience with VATS thymectomy is increasing. In patients with myasthenia gravis, thymectomy along with complete removal of all the anterior mediastinal fat is crucial to prevent recurrence and achieve remission as described by the thymectomy trial in non-thymomatous myasthenia gravis patients receiving prednisone therapy" (MGTX) trial in 2016 [13]. It is important to note that there are no randomized control trials comparing open trans-sternal approach to VATS in early stage thymoma with or without myasthenia gravis. Most comparative series with trans-sternal



[Table/Fig-5]: Response to surgery.

thymectomies have shown mean operative time lower than that of VATS, however, blood loss in VATS was lower as compared to open approach [14]. Mean chest tube duration, mean VAS pain scale, mean length of ICU and duration of stay in the hospital all were lower for VATS thymectomy patients as compared to trans-sternal approach [15].

Cardiac and pulmonary complications are almost similar for both of the methods. However, if late sequelae of sternotomy wound are accounted for then the complication rate increases to almost 15% for open trans-sternal approach [16]. In present study, operative time and blood loss to complete resection decreased progressively as to around (164.1±10 min and 178±47 ml). Similar operative time and blood loss have been reported by many authors [17-19]. Toker A et al., also demonstrated similar postoperative chest drain requirement (3 days), hospital stay (5.6 days) and mean VAS scores (4.8) [20]. Postoperative complications in present study comprised of only one case of clinically significant pneumonia and phrenic nerve palsy. Ye B et al., found postoperative complications in their analysis of trans-sternal and thoracoscopic thymectomy to be not different [21]. About 70.8% of the cases in present study were type AB thymoma [Table/Fig-6] similar to the analysis done by Detterbeck FC in which type A and type AB comprised an average of 58% and 66% of stage I as well as 25% and 36% of stage II patients, respectively [22]. Almost 92% achieved, R0 resection in present study. In most studies, 5-10% cases have R1 resection [23].

WHO Thymoma Type	Number of cases	Percentage
Type A	1	4.1%
Type AB	17	70.8%
Type B1	3	12.5%
Type B2	3	12.5%
Type B3	0	0
Other variants	0	0

[Table/Fig-6]: WHO Thymoma type according to histopathology

Almost 50% complete remission post operatively was obtained and no patient needed steroids or IVIG rescue in current study suggesting a good response to this surgery in most patients. Available literature suggest an extremely variable rates of complete remission (7-63%) [24].

Recent advances in minimally invasive surgeries include the use of uniportal technique, additional access via right chest port (bilateral) to improve dissection of the anterior mediastinal fat, 3D monitors to improve visualisation and Robotic thymectomy. The superiority of any of these techniques above conventional VATS thymectomy is yet to be proven [25-27].

The rarity of these tumours along with varied techniques are definite barrier against performing a multi-institutional randomised controlled trial to compare VATS and open trans-sternal thymectomies. Until such definite evidence is available, carefully selected patients of early stage thymoma with or without myasthenia gravis should be given a chance to undergo VATS thymectomy as it has been shown in most single institutional trials to be equivalent in treatment of myasthenia gravis and thymoma, while decreasing the morbidity and hospital stay.

Limitation(s)

Lack of a similar control group undergoing open trans-sternal thymectomy and a small sample size limit the capability of making definite recommendations in favour of video assisted thymectomy in this study.

CONCLUSION(S)

Minimally invasive techniques such as video assisted thymectomies, with its inherent low morbidity and excellent remission rates, if performed in properly selected patients have the potential to revolutionise the multimodal and often complex management of early stage thymoma with myasthenia gravis. However, caution is advised as these are technically demanding surgeries with a learning curve and should be performed at tertiary care centres with adequate Intensive Care Unit (ICU) facilities and multidisciplinary team approach.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 03, 2020
- Manual Googling: Apr 28, 2020
- iThenticate Software: Jun 10, 2020 (01%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Feb 24, 2020**
Date of Peer Review: **Mar 21, 2020**
Date of Acceptance: **May 03, 2020**
Date of Publishing: **Jul 01, 2020**