Review Article

Surgical approaches for thymectomy: a narrative review

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Background and Objective: Thymectomy continues to be a standard treatment strategy for patients with thymic neoplasms and myasthenia gravis. The total thymectomies performed has exponentially increased by 69.8% between 2012 and 2019. Trans-sternal and minimally invasive thymectomy increased by 62.8% and 83.7%, respectively. Our objective is to provide a narrative overview of the various approaches of thymectomy. We have briefly described the indications for thymectomy, discussed important preoperative considerations and an operative description of the different techniques of the procedure. We have aimed to summarize the pros and cons of each approach and narrated the technique we have adopted at the University of Minnesota.

Methods: A literature search was conducted encompassing original full-length articles, meta-analyses, review articles and case reports up to July 2024 from the MEDLINE and Google Scholar databases.

Key Content and Findings: Complete surgical resection remains the goal to decrease the risk of recurrence for non-myasthenic thymomas and thymic carcinomas. Surgical procedures have evolved from traditional open approaches to a wide variety of minimally invasive methods. A variety of factors specific to the tumor, patient and surgeon have to be considered while planning a thymectomy.

Conclusions: As of today, there is no consensus on the best surgical technique, with each approach providing specific pros and cons. Each technique may be a viable option in the management of thymic pathologies, thus preoperative evaluation in patients is necessary to optimize prognosis and outcomes.

Keywords: Thymectomy; subxiphoid subcostal thymectomy; thoracoscopic thymectomy; transcervical thymectomy

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Table 1 The search strategy summary

Items	Specification
Date of search	Up to July 31, 2024
Databases and other sources searched	MEDLINE, Google Scholar
Search terms used	"thymectomy", "minimally invasive thymectomy", "thoracoscopic thymectomy", "subxiphoid thymectomy", "robotic thymectomy" or any combination thereof
Timeframe	Up to July 31, 2024
Inclusion and exclusion criteria	All English language articles, including original full-length articles, meta-analyses, review articles and case reports were included. Any articles without details on thymectomy approach were excluded
Selection process	All articles selected using the above criteria were independently reviewed by all authors. Consensus was obtained after reviewing the inclusion and exclusion criteria set forth

Introduction

Since 1998 the incidence of thymectomies has continued to rise in the United States, with an estimate of 1,000 cases performed every year (1,2). The two primary indications include thymic neoplasms and non-thymomatous myasthenia gravis (MG). Throughout the years, advancements in surgical techniques, particularly minimally invasive methods, have revolutionized the way care is delivered. However, due to the lack of consensus regarding the best surgical approach to thymectomy, it is imperative to individualize the surgical strategy based on the clinical presentation and anatomical features. This includes a comprehensive assessment of the size and location of the tumor, invasion to adjacent structures, history of neoadjuvant therapy, anesthetic considerations, evaluation of the merits and pitfalls for each surgical approach, and individual surgeon's experience.

Thymic neoplasms are a rare entity. Population studies have shown an incidence of 2.5 to 5 per million, though lower rates are reported from the Surveillance Epidemiology and End Results (SEER) database (3-5). This has been attributed to missing smaller thymomas, which were previously thought to be benign (6). Despite the discrepancy in incidence rates, thymomas are the most common mediastinal tumor in adults (7) and comprise up to 1.5% of all mediastinal neoplasms (8). This group includes thymomas, neuroendocrine tumors of the thymus (NETT) and thymic carcinomas, with the latter comprising 14% of all thymic neoplasms (9-11). With incomplete resection, there is an increased risk of local recurrence for non-myasthenic thymomas and thymic carcinomas (8,12). Therefore, complete oncologic resection is a crucial prognostic factor for thymic tumors. We present this article in accordance with the Narrative Review reporting checklist (available at https://med.amegroups.com/article/view/10.21037/med-24-38/rc).

Methods

A search was conducted on the MEDLINE and Google Scholar databases. All articles published until July 2024 were considered. Search terms included "thymectomy", "minimally invasive thymectomy", "thoracoscopic thymectomy", "subxiphoid thymectomy", "robotic thymectomy" or any combination thereof. All article types including original full-length articles, meta-analyses, review articles and case reports were included (*Table 1*).

Clinical presentation

For patients with an indeterminate anterior mediastinal mass, the clinical history should focus primarily on identifying symptoms related to MG (such as weakness, diplopia, ptosis), B symptoms associated with lymphoma (fever, night sweats and weight loss), or symptoms suggestive of thyroid disease. Although some thymomas may be asymptomatic, approximately one third experience chest pain, cough, dyspnea, and up to half will additionally suffer from parathymic syndromes such as MG (7). With larger tumors, patients may experience symptoms related to invasion/compression of adjacent structures. When the superior vena cava is compromised, patients may present with headaches, upper body edema, distended neck veins, coughing, dyspnea and orthopnea. A symptom of particular concern is orthopnea, which may be indicative of a large anterior mediastinal tumor compressing on the trachea.

MG

In 2021 the prevalence of MG in the United States was estimated to be 37 per 100,000 persons, and globally it has been increasing in prevalence over the last decade (13). Furthermore, 15% of MG patients are associated with having a thymoma (7). Complete resection should be targeted in all thymoma cases regardless of MG type. Additionally, even in the absence of a thymoma, thymectomies still hold benefits as a treatment option for MG and acetylcholine receptor (AChR) antibody positive patients (14). A clinical trial in 2016 found transsternal thymectomy and alternate day prednisone to have more favorable outcomes than treating patients with prednisone alone, and had fewer recurrences after 3 years of follow-up (15). This study also demonstrated that patients, who underwent thymectomy, required fewer immunosuppressants and daily doses of prednisone. In terms of indications for thymectomies in MG, age is not typically an exclusion factor, and all thymomas, regardless of MG type, should be resected within the first 3 years of diagnosis if possible (16). Preoperative imaging with computed tomography (CT) can be used to help determine the course of treatment. CT scan can identify thymic hyperplasia, which has been shown to be a favorable predictor of improved outcomes (17). Some of the benefits following surgical treatment of MG include relieving weakness and averting potential complications from immunosuppressive therapy (14).

An added benefit of surgical treatment for thymomas, and specifically thymic carcinomas, is the ability to examine the pleural surfaces for metastases, and if possible, concomitant resection of such metastases during the thymectomy (18). Complete resection of such lesions has been associated with lower rate of complications and improved recovery (19,20).

Based on the clinical presentation and anatomy of the thymoma, the surgeon can make important treatment decisions. This includes identifying those patients with undiagnosed or uncontrolled MG that need referral to a neurologist prior to surgical resection or discovering patients with large tumors that may not be appropriate for a minimally invasive approach.

Anesthesia considerations

Careful preoperative evaluation and optimization of medical therapy are paramount in patients with MG, to reduce the risk of respiratory failure, aspiration, and myasthenic crisis. Specifically, anticholinesterase inhibitors such as pyridostigmine, and immunosuppressants when appropriate, should be continued until the day of surgery. Muscle relaxants are minimized or avoided when possible. Reducing the dose of glucocorticoids can help diminish the risk of postoperative infectious and wound healing complications (14). Consideration should be given to preoperative plasmapheresis or intravenous immunoglobulin (IVIG) therapy for patients at high preoperative risk for respiratory complications, such as those with preoperative neuromuscular weakness (21,22). Preoperative spirometry is a useful tool to assist in identifying such at risk patients (23).

An important preoperative concern is determining whether the patient can lay flat without orthopnea, since the presence of this symptom is worrisome for airway collapse on induction. This is especially true for large anterior mediastinal tumors. In such cases, these patients should undergo an incisional biopsy under awake and local anesthesia in an upright sitting position to obtain a diagnosis and determine an individualized treatment strategy. General anesthesia should be avoided as it could lead to catastrophic consequences due to tumor compression of the airway and result in inability to ventilate or oxygenate. In case of loss of airway secondary to airway compression by the tumor, a bail-out salvage maneuver would be to expeditiously sit the patient upright and utilize a rigid bronchoscope to establish airway access. Due to the emergent nature of such a dreadful crisis, timely cannulation for extracorporeal membrane oxygenation (ECMO) may not be feasible.

Additional anesthesia considerations include use of a double lumen endotracheal tube for thoracoscopic approaches to allow for single lung ventilation and collapse of a lung to improve visualization. Single lumen endotracheal intubation is also acceptable as long as intrathoracic carbon dioxide insufflation is maintained, and low tidal volumes are used. We recommend the use of an arterial line for continuous hemodynamic monitoring, and at least one large bore intravenous catheter in the lower extremities to be used for resuscitation, especially in case of potential significant hemorrhage secondary to injury of the superior vena cava or innominate veins. A central venous catheter and a urinary bladder catheter are usually unnecessary. The patient should have a type and screen with crossmatch for two units of packed red blood cells, and a sternal saw must be readily available on the field for an expeditious sternotomy if required.

Surgical approaches for thymectomy

Historically, thymectomy has been performed using open approaches, including trans-sternal, trans-cervical, or a combination of both techniques (maximal thymectomy). Advances in minimally invasive surgery (MIS) have revolutionized the approach to thymectomy. Beyond the standard open techniques, the modern-day thoracic surgeon has a range of options in the surgical treatment of thymus pathologies. Multiple reasons influence the choice of approach to thymectomy, including tumor factors (i.e., tumor size, laterality), patient factors (i.e., prior surgeries, body mass index or body mass index (BMI), narrow costal angle), and surgeon factors (i.e., experience with a specific technique during training, preference towards robotic surgery). Broadly, the approaches to thymectomy can be classified into two general categories, and further sub-classified according to operative technique:

- (I) Open thymectomy:
    - (i) Trans-sternal thymectomy
    - (ii) Trans-cervical thymectomy
    - (iii) Maximal thymectomy (trans-cervical + trans-sternal)
- (II) Minimally invasive [video-assisted thoracoscopic surgery (VATS) or robot assisted]:
    - (i) Trans-thoracic thoracoscopic (unilateral or bilateral)
    - (ii) Subxiphoid thoracoscopic
        - ❖ Uniportal
        - ❖ Multiportal subcostal

Principles of surgery

Regardless of the surgical approach to thymectomy, adherence to certain surgical principles is a must to achieve optimal outcomes. The goal of surgery is to achieve a total thymectomy with complete resection of the thymoma, the thymus, and the surrounding pericardial fat with wide macroscopic margins and negative microscopic margins on histopathology (R0 resection). This decreases the risk of recurrence and removes any additional synchronous thymoma that may have not been detected preoperatively. During thymectomy, the bilateral pleural spaces are accessed and evaluated for metastatic implants, and the bilateral phrenic nerves are identified. The phrenic nerves act as the lateral extent of the total thymectomy, and care is taken to preserve these. To reduce the risk of iatrogenic phrenic nerve injury, we advise gentle tissue handling close to the phrenic nerve. In case of tumor invasion into a phrenic nerve, this can be resected with impunity if, preoperatively, the ipsilateral diaphragm was evaluated and found to be paralyzed. In case of a functional diaphragm with an involved phrenic nerve, the nerve may be resected provided the patient has adequate pulmonary reserve. It is noted, however, that in cases of MG, respiratory decompensation may be provoked by resecting only one nerve. In cases of tumor involvement of the bilateral phrenic nerves, one phrenic nerve must be preserved to prevent bilateral diaphragmatic paralysis and postoperative respiratory failure. To ensure complete resection, the thymus along with the pericardial fat, are mobilized and resected between the bilateral phrenic nerves. In addition, the final specimen should include the superior thymic poles, which are identified and traced into the neck, as well as the pericardial fatty tissue all the way inferior onto the diaphragm. Depending on the extent of the thymoma and its invasion into adjacent organs, additional *en-bloc* resection of involved structures (with possible reconstruction) is necessary to achieve R0 resection. Unilateral involvement of the innominate vein does not require reconstruction, however, bilateral involvement or invasion into the superior vena cava would require vascular reconstruction of only one of the innominate veins, depending on surgeon's preference. If there is unresectable disease (such as bilateral phrenic nerve invasion), this can be debulked as safely as possible and clips can be left in place at the resection margins as markers for future radiation therapy. Gentle and careful tissue handling technique is of utmost importance to avoid violation of the tumor capsule, the occurrence of which would substantially increase the risk of tumor spillage and future local recurrence. For minimally invasive approaches, prior to extraction, the specimen should be placed in an extraction bag to prevent tumor spillage and drop metastases.

Iatrogenic phrenic nerve injury will lead to ipsilateral diaphragmatic paralysis. This can be addressed with diaphragmatic plication ideally at the time of the index operation, however, diaphragmatic plication could also be performed at a later time. The left recurrent laryngeal nerve is also at risk during surgical dissection in the area between the aortic arch and left main pulmonary artery, and injury of this will lead to ipsilateral vocal cord paralysis.

Trans-sternal thymectomy

Alfred Blalock in 1939 performed the first thymectomy via partial sternotomy in a patient with MG with thymoma (24). He then published a series of planned thymectomies for non-thymomatous MG in 1941 (25). The trans-sternal approach to thymectomy allows for excellent access and visualization of the thymus and mediastinal fat (19,20). This technique involves a standard median sternotomy incision from the manubrial jugular notch down to the xiphoid process. The incision can be extended cephalad to the neck, for a so called trans-cervical trans-sternal 'maximal' thymectomy, if necessary, to achieve complete thymic tissue resection. The trans-sternal approach is ideal for large tumors or in cases where bulky *en-bloc* resections and/or vascular reconstruction are anticipated. The advantage of this technique is excellent exposure at the expense of a large incision and its sequelae, including increased postoperative pain. Despite the excellent exposure of the trans-sternal approach, visualization of the distal left phrenic nerve remains a challenge. As minimally invasive techniques and technology continue to advance, it is likely the utilization of open thymectomy approaches will further decrease. Nevertheless, it is important to note that, oftentimes, open surgical approach may provide improved quality of resection of thymic tumors (including thymic carcinoid tumors).

Trans-cervical thymectomy

In 1969, Kirschner and colleagues reported trans-cervical resection for MG in 21 patients (26). They described a short uneventful postoperative course by avoiding the morbidity of sternotomy. Contraindications included large, inaccessible thymomas and low-lying preexisting tracheostomy. Cooper *et al.* showed that the transcervical approach could provide complete thymectomy with minimum morbidity in MG patients (27).

Trans-cervical approach to thymectomy (27) has the advantage of avoiding trans-thoracic incisions, less pain, decreased need for chest tubes, and shorter hospital stay (28,29). This technique is suited for thymectomy in the setting of non-thymomatous MG and has previously been shown to have comparable results to trans-sternal thymectomy (30).

Trans-cervical thymectomy may be performed with or without video assistance. Following single lumen endotracheal anesthesia, ensuring proper positioning is critical to the success of the operation. The patient's arms are tucked to the sides, the head is positioned at the top edge of the operating table, and the neck is extended using an inflatable balloon behind the shoulders. An approximately 5 cm transverse curvilinear cervical incision is created about 2 cm cephalad to the sternal notch and subplatysmal flaps are created up to the level of the thyroid cartilage and down to the level of the sternal notch. The cervical horns of the thymus are then dissected and divided between ligatures, taking care to ligate branches from the inferior thyroid vessels. The left cervical thymic horn is usually dissected and divided first as it typically extends higher in the neck. The thymus is then retracted anteriorly, and dissection then continues inferiorly and around the left innominate vein, taking care to ligate and divide thymic venous tributaries. A Cooper retractor is then used to retract the sternum anteriorly, and the inflatable bag is deflated. The substernal plane anterior to the thymus is further developed, followed by mobilization of the thymus from the pleurae laterally and the pericardium inferiorly and posteriorly. This part of the dissection is usually performed bluntly, with occasional use of an energy device. Care is taken to identify and protect the bilateral phrenic nerves, although proper visualization is extremely difficult, which is one of the main drawbacks of this approach.

Minimally invasive thoracoscopic thymectomy

Thoracoscopic thymectomy was introduced in 1992 with a goal to reduce the morbidity of sternotomy, improve patient acceptance and provide superior cosmesis (31,32). Minimally invasive thymectomy encompasses conventional trans-thoracic VATS, sub-xiphoid VATS, and robot-assisted thoracoscopic surgery (RATS) for both trans-thoracic and sub-xiphoid approaches. Minimally invasive techniques have been found to have improved postoperative outcomes along with less blood loss, faster recovery, lower complications, and shorter hospital stays compared to open approaches (12,19,20). Minimally invasive approaches had the best performance in MG and small thymomas without vascular invasion (12), long-term oncological outcomes were also equivalent in comparison (19,20). One study analyzed MIS with thymomas and found all resections to be complete with negative margins (12). Additionally, there was no significant difference in operative times. With robotic-assisted approaches there is improved precision, dexterity, ergonomics, and visualization of bilateral phrenic nerves (19,20,33). Concern has been reported in the literature regarding VATS having an increased risk of malignant pleural spread due to manipulation and possible tearing of the tumor with spillage tumor cells, however this remains controversial (17). The main concern with thoracoscopic thymectomy is an incomplete or compromised surgical excision given limited studies and availability to observe long-term postoperative outcomes (19,20). The most frequently reported difficulties that arise during minimally invasive thymectomy occur when the tumor is bulky, advanced, or invading into the chest wall or vessels (33). Despite these concerns, the quality of resection remains mostly unchanged compared to the historically done open approach, and this technique has shown to have lower morbidity and mortality (12,15,17,34). This further supports the idea of MIS becoming the preferred approach for thymectomy (17).

Both conventional thoracoscopic and robot-assisted approaches have been extensively adopted, though for both the surgical principles remain the same. Both unilateral and bilateral thoracoscopic approaches have been described. The patient is positioned in the lateral decubitus position. Lung isolation with a double-lumen endotracheal tube or bronchial blocker is usually required for visualization of the surgical field. Most commonly, three ports are placed in the chest, either right or left depending on the surgeon's preference. The thymus is dissected off the sternum and pericardium, followed by separating it off the phrenic nerve with sharp dissection. The horns are excised mostly from the right side. For the unilateral approach, the left-sided dissection is completed by pulling the thymus to the right. For the bilateral approach, additional ports are placed on the contralateral side to visualize the contralateral phrenic nerve and complete the dissection. There is no consensus on the preferred laterality for unilateral thoracoscopic thymectomy (35-37).

Subxiphoid subcostal thoracoscopic thymectomy

Kido *et al.* first described the subxiphoid subcostal thoracoscopic thymectomy technique in 1999 (38). They used a single transverse incision over the xiphoid, followed by xiphoid resection, and placed a sternal lifting system for exposure. The thymectomy was then performed via this single incision. As the technique evolved over the following decades, additional subcostal trans-thoracic ports were introduced to aid with better visualization. This technique allows for supine positioning, avoids lung isolation and its risks, and provides optimal bilateral phrenic nerve visualization. Uniportal access for subxiphoid thoracoscopic thymectomy has been described (39). At the University of Minnesota, we have adopted the conventional multi-port subxiphoid subcostal thoracoscopic approach for all thymectomies.

The patient is positioned supine with both arms abducted and a footboard to enable steep reverse Trendelenburg. We use a single lumen endotracheal tube and low tidal volume ventilation without positive end-expiratory pressure. We place a 15 mm subxiphoid port for initial access and advance it into the right pleural space. We then place two additional 5 mm subcostal ports approximately 5–8 cm away in each hemithorax. Under thoracoscopic visualization, we place additional 5 mm lateral subcostal ports in the anterior axillary lines bilaterally. The subcostal ports are inserted above the diaphragmatic insertion on the costal margin to reduce the risk of diaphragmatic hernia.

The dissection of the thymus is then performed keeping in line with standard surgical principles as previously described. The advantages of this approach are that the camera is freely moved between ports to help with careful visualization of both phrenic nerves (*Figure 1*). Subxiphoid thymectomy also provides excellent access to the most cephalad extent of the thymic horns. We also believe that this technique allows for superior evaluation of the thoracic cavity for tumor implants, and therefore improved resection and disease staging. Variations of this approach include a sternal retractor to increase the anteroposterior diameter of the mediastinum, which permits an increased working space. This is especially helpful in male patients with high BMI, in which cases visualization is more challenging.

Conclusions

The evolution of surgical techniques in the modern era allows for a wide array of surgical approaches to be safely used in the treatment of thymic pathologies. Complete resection of all thymic tissue remains the goal to achieve optimal results, while minimizing iatrogenic injury. The best surgical approach is the one that suits the individual patient's needs after careful evaluation of the patient's pathology and an assessment of the surgeon's preference.

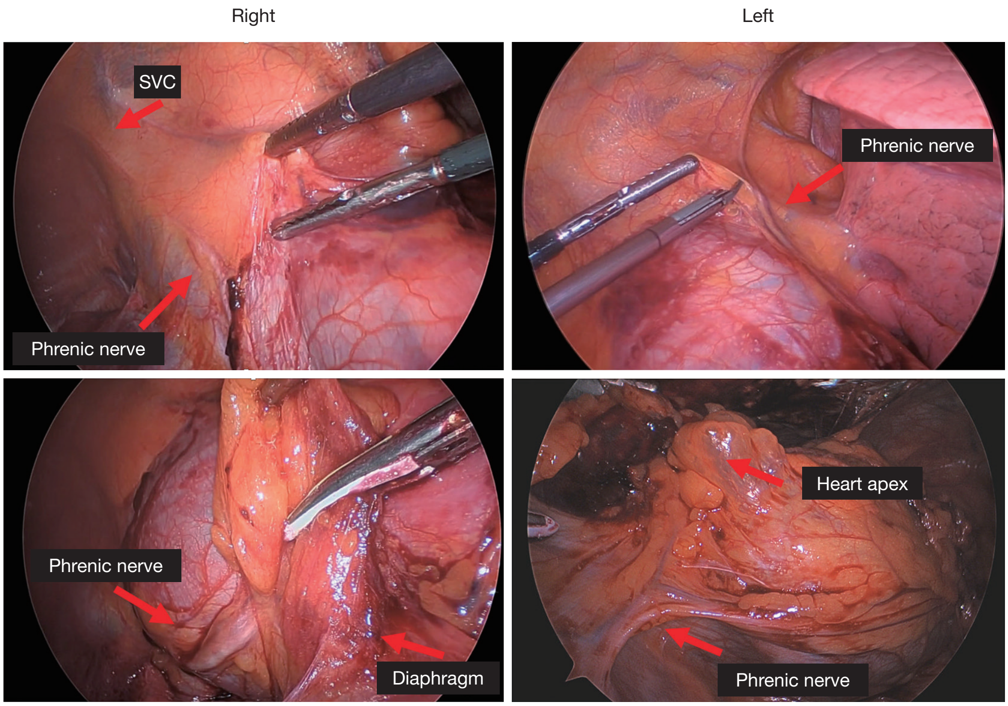

Figure 1 Intraoperative picture during subxiphoid subcostal thoracoscopic thymectomy. The right phrenic nerve is visualized lateral to the SVC. The entire thymic tissue is excised between the right and left phrenic nerves, adhering to the basic operative principles. SVC, superior vena cava.

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Footnote

Reporting Checklist: The authors have completed the Narrative Review reporting checklist. Available at https://med.amegroups.com/article/view/10.21037/med-24-38/rc

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