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Subxiphoid and subcostal thoracoscopic surgical approach for thymectomy

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Abstract

Background The continuous evolvement of minimally invasive thymectomy over the last decades has potential advantages over trans-sternal thymectomy with similar oncologic outcomes of thymoma and complete remission for myasthenia gravis patients. A variety of different minimally invasive approaches have been described previously. The aim of this article is to present our subxiphoid and subcostal approaches in thymectomy for patients with myasthenia gravis and thymomas and to investigate the early surgical outcomes of these patients.

Methods A retrospective analysis was performed of 95 patients who underwent thymectomy via a subxiphoid and subcostal approach for MG and/or thymoma at our department during the period of 2015 to 2017. The clinical characteristics and early surgical outcomes of these patients were reviewed and analyzed.

Results Complete thymectomy and extended thymectomy was accomplished through the subxiphoid and subcostal approach in 93 of the 95 (97.9%) patients. Two patients (3.2%) required conversion to sternotomy for the invasion of a thymoma. The mean operative time was 109 min (range 70–170 min), with the mean estimated blood loss of 47 ml (range 20–350 ml). Postoperative complications included two cases of myasthenic crisis: one case of pleural effusion and one case of wound infection. In a mean follow-up of 31 months no patients showed recurrence of the tumor. In 41 MG patients followed up for 31 months, the improvement rate was 87.8% and the rate of complete remission was 29.3%.

Conclusion Subxiphoid and subcostal thoracoscopic thymectomy may be a safe and feasible approach for treating MG and anterior mediastinal tumors

Keywords Thymectomy · Subxiphoid · Thoracoscopic · Thymoma · Myasthenia gravis

Thymectomy is most commonly considered to be an important part of the treatment of thymoma and myasthenia gravis (MG). A complete en-bloc thymectomy is crucial for tumor resection and complete remission of MG. The minimally invasive thymectomy has been performed frequently for the treatment of non-thymomatous MG [1], while a median sternotomy has traditionally been the preferred approach of thymectomy for patients with thymoma [2]. With benefits over trans-sternal thymectomy including better cosmetic results, less trauma, and fewer complications, minimally invasive thymectomy becomes the preferred operation in the treatment of thymoma and MG [3].

Several minimally invasive approaches have been applied in thymectomy, such as transcervical approaches, VATS (unilateral or bilateral), subxiphoid approaches, robotic techniques and a combination of these approaches [1, 4–7]. However, no consensus is reached on the optimum surgical approach in thymectomy. The subxiphoid approach was first reported by Kido et al. in 1999 [6]. Suda and colleagues introduced their experience on the uniportal subxiphoid approach for thymectomy [8]. However, a uniportal procedure does not allow easy manipulation. Hence recently, a novel subxiphoid and subcostal arch approach has been developed, which not only provides better operative views of the bilateral phrenic nerves and the superior horn of the thymus but also allows easy mastering of operation [9]. The aim of this article is to present our current technique utilizing the

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subxiphoid and subcostal approach in the surgery of thymus, specifically in thymectomy for non-thymomas myasthenia gravis and early-stage thymomas.

Materials and methods

Patients

Between January 2015 and December 2017, 95 consecutive patients with anterior mediastinal mass or myasthenia gravis underwent the subxiphoid and subcostal arch thoracoscopic thymectomy in our department. All the operations were performed by the same surgical team. These patients were retrospectively reviewed and analyzed, and this retrospective study was approved by the institutional review board, along with informed consents from all the patients.

The indications for the subxiphoid and subcostal arch thoracoscopic thymectomy were as follows: (I) patients with anterior mediastinal tumors which are not larger than 6 cm in diameter and no neoadjuvant therapy had been given; (II) patients with noninvasive tumors in the preoperative radiological examination; and (III) patients with non-thymomatous MG. The TNM staging system was used to define the pathological staging of thymoma [10]. The World Health Organization classification system was used to define the histology [11]. The diagnosis of myasthenia gravis was based on the clinical presentation, electromyographic studies, and serum level of acetylcholine receptor antibody. The Myasthenia Gravis Foundation of America (MGFA) classification was applied to classify the preoperative severity of MG [12]. In case of the advanced TNM stage-III thymomas or tumors larger than 6 cm, the trans-sternal approach is preferred. In case of non-thymomatous MG, the operation is proposed primarily to mildly to moderately affected patients in the MGFA class I–IIIb. In case of MG, a stable level of the disease is essential together with preoperative preparation. Any patients with preoperative generalized symptoms, respiratory difficulties, or bulbar symptoms are considered for plasmapheresis or intravenous immunoglobulins (IVIG) before surgery.

Surgical technique

Following the induction of general anesthesia and intubation with a single lumen endotracheal tube, the patient was placed in a supine position with a roll placed beneath the thoracic spine to elevate the chest. The operating surgeon stood between the patient's legs, the assistant was on the left or right side to operate the camera, and a monitor was placed at the cranial side of the patient. A 1.5-cm vertical incision was first made 1 cm caudal to the xiphoid process (Fig. 1), and vertical incisions could easily be extended for large tumor removal. There was no need to resect the xiphoid process. The fascia of the rectus abdominis muscle was then cut vertically, and the xiphoid was separated from the rectus abdominis at the site of attachment. The retrosternal space was created by blunt finger dissection, and the bilateral extra pleural space was enlarged. Under the guidance of the finger, two 0.5-cm extra pleural thoracic ports were created under the bilateral costal arches at the midclavicular lines (Fig. 1). Thereafter, a 10-mm, 30-degree angled thoracoscope was introduced into the retrosternal space. Artificial pneumothorax was created via insufflation with carbon dioxide (CO_2)

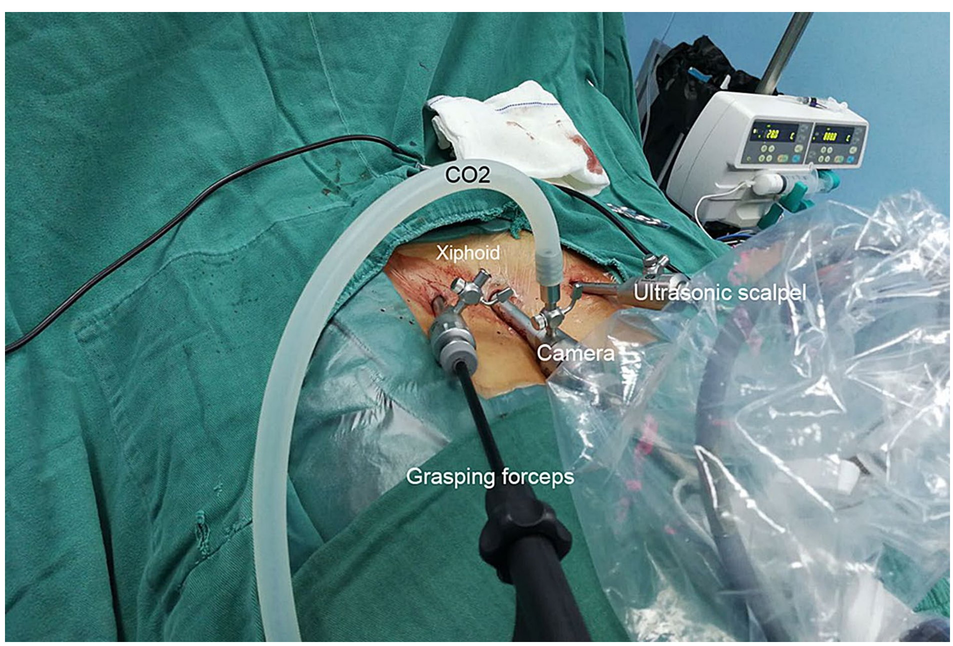

Fig. 1 The incisions and the setup of the surgical instruments. A 1.5-cm vertical subxiphoid incision for the camera; two subcostal arch incisions were created for the instruments at the midclavicular lines. Ultrasonic scalpel; CO2; Xiphoid; Camera; Grasping forceps

at a positive pressure of 8 cm H_2O to enlarge the anterior mediastinal space. An ultrasonic scalpel and thoracoscopic graspers were inserted into the retrosternal space through the bilateral operating ports, and the maneuverability of these devices was improved by holding graspers in the left hand and ultrasonic scalpel in the right hand (Fig. 1).

The procedure was a complete thymectomy for thymoma patients without myasthenia gravis (MG) (complete removal of the entire thymic gland along with the surrounding fat) and an extended thymectomy for patients with MG (removal of the bilateral mediastinal pleura, mediastinal and pericardiophrenic fatty tissues, and dissection of aorta-pulmonary window in addition to complete thymectomy). The decision to perform extended thymectomy was based on the presence of MG, regardless of the surgical approach. A surgery for thymoma met several requirements, including the "no-touch" technique, radical en-bloc removal of the whole tumor, and avoidance of rupture of the capsule. A VATS thymectomy was converted to the trans-sternal approach if tumor invasion of the great vessels or the pericardium had been suspected, or if there had been bleeding from a major vessel that could not be controlled.

Initially, the anterior border of the thymus is gradually detached from the posterior aspect of the sternum and up to the thoracic outlet (Fig. 2A). Bilateral mediastinal pleura were cut near the sternal surface up to the level of the right and left internal thoracic veins, which were left intact (Fig. 2B). The CO2 insufflation within the mediastinum displaces bilateral lungs and broadens the space behind the sternum, markedly improving the operative field. Next, the prepericardial fat tissue at the bilateral cardiophrenic angle was dissected and the bilateral phrenic nerves were confirmed. Dissection of the lateral edge of the thymus and the surrounding adipose tissue was performed along and anterior to the bilateral phrenic nerves up to the neck (Fig. 2C, D). The posterior border of the thymus was separated from the underlying pericardium up to identify the innominate vein. With careful dissection, the junction of the innominate vein and superior vena cava (SVC) was recognized. This plane of dissection was followed up the SVC to the right internal thoracic vein and across to the innominate vein. The left internal thoracic vein was followed superiorly and then posteriorly in the dissection until it inserts into the innominate vein. The thymus was then stripped off the innominate vein as far as was convenient (Fig. 2E), with the clipping or ligation of thymic veins. Through gently grasp and traction on the thymus, the superior horns were liberated from the neck with blunt or ultrasonic dissection (Fig. 2F, G). The thymus in the cervical region was dissected from the thyroid gland on the cranial side, right innominate vein on the right side, left innominate vein on the left side, and trachea and brachiocephalic artery on the dorsal side (Fig. 2H). Finally, the thymus and the adipose tissue were placed in a plastic bag and removed from the subxiphoid incision (Fig. 3A). If necessary, the dissection of the adipose tissue from the aorta-pulmonary window was completed at this stage. The resection borders were, bilateral phrenic nerves, the retrosternal space,

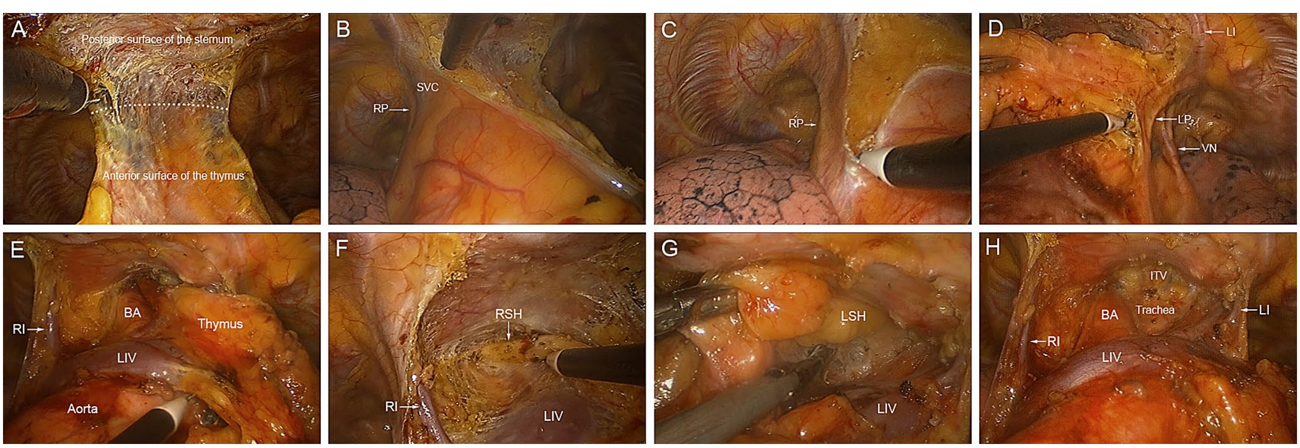

Fig. 2 **A** The anterior border of the thymus is detached from the posterior aspect of the sternum. Posterior surface of the sternum; Anterior surface of the thymus; **B** Right mediastinal pleura were cut near the sternal surface up to the level of the right internal thoracic vein. Right phrenic nerve; Right internal thoracic vein; **C** Dissection of the lateral edge of the thymus and adipose tissue was performed along the right phrenic nerve. Right phrenic nerve; **D** Dissection of the lateral edge of the thymus and adipose tissue was performed along the left phrenic nerve. Left phrenic nerve; Left internal thoracic vein; **E** The thymus was stripped off the innominate vein; Aorta; Left innominate vein; brachiocephalic artery **F** The right superior horn was dissected and pulled to the left side with traction; **G** The left superior horn was liberated from the neck with blunt or ultrasonic dissection; **H** A view of the cervical region after division of the superior horns of the thymus at the level of the thyroid. Left innominate vein; Left internal thoracic vein; Right internal thoracic vein; Trachea; Brachiocephalic artery; Inferior thyroid vein *RP* right phrenic nerve, *LP* left phrenic nerve, *RI* right internal thoracic vein, *LP* left phrenic nerve, *LI* left internal thoracic vein, *RSH* right superior horn, *LIV* Left innominate vein, *LSH* left superior horn, *ITV* Inferior thyroid vein, *BA* brachiocephalic artery

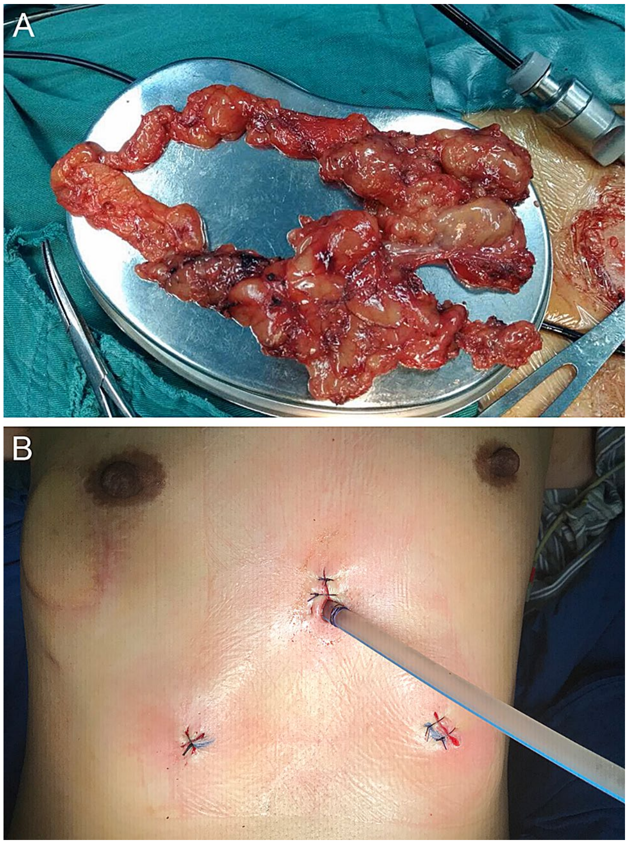

Fig. 3 **A** Resected thymus with the thymoma and adipose tissue. **B** Location of the incision and drainage tube

the pericardium and great vessels, the inferior border at the pericardial reflection including the subxiphoid space, and the lower neck regions. Hemostasis was assured and a drainage tube was inserted into the mediastinum through the subxiphoid incision (Fig. 3B).

Postoperative care

Early extubation was encouraged after surgery. Oxygen saturation monitoring and electrocardiography monitoring were performed in the early postoperative period. For patients with MG, the same medications used preoperatively restarted after the operation under the guidance of the neurologists. A subxiphoid drain could be removed after normal x-ray and with adequate clinical findings. The patient may be discharged the following day after the removal of subxiphoid tube.

Results

The patient characteristics are shown in Table 1. There are 34 men and 61 women ranging in age from 17 to 80 years (mean, 46 years). Forty-one patients (43.2%) were affected by MG. Before thymectomy, all patients with MG received anticholinesterase and 66.3% of the patients were given steroid therapy. Preoperatively, 6 patients were in stage I, 17 in stage IIA, 11 in stage IIB, 3 in stage IIIA, 2 in stage IIIB, 1 in stage IV, and 1 in stage V according to the Myasthenia Gravis Foundation of America (MGFA) classification.

Table 1 Demographic and Clinical Characteristics of Patients ($N=95$)

Variable	Number
Age(years)	45.6 ± 16.1
Male/Female	34/61
Cases with MG	41 (43.2%)
MGFA classification	
I	6 (6.3%)
IIA	17 (17.9%)
IIB	11 (11.6%)
IIIA	3 (3.2%)
IIIB	2 (2.1%)
IV	1 (1.1%)
V	1 (1.1%)
Extent of thymectomy	
Complete	43 (45.3%)
Extended	52 (54.7%)
Combined resection	2 (2.1%)
Pathology	
Thymoma	52 (54.7%)
Hyperplastic thymus	24 (25.3%)
Atrophic thymus	2 (2.1%)
Normal thymus	5 (5.3%)
Thymic cyst	12 (12.6%)
Thymoma pathology	
Size (cm)	3.45 ± 1.28
TNM stage	
I	48 (92.3%)
II	1 (1.9%)
IIIa	3 (5.8%)
WHO histological type	
A	9 (9.5%)
AB	5 (5.3%)
B1	5 (5.3%)
B2	22 (23.2%)
B3	11 (11.6%)

MG myasthenia gravis, *MGFA* Myasthenia Gravis Foundation of America

The operative approaches are presented in Table 1. Forty-three patients received complete thymectomy and 52 received extended thymectomy, and no preoperative biopsy was performed. If the lung was invaded, one of the ports under the costal arches was enlarged to 1 cm, and a wedge resection of the lung was made by using a stapler. During the resection, bilateral pulmonary ventilation was temporally suspended for a few seconds. No patient required additional access (cervical or lateral thoracoscopic incision).

Two patients with pulmonary invasion of tumor simultaneously underwent lung wedge resection, and no patient required additional access (cervical or lateral thoracoscopic incision). Two patients (3.2%) required conversion to sternotomy: one for invasion of a thymoma to the innominate vein, and the other for invasion to the pericardium.

Table 2 shows that the mean operative time was 109 min (range, 70-170 min), with the mean estimated blood loss (EBL) of 47 ml (range, 20–350 ml). All patients were extubated within 24 h except one patient for whom the mechanical ventilation was on before surgery for MG. The mean duration of postoperative chest drain was 2 days (range, 1–4 days) and the median postoperative hospital stay was 3 days (range, 2–10 days). There was no mortality and vascular or nerve injuries occurred in the study group. Two patients experienced a myasthenic crisis following the operation. One patient in stage IIb took corticosteroid and anticholinesterase agents but didn't get plasmapheresis or IVIG before surgery. The other patient in IIIb received preoperative IVIG, with corticosteroid and anticholinesterase therapy. The two patients required temporary mechanical ventilatory support postoperatively, and both patients recovered well when discharged. One pleural effusion necessitated unilateral guidewire inserted tube drainage, and one patient suffered wound infection.

The pathological diagnoses are presented in Table 1. There were 52 patients (54.7%) diagnosed with thymoma, 24 (25.3%) with hyperplastic thymus, 2 (2.1%) with atrophic thymus, 5 (5.3%) with normal thymus, and 12 patients (12.6%) with thymic cyst. Pathological findings verified the complete resection of tumor in all patients with thymoma. The mean diameter of the resected tumor was 3.45 ± 1.28 cm (range, 1.3 to 6.8 cm), and the TNM stage was I in 48 patients (92.3%), II in 1 patients (1.9%), and IIIa in 3 patients (5.8%). The World Health Organization histology was type A in 9 (9.5%), AB in 5 (5.3%), B1 in 5 (5.3%), B2 in 22 (23.2%), and B3 in 11 (11.6%). Postoperative radiotherapy was administered in 24 cases, all with stage II and III disease.

After a median follow-up of 31 months (range, 18–48 months), all the 95 patients were alive and no tumor recurrence happened. Moreover, 36 out of 41 patients with MG (87.8%) experienced some improvement. Complete stable remission (CSR) was found in 12 (29.3%) patients, pharmacological remission (PR) in 3 (7.3%), MM-2 (minimal manifestations) improvement in 8 (19.5%), and MM-3 improvement in 13 (31.9%) according to the MGFA classification of post-intervention status. The status of 5 (12.2%) patients remained unchanged, and none of the patients reported deterioration of MG.

Table 2 Operative data of patients who underwent subxiphoid-bilateral subcostal thymectomy (*N* = 95)

Variable	Measurement (mean ± SD)
Operation time	109.4 ± 20.7 min
Estimated blood loss	47.3 ± 46.0 ml
Postoperative drain duration	1.9 ± 0.7 d
Postoperative hospital stays	2.7 ± 0.6 d
Complications	
MG crisis	2
Pleural effusions	1
Wound infection	1
Postoperative radiotherapy	24
Follow-up	31.1 ± 9.7 mo
Complete stable remission (CSR)	12 (29.3%)
Symptom improvement	36 (87.8%)
Tumor recurrence	0

Discussion

Over the past several decades, thymectomy has been proved effective in treating MG and anterior mediastinal tumors, and various surgical techniques for thymectomy have been advocated. Although the median sternotomy firmly remains to be the gold standard for thymectomy [13], with the advancements in thoracoscopic instruments and techniques, the VATS thymectomy has become a viable surgical technique for treating thymic abnormalities [14] However, different approaches exist for VATS thymectomy, which includes the unilateral, bilateral, subxiphoid, transcervical, robotic, or a combination approach. The choice of surgical approach is usually based on the experience and preference of the surgeon. We recently changed the approach of VATS thymectomy from the lateral approach to the subxiphoid approach.

These reported thoracoscopic approaches for thymectomy have several limitations. The lateral VATS approach is associated with persistent postoperative pain due to intercostal nerve injury, an insufficient operative field in the neck region and difficulty in identifying the contralateral phrenic nerve [15]. Although the bilateral VATS approach increases the surgical exposure of the anterior mediastinum, more intercostal incisions are needed, which may increase operative trauma and postoperative pain [16]. In 2002, Hsu et al. reported the thoracoscopic thymectomy via subxiphoid incisions, and two ports were created at the bilateral intercostal space [17]. The subxiphoid incision was widely combined with the other minimally invasive incisions to create a hybrid approach for thymectomy by Takeo and Zielinski [1]. Suda et al. reported a uniportal thymectomy through the subxiphoid approach without any intercostal incision in

2012 [18]. However, this procedure requires to remove the xiphoid process and all the instruments inserted through a single port may interfere with each other, decreasing the maneuverability of instruments.

Although the VATS thymectomy has gained increasing popularity for the treatment of early-stage thymomas, some skepticism remains about the oncological results of this procedure. No randomized clinical trial has been designed to address the issue. Factors such as tumor size, tumor stage, and tumor histology should be considered when determining the indications for the VATS thymectomy. Traditionally, the VATS thymectomy was considered for thymomas less than 5 cm in diameter [7, 19]; however, with the improvement of technique, it seems that the size of tumor is not an absolute contraindication to VATS [20]**.** The maximum diameter is 6 cm of the thymomas in our series. The prediction of invasion of phrenic nerves, pericardium, and major vessels should suggest an open approach. Even according to these criteria, there were 2 conversions to sternotomy owing to unexpected invasion of adjacent structures. Indications for surgery with MG patients were patients whose disease is refractory to medical management or who cannot tolerate the medical regimen. Patients with significant cardiomegaly and cardiac severe arrhythmia would likely have poor operative access and experience hemodynamic destabilization during the instrumentation of the anterior mediastinum via the subcostal arch incision, so we would not advocate this subxiphoid approach in these patients.

The treatment of early-stage thymomas is based on complete surgical resection even in non-MG patients, and even if only a portion of the thymus is involved with a thymoma [21]. The ability to achieve a R0 resection is the key factor for successful treatment. Proponents of complete thymectomy advocate en-bloc resection of the tumor with the entire thymus gland and surrounding fat. However, the necessity of removing the whole thymus gland has been questioned for thymomas without MG [22] Recurrence rates were slightly higher after thymomectomy alone in early-stage patients [23, 24]. Our recommendation is to perform a complete thymectomy for tumors without MG. For myasthenia gravis patients without thymoma, the amount of thymus gland and the surrounding fat that should be removed for MG has also been a topic of controversy. The extent of surgery varies from removing only the thymus gland, to extensive thymectomy resecting the thymus and the anterior mediastinal adipose tissues, and to a maximal thymectomy that includes a neck dissection and skeletonization of all the mediastinal vessels [1, 21]. Most thoracic surgeons recommend to remove as much mediastinal adipose tissue as possible to avoid leaving ectopic thymus behind. Although total thymectomy is the goal of surgery, it has not been confirmed if this is necessary, nor is it clear that all these techniques achieve this goal [25]. There is either no consensus on the extent of surgery in case of thymomatous MG [21]. We prefer the extensive thymectomy in patients undergoing surgery for MG.

Regarding the novel subxiphoid and subcostal arch approach, several advantages are noted for the thoracoscopic thymectomy. First, the subxiphoid port provides an excellent operative view of the anterior mediastinum, the cervical region, and both pleural spaces, allowing adequate visualization of both phrenic nerves and of the superior horns of the thymus. Furthermore, with this approach, a lateral view was easily obtained through the subcostal arch ports. Second, the double-lumen endotracheal intubation is not necessary in this approach. Avoidance of separate ventilation could decrease the risk of pulmonary complications and may be beneficial to the patients who cannot tolerate the single-lung ventilation due to severe lung diseases or poor lung function. Third, with the help of artificial pneumothorax, the mediastinum is compressed and the bilaterally ventilated lungs are pushed aside, greatly improving the view of the operative field and allowing for safer dissection of the innominate vein and cervical horns. In our experience, low pressure CO_2 insufflation into the mediastinum does not alter the hemodynamic status of the patients. Another advantage of the approach is reduced postoperative pain and the absence of chest paraesthesia due to the avoidance of intercostal nerve injury and compression. There is also a clear cosmetic advantage with no visible scar in the neck and upper chest area. Compared with the uniportal subxiphoid thymectomy in which all surgical instruments inserted into a single port interfere with each other, in our procedure another two ports are introduced to greatly improve the surgical maneuverability and safety, leading to wider acceptance of the technique. The subxiphoid and subcostal thymectomy is an easy technique to learn for surgeons experienced in other lateral thoracoscopic procedures. The necessary skills can be acquired in a short time, about five patients, we now complete thymectomy in less than 120 min in most patients.

However, this approach has the following disadvantages. First, it is hard to completely remove the adipose tissue near the cardiac-diaphragmatic angles. Second, if a big tumor is located at the head-side area of the innominate vein, it is difficult to operate in the limited cervical space through this approach. Third, this approach is not applicable in advanced thymomas, similar to the other minimally invasive approaches.

Our group has used the subxiphoid and subcostal arch approach with good success in patients with early-stage thymomas, and 96.2% of thymoma patients had their resection completed through this approach. Intraoperative findings of invasions of the phrenic nerves and the big vessels, as well as the need to perform risky maneuvers, should induce the surgeon to convert to sternotomy. The supine position enables conversion to a median sternotomy extremely convenient if necessary. We had no cases of marginal or mediastinal recurrence with a mean follow-up of 31 months; however, it is too early to assess the real oncological value of this approach. It is vital that the thoracic surgeons work closely with the neurologists to achieve optimal preoperative management for the patients with significantly symptomatic MG. Plasmapheresis removes antibodies from the circulation and IVIG can bind antibodies. Both approaches can produce short-term clinical improvement and get the patient through the postoperative period. In our series, clinical improvement was observed in 87.8% of MG patients after 31 months of follow-up. There was no difference in clinical improvement after thymectomy between serie in a meta-anaylsis comparing 9 published series [26–29]. Our CSR rate of 29.3% is comparable with those in many other studies [30].

Despite several limitations in this study including small size, short follow-up, and its retrospective nature, we provide our initial experiences of thymectomy through this novel subxiphoid and subcostal arch approach. Excellent surgical exposures, reduced postoperative pain, and extensive dissection with greater maneuverability of instruments for the surgeon are the main advantages over the other approaches of thoracoscopic thymectomy. However, a longer follow-up will be required to confirm the oncological values and neurological outcomes of this new procedure. In the future, we even could convert this approach to robotic thymectomy through the same ports if the subcostal robotic instruments were long enough to reach the superior poles of the thymus.

Conclusion

The subxiphoid and subcostal arch thoracoscopic thymectomy may be a safe and feasible approach for treating MG and anterior mediastinal tumors. For MG patients, careful preoperative preparation, detailed evaluation, and postoperative vigilance can lead to a safe operation with the minimal postoperative morbidity.

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Compliance with ethical standards

Disclosures Author Xiaofeng Chen, Qinyun Ma, Xuan Wang, An Wang, and Dayu Huang have no conflicts of interest or financial ties to disclose.

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