



# Surgical management of thymic tumors: a narrative review with focus on robotic-assisted surgery

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**Background and Objective:** Thymic epithelial tumors, including thymomas and thymic carcinomas, represent the most common mediastinal tumors and account for up to 50% of all anterior mediastinal tumors. For early stages of these thymic tumors, complete resection of the entire thymus is the recommended treatment. The transition from open surgery to video-assisted thoracoscopic surgery (VATS) and recently to robotic-assisted thoracic surgery (RATS) has fundamentally altered the treatment of thymic tumors. While RATS has been widely implemented due to its many advantages including good visualization with magnification and three-dimensional vision, improved maneuverability and precise instrument control, different techniques have been described. This narrative review focuses on the main approaches and outcomes of RATS thymectomy. It compares the technical, perioperative and clinical outcomes of RATS thymectomy, in particular, with VATS and open thymectomy.

**Methods:** A non-systematic review for full text studies written in the English language was conducted using the PubMed search engine and literature was summarized.

**Key Content and Findings:** We present an overview of robotic-assisted resection for thymomas and review the main approaches and outcomes of RATS thymectomy. Critical points of the RATS approach, including surgical specifics and pitfalls, are presented. Technical advantages and disadvantages of each technique are discussed. The perioperative and clinical outcomes of RATS thymectomy are compared, where possible, to those for VATS and open thymectomy. Currently, retrospective analyses demonstrate comparable or even more favorable outcomes following a RATS approach in comparison to VATS and open approaches in terms of operating time, conversion rates, intraoperative complications, completeness of resection and mortality. Certain analyses also report better outcomes for patients undergoing RATS thymectomy in terms of blood loss, postoperative complications, duration of pleural drainage and length of hospital stay compared to VATS and open thymectomy.

**Conclusions:** Overall, RATS has shown promising results and could become the preferred technique for resection of thymic tumors. It shows good outcomes compared to VATS and open thymectomy in the current literature. However, especially for extended tumors with the need for extended resection and reconstruction, open thymectomy remains a valuable approach.

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## Introduction

The thymus is a primary lymphatic organ engaged in the proliferation and maturation of T-lymphocytes (1). It is comprised of two asymmetrical lobes that lie between the phrenic nerves and communicate in the midline, located behind the sternum and ventral to the pericardium, aortic arch, pulmonary artery, superior vena cava and brachiocephalic vein. During the course of adolescence, the thymus gland typically undergoes involution and recedes, becoming macroscopically indistinguishable from retrosternal fibrous adipose tissue (2).

Despite its normal involution, the thymic gland can sometimes harbor altered or abnormal cellular proliferation. This deviation from the typical cellular behavior can manifest as various conditions, including thymic tumors. Thymic epithelial tumors, including thymomas and thymic carcinomas, represent the most common mediastinal masses and account for around 20% of all mediastinal tumors and up to 50% of all anterior mediastinal tumors (3). Nevertheless, thymic tumors are very rare tumors, accounting for only around 0.2% up to 1.5% of all malignancies (4).

Thymomas may present with varied clinical manifestations. Slow, indolent growth is typical for thymomas, leading to around a third of all thymomas being diagnosed incidentally in radiological examinations of the chest (5). Occasionally symptoms including pain, cough, hoarseness, dyspnea can occur. Patients tend to present with symptoms once the tumor infiltrates or displaces surrounding structures. In cases of larger tumors, this infiltration may lead to complications such as superior vena cava syndrome due to local tumor compression (6,7).

As thymomas play a critical role in autoimmune pathogenesis, certain patients with tumors of the thymus may present with associated paraneoplastic syndromes. One of the most well-known associations is that between myasthenia gravis and thymomas, which was first identified by Alfred Blalock in the late 1930s. Blalock observed that resection of thymic tumors in patients with myasthenia gravis led to a striking improvement in their symptoms (8).

Approximately 30–50% of all patients with thymomas show symptoms of myasthenia gravis (6,9).

It is critical that these patients receive treatment by a specialist and are carefully evaluated by experienced neurologists before undergoing surgical resections, in order to effectively evaluate the risk of a postoperative myasthenic crisis (10,11). Therefore, it is recommended, that all patients with thymomas should be evaluated for symptoms of myasthenia gravis both by detailed history taking and, if necessary, a laboratory analysis of serum anti-acetylcholine receptor antibodies (12).

## Diagnostic procedures

Diagnosis is frequently incidental on a chest radiograph or computed tomography (CT) of the chest. An intravenous contrast-enhanced chest CT scan is the imaging modality of choice, and is essential for evaluating the precise configuration, margins, density, location and extension of the lesion (13). In CT scans, thymomas present as well-defined, homogeneous retrosternal soft tissue attenuation, which may appear round or lobulated (14). Typically, thymomas are located ventral to the great vessels and superior pericardium, however, various locations within the anterior-superior compartment of the mediastinum have been described (15). Irregular contours, necrotic or cystic components as well as focal calcification are associated with invasive thymomas (14).

Magnetic resonance imaging (MRI) of the chest is not routinely used in evaluation of thymic tumors. However, due to the absence of radiation exposure compared to CT scans, MRI can assist in the evaluation of subtle local invasion as well as cystic components. Furthermore, the ability to discriminate between thymic cysts and thymic malignancy can potentially help to avoid unnecessary thymectomy (6,13,16).

Additionally, fluorodeoxyglucose (FDG)-positron emission tomography CT (PET-CT) scans can be used to differentiate between subtypes of thymic epithelial tumors, with thymic carcinoma showing higher FDG uptake

compared to thymomas. However, PET-CT is not routinely used in the staging of thymic tumors, as thymic hyperplasia might also present with hypermetabolism (13,17). PET-CT scans have a role in the detection of local and distant metastasis for FDG-avid tumors as well as in evaluation of tumor recurrence (13,17,18).

As radiologic diagnostics have a high accuracy and can often differentiate thymomas based on imaging characteristics, pretreatment biopsy is not required if the probability of thymoma is high. Therefore, upfront surgical resection is both diagnostic and therapeutic. In all other cases and if a thymic tumor is unlikely, tissue biopsy is recommended (6,17,19). Additionally, as thymomas are usually encapsulated, biopsy, especially transpleural biopsy, risks tumor cell seeding and dissemination, which can convert an early stage thymoma into a stage IV disease with pleural dissemination (6,17,20,21).

### *Tumor stage and treatment*

Treatment strategies must be carefully adapted to each tumor stage. For most diagnosed unclear anterior mediastinal masses, surgical resection is the primary therapeutic approach. However, for cases where a thymic carcinoma is suspected or the mass appears to be not completely resectable due to local extension or infiltration, a multimodal therapeutic strategy should be evaluated in a multidisciplinary case discussion.

Employing the tumor, node, metastasis (TNM) staging system preoperatively enhances the efficacy in evaluating the extent and resectability of thymomas, thereby guiding upfront surgical resection as the primary diagnostic and therapeutic approach (6,17). Well-encapsulated tumors or tumors that are limited to the mediastinal fat and pleura are considered resectable tumors (TNM stage I including cT1a cN0 cM0 and cT1b cN0 cM0) (22). In contrast, locally advanced tumors with invasion of the pericardium (TNM stage II including cT2 cN0 cM0) or the unilateral phrenic nerve and even those tumors showing involvement of the lung (TNM stage IIIa including cT3 cN0 cM0) can be potentially resectable. Therefore, the indication for complete resection should be discussed in a multidisciplinary board (6,23). As TNM stage IIIa includes a very heterogeneous group of tumors, ranging from potentially resectable to unresectable tumors (e.g., those with involvement of the great vessels, myocardium, trachea, esophagus), a multimodal treatment approach should be considered for these cases as well as for TNM stage IIIb

(cT4 cN0 cM0) and above. In highly selected cases, surgery might even be indicated in TNM stage IVb tumors with easily resectable pleural and pericardial metastases (23,24).

Postoperatively, the Masaoka-Koga classification is employed to further stratify thymomas based on their pathological findings, thereby providing additional prognostic information and assisting in tailoring further adjuvant therapies (6,17,22-24).

### *Thymectomy*

Despite the evolving surgical approaches over the past decades, certain core principles remain fundamental to thymectomy. Foremost among these is the necessity for complete resection, which serves as the primary goal when determining indications for surgery, as completeness of resection is an independent prognostic factor (25-31). It is important to resect all thymic tissue including the primary bulk of the thymoma, the cranial horns of the thymus, any thymic tissue invading adjacent structures and ectopic of thymic tissue that may be contained in the surrounding mediastinal adipose tissue, especially for patients with myasthenia gravis, to prevent recurrence of disease (28,32). Simultaneously, it is important to avoid tumor disruption, thereby reducing the potential risks associated with tumor spillage and pleural dissemination. Emphasizing a minimal or “no-touch” technique and ensuring *en-bloc* resection remains key across all surgical approaches (33,34). If the tumor is not deemed completely resectable during surgery or potential tumor involvement close to the resection margins cannot be excluded, metallic clips can be placed at the margins of the surgical bed to mark the area of tissue removal. This allows for concentrated postoperative radiation in case of an incomplete resection. Incomplete resections or tumor debulking are not reported to improve prognosis, however, they may be an option in individual cases (17,35).

Historically, there are several established techniques for thymectomy. Traditional open approaches have been employed in the management of anterior mediastinal tumors and were considered the standard for numerous decades (36,37). The most common open surgical approach for thymomas is the transsternal approach (38). Other approaches have been described and include transcervical approaches, as well as thoracotomies (39-41).

After the first minimally invasive thymectomy performed in the 1990s (42), video-assisted thoracoscopic surgery (VATS) has established itself as a safe and widely applied

**Table 1** Search strategy summary

Items	Specification
Date of search	December 01, 2023 to January 06, 2024
Databases/sources searched	PubMed
Search terms used	Thymectomy, robotic thymectomy, robot thymectomy, robotic thymoma, robotic anterior mediastinum, RATS thymectomy, RATS thymoma, RATS anterior mediastinum, da vinci thymectomy, da vinci thymoma, da vinci anterior mediastinum, minimally invasive thymectomy, surgery anterior mediastinum, VATS thymectomy, VATS thymoma, VATS anterior mediastinum, open thymectomy, transsternal thymectomy, open surgery thymoma
Timeframe	January 01, 2003 to December 31, 2023
Inclusion and exclusion criteria	Inclusion: English language, full text articles (case studies, case reports, retrospective cohort series, systematic reviews, meta-analyses), studies of historical relevance or background  Exclusion: studies on other compartments of the mediastinum (non-anterior), non-thymomas or non-surgical treatment
Selection process	Both co-first authors screened the titles and abstracts of all articles identified in the search. Full-text articles were retrieved for all potentially relevant studies. The reviewers then independently assessed the full-text articles for inclusion in the review. Disagreements were resolved through discussion and consensus

RATS, robotic-assisted thoracic surgery; VATS, video-assisted thoracoscopic surgery.

approach for thymectomy due to advancements in surgical instrumentation and video technology (43,44). Currently, no standard approach for VATS thymectomy exists. Trocar positioning, number of trocars used as well as side of approach (left, right, bilateral, subxiphoidal) depend on various factors, such as tumor size and location, need for optimal exposure of several anatomical structures as well as surgeons' preference (45-48). While the introduction of VATS was a major milestone in the development of minimally invasive surgery, it still shows limitations such as limited maneuverability, two-dimensional view, amplified tremor due to long stiff instruments as well as a long learning curve. The use of a robotic platform can overcome these limitations, offering greater maneuverability of instruments (endo-wrist instruments), precise manipulation with tremor suppression, better ergonomics, three-dimensional visualization and an overall shorter learning curve. Since its first implementation robotic-assisted thoracic surgery (RATS) has gained more and more popularity in the field of minimally invasive thoracic surgery in the last 20 years. We present this article in accordance with the Narrative Review reporting checklist (available at <https://med.amegroups.com/article/view/10.21037/med-24-17/rc>).

## Methods

The literature research was conducted using the PubMed search engine. A comprehensive review of the English-language literature on RATS thymectomy was performed including case reports, retrospective and prospective cohorts, meta-analyses, systematic reviews and randomized controlled trials where available. Literature published between January 1, 2003 and December 31, 2023 was included, with some older, landmark references or cornerstone studies also cited. The search strategy is summarized in *Table 1*.

## Surgical treatment of thymomas

### *Robotic-assisted thymectomy*

The first reported robotic-assisted thymectomy took place in December 2000 (49). Similar to VATS, RATS approaches exhibit variations in trocar positioning and the number of trocars used. The subsequent section outlines the distinct approaches employed in RATS thymectomy.

In many centers that regularly conduct RATS thymectomies, patient positioning is standardized. For the resection of anterior mediastinal masses, the patient

is commonly positioned in a 30 to 45 degree semi-supine position with elevated hemithorax ipsilateral to the side of the approach (3,50). The ipsilateral arm is positioned lower than the operating table on an armrest, providing extensive space for the robotic arms. Meanwhile, the contralateral arm is supported on an additional armrest, abducted away from the chest, enabling a contralateral approach if necessary, which could be beneficial, for example, in case of massive bleeding, affording easier access for a median sternotomy (51).

While a unilateral three-trocar technique is frequently employed with incisions typically ranging between the third and fifth intercostal spaces (3,50-53). Some groups have adopted a four-trocar approach for extra mobility and flexibility (32,54).

The optimal side for RATS thymectomy remains a subject of debate. In practice, the dominant side of the tumor often dictates the side of the approach to ensure optimal visualization of the ipsilateral phrenic nerve and to manage potential pleural, pericardial or pulmonary involvement, as well as any adhesions (33). Typically, a left-sided approach is preferred, as it provides easier access to a larger portion of the thymic gland. Moreover, a composite anatomical analysis based on 50 consecutive resections of the thymus gland for myasthenia gravis by Jaretzki *et al.* revealed that in 72% of resected cases (55), the thymus gland is located laterally beneath the left phrenic nerve, offering improved identification and safer dissection around the nerve when directly visualized from the left side. Additionally, a major disadvantage of the right-sided approach, is the difficulty in identifying the left phrenic nerve, which increases the risk of intraoperative injury (33). Furthermore, since the right phrenic nerve runs near the superior vena cava, its path is more predictable and can be traced further along its caudal section (56). This allows for easier identification of the right phrenic nerve during a left-sided approach to thymectomy and reduces the risk of injury (33,57). Conversely, a right-sided approach may be helpful in reducing the risk of injuries to the heart and pericardium resulting from trocar and robotic arm insertion, given the absence of the cardiac apex (33). Further, the larger amount of space provided when entering the mediastinum from the right (due to the less prominent position of the heart and aorta on the right), is especially valuable in patients with mediastinal adiposity, left cardiac hypertrophy or a smaller thoracic cavity (e.g., in patients with Pectus excavatum) (33). In addition, the easier identification of the confluence of the superior vena cava and thus the right brachiocephalic vein,

may reduce the risk of injury to these structures through better visualization (33). Thus, as these approaches offer distinct advantages, it is critical that the operating team determines the optimal approach based on their experience and their favored technique while also considering individual patient anatomy.

In addition to the left- and right-sided approaches for RATS thymectomy described above, a subxiphoid approach has recently emerged as an alternative to the lateral approaches (58). The subxiphoid approach involves establishing surgical access to the patient's thoracic cavity via a subxiphoid incision for the camera trocar (59). Once observational access is established, the instrument trocars and robotic arms are inserted either subcostally (60) or intercostally bilaterally (51,58,59,61,62). Several authors have described placing the bilateral instrument trocars below the costal arches (subcostally), reducing the risk of intercostal damage and postoperative pain (60). Groups performing subxiphoid RATS thymectomies using multiple ports have suggested that the surgical view is superior to unilateral approaches, with some comparing it favorably to the perspective achieved through a transsternal approach (60). This approach offers a favorable surgical view of the upper mediastinum and the borders of the bilateral phrenic nerves (62). However, several groups have shown that the operative time, excluding console time, was notably greater in the subxiphoid group compared to the right- and left-sided groups due to the additional time required for subxiphoid incision, tissue dissection, bilateral pleura opening, and trocar placement (51). In light of these challenges, single-port RATS thymectomy has gained attention for its minimally invasive nature, primarily utilizing a subxiphoid technique. The single-port, or uniportal, subxiphoid approach involves a single incision below the sternum and offers the advantage of avoiding intercostal nerve injury, potentially reducing postoperative pain and improving cosmetic outcomes (63,64). Park *et al.* reported their experiences with uniportal subxiphoid RATS thymectomy, highlighting its technical feasibility and satisfactory patient outcomes. However, they also acknowledged that the uniportal subxiphoid approach has limitations, such as its current inability to perform complex procedures or remove particularly large tumors (63).

In multi-port RATS thymectomy, enlarging incisions for specimen retrieval and preventing specimen disruption is crucial, necessitating additional procedural steps. In contrast, uniportal RATS and VATS enable specimen extraction

through the same incision used for access, minimizing the need for incision enlargement and potentially reducing postoperative discomfort. Ensuring meticulous specimen orientation remains essential for precise pathological assessment and surgical accuracy in both multi-port and uniportal approaches, aligning with principles of no-touch technique and *en-bloc* resection (33,34,65,66).

### Outcomes after thymectomy (RATS vs. VATS vs. open)

Over the past decades, the evolution of thymectomy techniques from open surgery to VATS, and most recently to RATS, has been paralleled by significant improvements in patient outcomes. VATS holds a slight advantage due to its longer history of clinical use and wider adoption compared to RATS. Consequently, surgeons have accumulated more extensive experience and familiarity with VATS techniques (67). Additionally, certain surgeons favor the hands-on and tactile feedback offered by conventional VATS instruments over robotic instruments (68). However, several studies have indicated that VATS exhibits a less steep learning curve. This phenomenon is mainly linked to the challenge of developing essential skills, such as depth perception and video-hand-eye coordination, which are crucial for achieving competence in VATS procedures (68,69).

From a technical perspective, RATS offers several advantages over VATS. The RATS approach provides a genuine three-dimensional view and up to seven degrees of freedom for most instruments (70). It allows for adjusting the ratio of instrument movements and freezing instruments during repositioning (71). VATS instruments, which exhibit stiffness and elongation, have a tendency to amplify the motion of surgical instruments. Conversely, RATS offers a notable benefit owing to its sophisticated tremor filtering capabilities (50,72,73). These factors have led to rapid learning curves for RATS thymectomies, often requiring only 15 to 20 cases (74). However, it is essential to acknowledge that the RATS technique also has certain disadvantages, including longer setup times (which improve markedly with operating room experience) and longer intraoperative instrument change intervals. Additionally, the acquisition of new robotic instruments is costlier (50).

Open thymectomy was originally favored for its superior visualization of the situs, as it offers unparalleled visibility of the surgical field due to the wide access provided (75).

For patients undergoing transsternal thymectomy, a rapid emergency response is feasible in the event of intraoperative complications, such as significant bleeding. Although, there has been a shift toward minimally invasive approaches in the past two decades, the open approach nevertheless remained a cornerstone for the resection of particularly large thymomas with major invasion of adjacent structures (76).

During the late 2000s, many authors advised against routinely employing minimally invasive surgery for thymomas exceeding 4 cm in size, favoring an open approach instead (77). More recently, several studies have shown that thymomas exceeding 5 cm can be successfully resected in a minimally invasive manner (3,53,76,78). Currently there is no consensus regarding the maximum tumor size for minimally invasive surgery (79).

In-depth comparative outcomes between RATS, VATS, and open thymectomy are summarized in *Table 2*, with a detailed comparison of the outcomes discussed in the following paragraphs.

### Duration of operation

In addition to the aforementioned technical differences, operative, perioperative and short-term results vary between the techniques. In extensive meta-analyses conducted by Hess *et al.*, O'Sullivan *et al.*, and Shen *et al.*, the mean duration of surgery for thymectomies performed using RATS, VATS, and open approaches showed no statistically significant differences among the examined studies (80-82). The mean operating time among the examined studies for RATS thymectomies ranged from 71 minutes (n=51) (87) to 224.5 minutes (n=14) (89). For VATS thymectomies mean operating time ranged from 79 minutes (n=35) (87) to 198 minutes (n=79) (95) and for open thymectomies, mean operating time ranged from 88 minutes (n=44) (96) to 243.8 minutes (n=22) (89). Nevertheless, a high degree of heterogeneity in recorded operating times was noted by numerous authors and can potentially be attributed to differences in the experience of surgeons across various centers. Additionally, it was noted by several authors that various studies included in these meta-analyses may define operating times differently. Commonly these are skin incision to skin suture, or procedure time (either including or excluding docking time of the robotic system), or even total operating room occupation (81,87,97-99). In many cases, the operating time may not be defined within the text,

**Table 2** Comparative outcomes: RATS vs. VATS vs. open thymectomy

Outcome	Approach for thymectomy		
	RATS	VATS	Open
Duration of operation	Meta-analyses show no statistically significant differences in mean duration of surgery between RATS, VATS, and open thymectomies. Operating times differ significantly among studies due to variations in surgical expertise and particularly in the definitions used for measuring operating time (80-82)		
Intraoperative complications	No significant differences in intraoperative complication rates were found among the three thymectomy approaches, suggesting comparable safety with appropriate patient selection (81)		
Intraoperative blood loss	RATS results in significantly lower intraoperative blood loss compared to open thymectomy (173 mL). The reported significant difference in blood loss compared to VATS thymectomy is minimal (24 mL) (81-83)	Compared to open thymectomy, VATS results in lower blood loss, while showing a slightly higher blood loss (24 mL) compared to RATS (81-83)	Open thymectomy's higher blood loss is primarily due to sternotomy's invasiveness. RATS demonstrates significantly lower blood loss compared to open thymectomy, while VATS also shows reduced blood loss, underscoring the benefits of minimally invasive approaches (81-83)
Conversion rate	Statistical analysis indicates minimal heterogeneity and no significant difference in conversion rates between RATS and VATS approaches (81); low conversion rates highlight the impact of precise patient selection, intraoperative vigilance, surgical skill, and technological advances in reducing open procedures		
Complete resection rate	There was no difference in the rate of complete resection between minimally invasive and open thymectomy approaches. Complete resection rates are consistently high across all approaches (81,84-86)		
Duration of pleural drainage	RATS shows lower (87) to significantly lower (82) drainage duration compared to VATS	VATS shows higher (87) to significantly higher (82) drainage duration compared to RATS	Minimally invasive approaches also demonstrate shorter (88) to significantly shorter (80,87) drainage durations compared to open thymectomy
Volume of pleural drainage	RATS exhibits significantly lower (82,87) pleural drainage volume compared to VATS	VATS exhibits significantly higher (82,87) pleural drainage volume compared to RATS	Minimally invasive approaches also show lower (88) to significantly lower (87) drainage volumes compared to open thymectomy
Length of hospital stay	RATS shows comparable (81) up to significantly shorter LOS compared to VATS (82,87) and shorter (89) to significantly shorter (81) LOS compared to open thymectomy	VATS shows comparable (81) up to significantly longer LOS compared to RATS (82,87) and shorter (88) to significantly shorter (87,90) LOS compared to open thymectomy	Open thymectomy shows longer (88,89) to significantly longer (81,87,90) LOS compared to minimally invasive approaches
Postoperative complications	RATS consistently shows low complication rates (81-84,87) and significantly lower rates compared to open thymectomy (81,87,91). Furthermore, RATS demonstrates comparable (87) or marginally lower (81,82,84) postoperative complication rates than VATS, with certain studies indicating significantly reduced rates (82)	VATS shows low complication rates overall (81,87). VATS and open thymectomy generally exhibit comparable complication rates (88). Moreover, VATS shows postoperative complication rates that are comparable (87) to or slightly higher (81,82,84) than those of RATS, with some studies indicating significantly higher rates (82)	Open thymectomy also demonstrates low complication rates (83,92), comparable to minimally invasive approaches (80,88), although some studies indicate significantly higher rates of postoperative complications compared to RATS thymectomy (81,87,91,92)
Mortality	All three approaches report minimal or no mortality within the first 30 days after thymectomy (80,81), indicating comparable safety and efficacy in minimizing short-term risks		
Recurrence	Data comparing recurrence rates among RATS, VATS, and open thymectomy are limited. Studies indicate no significant differences in recurrence rates between minimally invasive and open thymectomy (78,80,88), while RATS studies report no recurrences with small sample sizes (93,94)		

RATS, robotic-assisted thoracic surgery; VATS, video-assisted thoracoscopic surgery; LOS, length of hospital stay.

making interpretation difficult.

### **Robotic surgery safety measures**

While the robotic arms allow for a greater range of motion in highly confined spaces, the lack of tactile feedback has been a concern for some surgeons (100,101). Recent developments highlight the potential for future integration of haptic feedback systems into robotic-assisted surgery, which may be immensely beneficial (101).

As described above a left-sided approach poses challenges in visualizing and identifying the right phrenic nerve and vice-versa (56). Nevertheless, due to the vena cava's prominent position as a leading structure in the right hemithorax, identifying the right phrenic nerve from the left is comparatively more straightforward (33,57). To minimize the risk of phrenic nerve injury, contralateral thoroscopic surveillance of the contralateral nerve during VATS thymectomy has been described (102). However, this is rarely implemented in clinical practice due to increased surgical trauma, and need for a larger operating team and material, as well as only limited benefits (103).

In addition, the risk for intraoperative injury to vascular structures, and consequent minor or major bleeding must always be considered. Bleeding is primarily caused by injuries to the internal mammary vessels and the thymic veins (104,105). Significant bleeding can furthermore occur in cases of accidental injury to the left brachiocephalic vein, the superior vena cava or the ascending aorta (105,106). As they can be potentially catastrophic, all precautions to prevent injury and to control significant bleedings must be taken. Continuous identification of veins throughout the operation is crucial, as strands of tissue may unexpectedly contain smaller branches of thymic veins. As there is no tactile feedback in robotic-assisted interventions, the surgeon must pay close attention to any visual indications of tissue strain. It may be possible to control bleeding by compression, clipping, stitching or application of a vascular patch. A strategy for addressing and mitigating massive bleeding must always be at hand during RATS thymectomies and the surgical team must be prepared for open surgery. In RATS, emergency conversions to open surgery pose a challenge. This occurs because the surgeon, while operating from the control console, is not in a sterile environment. Additionally, the presence of robotic arms can significantly hinder access to the patient (107). Therefore, it is necessary to have an additional surgeon who remains consistently sterile and stays close to the patient at all times.

Furthermore, thorough instruction of the entire operating team regarding procedures and intraoperative complications is necessary (108).

### **Intraoperative complications**

The rate of intraoperative complications for RATS thymectomies was comparable to those reported for the VATS approach with pooled analysis demonstrating a range of 0% to 9% versus 0% to 11%, respectively (81,84). Among the twelve studies analyzed by O'sullivan *et al.*, which reported intraoperative complications in RATS thymectomies, seven studies indicated a 0% rate of intraoperative complications (81). The rate of complications is reported by several studies, however precise information on the occurrence of specific intraoperative complications is limited in the available studies, making it challenging to provide a quantitative overview of individual complication rates.

While a 0% intraoperative complication rate was reported for VATS thymectomy by Kamel *et al.* (n=7) (83), higher rates of intraoperative complications were reported at 5.7% by Qian *et al.* (n=35) (87) and at 11% by Rowse *et al.* (n=45) (84). Qian *et al.* describe one case of hemorrhage due to pleural adhesions in their VATS group, however, they do not relate the second case of intraoperative complication (87). The complications observed by Rowse *et al.* where small pericardiotomies of 2–3 mm in four patients and an injury to the internal mammary artery in one patient undergoing VATS thymectomy (84).

The systematic review by O'sullivan *et al.* further examined six separate studies for intraoperative complications during open thymectomy (81). Four studies reported a 0% intraoperative complication rate (89,99,109,110). Before statistical matching, Kamel *et al.* reported a 17% intraoperative complication rate (83). The importance of this value must be questioned as an outlier; however, the number of cases was only twelve and after propensity-matching the rate decreases to 4.5% (83). The specific intraoperative complications are not described. Qian *et al.* observed a 5.4% intraoperative complication rate for open thymectomy, whereby, among 37 patients, two cases of intraoperative hemorrhage occurred (87).

Summarily, these results indicate that there is no statistically significant difference in the rates of intraoperative complications between the three approaches for thymectomy. While this may be surprising considering



the intrinsic invasiveness of open thymectomy and the ostensible advantages of minimally invasive surgery, this indicates primarily that all three approaches are safe relative to one another when patients are well selected. Further research will be necessary to specify the rates of individual intraoperative complications. Additionally, increased experience with the robotic platform could potentially lead to a reduction in intraoperative complication rates, making it comparatively more advantageous in the future.

### ***Intraoperative blood loss***

Intraoperative blood loss is reported to be low for RATS thymectomy, though heterogeneity in data is very high. Across the available literature, estimated mean blood loss during RATS thymectomy ranged from less than 10 mL (n=6) reported by Renaud *et al.* (110) to 103.6 mL (n=117) as described by Kang *et al.* (92). Kamel *et al.* also reported very low mean blood loss of 20 mL among 70 patients (83). Among the studies included for blood loss in pooled analyses by O'sullivan *et al.*, this parameter did not exceed 100 mL in seven of nine studies (81).

In contrast, among the seven studies focused on comparing RATS and open thymectomy, six revealed mean blood loss of over 100 mL for open thymectomy (transsternal approach). Hereby, median blood loss ranges from 150 mL as reported by Kamel *et al.* (n=22) (83) and Kneuertz *et al.* (n=34) (76) to a mean blood loss of 466.1 mL reported by Ye *et al.* (n=51) (94) for transsternal thymectomies.

For the VATS approach, Kamel *et al.* reported a median intraoperative blood loss of 10 mL for seven cases (83). Shen *et al.* included seven studies with a total of 253 cases in their analysis for intraoperative blood loss among VATS procedures (82). Five of these seven studies indicate a mean intraoperative blood loss of less than 100 mL. O'sullivan *et al.* similarly found that among four studies, three studies reported less than 100 mL of blood loss during VATS thymectomy (81). Pooled-analysis of the seven studies that compared RATS and open thymectomy specifically indicates that mean blood loss is significantly lower for RATS groups (P=0.01) (81). However, analysis by O'sullivan *et al.* found no significant difference in terms of blood loss between RATS and VATS (81). Contrastingly, in their 2022 meta-analysis of seven studies that compared RATS versus VATS thymectomies, Shen *et al.* found that pooled analysis demonstrates that the RATS (n=196) approach yielded significantly less blood loss than VATS

(n=253) (P=0.009) (82). The weighted mean difference for blood loss for RATS versus open thymectomy lay at 173 mL according to the analysis by O'sullivan *et al.*, and 24 mL for RATS versus VATS according to Shen *et al.* (81,82). The higher intraoperative blood loss observed for open thymectomy is predominantly attributable to the invasiveness of sternotomy, as opposed to the reduced incisions employed in minimally invasive techniques. While O'sullivan *et al.* question the clinical relevance of a 173 mL reduced blood loss and one may question the relevance of a 24 mL difference as well, these results nevertheless reinforce the advantages of minimally invasive surgery.

### ***Conversion rates***

In addition to significant intraoperative blood loss or vascular injury, conversion was necessary for marked pleural adhesions or significant local tumor invasion of vascular structures, the phrenic nerve or pericardium (80). Nevertheless, conversion rates during RATS thymectomies reported in literature are relatively low. Nine out of thirteen studies analyzed by O'sullivan *et al.* reported a 0% conversion rate (81). Higher conversion rates were reported by several authors, whereby the highest conversion rate reported was 7.1% by Balduyck *et al.* (n=14) (89) and Kamel *et al.* (n=70) (83). One patient reported by Balduyck *et al.* required conversion to a median sternotomy due to invasion into the subclavian vein (89). Kamel *et al.* reported a total of five conversions to an open approach out of 70 patients with three conversions attributed to advanced local invasion into surrounding structures (including the aorta and innominate vein) and two conversions for dense pleural adhesions (83). Similarly, Marulli *et al.* documented two cases where the decision to convert was made due to the size of the specimen and the suspected infiltration into the pericardium (99). Wilshire *et al.* performed one conversion due to challenges in accurately defining tumor margins (111).

Similarly, low rates of conversion to open thymectomy were reported by groups performing VATS thymectomies. Hereby, the reported conversion rates ranged from 0% (n=45) (87) to 1.3% (n=79) (95) and 4% (n=25) (85).

The specific reasons for transitioning to an open procedure were not extensively detailed in the aforementioned studies, except in one case reported by Ye *et al.*, where the reason was an intraoperative injury to the left innominate vein (85). Statistical analysis of these results indicates minimal heterogeneity and no significant

difference in conversion rates between RATS and VATS approaches (81). The low conversion rates for both RATS and VATS thymectomy indicate that with meticulous patient selection, careful intraoperative monitoring, high expertise from surgical teams, and the advancements in technology available today, an optimized response to intraoperative challenges is possible and the need for conversion to open procedures is decreased significantly.

### *Complete resection*

Complete resection is the cornerstone of surgical treatment for thymoma. The resection boundaries for thymectomy should encompass all thymic and perithymic tissue located between the phrenic nerves, extending from the innominate vein superiorly to the diaphragm inferiorly (84). The meta-analysis by O'sullivan *et al.* includes nine studies that compare complete resection rates between RATS and open thymectomy (81). Among these studies, seven reported a 100% complete resection rate for RATS among a total of 267 patients. Kneuert *et al.* indicate the lowest complete resection rate at 90% among 20 patients for RATS thymectomy and 85% for open thymectomy among 34 cases (76). It must be noted however that this study specifically focused on large thymomas with a median size of 6.0 cm, which may have made complete resection more challenging. In 2017, Burt *et al.* provided data from their large international registry study. Hereby, complete resection was achieved in 92% of 146 patients undergoing RATS thymectomy (86). Also, among 2028 patients that underwent open thymectomy, complete resection was achieved in 86% of patients (86). However, Burt *et al.* report that after propensity matching and balancing of all variables, the rate of complete resection did not differ between minimally invasive or open thymectomy (86). Similarly, O'sullivan *et al.* concluded after pooled analysis that no statistically significant difference in complete resection rate and decreased positive margin rate could be demonstrated between open and RATS thymectomy (81). With regard to the VATS approach, Burt *et al.* reported a 95% complete resection rate among 315 patients that underwent VATS thymectomy (86). Rowse *et al.* and Ye *et al.* furthermore reported a 100% complete resection rate among all patients undergoing RATS (n=11 and 21) and VATS thymectomy (n=45 and 25) (84,85). Subsequent statistical analysis indicates that there is no significant difference in complete resection rates between RATS and VATS thymectomy (81). The absence of statistically significant differences in

complete resection rates should not come as a surprise. Each of the approaches (transsternal, VATS and RATS) offers unique benefits in terms of surgical technique and visualization. Rather than relying solely on tradition or personal preference, clinicians should meticulously evaluate individual anatomical and pathoanatomical factors that favor a specific surgical technique. Ultimately, the resection rates achieved across all three methods are comparable.

### *Duration and volume of pleural drainage*

In terms of postoperative parameters, limited data comparing duration and volume of pleural drainage between RATS, VATS and open thymectomy is available. In the pooled analysis of seven studies conducted by Shen *et al.*, comparing RATS and VATS among a total of 603 patients, it was observed that postoperative duration of pleural drainage was lower for RATS compared to VATS (82). Specifically, the weighted mean difference indicates a shortening of approximately one day for patients undergoing RATS thymectomy (82). The shortest mean duration of postoperative pleural drainage was reported at 1.1 days by Ye *et al.* (n=21) (85) and the longest was 3.1 days as reported by Şehitogullari *et al.* (n=21) (112). Six of seven studies reported a duration of less than three days for RATS thymectomy (82).

Among VATS thymectomies, Li *et al.* reported a mean duration of postoperative pleural drainage of 2.34 days for 35 patients, the lowest mean of postoperative pleural drainage duration reported for this approach (113). Şehitogullari *et al.* reported the longest mean duration of postoperative pleural drainage for the VATS thymectomy at 5.1 days for 24 cases (112). Only two of seven studies reported an average duration of under three days for patients undergoing VATS thymectomy (82). Though, pooled analysis by Shen *et al.* indicates significantly shorter duration of postoperative pleural drainage for RATS compared to VATS ( $P < 0.001$ ), the clinical significance of this discrepancy might be debatable, particularly given the considerable heterogeneity observed in the available data on this parameter. However, when contrasting this parameter between minimally invasive and open surgical approaches, the difference becomes more apparent and, therefore, potentially more clinically significant. Among ten studies analyzed by Hess *et al.* in a meta-analysis comparing minimally invasive and open thymectomy, none of the authors reported a median duration of postoperative pleural drainage of less than 2.4 days after open thymectomy (80,114). In the open thymectomy groups, the mean duration

of postoperative pleural drainage extended beyond three days in eight out of ten studies, with Lee *et al.* reporting a mean duration of 5.3 days for 59 patients undergoing extended transsternal thymectomy (80,115). Consequentially, in seven out of ten studies, a statistically significant reduction in pleural drainage duration was noted when comparing minimally invasive and open approaches (80).

In thymectomy patients, an additional valuable metric for assessing tissue damage and postoperative healing is the total volume of pleural drainage. This metric reflects the quantity of fluid accumulated over the entire duration of pleural drainage. Shen *et al.* conducted an analysis of data from five studies involving 217 patients who underwent RATS thymectomy and 225 patients undergoing VATS thymectomy. The findings revealed that the pleural drainage volume was 80.81 mL lower in patients undergoing RATS compared to VATS (82). Among the studies included in the meta-analysis, Li *et al.* reported the lowest mean volume of drainage for RATS with 209.5 mL (n=60) (113), with Wang *et al.* documenting the highest mean volume of pleural drainage of 398.02 mL (n=58) (82,116).

In VATS thymectomy, Li *et al.* observed low median volume of pleural drainage of 217.04 mL (n=60) (113), while Qian *et al.* reported the highest mean volume of pleural drainage of 613.9 mL (n=35) (87).

While comprehensive meta-analyses comparing volume of pleural drainage across RATS, VATS and open thymectomies are scarce, Qian *et al.* report that the mean volume of pleural drainage was 352.2 mL for RATS (n=51), 613.9 mL for VATS (n=35) and 980.00 mL for open thymectomy (n=37) (87). Similarly, in a systematic review conducted by Xie *et al.* comparing VATS and open thymectomy, it was found that among three studies involving a total of 424 patients, weighted mean volume of pleural drainage was lower in VATS (408.4 mL) compared to open thymectomy (732.1 mL) (88).

The duration and volume of pleural drainage provide valuable insights into fluid dynamics within the pleural space following thoracic surgery. These parameters serve as indicators of healing, inflammation, infection, or residual fluid. Reductions in both drainage volume and duration are favorable outcomes associated with minimally invasive surgery, including RATS, suggesting decreased tissue trauma and improved postoperative recovery. It is important to acknowledge that traditional open surgical techniques are significantly more invasive and tissue-damaging. However, it is worth noting that open surgery is often necessary for particularly large thymomas, which may confound

the interpretation of these parameters. Nevertheless, minimizing pleural drainage duration and volume may positively impact postoperative hospital stays for patients.

### *Length of hospital stay (LOS)*

There is significant heterogeneity in the mean LOS reported among groups, reflecting variations in postoperative care protocols, differences in hospital policies or resources, insurance policies and patient comorbidities. Qian *et al.* reported statistically significant differences in the mean hospital stay with 4.3 days for RATS, 5.5 days for VATS and 6.6 days for open thymectomy (87). Similarly, Xie *et al.* showed an average hospital stay of 9.8 days for open thymectomy, compared to 7.0 days for VATS (88), and Friedant *et al.* noted a significantly shorter LOS for minimally invasive thymectomy (RATS and VATS) with a mean LOS of 8 days compared to open thymectomy with a mean LOS of 9 days (90). Additionally, the meta-analysis by O'sullivan *et al.* demonstrated that among 382 RATS thymectomies and 442 open thymectomies a mean weighted difference in LOS of over two days between RATS and open thymectomies, with RATS having a significantly shorter LOS (81). However, the shorter LOS (0.81 days) for RATS compared to VATS was not statistically significant (81). In a more recent meta-analysis by Shen *et al.*, RATS (n=688) showed a significantly shorter LOS, with a mean difference of 1.07 days less compared to VATS (n=730) (82). In terms of trends for LOS, among the 13 studies analyzed by O'sullivan *et al.*, 9 reported a LOS of 4 or less days for RATS, while only 3 reported the same for open thymectomy (81). Furthermore, 10 of 13 studies reported average LOS of 5 or more days after open thymectomy, while only 1 study reported such values for RATS (81). Similarly, among the 11 studies analyzed by Shen *et al.*, 8 reported LOS of 4 or more days after VATS thymectomy (82). It is conceivable that studies with larger sample sizes would be necessary to detect a more pronounced difference in LOS between RATS and VATS. An outlier among the RATS groups was the study by Balduyck *et al.* whereby mean LOS was 9.6 days for 14 patients undergoing RATS thymectomy and 11.8 days for 22 patients undergoing transsternal thymectomy (89). While it is stated that patients were released from the hospital once they were able to move around independently and when postoperative pain was effectively managed with oral analgesic medication, no specific reasoning for the extended LOS for RATS could

be found (89). Considering the intrinsic invasiveness of the open approach, open thymectomies tend to result in higher surgical trauma due to the performed sternotomy and may require the use of an epidural catheter or similar for pain management as well as more intensive monitoring, support and physiotherapeutic aid, which may be associated with a longer hospital stay.

### **Postoperative complications**

Postoperative complications are a significant concern following thymic surgery, warranting careful monitoring and management. Current research suggests that the rate of postoperative complications is highly heterogeneous between various centers and types of complications that arise can be very diverse. Thirteen studies examined by O'Sullivan *et al.* included data comparing rates of postoperative complications for RATS and open thymectomy. In these studies, 382 patients underwent RATS thymectomy and 442 had an open approach (81). Statistical analysis demonstrated a significantly lower postoperative complication rate in the RATS group with low heterogeneity ( $P < 0.0001$ ) (81). The lowest rates of postoperative complications after RATS thymectomy were reported at 0% by Qian *et al.*, Renaud *et al.* and Seong *et al.* for a total of 91 patients (87,93,110). In contrast, higher rates of postoperative complications after RATS were reported by Wilshire *et al.* and Balduyck *et al.* (89,111). Wilshire *et al.* state that five minor and one major event occurred among 23 patients (26%) while Balduyck *et al.* describe phrenic nerve paralysis in two patients and a deep-vein thrombosis in one, among 14 patients (21.4%) (89,111). Kamel *et al.* reported an 8% postoperative complication rate for a larger case number of 70 patients undergoing RATS thymectomy (83). Hereby, three patients experienced a myasthenic crisis, three suffered postoperative pneumonia, and two patients had prolonged air leakage (83). Other postoperative complications that have been described after RATS thymectomy include tension pneumothorax, hemorrhage, wound infection, atelectasis of the lung, pleural effusion, among others (80). Extensive trials are essential to specify the rates of complications, particularly for RATS, given its comparatively less established status and the limited accumulated experience.

For open thymectomy, no postoperative complications were observed by Kamel *et al.* for 22 patients (83). The study by Weksler *et al.* reported particularly high postoperative complication rates for the open approach (91). Among

35 open thymectomies, 20 postoperative complications arose (57%), while only one complication was observed after fifteen RATS thymectomies (6.7%) (91). These included seven cases of supraventricular arrhythmia (six patients in the transsternal group and in one in the RATS group), sternal dehiscence, atelectasis, renal failure, respiratory failure, change in mental status, severe subcutaneous emphysema, and chylothorax (91). Furthermore, Kang *et al.* reported a lower postoperative complication rate of 14% (12% after propensity score matching) for a particularly large number of open thymectomies ( $n=312$ ) (92). Major complications included postoperative bleeding and reintubation, pleural or pericardial effusion, diaphragmatic paralysis and vocal cord palsy (92). Other common postoperative complications after open thymectomy were impaired wound healing and wound infection (80). In addition, sternal instability and dehiscence, respiratory infections (especially pneumonia), and in the long term, pathological scarring are reported (10,80).

Both O'Sullivan *et al.* and Shen *et al.* have performed statistical analysis comparing rates of postoperative complications between RATS and VATS thymectomy. O'Sullivan *et al.* reported that pooled analysis of five studies, with 212 RATS and 244 VATS thymectomies from the period 2011 to 2017, showed no statistically significant differences in postoperative complication rates (81). However, the more recent analysis by Shen *et al.*, that incorporates eight studies from a broader and more recent time frame (2013–2020), showed that the rate of postoperative complications was significantly lower in the RATS group ( $n=260$ ) than in the VATS group ( $n=338$ ) ( $P=0.02$ ) (82). This observation suggests that the improved outcomes in RATS may be attributed to the increased accumulation of surgical expertise and advancements in robotic technology over time, reflecting a learning curve and refinement in RATS techniques that have resulted in better postoperative outcomes compared to earlier studies. With regard to the specific postoperative complications reported after VATS thymectomy, these are tendentially similar to those reported for RATS thymectomy. For instance, Rowse *et al.* reported seven postoperative complications among 45 patients, including phrenic nerve palsy, pericarditis, atrial fibrillation and pleural effusion (84). Myasthenic crises are feared complications after all forms of thymic surgery and special attention must be paid postoperatively for stigmata of respiratory failure. Strategically optimizing pharmacotherapy (including parasympathomimetics, corticosteroids, immunomodulators

and biologicals) is crucial for facilitating successful patient adaptation during and after surgery. This approach aims to detect and manage myasthenic crises effectively. While data for RATS is sparse, a meta-analysis conducted by Geng *et al.* with fifteen studies and 2,626 patients undergoing surgery for myasthenia gravis, found that the risk of a myasthenia crisis is increased with lengthier surgeries and more blood loss (117). This observation suggests that myasthenic crises may occur more frequently after open thymectomy, likely due to the observed increased blood loss. However, robust large-scale studies are needed to establish more definitive evidence. The higher incidence of postoperative complications following open thymectomy, compared to minimally invasive approaches, is anticipated due to the greater tissue trauma inherent in open procedures. Factors such as larger incisions (including sternotomy), heightened blood loss, and increased tissue manipulation contribute to the elevated rate of complications after open thymectomy. Given that managing complications can be intricate and discomforting for patients, minimizing these complications remains a notable advantage of minimally invasive techniques, particularly RATS.

### **Mortality**

For all three approaches to thymectomy, there were few or no reported mortalities in the first 30 days after surgery (80,81). The meta-analysis by O'sullivan *et al.* indicates that of ten studies comparing mortality between RATS and open thymectomy, no deaths were recorded among 342 RATS thymectomies, and only one death was recorded within one study in the open cohort among a total of 453 open thymectomies (81). Similarly, in three studies comparing RATS and VATS, no deaths were recorded among 136 RATS thymectomies and 159 VATS thymectomies (81). Pooled analysis showed equivalent results between all of the groups and minimal heterogeneity (81). Hess *et al.* report similar findings for mortality in their meta-analysis comparing minimally invasive and open approaches for thymectomy (80). Specifically, while no deaths after minimally invasive surgery were recorded (80), Jurado *et al.* (n=186) and Weksler *et al.* (n=35) reported one death after open thymectomy (91,118). Jurado *et al.* report a pulmonary embolism on the third postoperative day as the cause of death, while Weksler *et al.* do not specify the cause of death in their reported case (91,118). After statistical analysis by Hess *et al.*, the 30-day mortality did not differ significantly between minimally invasive and open

thymectomy (80). The uniformity in 30-day postoperative mortality rates across all three surgical approaches suggests comparable safety profiles and overall efficacy in terms of short-term outcomes. This indicates that while each approach may differ in terms of technique and invasiveness, they are all similarly effective in minimizing the risk of mortality within the immediate postoperative period in well selected patient groups.

### **Recurrence**

While comprehensive data comparing recurrence rates among all three surgical approaches are scarce, insights can be gained through the examination of specific comparative studies. The systematic review by Hess *et al.* compares the recurrence rates following minimally invasive thymectomy, specifically VATS (n=764) and RATS (n=74) as one group against open thymectomy (n=1,230). Analysis of the twenty studies included, showed no statistically significant difference in recurrence. Pleural recurrence or dissemination was more frequently observed than local recurrence in both groups (80). Similarly, Xie *et al.* compared recurrence for VATS (n=540) and open (n=521) thymectomies in their systematic review. Hereby, recurrence-free survival was tracked for up to ten years among 14 studies. VATS was associated with 5-year overall survival and 10-year recurrence-free survival that were similar to or higher than those seen with open thymectomy (88). Agatsuma *et al.* also observed no statistically significant difference in recurrence-free survival and overall survival rates between their propensity score-matched VATS (n=140) and open thymectomy (n=140) groups (78). Additionally, Ye *et al.* (RATS, n=23) and Seong *et al.* (RATS, n=34) specifically compared recurrence rates between RATS and open thymectomies (93,94). Thymoma recurrence was monitored using chest CT scans at 6 and 12 months post-surgery, followed by annual scans in the study by Ye *et al.* (94). In the study by Ye *et al.*, no recurrences were observed during the postoperative follow-up period, which extended for 16.9 months (range, 1–48 months) in the RATS group and 18.1 months (range, 1–48 months) in the open thymectomy group (94). Additionally, Seong *et al.* reported no recurrences in either study group during a mean follow-up duration of  $1.11 \pm 0.21$  years for the RATS group and  $1.85 \pm 0.19$  years (range, data not specified) for the open thymectomy group (93). These studies, however, have relatively small sample sizes.

Data on recurrence rates after RATS thymectomy are

currently limited, and long-term follow-up is not yet widely available, likely due to the recent adoption of this approach in thymic surgery. Nevertheless, existing data suggests that RATS thymectomy shows comparable local and pleural recurrence rates to both VATS and open thymectomy.

## Limitations

Our narrative review encountered several limitations, and the findings necessitate cautious interpretation. The studies under review predominantly followed a retrospective, non-randomized, and purely observational design, given the absence of prospective, multicenter trials. Consensus among all authors underscores the need for additional investigation, particularly through larger, robustly designed randomized trials, to comprehensively assess oncological outcomes and long-term patient outcomes in this field.

## Conclusions

Meticulous staging and diagnostics as well as an efficient multidisciplinary approach to therapeutic decisions are critical for the successful treatment of patients with thymomas. Complete resection of the entire thymus is the preferred primary treatment approach and each surgical approach to thymectomy, whether open, VATS, or RATS, presents unique technical, perioperative and clinical advantages, as well as disadvantages depending on tumor stage and local extension of disease. Minimally invasive thymectomy using RATS is frequently performed from the left side as many thymomas are located left-sided of the patient's median. Additionally, right-sided and subxiphoidal approaches are feasible alternatives. Open, VATS and RATS thymectomies showed comparable operating times, and achievement of complete resection with similar conversion rates between VATS and RATS. In terms of LOS, estimated intraoperative blood loss and postoperative complications, significant differences favoring RATS are reported. Despite ongoing debate regarding the optimal approach, current research supports the feasibility and safety of RATS techniques in achieving excellent outcomes. Future studies and advancements in technology may further refine the role of RATS thymectomy in the management of thymomas.

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