Video-assisted thoracoscopic surgery is safe and reliable for large and invasive primary mediastinal tumors

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Abstract

Introduction: Video-assisted thoracoscopic surgery (VATS) was not considered for the treatment of primary mediastinal tumors of large sizes or with local invasion.
Aim: To investigate the clinical outcomes of VATS for large and invasive mediastinal tumors.
Material and methods: One hundred and thirteen patients with primary mediastinal tumors were treated by VATS. Twenty-nine patients had bulky tumors (diameter > 6 cm) and 5 patients had invasive tumors. Clinical data were documented and compared.
Results: No patients suffered from any complications after VATS. No relapse or metastasis occurred in the patients with bulky tumors, while 1 patient with invasive thymoma suffered a relapse after VATS. The 2-year disease-free survival and overall survival in patients with bulky tumors were 100% and 100%, while those in patients with invasive tumors were 75% and 100%. There were no differences in hospital stay after VATS between the patients with bulky tumors and smaller tumors, nor between the patients with invasive tumors and non-invasive tumors. Patients with bulky tumors lost more blood than those with smaller tumors, while more blood loss occurred in patients with invasive tumors than non-invasive tumors. Longer operative time was needed for patients with bulky tumors and invasive tumors. Mediastinal tumors with large size or invasion should not be contraindicated for VATS. The prognosis of such patients treated with VATS was comparable to that of traditional open surgery.
Conclusions: VATS is a safe and effective procedure for large and invasive mediastinal tumors.

Key words: prognosis, mediastinal tumor, video-assisted thoracoscopic surgery.

Introduction

Open surgery, e.g., sternotomy or thoracotomy, was the traditional and conventional surgical route for the treatment of primary mediastinal tumors. With the development of mini-invasive technology, e.g., video-assisted thoracoscopic surgery (VATS), most primary mediastinal tumors can be radically resected with VATS. VATS has advantages over open surgery because of less trauma and pain, a better cosmetic effect and quicker recovery, especially for the elderly and patients with poor cardiopulmonary function [1, 2]. However, in general, VATS was believed not suitable for primary mediastinal tumors with large size (maximal diameter > 5 cm) or local invasion because of poor exposure and a higher risk of blood loss and tissue injury.

Aim

In this study, 113 patients with primary mediastinal tumors were treated with VATS. Twenty-nine

patients had solid tumors with maximal diameter > 6 cm and 4 patients with invasive tumors were treated radically with VATS. Here we present data to show that VATS remains a safe and reliable procedure for large and invasive mediastinal tumors.

Material and methods

Patients

This study was approved by the Clinical Ethics Committee, the First Affiliated Hospital, Chongqing Medical University and conducted in accordance with the principles and guidelines laid down in the Declaration of Helsinki. One hundred and thirteen patients with primary mediastinal tumors treated in our medical center between January 2011 and December 2018 were included in our study. All the patients were treated under VATS. Patients who underwent VATS but converted to open surgery were excluded. All patients had chest computed tomography or magnetic resonance imaging for evaluating the location, texture, size, and invasion of the tumor. Computed tomography (CT) angiography and three-dimensional reconstruction of vessels were required to evaluate the association between the tumor and adjacent vital vessels. No patients received needle biopsy or mediastinoscopy before surgery. Seventeen patients with myasthenia gravis (MG) were given anticholinesterase to control symptoms before surgery under the guidance of neurologists.

Pathology

Pathology of these patients included thymoma (Masaoka stage I, 44/113), thymoma (Masaoka stage II-III, 4/113), thymic squamous cell carcinoma (2/113), Schwannoma (22/113), ganglioneuroma (2/113), thymic hyperplasia (4/113), mature teratoma (6/113), mediastinal lipoma (2/113), hemangioma (2/113), thymic cyst (14/113), bronchial cyst (8/113), pericardial cyst (1/113), epidermoid cyst (1/113), and mesenchymoma with cystic degeneration (1/113).

Surgical methods

General anesthesia and double-lumen endotracheal tube intubation were administered before the operation. The patients were placed in the supine position or lateral recumbent position. For the supine position, the observation port was placed in the subxiphoid region, while the operation ports were placed under the arch of ribs on both sides. For the lateral recumbent position, the observation port was placed at the 6th or 7th intercostal space on the mid-axillary line, while the operation ports were placed at the 3rd or 4th intercostal space on the anterior-axillary line and 6th or 7th intercostal space on the scapula line. Tumors were separated with an ultrasonic scalpel in combination with blunt separation. Titanium or biological clips were used to ligate surrounding vessels or thymic veins. The principle of tumor-free manipulation was followed during the surgery. Thymoma was treated with thymectomy, while thymoma complicated with MG, aplastic anemia (AA) or systemic lupus erythematosus (SLE) were treated with extended thymectomy. Thymomas (Masaoka stage II–III) with local invasion were treated with thymectomy or extended thymectomy as well as resection of the invaded tissues in order to achieve R0 resection. However, if radical surgery could not be achieved, palliative surgery was an alternative way.

Statistical analysis

SPSS19.0 (Chicago, IL, USA) software was used for statistical analysis. Age, maximum diameter, intraoperative blood loss, operative time, hospital stay and duration of follow-up were analyzed by quartile statistics and presented as medians. The non-parametric rank sum test was used to compare the same variable of different groups. $P < 0.05$ indicated a statistically significant difference. The prognosis was evaluated with 2-year OS and 2-year DFS. The 2-year OS was defined by the percentage of patients who have survived for 2 years after surgery, while 2-year DFS was defined by the percentage of patients who have survived for 2 years after surgery without relapse or metastasis.

Results

The demographical and clinical data are summarized in Tables I–III. There was no mortality during the perioperative period. Atrial fibrillation occurred in 1 patient without any cardiac symptoms. Three-quarters of primary mediastinal tumors (84 cases) in our study were < 6 cm in maximal diameter, while only one-quarter of the tumors (29 cases) were > 6 cm in maximal diameter. Pathology of the tumors with maximal diameter > 6 cm included thymoma

Table I. Demographic data of patients with primary mediastinal tumors treated with video-assisted thoracoscopic surgery

Parameter	Total (n = 113)	Diameter > 6 cm (n = 29)	Diameter < 6 cm (n = 84)	*P*-value	Non-invasion (n = 108)	Invasion (n = 5)	*P*-value
Gender:							> 0.05
Male	52	30	22	> 0.05	50	2	
Female	61	41	20		58	3	
Average age [years]	50	53	47	> 0.05	50	44	> 0.05
Maximal diameter [cm]	4.6	7	4.2	< 0.01	4.6	5.1	> 0.05
2-year DFS (%)	99.1	100	98.8	–	100	75	–
2-year OS (%)	100	100	100	–	100	100	–
Follow-up [months]	30	31	27	–	30	32	–
Radical or palliative:							
Radical	112	28	84	–	108	4	–
Palliative	1	1	–		–	1	
Blood loss [ml]	100	230	80	< 0.001	90	270	< 0.01
Hospital stay [days]	5	4.7	5.1	> 0.05	5	6.2	> 0.05
Operative time [min]	90	145	76	< 0.001	75	180	< 0.001
Piecemeal or *en bloc*:							
Piecemeal	3	3	0	–	2	1	–
En-bloc	110	26	84		106	4	

DFS – disease-free survival, OS – overall survival.

Table II. Clinical symptoms of patients with primary mediastinal tumors treated with video-assisted thoracoscopic surgery

Symptom	Total (n = 113)	Diameter > 6 cm (n = 29)	Diameter < 6 cm (n = 84)	Invasion (n = 5)	Non-invasion (n = 108)
Cough	15	10	5	1	14
Chest pain	16	8	8	3	13
Chest distress	11	6	5	1	10
Dizziness	2	–	2	–	2
Myasthenia gravis	17	4	13	–	17
Dermal hypoesthesia	1	–	1	–	1
Systemic lupus erythematosus	1	–	1	–	1
Aplastic anemia	1	–	1	–	1

(Masaoka stage I–III, 10/29), thymic squamous cell carcinoma (2/29), thymic cyst (4/29), neurogenic tumors (8/29), mature teratoma (1/29), bronchial cyst (1/29), pericardial cyst (1/29), mediastinal lipoma (1/29), and epidermoid cyst (1/29). Five patients had invasive mediastinal tumors, including thymoma (Masaoka stage II–III, 3/5), immature teratoma (1/5), and thymic squamous cell carcinoma (1/5). Four of these 5 patients with invasive tumors were treated with radical VATS, whereas 1 patient with thymoma (Masaoka stage III) was treated with palliative surgery. More blood loss was observed in

Table III. Clinical data of patients with primary mediastinal tumors treated with video-assisted thoraco-scopic surgery

Parameter	Total (n = 113)	Diameter > 6 cm (n = 29)	Diameter < 6 cm (n = 84)	Invasion (n = 5)	Non-invasion (n = 108)
Tumor location:					
Anterior and superior	74	24	50	5	69
Anterior and inferior	1	–	1	–	1
Middle	10	1	9	–	10
Posterior and superior	21	2	19	–	21
Posterior and inferior	7	2	5	–	7
Invaded tissues:					
Superior vena cava	2	1	1	2	–
Pericardium	5	2	3	5	–
Lung	5	2	3	5	–
Surgical mode:					
Pulmonary wedge resection	4	2	2	4	–
Lobectomy	1	–	1	1	–
Partial pericardiectomy	5	2	3	5	–
SVC angioplasty	2	1	1	2	–

patients with large tumors ($p < 0.001$) and invasive tumors ($p < 0.01$). Longer operative time was also seen in patients with large tumors ($p < 0.001$) and invasive tumors ($p < 0.001$). However, there were no differences in hospital stays after surgery between large tumors and smaller tumors ($p > 0.05$), as well as between invasive and non-invasive tumors ($p > 0.05$, Table I).

Five patients (5/113) were lost during follow-up. The median duration of follow-up was 30 months for the rest of the 108 patients. One patient with a large thymoma (Masaoka stage III) suffered a relapse at 12 months after radical surgery. This patient refused to undergo a second operation, but instead was treated with chemoradiotherapy, and has survived since the latest follow-up with slow progression of the lesion. One patient with a large thymoma (Masaoka stage III) was treated with palliative surgery plus I^{125} implantation and progressed slowly during follow-up. No relapse or metastasis appeared in other patients during follow-up. The 2-year DFS and 2-year OS for patients with large tumors were 100% and 100%, while those for invasive tumors were 75% and 100%, respectively (Table I).

All 17 patients with MG, including 14 thymomas (Masaoka stage I) and 3 cases of thymic hyperplasia, were followed up for over 24 months after extend-

ed thymectomy. MG symptoms did not improve in 6 patients: 5 thymoma (Masaoka stage I) and 1 thymic hyperplasia. The dosage and frequency of anticholinesterase medicine remained the same as before the surgery. MG symptoms significantly improved in 9 patients: 7 thymoma (Masaoka stage I) and 2 thymic hyperplasia. The dosage and frequency of drug use were reduced gradually during follow-up. MG symptoms completely disappeared in 2 patients with thymoma (Masaoka stage I). Anticholinesterase medicine was discontinued as a result. One patient with thymoma (Masaoka stage I) and SLE was followed up for 18 months. The symptoms and laboratory parameters of SLE gradually normalized. One patient with thymoma (Masaoka stage I) and AA was followed up for 24 months. There was no improvement of AA symptoms, and blood transfusion, as well as hormonal and immunosuppressive therapy, continued after surgery.

Discussion

VATS shortens hospital stay and causes less morbidity in comparison with traditional thoracotomy or sternotomy [3, 4]. In general, VATS is not recommended for mediastinal tumors with a diameter > 5 cm or local invasion. However, in this study, there

was no difference in hospital stay after surgery between patients with large tumors (maximal diameter > 6 cm) and those with smaller tumors (maximal diameter < 6 cm), and no difference in hospital stays between those with invasive tumors and those with non-invasive tumors. Our data suggest that large or invasive mediastinal tumors do not essentially prolong recovery time after VATS. The absence of increased complications in patients with large or invasive tumors indicates that VATS is safe and reliable for such mediastinal tumors.

Thymic tumors, e.g., thymoma, thymic hyperplasia and thymic squamous cell carcinoma, are primarily located at the anterior and superior mediastinum, where the space is limited yet rich in vital vessels and nerves. Thymectomy or extended thymectomy was the standard procedure for thymic tumors with or without endocrine or hematologic disorders, e.g., MG, SLE and AA [5, 6]. The extent of resection by VATS through a subxiphoid route was comparable to that by open surgery through sternotomy, suggesting that VATS can achieve satisfactory resection and good prognosis. However, limited space and poor exposure may lead to higher risks of blood loss and vital tissue injury [7, 8]. Therefore, VATS through a subxiphoid route was technically more difficult than open surgery through sternotomy. Left innominate vein and SVC are the most vulnerable organs during surgical resection of mediastinal tumors in the anterior and superior mediastinum. According to our experience, careful manipulation of surrounding vessels and the thymic vein is critical during VATS. Improper handling causes blood loss, obscures the field of vision, and may thus elongate the surgical procedure.

Our study shows that it is feasible and safe to treat large thymic tumors (maximal diameter > 6 cm) by VATS through a subxiphoid route. We did not observe prolonged hospital stay or increased perioperative complications after VATS. Our data suggest that large thymic tumors with maximal diameter > 6 cm are not a contraindication for VATS. In addition, no relapse or metastasis was seen after VATS. Thymoma (Masaoka stage II–III) was characterized by local invasion into surrounding tissues, e.g., SVC, pericardium and pulmonary parenchyma. In this study, 3 patients with thymoma (Masaoka stage II–III) were treated with radical VATS through a subxiphoid route. The involved pulmonary parenchyma can be resected with linear stapling devices, while the involved pericardium can be excised by ultrasonic scalpel. If SVC is involved, angioplasty with linear stapling devices or biological clips can be used. Therefore, we believe invasive thymic tumors are not an absolute contraindication to VATS. Most of the large thymic tumors (maximal diameter > 6 cm) were resected *en bloc* by VATS. However, in certain cases, piecemeal resection was needed for large or invasive tumors because of poor exposure during the operation. The principles of tumor-free manipulation should be followed to avoid cancer cell dissemination. It has been reported that the clinical outcomes of VATS were comparable to those of open surgery for thymoma [3, 9]. Palliative surgery is an alternative treatment that can prolong survival and produce a good prognosis even left with residual lesions.

Neurogenic tumors are primarily located in the posterior mediastinum, where the space is relatively large with less vital tissues [10]. This allows for better surgical exposure and fewer complications of vital tissues. Eight large neurogenic tumors were included in this study. However, neurogenic tumors may cause diverse clinical symptoms which are associated with direct compression of nerves, e.g., chest and back pain [10, 11]. Neurogenic tumors should be cautiously resected by ultrasonic scalpel to avoid nerve injury [12]. Also, 1 case of large mature teratoma was included in this study. Teratoma often adheres tightly to the surrounding tissues and increases the risk of VATS. Teratoma adhering to the pericardium and the lung was treated by tumor resection plus partial pericardiectomy and wedge resection of the lung by VATS. Mediastinal cysts of various sizes can be removed by aspirating the cystic fluid in advance to shrink the tumor. If the cyst wall cannot be completely removed, electrocoagulation, chemical dipping, suture or ligation are alternatives [13–16].

Conclusions

Large and invasive mediastinal tumors should not be contraindications to VATS. VATS is a reliable and safe procedure for resection of large and invasive mediastinal tumors. The prognosis of VATS for such tumors is comparable to that of traditional open surgery. Meanwhile, VATS causes less surgical trauma and perioperative pain.

Conflict of interest

The authors declare no conflict of interest.

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