

Minimally invasive mediastinal surgery

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In the past, mediastinal surgery was associated with the necessity of a maximum exposure, which was accomplished through various approaches. In the early 1990s, many surgical fields, including thoracic surgery, observed the development of minimally invasive techniques. These included video-assisted thoracic surgery (VATS), which confers clear advantages over an open approach, such as less trauma, short hospital stay, increased cosmetic results and preservation of lung function. However, VATS is associated with several disadvantages. For this reason, it is not routinely performed for resection of mediastinal mass lesions, especially those located in the anterior mediastinum, a tiny and remote space that contains vital structures at risk of injury. Robotic systems can overcome the limits of VATS, offering three-dimensional (3D) vision and wristed instrumentations, and are being increasingly used. With regards to thymectomy for myasthenia gravis (MG), unilateral and bilateral VATS approaches have demonstrated good long-term neurologic results with low complication rates. Nevertheless, some authors still advocate the necessity of maximum exposure, especially when considering the distribution of normal and ectopic thymic tissue. In recent studies, the robotic approach has shown to provide similar neurological outcomes when compared to transsternal and VATS approaches, and is associated with a low morbidity. Importantly, through a unilateral robotic technique, it is possible to dissect and remove at least the same amount of mediastinal fat tissue. Preliminary results on early-stage thymomatous disease indicated that minimally invasive approaches are safe and feasible, with a low rate of pleural recurrence, underlining the necessity of a “no-touch” technique. However, especially for thymomatous disease characterized by an indolent nature, further studies with long follow-up period are necessary in order to assess oncologic and neurologic results through minimally invasive approaches. Furthermore, increased robotic experience and studies, including randomized controlled trials, are needed to validate the findings of the current literature.

Keywords: Mediastinum; minimally-invasive surgery; video-assisted thoracic surgery (VATS); robotic; thymectomy



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Introduction

In the past, mediastinal surgery was associated with the necessity of a maximum exposure, which was accomplished with various approaches, including median sternotomy, posterolateral thoracotomy, unilateral anterior thoracotomy with partial sternotomy (hemi-clamshell), and bilateral anterior thoracotomy with transverse sternotomy (clamshell). These approaches were associated with high morbidity and long post-operative stays. In the early 1990s,

many surgical fields, such as thoracic surgery, observed the development of minimally invasive techniques.

Video-assisted thoracic surgery (VATS) is a minimally invasive technique that permits reduced operative trauma compared to open surgery, but is not routinely performed as a therapeutic approach for mediastinal mass resections. Some surgeons are hesitant to utilize VATS, especially for anterior and upper mediastinal lesions, as the mediastinum is an impervious space in the thorax that contains vital structures at risk of injury during surgery (1-4).

Furthermore, although VATS gives clear benefits, it also has some disadvantages for the operator, such as long instruments placed through fixed entry points creating a fulcrum effect, bi-dimensional screen vision of the surgical field, and the creation of an unnatural visual effect that can cause the surgeon to lose orientation and the eye-hand-target axis when the camera is under an assistant's control.

In order to overcome these limitations, some robotic systems have been developed over the last two decades. For the purposes of this article, we define robotic surgery as a surgical procedure that utilizes a device with computer enhanced technology, during which the interaction between surgeon and patient is under the direct control of the surgeon. The Automated Endoscopic System for Optimal Positioning was the first robotic arm approved by the US Food and Drug Administration (FDA) to be used in laparoscopic surgery (5). Subsequently, the same company (Computer Motion Inc., Goleta, CA, USA) developed the ZEUS system to assist surgeons in minimally invasive surgery (6,7). At the same time, the da Vinci Surgical System was developed by Intuitive Surgical (Sunnyvale, CA, USA) and cleared by the FDA for laparoscopy, thoracoscopy and intracardiac mitral valve repair. Currently, the da Vinci Robotic system is the only complete surgical system applied in a wide range of surgical procedures.

The first thoracoscopic resection of mediastinal lesions, including thymectomy and a neurogenic tumor of the posterior sulci was reported by Roviario *et al.* in 1994 (1). Eight years later, Yoshino *et al.* reported the first application of robotic system for the removal of the thymus and a posterior mediastinal mass (8,9). Since then, the application of minimally invasive approaches, including robotic systems, has been increasingly spreading worldwide. Herewith, we describe the state of the art regarding different procedures, including thymectomy and posterior mediastinal lesion removal.

Thymectomy

The most frequent indications for thymectomy are myasthenia gravis (MG) and thymomatous disease, and the most common approach remained median sternotomy until the 1960s, when a series of almost 60 transcervical thymectomies was performed without significant complications or mortality (10). However, considering the results of some studies showing that thymic tissue could reside within the mediastinum or neck outside of the gland, many surgeons felt that maximum exposure techniques were

more appropriate to ensure complete resection (11).

The debate between trans-cervical and trans-sternal thymectomies continued until a less invasive approach involving video-thoracoscopic surgery was developed in thoracic surgery (12,13). A large amount of data has been published regarding minimally invasive thymectomy for MG, reporting interesting results. Both unilateral and bilateral VATS techniques have been applied for thymectomy, and have been demonstrated to result in less operative trauma, lower morbidity and shorter hospital stays when compared to the trans-sternal approach (14-19). The operative times were acceptable and conversion rate was low (*Table 1*). Additionally, Rückert *et al.* reported better preservation of lung function with minimally invasive approaches compared to median sternotomy (20). Some authors preferred the right-side approach due to the relatively larger chest cavity and optimal visualization of the superior vena cava and the right phrenic nerve (21,22). Other authors preferred the left-side approach, underlining that the left pericardio-phrenic and aorto-pulmonary window fat tissues can be more easily reached from the left (23,24).

It is important to say that one of the most important keypoints of the minimally invasive technique for the treatment of MG is represented by the neurological outcomes, which are related to the necessity of resecting all thymus and peri-thymic fat tissue [extended thymectomy according to the Masaoka criteria (25), considering the distribution of thymic tissue and ectopic thymic tissue (11)].

Lee *et al.* compared the trans-sternal approach with bilateral VATS, observing no differences in the extent of the resected specimen (19). Meanwhile, Liu *et al.* reported that unilateral VATS offered long-term neurological outcomes equivalent to that of bilateral VATS (21). Other authors reported interesting mid-term neurologic results on 107 consecutive non-thymomatous myasthenic patients who underwent unilateral VATS, with the sidedness of the approach based on individual cases and the computed tomography (CT) status of the thymus (26). However, VATS has some disadvantages, including planar vision of the operative field and the lack of ability to articulate the tips of the thoracoscopic instruments. Robotic systems can overcome these limitations, combining the advantages of VATS (less operative trauma, short hospital stay and cosmetic results) with three-dimensional (3D) vision and the ability to articulate the tips of the instrument inside the chest cavity. Excellent results were reported in several series (23,27-30), showing low conversion rate, low morbidity and adequate operative time. In a recent study, Cakar *et al.*

Table 1 Literature data on minimally invasive thymectomy for MG

Author, year	Sample size	Approach	Side	Operative time (minutes)	Conversion rate (%)	Mortality (%)	Morbidity (%)	Follow-up	CSR (%)
Tomulescu, 2006	107	VATS	R/L	90	0	0	9	34.6	15
Sauchenco, 2002	38	VATS	R	NR	2.6	0	NR	53	14
Mineo, 2000	31	VATS	L	165	3.2	0	NR	39.6	36
Rückert, 2011	79	VATS	L	198	1.3	0	2.5	42	20.3
	74	Robotic	L	187	1.4	0	2.7	42	39.3
Marulli, 2013	100	Robot	L	120 ^a	0	0	6	67 ^a	28.5
Cakar, 2013	9	Robot	R	154 ^a	0	0	11	13 ^a	NR
	10	Open	–	110 ^a	–	0	30	74 ^a	NR
Liu, 2015	31	VATS	Bilat	169	0	0	16	5.2 ^{ab}	46.6
	72	VATS	R	152	0	0	19	5.2 ^{ab}	46.6
Lee, 2011	55	VATS	Bilat	112	3.6	0	2	NR	NR
	59	Open	–	130	–	0	5	NR	NR
Keating, 2011	57	VATS	R	NR	0	1.8	14	36	28

MG, myasthenia gravis; VATS, video assisted thoracoscopic surgery; CSR, complete stable remission rate. Side: R, right; L, left; bilat, bilateral. Operative time is expressed as a mean, unless otherwise stated. Follow-up period is expressed as a mean in months, unless otherwise stated. NR, not reported; a, median; b, years.

observed that robotic thymectomy in patients with MG provided at least the same benefits as open trans-sternal thymectomy with regard to improvement of neuro-muscular symptoms and drug dose reduction, but with a lower rate of complication and reintervention: the clinical outcomes of remission favored the robotic approach (31). Thus, the authors suggested that, with a unilateral robotic technique, it is possible to dissect and remove at least the same amount of mediastinal fat tissue, in addition to thymic tissue, as with the trans-sternal approach. Additionally, Rückert *et al.* reported an improved neurological outcome for the robotic thymectomy in respect to thoracoscopic thymectomy, for patients affected by MG (32). Another criticism is represented by thymomatous disease. Since 1993, some papers have attested to the possibility of performing thymectomy for Masaoka Stage I and II thymomas with VATS (1-3). The first paper describing the robotic resection of a Masaoka Stage I thymoma was published by Yoshino *et al.* in 2001. In spite of this data, few papers evaluated the role of minimally-invasive approach and some authors advocated the necessity of median sternotomy due to the high risk of tumor spread inside the chest cavity (8). In 2010, Agasthian *et al.* reported a local recurrence rate of 3.4% in patients who underwent VATS thymectomy for thymoma (33), while two recent papers compared the VATS

and the open approaches for thymomas (16,34). Cheng *et al.* observed no local or pleural disease recurrence for Stage II thymoma, either in the open or in the VATS groups (16), and similar outcomes were published by Pennathur *et al.* (34) in a larger comparative study, reporting no significant difference in disease recurrence and overall survival between the two groups. Comparable results were obtained by He *et al.* and Liu *et al.* in comparative studies, which analyzed the trans-sternal approach and the VATS one (35,36). In another study in 2012, focused on robotic thymectomy for thymoma, the authors emphasized the excellent visualization provided of the mediastinal field, including all thymic and peri-thymic tissues and the thymoma capsule, that allowed a safe manipulation of mediastinal tissue. In these series, no disease recurrence was observed (37). A recent paper by Ye *et al.* compared 25 VATS thymectomies and 21 robotic thymectomies for stage I thymoma. Robotic thymectomy appeared to be feasible, safe and equally minimally invasive as VATS, and resulted in a shorter drainage period and reduced hospital stay compared with the VATS approach (38). A multicentre European study on 79 thymomas resected with the robotic approach showed good surgical results with no mortality, low morbidity, and short hospital need to insert reference for this study. With regard on oncologic results, only one case of disease relapse

Table 2 Literature data on minimally invasive thymectomy for thymoma

Author, year	Sample size	Approach	OT	CR	Mortality (%)	Morbidity	Follow-up	Disease recurrence
Cheng, 2005	12	VATS	193	0%	0	NR	33.9	0%
	10	Open	207	–	0	NR	33.9	0%
Pennathur, 2011	18	VATS	NR	NR	0	NR	27 ^b	0/18
	22	Open	NR	–	0	NR	58 ^b	1/22
Mussi, 2012	14	Robotic	139	14%	0	14.3%	14.5	0%
He, 2013	15	VATS	202	0/15	0	26.7%	12–61 ^a	0%
	18	Open	141	–	0	33.3%		0%
Liu, 2014	76	VATS	142	1/76	0	NR	61.9	2.6%
	44	Open	150	–	0	NR	69.7	2.3%
Ye, 2013	25	VATS	104	1/25	0	1/25	25.2	0%
	21	Robotic	96	0%	0	1/21	17.5	0%
Marulli, 2012	79	Robotic	140 ^b	8.9%	0	17.1%	40 ^b	0.7%

VATS, video assisted thoracoscopic surgery; Open, transternal approach; OT, operative time expressed as a mean in minutes, unless otherwise stated; CR, conversion rate. Follow-up period is expressed as a mean in months, unless otherwise stated. NR, not reported; a, range; b, median.

occurred (1.3%), a percentage that is comparable with other thoracoscopic series (29) (Table 2). However, considering the indolent nature of thymomatous disease, long follow-up period is necessary in order to assess the long-term oncologic results. Thus, further studies on larger series are necessary to confirm the good results of minimally-invasive approaches.

Posterior mediastinal lesion resection

The most frequent lesions occurring in the posterior mediastinum are represented by neurogenic tumors, which are generally asymptomatic and diagnosed incidentally. These tumors are usually benign and arise in the costovertebral sulci from sensitive fibres of intercostal nerves, from the sympathetic chain or, less frequently, from the vagus nerve. In the past, thoracotomy was the traditional surgical approach, but at the beginning of the 1990s, VATS was introduced to the thoracic field and applied for the removal of posterior mediastinal lesions (1). VATS minimized the trauma incision, reduced hospital stays, and provided an appropriate view of the posterior mediastinum (39-41). However, the removal of dumbbell-type lesions may be considered challenging (42) and, in this sense, a combined neurosurgical and thoracoscopic approach would be an excellent strategy (43).

Another criticism is represented by tumors lodged in

the superior sulcus, close to the stellate ganglion, where careful bipolar dissection is recommended. In this setting, the features of the robotic system could help surgeons. At the beginning of the 21st century, some papers reported the removal of a posterior-mediastinal mass with the aid of robotic systems, emphasizing its safety and feasibility (9,44). Subsequently, studies on the application of robotic systems for removal of mediastinal lesion, including neurogenic tumors, have highlighted features such as depth perception, tremor filtration and 7-degree articulation of the instrument tips that have permitted a precise isolation of the anatomic structures and safe manipulation of the tissues. Melfi *et al.* reported no mortality and a morbidity rate of 7.2% (30). A heterogeneous study of Cerfolio *et al.*, comprising different kind of surgical procedures, reported no mortality and low morbidity rate (12%): one esophageal perforation, four atrial fibrillations, two pneumothoraces, one case of gout and one prolonged air leak (45). Nakamura *et al.* published their Japanese experience with robotic-assisted resection of posterior mediastinal masses, where no conversions or complications were reported (46).

Other small studies have demonstrated that operating tumors in the posterior mediastinum is feasible with the robotic-assisted approach (47,48). Other pathologies uncommon to the posterior mediastinum, such as thyroid goiters, have also been resected using robotic-assisted systems (49,50). Additionally, in 2010, Chon *et al.* observed



Video 1 Minimally invasive mediastinal surgery.

Available online: <http://www.annalscts.com/article/view/9053/9657>

that robotic-assisted resection of double primary tumors within different areas of the mediastinum (anterior and posterior) is possible with a single-stage operation (51).

Ectopic mediastinal parathyroid adenoma removal

Primary hyperparathyroidism is the most common cause of hypercalcemia. Usually, the culprit gland or glands are located in the cervical region, but can also be found in ectopic locations in 15% to 20% of cases (52), including the mediastinum, which in the past was accessed through a median sternotomy or thoracotomy.

With improved technology, more minimally invasive approaches such as VATS are being used (53,54). Additionally, several case series have reported the application of robotic systems to resect ectopic parathyroid glands located in the mediastinum, demonstrating its safety and feasibility (55-58). Profanter *et al.* underlined the advantage of the robotic-assisted system in respect to VATS when dissecting tissue in areas such as the aortopulmonary window (55). Transient weakness of the left recurrent laryngeal nerve was the only postoperative complication recorded in these series, and this complication had completely resolved by 8 months (56).

Other mediastinal pathology

At the beginning of the last century, VATS began to be applied also for resection of lesions occurring less commonly within the mediastinum, such as pleuropericardial cysts, lipomas, teratomas or fibrous tumors of the mediastinum. Roviario *et al.* reported the application of VATS for a wide

range of mediastinal lesions, highlighting that VATS provides good exposure of the entire mediastinum, ensures adequate room for surgical manoeuvre, and results in greatly reduced surgical trauma (1). Martinod *et al.* reported a series of bronchogenic cysts removed with thoracoscopic approach (59), while Umemori *et al.* reported the successful VATS resection of pleuropericardial cysts of the mediastinum (60).

In 2004, Bodner *et al.* reported the application of the robotic system for the treatment of various mediastinal lesions, and Meehan *et al.* described their experience with robotic-assisted resections of mediastinal lesions in children, including teratomas and germ cell tumors (61). Another paper by Melfi *et al.* documented the resection of nine pleuropericardial cysts and three teratomas (30). The results from both of these series demonstrate that even uncommon pathologies within the mediastinal borders can be extirpated with good results.

Conclusions

During the 20th century, less invasive surgical approaches were developed to access the mediastinum. VATS has the potential to reduce morbidity, postoperative pain levels and length of hospital stay. However, this technique has some limitations. These include the planar vision intraoperatively, with the loss of depth perception; the limited maneuverability of thoracoscopic instruments, making it difficult to operate around corners; the fulcrum effect of instruments inserted through the chest wall; and the non-ergonomic positions that the surgeon often has to adopt.

Robotic systems can be considered a natural progression of VATS, offering a high-definition 3D vision, tremor filtration and a 7-degree articulation of the instruments inside the chest cavity. These features appear to be highly useful in a remote and tiny space such as the mediastinum (*Video 1*).

Despite these positive results, randomized controlled studies are necessary in order to confirm the benefits of minimally invasive approaches, especially for thymectomy, both from a neurological and oncological point of view.

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Footnote

Conflicts of Interest: Franca Melfi is an official proctor for

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