4 Surgical Approach to Thymic Lesions

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4.1 History

The first thymectomy was performed in 1911 by Sauer Bruch via a transcervical route [1]. Nearly two decades later Alfred Blalock and colleagues performed the first trans-sternal thymectomy in a case of thymoma with myasthenia gravis (MG) and they noted the resolution of myasthenia [2]. Subsequently the indication of thymectomy was extended to even non-thymomatous patients of MG with encouraging results and remission rates of up to 15–50%, thus establishing surgery as a potential therapeutic modality for MG [3, 4].

The next major paradigm shift happened with the description of ectopic thymic tissue in mediastinal fat beyond the confines of thymic gland by Masaoka et al. [5]. This brought in the concept of extended thymectomy as a preferred surgical option. This entails complete removal of thymus along with mediastinal fat. Subsequently even more radical maximal thymectomy was described by Jaretzki et al. [6] which includes removal of even cervical fat through an additional incision in the neck. The advent of minimal invasive surgery has prompted the surgeons to adapt these techniques in the management of thymic diseases which minimize the morbidity associated with open techniques. Currently, minimal invasive techniques are preferred and increasing number of studies have confirmed the safety and efficacy of these techniques in the treatment of MG [7, 8, 9]. The evolution of surgical approaches to thymus has been summarized in Table 4.1. The first video-assisted thoracoscopic surgery (VATS) thymectomy was performed by Sugarbaker from Boston and the Belgium group in 1993 [10]. VATS thymectomy has become increasingly popular due to low procedural morbidity and mortality, improved cosmesis, and lesser degree of access trauma. There is increasing data to support equal efficacy with VATS thymectomy when compared to open thymectomy for non-thymomatous MG [11]. Francesco Paolo Caronia et al. did the first uniportal VATS thymectomy in 2015 [12].

4.2 Indications for Thymectomy

Patients with thymoma with or without MG warrant a thymectomy. MG in general is an indication for thymectomy, with early onset myasthenia patients benefitting the most [13, 14]. Conditions like AChR antibody-negative, anti-MUSK antibody-positive, pure ocular MG and late-onset non-thymomatous MG have poor response to thymectomy [11, 15].

Other rare indications for thymectomy are thymic cyst, thymic carcinoid, thymic carcinoma, ectopic intrathymic parathyroid, symptomatic thymic hyperplasia, and pure red cell aplasia.

Table 4.1 Evolution of surgical approaches to thymus

Approaches	Year	Author
Transcervical [1]	1911	Sauerbruch F.
Transsternal [2]	1939	Alfred Blalock et al.
Extended thymectomy [5]	1975	Masaoka et al.
Maximal thymectomy [6]	1988	Alfred Jaretzki et al.
VATS thymectomy [10]	1993	Sugarbaker et al.
VATET [11]	1996	Scelsi et al.
Uniportal thymectomy [12]	2015	Francesco Paolo Caronia et al.

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4.3 Surgical Anatomy of Thymus

ITMIG (international thymic malignancy interest group) system classifies the mediastinum into three compartments, the anterior prevascular compartment, the middle visceral compartment, and the posterior prevertebral compartment. The thymus lies in the prevascular compartment which is bounded superiorly by the thoracic inlet, inferiorly by the diaphragm, anteriorly by the posterior border of the sternum, laterally by the mediastinal pleura, and posteriorly, the anterior aspect of the pericardium [16].

The thymus gland has an H-shaped configuration which consists of elongated left and right lobes that join at their central portions just caudal to the left innominate vein (Fig. 4.1). The cephalad ends of each lobe become thin and are generally well defined, whereas the caudal ends of each lobe are thicker and less easily definable as they fade into surrounding mediastinal fat as one approaches the diaphragm. The gland is enveloped in a fibrous capsule which allows the surgeon to apply traction and also helps in differentiating from the surrounding fat.

The gland itself, by virtue of its capsule, has a smoother, more lobulated appearance while the fat has a less coalesced, less solid appearance. Making this differentiation is particularly challenging during the most caudal portion of a thymic dissection as one approaches the diaphragm and above the innominate vein.

The presence of mediastinal ectopic foci of thymic tissue may be observed in a range from 20% up to 72% [5, 6, 17]. Ectopic foci of thymic tissue have been found in the neck, either fused or close to the parathyroid and thyroid glands (Fig. 4.2). Ectopic foci of thymus have also been reported in the base of skull, main bronchi, and in the parathyroid gland. Thus, total and complete removal of the thymic tissue to achieve a favorable clinical outcome is theoretically impossible, and it just indicates that ectopic thymic tissue is a marker for poor outcome after surgery.

The blood supply to the body of the thymus is derived from small branches which arise from the superior and inferior thyroid arteries, the internal mammary vessels, and less importantly from the pericardiophrenic vessels. The venous drainage, on the other hand, is primarily through 1–3 larger branches that drain directly off of the posterior aspect of the gland into the left innominate vein.

Lymph Node Dissection in Thymic Carcinoma Lymph node dissection is not very well described in thymic malignancies as compared to other thoracic malignancies. The incidence of nodal metastases in patients with thymic carcinoma ranges from 26.8% to 41% [18–20].

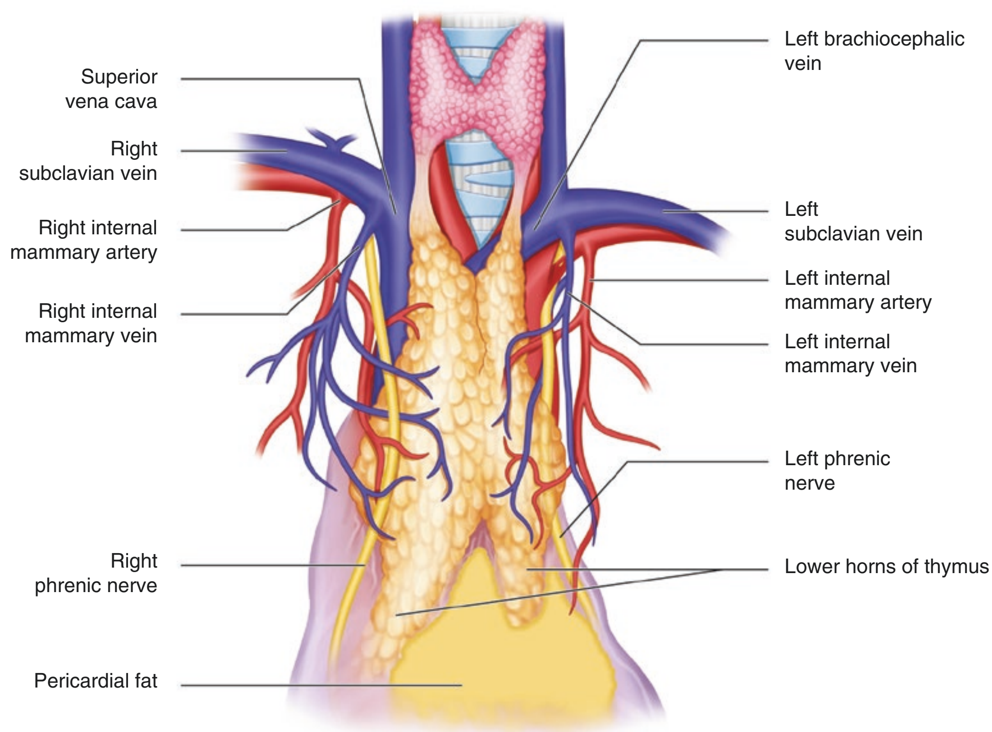


Fig. 4.1 Anatomy of thymus. *RIMA* Right internal mammary artery, *RIMV* Right internal mammary vein, *LIMA* Left internal mammary artery, *LIMV* Left internal mammary vein, *SVC* Superior vena cava

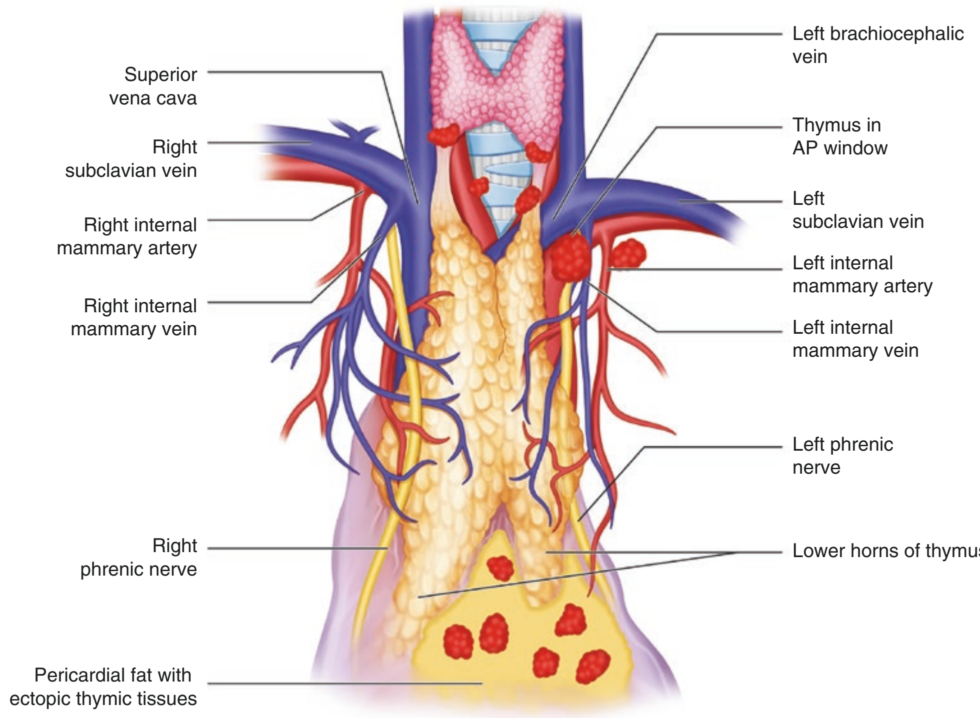


Fig. 4.2 Areas of potential ectopic thymic tissue. *RIMA* Right internal mammary artery, *RIMV* Right internal mammary vein, *LIMA* Left internal mammary artery, *LIMV* Left internal mammary vein, *SVC* Superior vena cava and *AP* Aorto-pulmonary

The first ITMIG recommendations were given in 2011 [21]. They recommended that any suspicious lymph node should be removed. In thymomas with adjacent organ involvement, routine removal of anterior mediastinal lymph nodes and a systematic sampling of intrathoracic lymph nodes is recommended. For thymic carcinoma, the systematic removal of anterior mediastinal, intrathoracic, supraclavicular, and lower cervical lymph nodes was recommended.

There has been a renewed interest in lymph node dissection and according to the new ITMIG/IASLC (2014) [16] lymph node map they are classified as the anterior region (N1) including the lower anterior cervical, peri-thymic, prevascular, para-aortic, ascending aortic, superior phrenic, supradiaphragmatic, inferior phrenic, and pericardial node groups. The deep region (N2) includes the deep cervical, supraclavicular, upper and lower paratracheal, subaortic, subcarinal, hilar, and internal mammary node groups. All nodes outside the anterior and deep regions were regarded as M components.

By defining node areas both anatomically and on CT images, clinical and pathological staging is improved. Involved nodes should be classified as in either the "anterior region" or "deep region" according to the boundaries described; if possible, the specific location of the node should be recorded as well.

4.4 Principle of Surgery

Aim is to achieve complete clearance of mediastinal fat along with complete excision of thymus in non-thymomatous myasthenia gravis. Thymectomy is done in patients of thymoma, although some recent studies are promoting thymomectomy in early-stage thymoma [22].

4.5 Surgical Approaches

The surgical decision is influenced by the extent of the planned resection (simple or extended thymectomy), status of thymus (atrophic, normal, hyperplasia, or thymoma), location of the gland (left or right), and involvement of major vascular structures. Other factors which influence surgical approach are the general and respiratory condition of the patient.

Thymus extends in body cavities (neck and thoracic cavity) and approaches to thymus have been described from both regions. Additionally, subxiphoid and subcostal approaches are also described (Fig. 4.3).

The role of VATS thymectomy in large thymomas is still debatable. The involvement of phrenic nerve, innominate vein, or other major vascular structures is a contraindica-

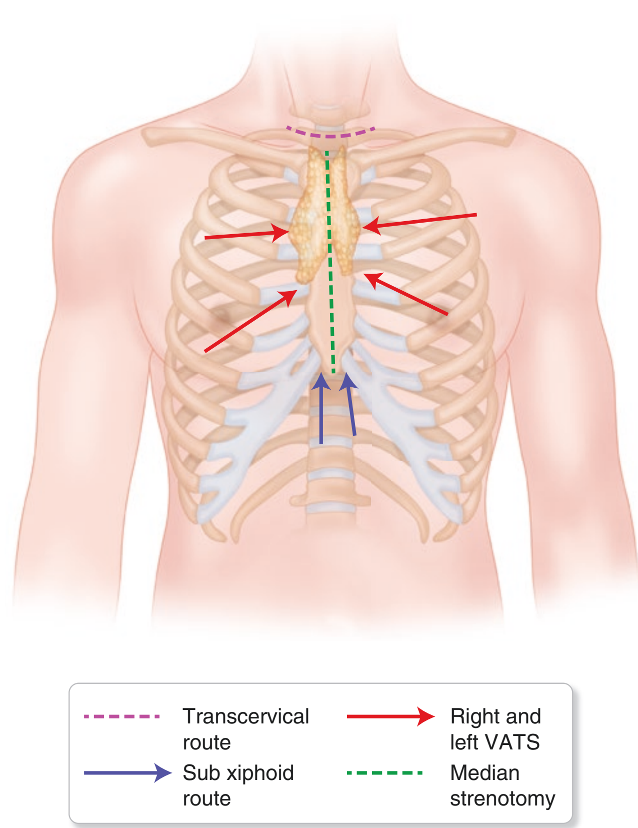


Fig. 4.3 Various surgical approaches to thymus

tion for VATS, either diagnosed preoperatively or intraoperatively [21].

According to the European Society for Medical Oncology (ESMO) guidelines on thymic tumors [23], the standard surgical approach in resectable disease remains median sternotomy. Resectable tumors include all stage I/II disease (according to Masaoka-Koga stage) and selected stage III tumors. The ESMO guidelines however recognize that MIT (minimally invasive thymectomy) is an option for presumed stage I and II "in the hands of appropriately trained surgeons."

According to the ITMIG policies, a minimally invasive thymectomy should comprise of the following [21].

1. A minimally invasive resection of a thymic malignancy should involve no rib spreading or sternal cutting. The intent should be to perform a complete resection, and a significant portion should be done with visualization on a video monitor.
2. Resection should involve the thymoma, thymus, and mediastinal fat.
3. Dissection and visualization of innominate vein and both phrenic nerves should be done.
4. Conversion to open is required if oncologic principles are being compromised or violated: e.g., perforation of the capsule, incomplete resection, risk of a discontinuous (not en bloc) resection, or disruption of the tissues exposing the tumor.
5. The access incision for retrieval of the thymoma should be large enough to prevent specimen disruption.
6. Exploration of pleura should be done if the thymoma invades the mediastinal pleura.
7. Retrieval in the bag.
8. Examination of the removed specimen to assess for completeness of the resection is required.
9. Communication with pathologist about suspicious areas is essential. The issues are orientation of the specimen, marking of several routine areas both on the specimen and in the patient, and identification of areas of tissue disruption that were not "closed" during the dissection.

4.6 VATS Thymectomy

VATS thymectomy has been performed in a left lateral, lateral semi-supine, and supine position.

Figure 4.4 shows patient positioning for VATS thymectomy in supine position.

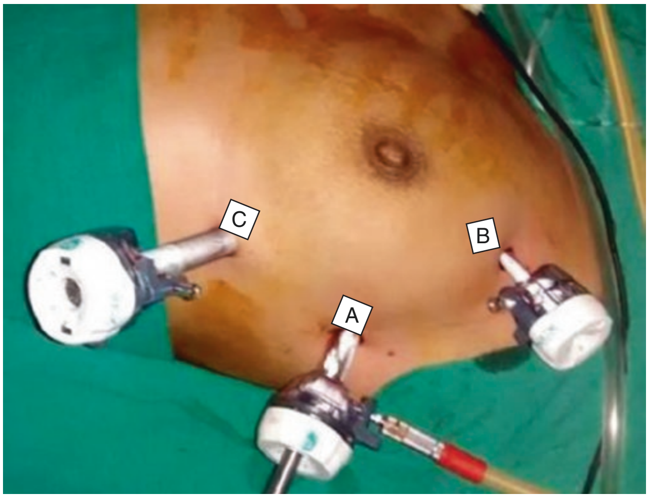
The first port is placed in the fourth or fifth intercostal space. Once the first port is placed, a combination of carbon dioxide insufflation and lung isolation is used for creation of space. The rest of the ports are placed under direct vision.

Port position is as shown in Fig. 4.5 for left VATS thymectomy.

Once the thoracic cavity is entered a thorough assessment of the lesion is done along with assessment for any pleural deposits. The view from the right and left lateral ports is shown in Figs. 4.6 and 4.7.

Step 1: Identification of phrenic nerve and internal mammary vessels.

Fig. 4.4 Patient positioning for VATS thymectomy. Arm tucked below the level of the table exposing the lateral chest wall for port placement and manipulation



A-Camera port (10 mm)
B-5 mm working port
C-10 mm working port, also used for specimen extraction

Fig. 4.5 Port placement for VATS thymectomy

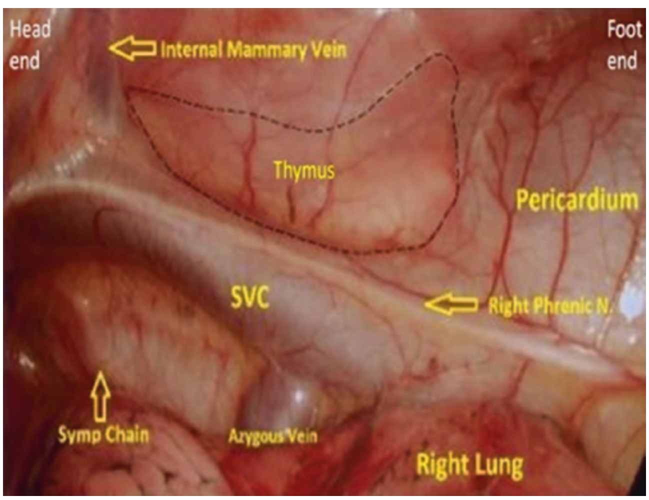


Fig. 4.6 View of anterior mediastinum from right VATS

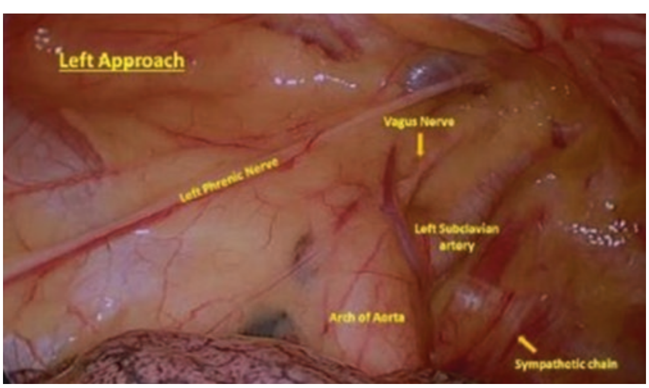


Fig. 4.7 View of anterior mediastinum from left VATS

Initially dissection starts by dividing the mediastinal pleura medial and parallel to the phrenic nerve as shown in Fig. 4.8.

Step 2: The pleural incision is extending from lateral to medial as depicted in Fig. 4.9 toward the opposite pleura.

Step 3: The next part of dissection begins at the inferior border at the pericardial reflection just medial to the phrenic nerve and proceeds from lateral to medial (Fig. 4.10). The end point of this dissection is identification of contralateral pleura and the contralateral phrenic nerve.

Step 4: Identification of thymic veins draining into the innominate vein (Fig. 4.11). Once the veins are identified they are dissected, ligated using polymer or titanium clips, and divided (Fig. 4.12).

Step 5: Taking down both the thymic horns is an important part of dissection. A series of blunt and sharp dissection is used to bring the thymic horns down (Figs. 4.13 and 4.14).

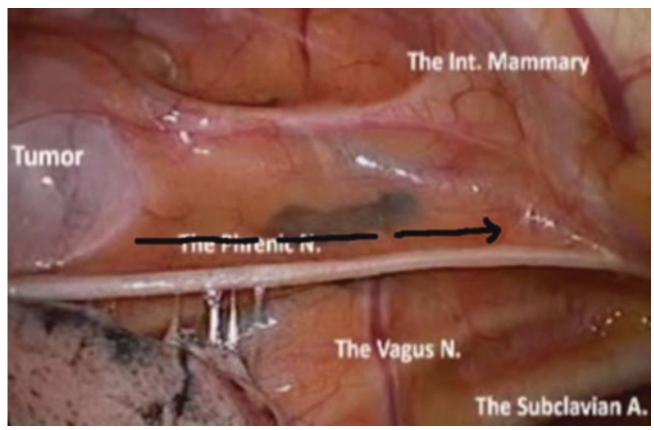


Fig. 4.8 View of left VATS. Dissection starts by dividing the mediastinal pleura medial to phrenic nerve along the dotted lines

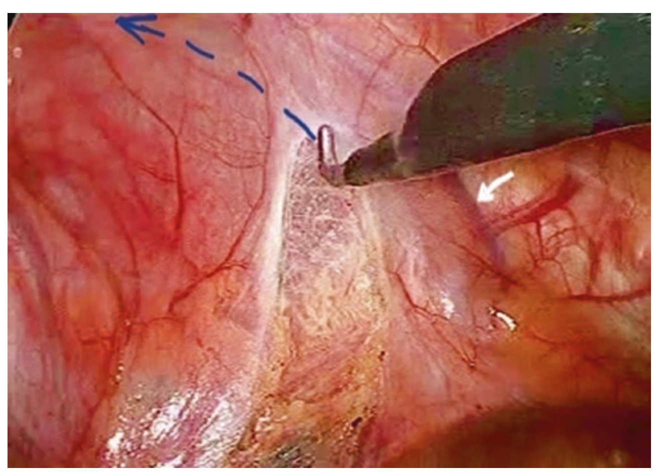


Fig. 4.9 Extension of the pleural incision from lateral to medial in the direction of the dotted lines toward the opposite pleura

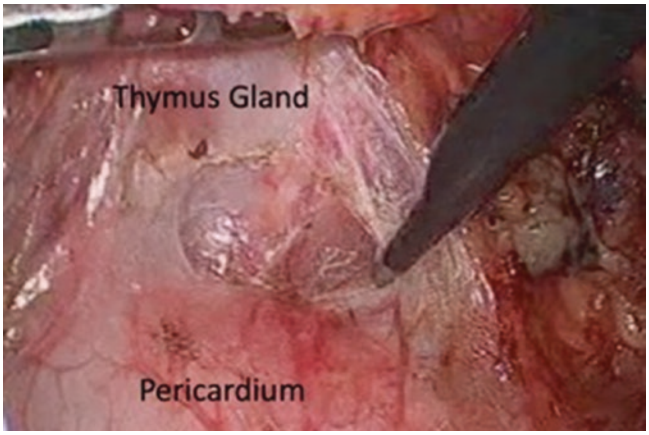


Fig. 4.10 Thymus dissected from its attachments to the pericardium

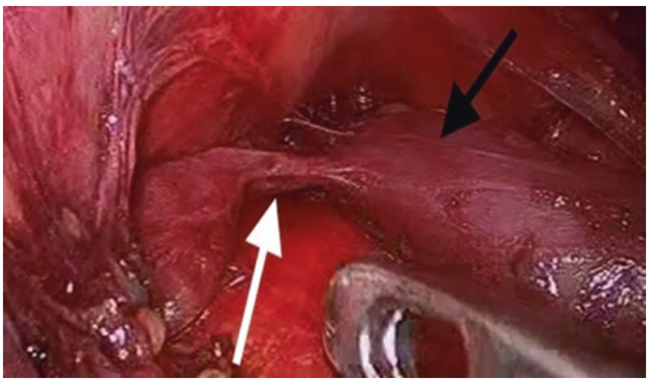


Fig. 4.11 Identification of thymic veins. *White arrow* thymic vein, *Black arrow* Brachiocephalic vein

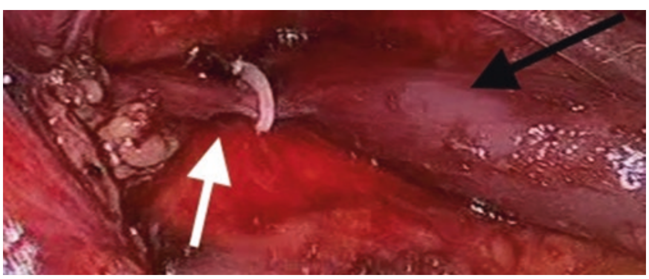


Fig. 4.12 Identification of thymic veins and clipping them with polymer clips. *White arrow* Thymic vein clipped with polymer clips, *Black arrow* Brachiocephalic vein

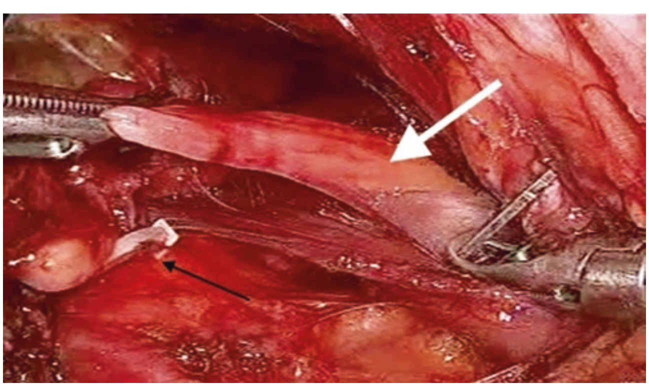


Fig. 4.13 Dissection of the left thymic horn going above the brachiocephalic vein. *White arrow* Left thymic horn going above the brachiocephalic vein, *Black arrow* Clipped thymic vein

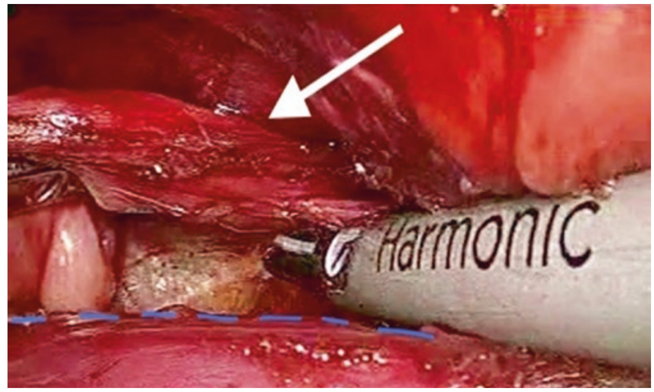


Fig. 4.14 Dissection of the right thymic horn going above the brachiocephalic vein. *White arrow* Right thymic horn going above the brachiocephalic vein, *Blue dotted lines* brachiocephalic vein

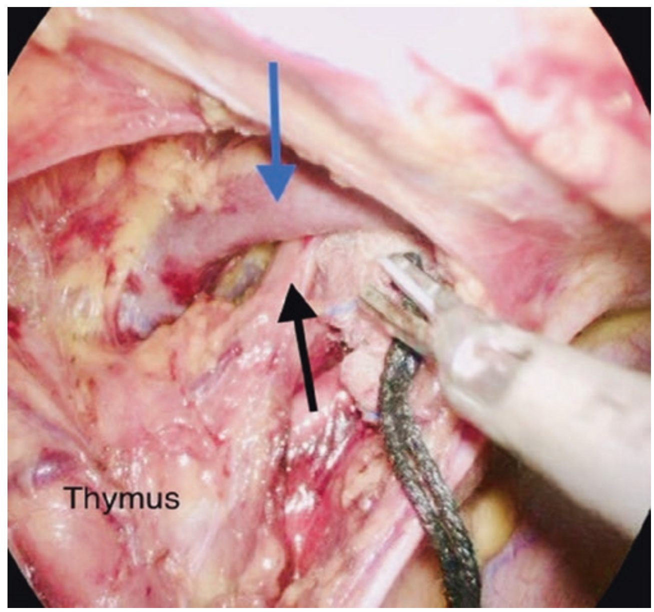


Fig. 4.15 Dissection of the right thymic horn going under the brachiocephalic vein. *Black arrow* Right thymic horn going under the brachiocephalic vein, *Blue arrow* brachiocephalic vein

Caution should be taken as sometimes the thymic horns can go underneath the innominate vein as shown in Fig. 4.15.

(Note: the order of steps 3, 4, and 5 is not fixed and is interchangeable depending on the anatomy, underlying disease, and body habitus of the patient.)

Step 6: Clearance of the cardiophrenic fat pad ensuring clearance of all anterior mediastinal fat (Fig. 4.16).

In some cases, the tumors infiltrate the adjacent organs as shown in Figs. 4.17 and 4.18. An R0 resection is recommended even in such conditions.

The specimen is retrieved in a bag (Fig. 4.19).

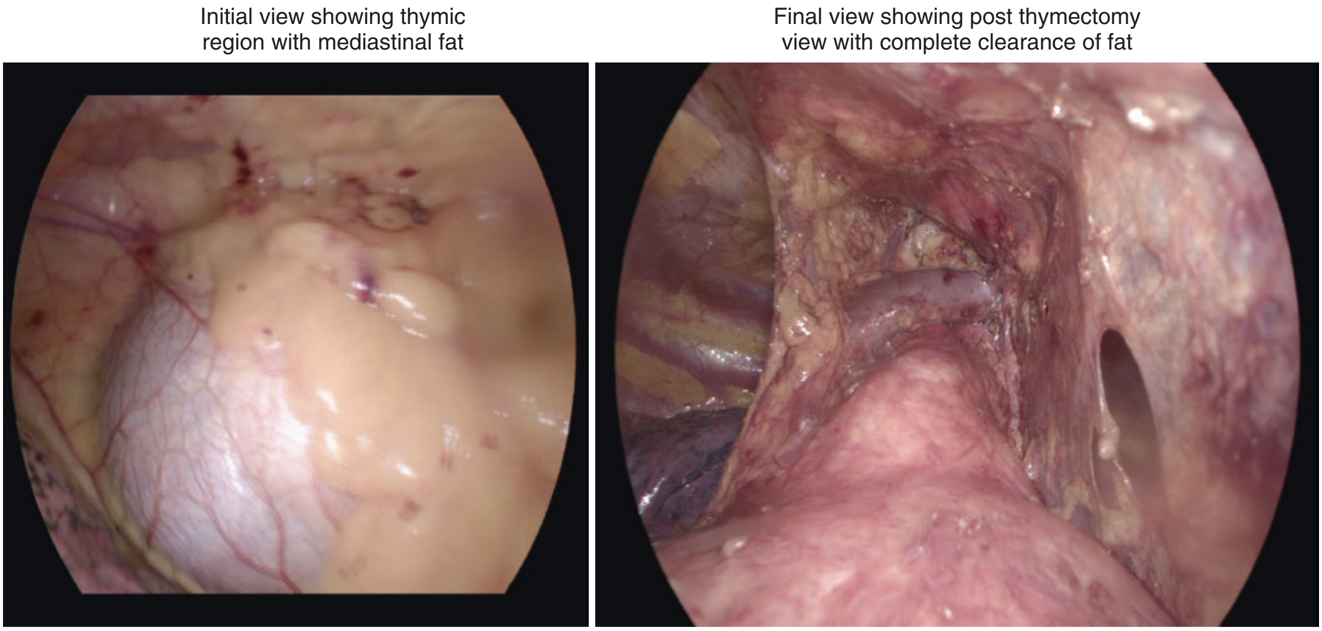


Fig. 4.16 View of the anterior mediastinum after completion of thymectomy

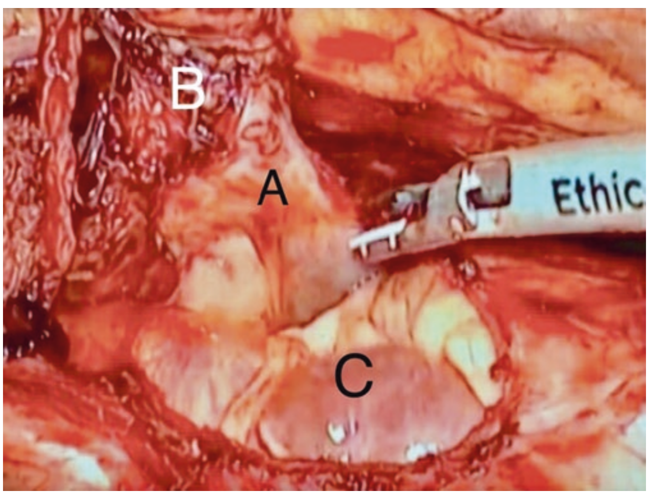


Fig. 4.17 Thymoma with adjacent organ involvement. *A* Pericardium, *B* tumour invading pericardium, *C* Cardiac chambers

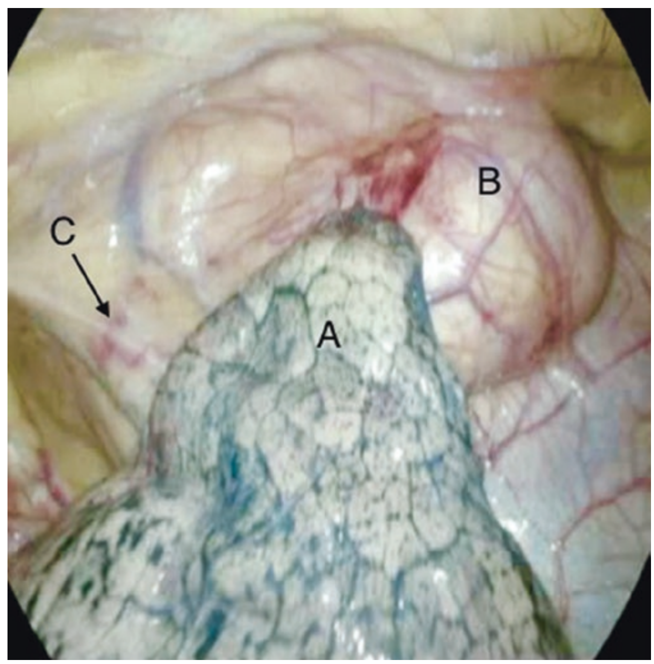


Fig. 4.18 Thymoma with adjacent organ involvement. *A* Adjacent lung parenchyma, *B* tumour invading lung, *C* Phrenic nerve

Fig. 4.19 Specimen retrieved in bag

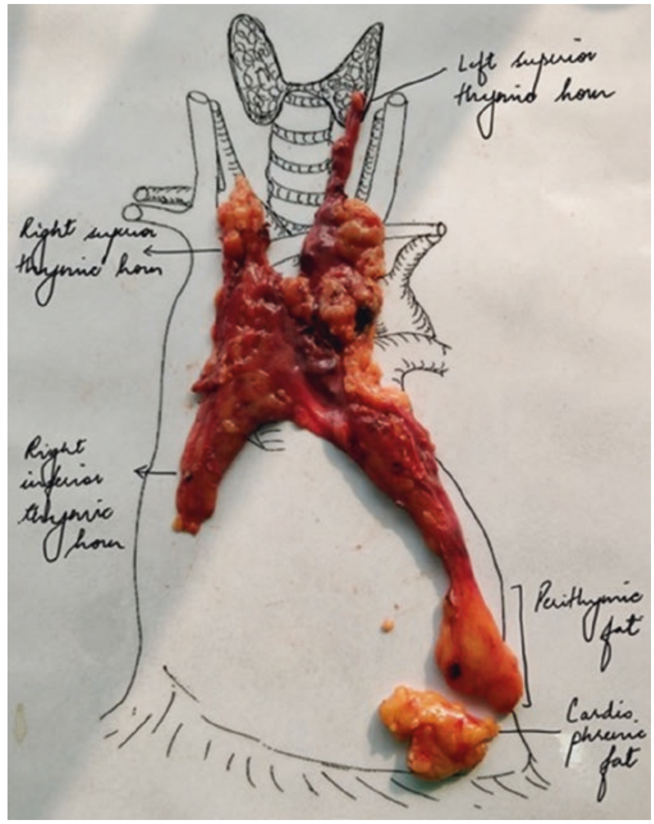


Fig. 4.20 Mediastinal board in use for specimen orientation

Table 4.2 Prognostic factors of thymectomy outcome in MG [23–26]

Preoperative	Age of onset of MG	<50 years have good outcome
	Duration of disease	<12 months of symptoms have good prognosis
	Stage of myasthenia	Mild MG—best prognosis
	Medications	High pyridostigmine dose—worse outcome Preoperative steroids have less remissions
	Gender	Females have better outcome
	Antibody status	Anti-MUSK antibody has negative impact
Postoperative	Histopathological stage	Presence of germinal centers has a higher chance of complete remission
	Clinical outcome over time	Response is best after 6 months

Prognostic factors of thymectomy outcome in patients of MG are outlined in Table 4.2

4.7 Surgeon and Pathologist in Thymic Tumors/Malignancies

A properly oriented specimen with labeling is a prerequisite for correct diagnosis (Figs. 4.20, 4.21, and 4.22). Labeling the involved structures, organs, or areas of likely residual microscopic or macroscopic disease is the primary responsibility of the operating team. In this regard the use of mediastinal board and a proper communication with the pathologist is of prime importance. Mediastinal boards are drawings of the mediastinum on which the surgeon can put the specimen for orientation to show the way the tumor was located in the mediastinum and can even draw further on that board with a marker and highlight certain margins in question. These boards are laminated for their reuse. They can be brought to the grossing room fresh by the OT staff or surgeon. If transportation is an issue, these boards can be put in a large container. In regard to pinning the specimens to the board, a pinboard can be put underneath the laminated sheet and then the specimen can be pinned to the board. Alternatively, margins can be drawn on a towel and specimen can be sewed on the towel for orientation (personal communication with Anja Roden, MD, Mayo Clinic, Rochester).

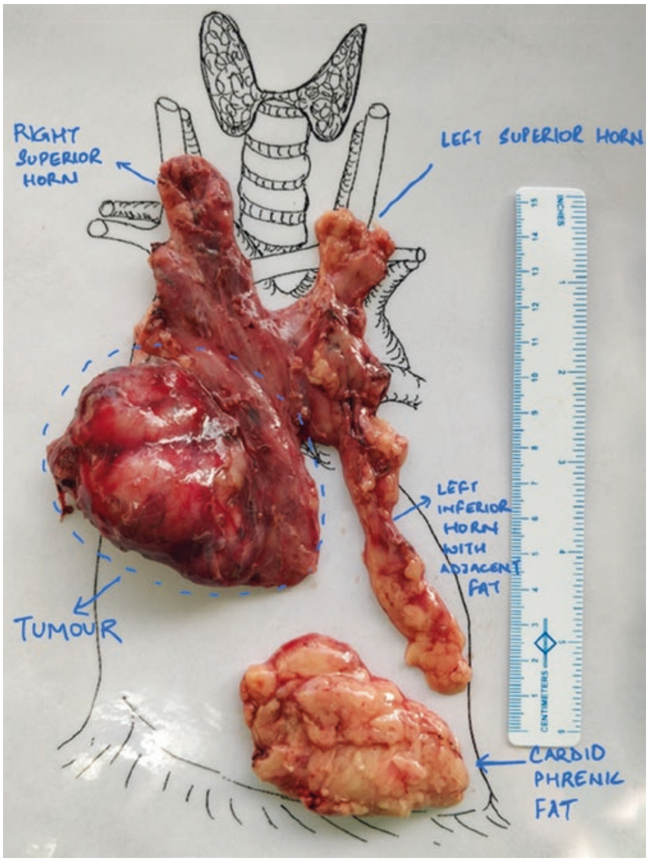


Fig. 4.21 Mediastinal board in use for specimen orientation

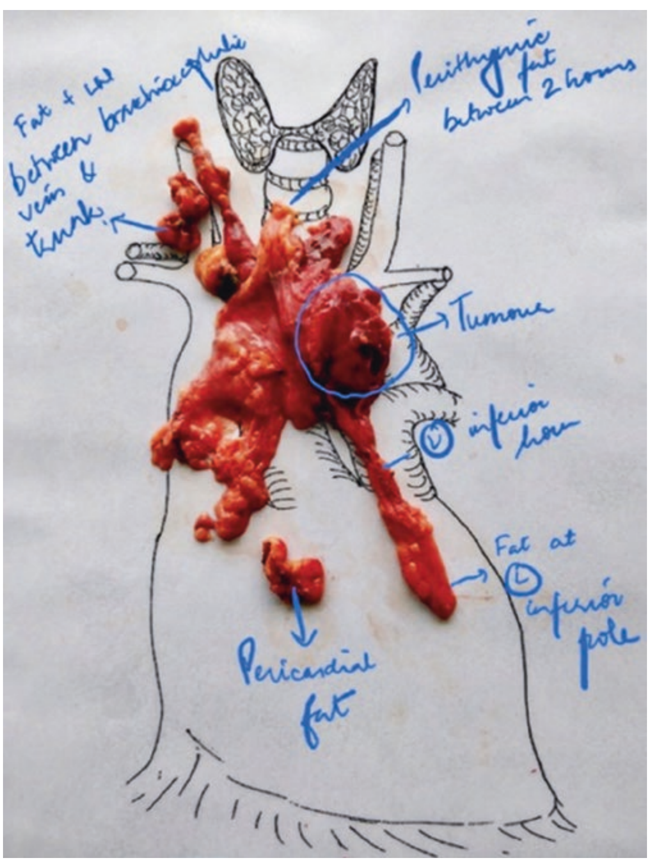


Fig. 4.22 Mediastinal board in use for specimen orientation

The final diagnosis should encompass WHO classification and the Masaoka-Koga staging of thymic tumors. Staging according to the proposed IASLC/ITMIG/TNM system is optional but carry significance in thymic carcinomas as lymph node metastases play an important role in prognostication.

4.8 Conclusion

Surgeon plays an important role in the management of thymic disorders, particularly in myasthenia gravis with or without thymoma. Minimally invasive thymectomy is preferred for myasthenia gravis and early thymoma due to lower morbidity compared to open thymectomy. Open thymectomy is still a preferred approach for locally advanced thymomas.

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