

# Characteristics of Thymoma Successfully Resected by Videothoroscopic Surgery

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## Abstract

**Purpose.** The inclusion criteria were established for a videothoroscopic resection of early-stage thymoma. We retrospectively evaluated the validity of these criteria in the treatment of early-stage thymoma.

**Methods.** The computed tomography (CT) image characteristics and clinical information comprised these criteria. The image considerations included the location of the tumor in the anterior mediastinum, a distinct fat plane between the tumor and vital organs, unilateral tumor predominance, tumor encapsulation, the existence of residual normal-appearing thymic tissue, and no mass compression effect. All enrollees were expected to be free of pleural effusion, pericardial effusion, paralysis of the hemidiaphragm, and the encasement of great vessels. An elevation of either the serum  $\alpha$ -fetoprotein or  $\beta$ -human chorionic gonadotropin levels, severe chest pain, superior vena cava syndrome, hoarseness, and age less than 20 years excluded the patient from enrollment. The heterogeneous content of the tumor was not an exclusion criterion, and the tumor size was not considered important. According to the above criteria, 44 patients were enrolled between November 1999 and November 2005.

**Results.** Twenty-seven patients had stage I thymoma and 17 had stage II thymoma. All patients successfully underwent a complete tumor resection using a three-port endoscopic technique. There was no open conversion.

**Conclusions.** Based on these criteria, we can select suitable patients to confidently perform a thoracoscopic resection of early-stage thymoma.

**Key words** Thoracoscopy · Thymoma · Minimally invasive surgery · Thymomectomy · Mediastinum

## Introduction

Thymoma is the most common primary tumor in the anterior mediastinum in adults.<sup>1</sup> A total surgical resection of the tumor is curative for resectable tumors.<sup>2,3</sup> For Masaoka stage I thymoma, a videothoroscopic (VTS) resection has already been accepted as an alternative approach to a well-established sternotomy.<sup>4–9</sup> For stage II thymoma, we have reported our preliminary findings showing beneficial results using a VTS resection.<sup>8,10</sup> To our knowledge, there has been no report in the literature describing the criteria for the selection of thymoma that can be resected by VTS. We therefore reviewed the image characteristics of computed tomography (CT) and the clinical information of all our VTS-resected tumors, and summarize the results. All these patients were selected under the preliminary criteria which were set up to decide whether a VTS resection can be successfully performed to treat early-stage (Masaoka I and II) thymoma.

## Patients and Methods

Between November 1999 and November 2005, 101 cases of primary mediastinal lesions were resected with a curative intent. Of these, 44 patients (25 women, 19 men) were enrolled for a VTS resection. The CT image characteristics and clinical information comprised these enrollment criteria. Computed tomography image considerations included the location of the tumor in the anterior mediastinum, a distinct fat plane between the tumor and vital organ, unilateral tumor predominance, tumor encapsulation, existence of residual normal-appearing thymic tissue, and no mass compression effect. The enrollees were expected to be free of pleural effusion, pericardial effusion, paralysis of hemidiaphragm, and the encasement of great vessels. The elevation of the serum  $\alpha$ -fetoprotein (AFP) or  $\beta$ -human

**Table 1.** Patient profiles

Stage	Age (years)	Sex (male:female)	Mean size (cm)	Follow-up (months) <sup>a</sup>
I	40.4 ± 18.8	9:18	7.1 × 3.9 × 2.1	39.6
II	42.3 ± 14.9	9:8	8.5 × 4.9 × 2.6	26.6

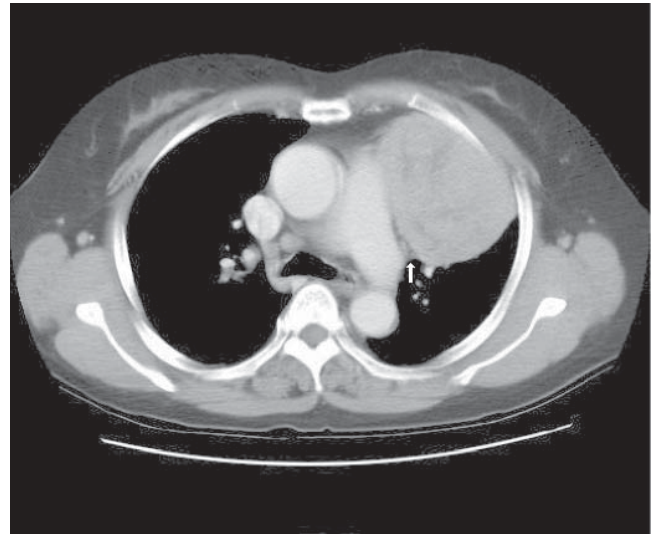
<sup>a</sup> All patients were alive during the follow-up period

chorionic gonadotropin (hCG) levels excluded the patient from enrollment. Other exclusion criteria included severe chest pain, superior vena cava syndrome, and hoarseness. An age of less than 20 years was considered to be a relative exclusion criterion. The heterogeneous content of the tumor was not an exclusion criterion, and the tumor size was not considered important.

The patients were placed in the lateral decubitus position with the chest wall draped as for a thoracotomy. They all underwent a complete thymoma resection using a three-port endoscopic technique, with the camera port in the 6th intercostal space (ICS), posterior-axillary line. The locations of the other two ports were selected after the target tumor was visualized, usually in the 4th ICS, mid-axillary line and 5th ICS, anterior-axillary line, respectively. The sizes of the three port-incisions were all 1 cm at the beginning of the procedure. At the end, one of the port sites was extended to remove the mass, usually about 2–3 cm in size without spreading. The dissection plane was initiated from the pericardial area towards the neck base. The normal thymus tissue, if it existed, was removed together with the tumor. In the case of a large tumor, which obstructed the manipulation space, the tumor was removed from the thoracic cavity before the normal thymus tissue was dissected. The peri-tumor loose tissue was swept away from the tumor by a blunt dissection, and the adhesion band was dissected by a coagulation hook. Injury to the phrenic nerve was strictly avoided. The thymic vein and other large vessels were clipped with endo-clippers. If the freed mass was too large to be removed with a retrieval bag, we then would cut it piece by piece in a double-layered bag for removal. One chest tube (32 F) was routinely retained after the operation. The diagnoses of all resected lesions and their stages were confirmed by clinical and histopathological examinations. Adjuvant radiation therapy was regularly given for all cases of stage II thymoma. Regular chest radiography, and CT if needed, were performed during the follow-up examinations.

## Results

There were no deaths, open conversion, or major complications in these 44 patients. The mean age of the patients was 41.1 ± 17.2 years. The mean blood loss was



**Fig. 1.** Computed tomography image. The thymoma has a one-sided predominance and is well encapsulated. The fat plane between the tumor and pulmonary vessel is preserved (arrow)

118.6 ± 84.0 ml and the mean operation time was 194.0 ± 76.0 min. Twenty-seven patients had Masaoka stage I thymomas and 17 had stage II thymomas. The mean duration of hospitalization was 7.6 ± 6.9 days. All patients survived without any sign of recurrence during the follow-up period of 34.6 months. The patient profiles are summarized in Table 1.

Among these 44 patients, the level of serum AFP and β-hCG were all within the normal limits. None had malignant clinical presentations of severe chest pain, superior vena cava syndrome, or hoarseness. On CT, the anterior mediastinal location of the tumor, tumor encapsulation, and a distinct fat plane between the tumor and vital organ were found in all 44 patients. The predominant location of the tumor was on the unilateral side (Fig. 1) and this was detected in 40 of the 44 patients (91.0%). The existence of a residual normal-appearing thymic tissue (Fig. 2) on CT imaging was found in 38 patients (86.4%). All were free of pericardial effusion, paralysis of the hemidiaphragm, and mediastinal great vessel encasement. There was only one case with minimal pleural effusion on the ipsilateral side of the tumor (2.3%). There was no mass compression affecting the heart in any patient (Fig. 3). The heterogeneous content of the tumor (Fig. 2) was not an exclu-

sion sign; 14 patients (31.8%) had heterogeneous tumor content on CT image. The mean size of the resected tumors was  $7.8 \times 4.4 \times 2.4$  cm with the largest tumor being 18 cm long. The data profiles are summarized in Table 2.

## Discussion

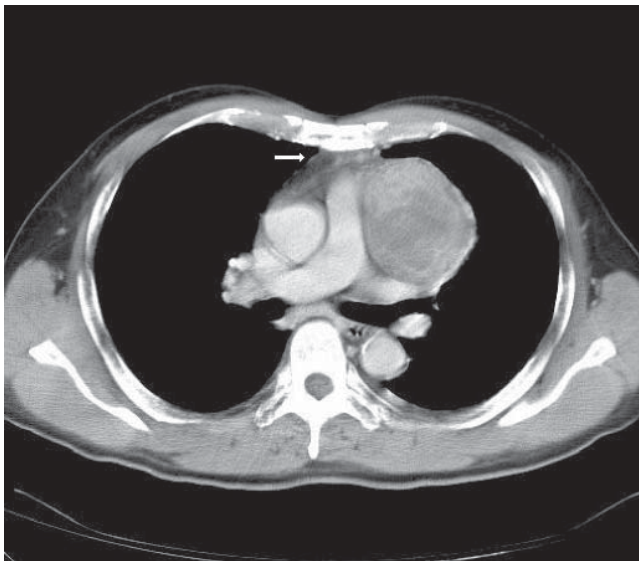
The objective treatment of thymoma is the complete removal of the tumor and all involved structures.<sup>2,8,11</sup> The extension of the resection is almost the same for both the videothoracoscopic surgery (VTS) and trans-sternal approaches.<sup>10,12</sup> We use the term “videothoracoscopic surgery” instead of “video-assisted thoracoscopic surgery” in this article to emphasize that there is no accessory thoracotomy needed in the VTS procedure. Therefore, VTS surgery, which has the advantage of

a small incision and rapid recovery, offers a better-tolerated approach to treat thymoma. Because it is minimally invasive and has an acceptable resection extent, we thus consider resection of thymomas by VTS to meet both anatomic and surgical requirements for successful treatment. The mean duration of 7.6-day hospitalization was somewhat long for a three-port minimally invasive technique, and this might be due to the associated myasthenia gravis (MG) in 15 patients (34.1%).

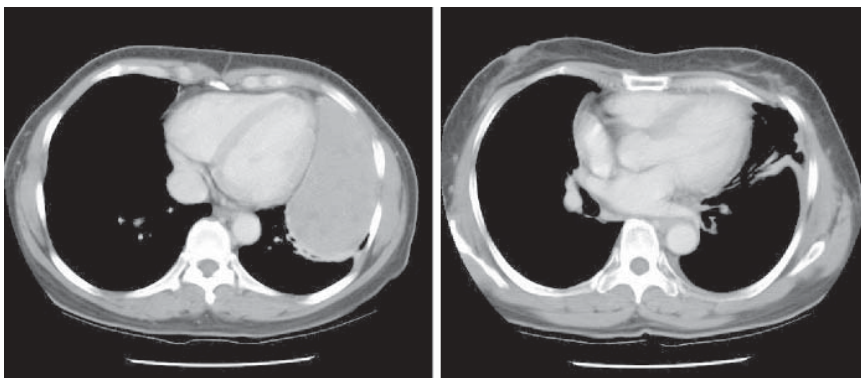
Thymoma has been reported to be best detected by chest CT, with an 85% sensitivity, a 98.7% specificity, and a 95.8% accuracy rate.<sup>13</sup> Most thymomas are located in the upper anterior mediastinum.<sup>14,15</sup> Therefore, one of our image characteristics is the anterior mediastinal location of the tumor. Although there is no hallmark to identify an anterior mediastinal mass as a thymoma, the existence of thymoma can be speculated if there is any residual normal thymic tissue beside the mass.

Thymoma usually arises from a single thymic lobe and then it typically extends unilaterally to one side of the mediastinum, but bilateral extension is rarely observed.<sup>16</sup> For a VTS complete resection of thymoma, the tumor location on the unilateral side is the most important consideration. It is difficult to remove a bilaterally extending tumor via a one-sided approach, especially endoscopically. However, for small-sized thymomas, a central location is not a contraindication for an endoscopic approach as shown in our four cases.

The CT images of tumor encapsulation and a distinct fat plane between the tumor and vital organ are indicative of noninvasiveness, in contrast to the thymomas showing malignant CT characteristics as demonstrated by invasion or tumor spread.<sup>17</sup> A lack of mediastinal fat obliteration does not rule out capsular invasion, but when these planes are preserved, then extensive invasion and disease are unlikely.<sup>1</sup> We therefore select our VTS cases strictly to make sure that they fulfill this criterion. This is one of the reasons that we have no open conversion in all our VTS cases.



**Fig. 2.** Computed tomography image. The existence of normal thymic tissue (*arrow*) and the heterogeneous content of the tumor in a case of a thymoma resected by videothoracoscopic surgery



**Fig. 3a,b.** Computed tomography image. **a** The mass compression effect to the heart is negative in a case of a thymoma resected by videothoracoscopic surgery (VTS). **b** A film of the same patient 2 weeks post-VTS resection taken for radiation therapy which showed a complete VTS resection

**Table 2.** Clinical data and computed tomography image profiles

	Positive No.	Percentage
Clinical characteristics		
AFP and hCG	0	0
Severe chest pain	0	0
Superior vena cava syndrome	0	0
Hoarseness	0	0
Age less than 20 years	2	4.5
Image characteristics		
Anterior mediastinal location of the tumor	44	100
Tumor encapsulation	44	100
Distinct fat plane between tumor and vital organ	44	100
Predominant location of tumor in unilateral side (Fig. 1) detected in 14 patients (87.5%)	40	91.0
Existence of normal-appearing thymic tissue	38	86.4
No pericardial effusion	44	100
No paralysis of hemidiaphragm	44	100
No mediastinal great vessel encasement	44	100
No pleural effusion	43	97.7
No mass compression effect to the heart	44	100
Heterogeneous content of the tumor	14	31.8

AFP,  $\alpha$ -fetoprotein; hCG,  $\beta$ -human chorionic gonadotropin

There is no mass compression effect to the adjacent heart on CT images in all our 44 cases, which may be a sign of elastic content. The elastic nature of the tumor is beneficial for tumor manipulation, which is a key point for successful VTS performance. The CT images of pleural effusion, pericardial effusion, great vessel encasement, and paralysis of the hemidiaphragm are indicative of more invasive tumors, and therefore they are classified as VTS-unresectable. Despite a well-described propensity for pleural metastasis, pleural effusions are rarely associated with thymoma.<sup>18</sup> Indeed, we have rarely encountered any operable thymoma, even in an open sternotomy, which involves pleural or pericardial effusion. Pericardial and pleural effusions are frequently seen on imaging of thymic carcinoma,<sup>14</sup> but not in thymoma. Mediastinal lymph node involvement is the major cause of pleural and pericardial effusion in cases of advanced mediastinal malignancy, which is rarely seen in noninvasive thymoma.

The heterogeneous content of the tumor is not an exclusionary sign from the macroscopic view that although most thymomas are solid, necrosis, hemorrhage, and cystic degeneration can be seen in up to 33% of all cases.<sup>1</sup> Furthermore, in our experience, the VTS resection of thymoma is not contraindicated even if the tumor border is irregular or local lung infiltration is noted on CT imaging. We can remove the locally involved lung tissue endoscopically. Whether the tumor size is a prognostic marker across the various thymomas and thymic carcinoma subtypes is still not clear.<sup>11</sup> A large tumor size is not considered an absolute contraindication to VTS-resected surgery based on the fact that a tumor measuring 18cm in size was VTS-resected in our

study. A large tumor size, however, does interfere with the VTS procedure while also increasing the chance of an open conversion.

In general, the differential diagnoses of patients presenting with a mass in the anterior mediastinal compartment are also guided by the patient's age, sex, and associated symptoms, besides the appearance on CT.<sup>19</sup> Clinically, an elevation of serum AFP or of  $\beta$ -hCG is an indicator of a germ cell tumor,<sup>20</sup> and therefore such patients are excluded from our list. Age is also a consideration. If the patients are under 20 years of age they are excluded from our list because thymomas are less likely.<sup>21</sup> However, two of our patients were less than 20 years old and they were enrolled for a VTS thymomectomy owing to an association with MG, which highlighted the thymoma risk. The patients demonstrating either locally advanced or disseminated thymoma at the time of presentation are usually symptomatic with significant chest pain, in contrast to those with localized thymoma and vague chest pain.<sup>19</sup> We therefore excluded the former patients from our list.

Magnetic resonance imaging (MRI) rarely adds much additional information to an optimally performed contrast-enhanced CT scan, particularly in the era of multidetector CT (MDCT) scans.<sup>15</sup> However, Sakai et al. demonstrated that Masaoka Stage I and II thymomas have an earlier peak enhancement than Stage III thymoma.<sup>22</sup> However, their findings are inconclusive. The role of positron emission tomography (PET) in the evaluation of thymoma is also not conclusive.<sup>23,24</sup> For cases suspected to be thymoma, MRI and PET are not used for a routine evaluation in our institute.



Adjuvant radiation therapy for stage II thymoma is widely advocated, but the evidence supporting it remains controversial.<sup>25</sup> According to the reports of Singhal et al.<sup>25</sup> and Mangi et al.,<sup>26</sup> adjuvant radiation therapy does not improve the prognosis of completely resected stage II thymoma. Therefore, the adjuvant radiation therapy used in our study is not considered to affect the outcome.

We believe this is the first report in the literature confirming the criteria set up for performing a successful resection of thymoma by VTS. The paper would offer significantly more insight into these criteria if we could describe the characteristics of lesions where VTS was attempted but proved to be unsuccessful. However, there was no conversion to an open sternotomy based on these criteria.

## Conclusion

Based on these criteria, it is desirable to distinguish thymomas from more advanced ones in order to select suitable patients for a VTS resection.

## References

1. Maher MM, Shepard JO. Imaging of thymoma. *Semin Thorac Cardiovasc Surg* 2005;17:12–9.
2. Mehran R, Ghosh R, Maziak D, O'Rourke K, Shamji F. Surgical treatment of thymoma. *Can J Surg* 2002;45:25–30.
3. Ströbel P, Marx A, Zettl A, Müller-Hermelink HK. Thymoma and Thymic Carcinoma: An Update of the WHO Classification 2004. *Surg Today* 2005;35:805–11.
4. Tarrado X, Ribo JM, Sepulveda JA, Castanon M, Morales L. [Thoracoscopic thymectomy]. *Cir Pediatr* 2004;17:55–7.
5. Yoshino I, Hashizume M, Shimada M, Tomikawa M, Tomiyasu M, Suemitsu R, et al. Thoracoscopic thymectomy with the da Vinci computer-enhanced surgical system. *J Thorac Cardiovasc Surg* 2001;122:783–5.
6. Yim AP. Video-assisted thoracoscopic resection of anterior mediastinal masses. *Int Surg* 1996;81:350–3.
7. Roviario GC, Rebuffat C, Varoli F, Sonnino D, Vergani C, Maciocco M, et al. Major thoracoscopic operations: pulmonary resection and mediastinal mass excision. *Int Surg* 1996;81:354–8.
8. Cheng YJ, Wu HH, Chou SH, Kao EL. Video-assisted thoracoscopic management of mediastinal tumors. *JSLs* 2001;5:241–4.
9. Kaiser LR. Thymoma. The use of minimally invasive resection techniques. *Chest Surg Clin North Am* 1994;4:185–94.
10. Cheng YJ, Kao EL, Chou SH. Videothoracoscopic resection of stage II thymoma: prospective comparison of the results between thoracoscopy and open methods. *Chest* 2005;128:3010–2.
11. Strobel P, Bauer A, Puppe B, Kraushaar T, Krein A, Toyka K, et al. Tumor recurrence and survival in patients treated for thymomas and thymic squamous cell carcinomas: a retrospective analysis. *J Clin Oncol* 2004;22:1501–9.
12. Mack MJ, Scruggs G. Video-assisted thoracic surgery thymectomy for myasthenia gravis. *Chest Surg Clin North Am* 1998;8:809–25, viii;discussion 827–34.
13. Ellis K, Austin JH, Jaretzki A. Radiologic detection of thymoma in patients with myasthenia gravis. *AJR* 1988;151:873–81.
14. Strollo DC, Rosado-de-Christenson ML, Jett JR. Primary mediastinal tumors: part II. Tumors of the middle and posterior mediastinum (see comment). *Chest* 1997;112:1344–57.
15. Wright CD, Mathisen DJ. Mediastinal tumors: diagnosis and treatment. *World J Surg* 2001;25:204–9.
16. Rosado-de-Christenson ML, Galobardes J, Moran CA. Thymoma: radiologic-pathologic correlation. *Radiographics* 1992;12:151–68.
17. Vail CM, Ravin CE. Mediastinal masses. In: Freundlich IM, Bragg DG, editors. *A radiologic approach to diseases of the chest*. Baltimore: Williams & Wilkins; 1992. p. 361.
18. Verstandig AG, Epstein DM, Miller WT Jr, Aronchik JA, Geftter WB, Miller WT. Thymoma—report of 71 cases and a review. *Crit Rev Diagn Imaging* 1992;33:201–30.
19. Cameron DW, Kenneth AK. Surgical treatment of thymic tumors. *Semin Thorac Cardiovasc Surg* 2005;17:20–6.
20. Klein EA. Tumor markers in testis cancer. *Urol Clin North Am* 1993;20:67–73.
21. Wychulis AR, Payne WS, Clagett OT, Woolner LB. Surgical treatment of mediastinal tumors: a 40 year experience. *J Thorac Cardiovasc Surg* 1971;62:379–92.
22. Sakai S, Murayama S, Soeda H, Matsuo Y, Ono M, Masuda K. Differential diagnosis between thymoma and non-thymoma by dynamic MR imaging (see comment). *Acta Radiol* 2002;43:262–8.
23. Liu RS, Yeh SH, Huang MH, Wang LS, Chu LS, Chang CP, et al. Use of fluorine-18 fluorodeoxyglucose positron emission tomography in the detection of thymoma: a preliminary report. *Eur J Nucl Med* 1995;22:1402–7.
24. Sasaki M, Kuwabara Y, Ichiya Y, Akashi Y, Yoshida T, Nakagawa M, et al. Differential diagnosis of thymic tumors using a combination of 11C-methionine PET and FDG PET. *J Nucl Med* 1999;40:1595–601.
25. Singhal S, Shrager JB, Rosenthal DI, LiVolsi VA, Kaiser LR. Comparison of stages I–II thymoma treated by complete resection with or without adjuvant radiation. *Ann Thorac Surg* 2003;76:1635–41;discussion 1641–52.
26. Mangi AA, Wright CD, Allan JS, Wain JC, Donahue DM, Grillo HC, et al. Adjuvant radiation therapy for stage II thymoma. *Ann Thorac Surg* 2002;74:1033–7.