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Clinical Experience with Thymic Cystectomy: A Single-Institution Study of 117 Cases from 2013 to 2019

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Background: The aim of this study was to summarize the clinical experience of thymic cysts treatment from a single center.





Material/Methods: Clinical data, imaging, pathological results, and follow-up results of thymic cyst patients who underwent surgery from January 2013 to September 2019 were retrospectively reviewed.

Results: A total of 117 patients were enrolled, including 76 asymptomatic patients and 41 symptomatic patients. The average diameter of thymic cysts, the cysts in asymptomatic patients, and those in symptomatic patients were 31.93 ± 19.92 mm, 29.28 ± 17.97 mm, and 36.85 ± 22.50 mm, respectively. The number of cysts ranged from 1 to 3 cm, 3 to 6 cm, and >6 cm in 73 cases (62.4%), 32 cases (27.3%), and 12 cases (10.3%), respectively. There was no correlation between the size of thymic cysts and the presence or absence of symptoms. Only 20 cases (17.1%) were correctly diagnosed as thymic cysts before surgery. There were 67 patients (57.3%) who underwent video-assisted thoracic surgery (VATS) and 50 cases (42.7%) underwent open surgery. Cystectomy was performed in 93 cases (79.5%) and 24 cases (20.5%) underwent simultaneous resection of thymic cysts and other thoracic tumors. Compared with the thoracotomy group, the VATS group had shorter hospital stay and chest tube indwelling time. No serious complications occurred after surgery. The median follow-up time was 45.0 months (range 4.0–84.0 months) and there was no recurrence.

Conclusions: Attention should be paid to the accuracy of preoperative diagnosis of thymic cysts and the reduction of asymptomatic thymic cystectomy. For patients who have both thymic cysts and other thoracic tumors, simultaneous surgery is safe and feasible.

MeSH Keywords: **Mediastinal Cyst • Thoracic Surgery • Treatment Outcome**

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Background

Thymic cysts are rare, and are located in the anterior superior mediastinum. Most thymic cysts cause no obvious symptoms and the main treatment strategy is follow-up [1]. In recent years, incidental mediastinal nodules have become easier to detect with the wide application of CT scans. It is reported that the prevalence of incidental anterior mediastinal lesions is 0.9%, 0.45%, and 0.73% in different populations, [2–4, respectively]. Yoon et al. found that 85.2% of mediastinal lesions were smaller than 2 cm, and their CT features were difficult to distinguish from thymic epithelial tumors (TETs). Of the 51 resected lesions, 62.8% were thymic cysts [4]. These results suggest a higher incidence of thymic cysts than ever before.

Considering that once the tumor exceeds 3 cm, the growth rate will increase and the surgery will become complicated, surgical treatment is recommended for patients with the tumors larger than 3 cm or who have symptoms [5].

It is difficult to distinguish thymic cysts smaller than 3 cm from TETs unless there are typical manifestations, such as being located in the anterior mediastinum, round shape, clear border, and CT <20 Hounsfield units (Hu). The smaller lesions are often misdiagnosed as TETs. Thymic cyst is a benign disease, but they can rupture or even progress to malignancy during long-term follow-up. Therefore, thymic cystectomy is the recommend treatment strategy. In clinical practice, cystectomy is mostly used for thymic cysts <3 cm [4,6–8].

Currently, there is controversial on surgery of asymptomatic lesions smaller than 3 cm. The controversial is mainly because postoperative pathological results found that most of these small lesions are benign. Surgery needs to be cautious since it is not clear whether early surgery has better clinical benefits [4]. In addition, inadequate knowledge of thymic cysts and preoperative misdiagnosis lead to unnecessary operations, complications, and wasted medical expenditures [9,10].

At present, there is no consensus on the surgical treatment of thymic cysts and there has been no large-sample clinical research. The choice of treatment is mostly dependent on clinical experience and knowledge. In this retrospective study, we collected data on thymic cysts that were surgically removed and pathologically confirmed in our hospital in the past 6 years, and summarized and analyzed the results to improve understanding of thymic cysts and provide evidence for clinical management.

Material and Methods

Study population

This retrospective study was approved by the Institutional Review Board (IRB No. 2020KY004) and informed consent was waived.

Patients and clinical data

All patients were initially diagnosed and treated.

Data collection

Medical records of 117 patients with thymic cysts at Shanghai General Hospital from April 2013 to September 2019 were collected in detail, including age, sex, past history of surgery and tumor, symptoms at presentation, preoperative chest CT report, surgical approach, simultaneous operation, surgical results and pathological diagnosis, postoperative complications, and recurrence.

Chest CT scan and diagnosis

In our institution, all patients received a chest CT from the lung apex to the adrenal gland at suspended maximum inspiration with 64-slice spiral CT. Slice thickness was 1.25 mm. Two board-certified experienced chest radiologists read the chest CT scans and identified the presence of the lesion in the mediastinum. They measured the longest diameter of the lesion using an electronic caliper and assessed mean CT attenuation by drawing a round region of interest. The lesion could be diagnosed as thymic cyst based on typical performance, size, location, margin, shape, and CT value. Simultaneously, the lungs, pleura, diaphragm and ribs were also observed.

Surgery and postoperative management

Surgeons performed the operation based on their clinical experience and skills. Surgical approaches included neck incision, mid-sternal incision, thoracotomy, and VATS incision. The surgical methods used were cystectomy or thymectomy. At the same time, some patients underwent lung resection or other mediastinal tumor resection.

Postoperative treatments were performed in accordance with routine thoracic surgery, including oxygen therapy, chest drainage, analgesic treatment, respiratory rehabilitation, and postoperative chest radiographs.

Pathological diagnosis

Thymic cysts were diagnosed according to pathological diagnostic criteria of the WHO. Two experienced pathologists

independently performed diagnosis and then reached a consensus.

Follow-up

The patient received first follow-up and CT scan at 3 months after the operation. Follow-up was completed yearly by telephone or at an outpatient department, and the deadline for follow-up was September 2019.

Statistical analysis

Differences were compared using the *t* test and analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables. A *P* value <0.05 was considered statistically significant. SPSS 20.0 software (2011; IBM, Armonk, NY, USA) was used for statistical analysis.

Results

Patient general information

A total of 117 patients with complete medical information were included in the study (Table 1). There were 57 males and 60 females, with an average age of 56.3 years (range, 18–81 years). Three patients had a history of malignant tumors, including 1 case of rectal cancer, 1 case of breast cancer, and 1 case of brain tumor. Nineteen cases had surgery history, including tumor resection, fracture internal fixation, and appendicitis resection. Common medical diseases included hypertension, diabetes, and pulmonary nodules. Twenty-six patients had a history of smoking and 3 patients had a history of smoking cessation. Seventy-six patients had no symptoms. Among of the 41 symptomatic patients, 16 cases had chest or back pain and posterior sternum discomfort, 23 cases had chest tightness, cough, and fever, 1 case had muscle weakness, and 2 cases had limb fractures.

CT scan results

Location of the thymic cyst

Among the 117 cases of thymic cysts, 113 were located in the anterior superior mediastinum, 2 were cervical, 1 was in the mediastinum, and 1 was in the posterior mediastinum.

Size of the thymic cyst and distribution

The average diameter of thymic cysts was 31.93 ± 19.92 mm (range, 10–112 mm), the average diameter of cysts in asymptomatic patients was 29.28 ± 17.97 mm (range, 10–100 mm), and that of symptomatic patients was 36.85 ± 22.50 mm (range, 9–112 mm). The number of thymic cysts ranged from 1–3 cm,

3–6 cm, and >6 cm in 73 cases, 32 cases, and 12 cases, respectively.

CT value of the thymic cyst

Fifty-one patients underwent plain CT scan, and the average CT value was 30.25 ± 16.12 Hu (range 4–60 Hu). Eight-six patients underwent enhanced CT scan, and the average CT value was 38.91 ± 22.02 Hu (range 5–95 Hu). Twenty people received both plain and enhanced CT scans, and the average CT values were 26.7 ± 16.33 Hu (range, 4–53 Hu), 43.4 ± 22.09 Hu (range, 6–84 Hu), respectively. A total of 71 patients received plain CT scan, and the CT values of 20 cases (17.1%) were smaller than 20 Hu.

Relationship between thymic cyst size and symptoms

In the asymptomatic group, cysts were 1–3 cm, 3–6 cm, and >6 cm in 50 cases, 21 cases, and 5 cases, respectively. In the symptomatic group, there were 23 cases, 11 cases, and 7 cases whose cysts were in the range of 1–3 cm, 3–6 cm, and >6 cm, respectively. There was no statistically significant difference between the 2 groups (Table 2).

Pathology results

All thymic cysts were benign, of which 107 were monocular and 10 were multilocular. The surgical pathology included 3 cases of lung cancer, 9 cases of lung benign nodule, 4 cases of thymoma, 1 case of thymic squamous cell carcinoma, 4 cases of thymic hyperplasia, 1 case of mature teratoma, 1 case of neuroilemmoma, and 1 case of ectopic thyroid gland.

Surgical data

The thymic cysts were removed by open surgery or VATS in 117 patients based on the surgeon's clinical skills and judgement. Surgery was performed with endotracheal intubation and general anesthesia. Frozen pathology was performed intraoperatively. The preoperatively diagnosed tumors or other thoracic tumors found intraoperatively were removed simultaneously.

Sixty-seven patients underwent VATS, 37 underwent thoracotomy, 11 underwent mid-sternal incision, and 2 underwent neck incision.

Among the 24 patients who also had other thoracic tumors, lung cancer, benign pulmonary nodules, thymoma, thymic hyperplasia were most common, and thymic carcinoma, teratoma, hamartoma, and ectopic thyroid gland were rare (Table 3).

The average diameter of cysts, surgery time, chest tube indwelling time, and length of hospital stay in the cystectomy

Table 1. Clinical characteristics of 117 thymic cyst patients.

Variables		Number	
Total		117	
Sex	Male	57	
	Female	60	
Age		56.6±13.3	
Past history	Malignancy	3	
	Surgery	19	
Smoking status	Smoking	26	
	Smoking cessation	3	
	Never	88	
Clinical symptom	Asymptom	76	
	Symptom	Cough, dyspnea, fever	22
		Pain	16
		Myasthenia gravis	1
		Other	2
CT scan	Location	Neck	2
		Anteriomediastinum	113
		Middlemediastinum	1
		Posteriormediastinum	1
	Size	1~3 cm	73
		3~6 cm	32
		>6 cm	12
CT Attenuation	Non-enhanced (n=31)		30.25±16.12
	Enhanced (n=66)		38.91±22.02
	Both (n=20)	Non-enhanced	26.7±16.33
		Enhanced	43.4±22.09
Surgical approach	VATS		67
	Thoracotomy		37
	Sternotomy		11
	Neckincision		2

Table 2. Relationship between tumor size and clinical symptoms.

	Asymptom (76)	Symptom (41)	P-value
<3 cm	50	23	0.1398
3–6 cm	21	11	0.2020
>6 cm	5	7	0.5177

group were 30.70±18.54 cm, 67.83±26.6 min, 3.67±1.43 days, and 9.98±3.56 days, respectively, whereas those in the cystectomy combined with other thoracic tumor resection group were 36.71±24.40 cm, 68.57±15.37 min, 5.4±1.51 days, and 13.93±3.71 days, respectively. There was no significant difference between the 2 groups in cyst size and surgery time.

However, the chest tube indwelling time and length of hospital stay in the cystectomy group were significantly shorter than those in the cystectomy combined with other thoracic tumor resection group, and the difference between these 2 groups was statistically significant (Table 4).

Table 3. Pathological diagnosis and surgical approach of 24 thymic cysts combined with other thoracic tumor.

	Pathological diagnosis	Number	VATS	Open surgery		
				Thoracotomy	Sternotomy	Neck incision
Lung cancer	Invasive adenocarcinoma	2	1	1		
	Minimally invasive adenocarcinoma	1		1		
	Carcinoma <i>in situ</i>	1		1		
Lung benign nodule	Atypical adenomatous hyperplasia	1	1			
	Granuloma	1		1		
	Bronchiectasis	1	1			
	Fibrous calcified tissue	4	2	2		
	Hamartoma	1		1		
Thymoma	B1	2	1	1		
	B2	2		2		
Thymic squamous cell carcinomas	1				1	
Thymic hyperplasia	4	3	1			
Mature teratomas	1				1	
Neurilemmoma	1					1
Ectopic thyroid gland	1			1		

Table 4. Surgical results of patients combined with and without other thoracic tumor.

Characteristic	With concomitant tumor (23)	Without concomitant tumor (92)	P-value
Size of thymic cysts(mm)	36.71±24.40	30.70±18.54	0.18874
Operation time/min	68.57±15.37	67.83±26.6	0.92105
Chest tube indwelling(day)	5.4±1.51	3.67±1.43	0.00189
Hospital stays(day)	13.93±3.71	9.98±3.56	0.00065

Two cases of neck incision were deleted.

Table 5. Surgical results of different surgical approaches in patients combined with thoracic tumor.

Characteristic	VATS (9)	Thoracotomy (12)	P-value
Size of thymic cysts (mm)	40.89±26.21	27.75±18.14	0.18968
Operation time/min	73.33±15.28	67.27±15.87	0.56615
Chest tube indwelling (day)	4.33±0.58	5.86±1.56	0.15158
Hospital stays (day)	13.67±4.16	14±3.79	0.89668

Two cases of median incision and one case of neck incision were deleted.

The average diameter of cysts, surgery time, chest tube indwelling time, and length of hospital stay in the VATS group were 40.89 ± 26.21 cm, 73.33 ± 15.28 min, 4.33 ± 0.58 days, and 13.67 ± 4.16 days, respectively. Those in the open surgery group were 27.75 ± 18.14 cm, 67.27 ± 15.87 min, 5.86 ± 1.56 days, and 14 ± 3.79 days, respectively. Compared with the thoracotomy group, the tumors were larger, the operation time was longer, and the chest tube indwelling time and hospital stay were shorter in the VATS group, but the differences were not statistically significant (Table 5).

Discussion

The relationship between tumor size and symptoms and surgical indication

In the present study, 76 cases (64%) were found on physical examination and had no symptoms, while 42 cases (36%) were symptomatic, of which, 23 cases (19%) complained of respiratory symptoms and 16 cases (13%) complained of chest pain. Wang et al. reported that among 108 thymic cysts, 70% cases were asymptomatic, 25% cases had respiratory symptoms, and 5% cases had chest pain [7]. Our results are in line with their study. Asymptomatic patients detected by physical examination were more than those with thymic cysts diagnosed with clinical symptoms.

The thymic cyst symptoms were mainly caused by enlargement of the tumor, which results in volume effect and leads to retrosternal pain or discomfort.

Some patients went to the hospital because of respiratory symptoms and the mediastinal lesions were therefore detected earlier with CT scan. In this study, patients with thymic cysts had a 50% chance of developing symptoms when the cyst was larger than 6 cm, while in the 3–6 cm range, 30% of them developed symptoms. If they were smaller than 3 cm, the chance of developing symptoms was only 20%. Through statistical analysis, we found that there was no correlation between the size of thymic cysts and the presence or absence of symptoms, and there is currently no literature on this relationship. These findings remind us of the importance of early detection and medical examination.

The traditional view is that surgery is considered only when thymic cysts are symptomatic. However, the current literature does not mention which are the specific symptoms and how large cysts may cause symptoms or require surgery. Currently, surgical indications for thymic cysts are considered to be cysts larger than 3 cm in diameter or associated with clinical symptoms such as chest pain and breathing discomfort. In clinical practice, surgical treatment can be also considered for some

small tumors suspected to be solid or growing rapidly, or combined with other thoracic tumors that require surgery.

In this study, the average diameter of thymic cysts was 31.93 ± 19.92 mm. According to the size distribution of cysts, there were 73 cases (62.4%) with a diameter of < 3 cm and 44 cases (37.6%) with a diameter of > 3 cm. Most studies reported that the average diameter of surgically resected thymic cysts was in the range of 1.5–2.5 cm [2,4,6,8]. Wang et al. reported that the average size of the 108 surgery-resected thymic cysts was 48.3 ± 33.7 mm at the largest diameter (range, 5–160 mm) and the average size of the retrosternal thymic cysts was 22 ± 8 mm [7].

In clinical practice, thymic cysts < 3 cm account for a large proportion of surgical resections. Surgical removal is controversial in asymptomatic patients and in patients with tumors smaller than 3 cm [4,10]. Henschke and Yoon suggested that most anterior mediastinal lesions are stable, and some of them might become smaller [3,4]. Considering that most cysts grow very slowly and sometimes become smaller, conservative treatment seems reasonable. However, another study indicated that the size of thymic cyst in 6 cases increased by 24–211% from the initial average diameter of 14.6 mm; 1 case increased by 6%, and 1 case decreased by 8% among 8 patients with an average follow-up of 6.5 years. These results suggest that these tumors grow over time, even if they are benign cysts, and will eventually need to be removed by surgery [2]. Therefore, lesion hyperplasia is not always a malignant mass and thymic cysts are also growing. Follow-up is ineffective. In addition to increasing the psychological burden, multiple CT examinations increase the risk of radiation and examination costs, and the pathology is always unclear. Even if the imaging diagnosis is benign, it might be malignant. Therefore, most surgeons prefer to perform surgery. The consequence is that surgical excision may be over-used for asymptomatic patients and for patients with small tumors, with increased complications and costs [9,10].

Based on the above discussion, we believe that considering the inaccuracy of the preoperative diagnosis and the uncertainty of tumor development, surgery for asymptomatic patients and for patients with lesions smaller than 3 cm should be carried out with caution. The purpose of this study was to improve the accuracy of preoperative diagnosis and reduce unnecessary surgical resection. It is necessary to establish a database as soon as possible to verify whether early surgery is needed.

Interpretation of CT scans

CT is a reliable method for diagnosing thymic cysts. CT sensitivity of diagnosis is affected by the size and the CT value of cysts, especial for cysts with diameter < 3 cm or CT value > 20

Hu [9]. In this study, 31.3% (16/51) of CT scans had a CT value <20 Hu, which was consistent with typical thymic cysts performance. The average CT value of plain CT was 30.25 ± 16.12 Hu (range, 4–60 Hu). The CT value is close to the density of soft tissue, which is often suspected of benign thymoma or other disease. In our study, 17.1% (20/117) of cases were correctly diagnosed with thymic cysts and confirmed pathologically. Seventeen cases (14.5%) were misdiagnosed as thymoma and 80 cases (68.4%) were diagnosed as mediastinal masses. Thus, the accuracy of the preoperative diagnosis was close to 20%. The results of this study are similar to those of other studies. For example, Araki et al. reported 18 cases of thymic cysts with an average CT value of 45 Hu. The CT value of 15 cases (83%) patients was larger than 20 Hu, and 11 cases (61%) were misdiagnosed with thymoma [11]. Therefore, diagnosis of thymic cysts only based on CT value and morphology is not reliable, and the accuracy of preoperative diagnosis is not high.

It was reported that the CT value of the viscous cystic fluid was 32.7 ± 11.3 Hu, while that of the clear cystic fluid was 10.6 ± 6.9 Hu ($P < 0.05$). This indicates the nature of the cystic fluid could affect the CT value [7]. If the cyst fluid is clear, the CT value reflects the water density. If the fluid is rich in protein or has bleeding and infection, it shows a high CT value. These phenomena are common in the clinic and cannot be known before surgery. Therefore, thymic cysts can be accurately diagnosed for low CT value, and cystic lesions cannot be excluded for high CT value.

The accuracy of preoperative CT diagnosis is low in our institution. Considering China's realistic medical environment and health law system, radiologists are more willing to adopt the cautious and conservative strategy. Thymic cysts can be identified in patients with typical manifestations such as anterior superior mediastinum, water density, clear boundary, and thin wall. If the lesion does not have typical morphology or high CT value, radiologists tend to diagnose thymic tumors or mediastinal masses. In fact, these diagnoses of thymic tumors or mediastinal masses are not obviously wrong and are acceptable. In addition, Chinese patients have more risk of infection, which may be the cause of turbidity of thymic cyst fluid, leading to high CT value, which affects the judgement of radiologists.

In recent years, MRI has been used for diagnosis of thymic cysts. The MRI manifestations of thymic cysts are T1 low signal and T2 high signal. Tomiyama et al. reported that the accuracy of CT and MRI for diagnosing of thymic cysts were 46% and 71%, respectively. The diagnostic accuracy of MRI in thymic cysts with hemorrhage or inflammation may be better in distinguishing anterior mediastinal tumors [12]. According to the consensus of the ESTS, CT is more reliable in diagnosing thymic cysts, and is superior to or equivalent to MRI in the

diagnosis of anterior mediastinum [13]. If it is used for further differential diagnosis, especially for soft tissue lesions, MRI and PET-CT examinations can also provide more diagnostic information [14,15].

In our hospital, CT is generally the first choice. CT was used to diagnose mediastinal tumors and this also meets the restrictions of medical insurance policies. In addition, CT can check for lesions in lungs, ribs, pleura, and chest wall. In this study, lung nodules and larger mediastinal tumors were clearly diagnosed before surgery. However, some small thymomas and thymic carcinomas were not diagnosed before surgery, probably because the bigger thymic cysts covered the small tumors.

Simultaneous operation

Thymic cysts combined with other thoracic tumors were previously thought to be rare [7,16]. In recent years, with the wide use of CT scans, many incidental and asymptomatic lung nodules and mediastinal masses diseases were detected. Based on the large population of China, even with a small incidence of diseases, there are a large number of patients. In this study, patients with pulmonary nodules or other mediastinal masses accounted for about 20% of patients (Table 3). Another explanation is that our hospital is a bigger regional medical center and more patients with complex diseases are referred by practitioners

Few studies have reported the feasibility and safety of simultaneous surgery for thymic cyst in patients who also have other thoracic tumors. In this study, we successfully performed resection for lung nodules or other mediastinal lesions during the removal of thymic cysts. The results showed that the size of thymic cysts and operation time in the simultaneous operation group were similar to those of the single cystectomy group. The length of hospital stay and chest tube indwelling time in the single cystectomy group were shorter than in the simultaneous operation group. Although simultaneous operations involve more trauma and slower recovery, the results indicate the safety and feasibility of simultaneous surgery.

In recent years, VATS has been recommended in mediastinal tumor resection because it involves less trauma, shorter hospital stay, and less pain, and results in less visible scarring [17,18]. For patients with thymic cysts combined with other thoracic tumors, which is an advantage of simultaneous excision, VATS or thoracotomy? In this study, compared with the thoracotomy group, the VATS group has some advantages, which may be due to causing less trauma and faster recovery (Table 5). In terms of operation time, there is no obvious advantage in the VATS group compared with the thoracotomy group because the open surgery for thymic cyst resection is simple. In addition, the VATS surgery time will not be significantly reduced

for beginners, because a learning process is required. Overall, the operation time, chest tube indwelling time, and length of hospital stay in our study are similar to those reported in the literature [7,19]. With increasing technical proficiency, the advantages of VATS surgery will become apparent for patients with thymic cysts combined with other thoracic tumors.

Pathological results and follow-up

In this study, all thymic cysts were benign after pathological diagnosis. No recurrence of thymic cysts was found during long-term follow-up, indicating the effectiveness of surgical treatment and the benign nature of the thymic cysts.

Malignancy is possible with any benign tumor, including thymic cysts, but the incidence is very low and only a few cases have been reported [20].

Limitation

The limitations of this study include its single-center and retrospective design.

Conclusions

The diagnosis and treatment of thymic cysts require further research. The accuracy of preoperative diagnosis based on CT examination should be further improved, and the use of resection for asymptomatic or smaller thymic cysts should be reduced. For thymic cysts combined with other thoracic tumor, simultaneous surgery is safe and feasible.

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Conflicts of Interest

None.

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