

Video-assisted thoracoscopic thymectomy for early-stage thymoma: A review

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Abstract

Minimally invasive thoracoscopic surgery has become a popular technique to remove lung and mediastinal tumors. Video-assisted thoracic surgery (VATS) thymectomy has been performed for early-stage (Masaoka stages I/II) thymomas during the past two decades. Several reports have stated that VATS thymectomy for early stage thymomas appears safe and feasible. This technique is associated with a shorter hospital stay and has oncologic outcomes comparable with those of trans-sternal thymectomy. Other researchers have found no difference in the short-, mid-, or long-term prognosis between VATS and trans-sternal thymectomy. However, evaluation of the long-term oncologic outcomes of VATS thymectomy for early stage thymoma using national registries and randomized controlled trials is difficult because thymoma is a rare tumor. The present study was performed to investigate the history of, indications for, advantages and disadvantages of, and future potential problems associated with VATS thymectomy for treatment of early stage thymoma (Masaoka stages I/II).

Introduction

Thymoma is a common primary tumor that appears in the anterior mediastinum [1] and represents 50% of all anterior mediastinal tumors [2]. The incidence of thymomas, however, is low (0.15 cases per 100,000 person-years) [3].

According to the Japanese Association for Thoracic Surgery, video-assisted thoracic surgery (VATS) thymectomy was performed to treat 765 (35.8%) of 1904 thymomas in 2013, and this number has increased each year since then [4]. The National Comprehensive Cancer Network (NCCN) guidelines [5], however, note that minimally invasive procedures are not yet routinely recommended because of the lack of long-term data. Additionally, VATS thymectomy should be performed in specialized centers by surgeons with experience using these techniques. We herein discuss the use of VATS thymectomy for early stage thymoma (Masaoka stages I/II) [6].

Definitive surgery for early stage thymoma

The most relevant prognostic factors for thymoma are the tumor stage [7-9], World Health Organization histologic type [7,8,10], and completeness of the resection [11-13]. The NCCN guidelines [5] state that the goal of open surgery is complete resection.

What, then, should be the extent of definitive surgery for treatment of clinically early-stage thymoma? Of 122 thymomas reviewed at the Massachusetts General Hospital [14], 28.5% surgeries reported to be pathologically encapsulated showed microscopic evidence of true capsular invasion. Among other series involving >100 patients, an average of 81% of all recurrences were local, 9% were distant, and 11% involved both sites [15-18]. Among patients with recurrence, the pleural space or lung was involved in 58% (most often as a nodule under the parietal pleura), pericardium or mediastinum in 41%, bone in 10%, and liver in 8% [15-18]. This high incidence of local recurrence is a characteristic feature of thymomas.

Thymomas do not commonly metastasize to regional lymph nodes. A survey of 1327 patients from 115 specialized institutions certified by the Japanese Association of Chest Surgery revealed a 2% (19/1064)

incidence of lymph node metastases in patients with a thymoma (0.4% in stage I, 6.0% in stage III) [19]. However, how often nodes were examined in that study was unclear. Moreover, no routine policy appears to have been in place regarding whether (or which) nodes were biopsied or dissected. Detterbeck et al. [20] recommended removal of adjacent nodes and anterior mediastinal nodes even for stage I/II thymomas. Whether removal of lymph nodes is needed for early stage thymomas is controversial. However, it is at least necessary to perform complete resection for early stage thymoma.

Complete resection of thymomas

Zielinski et al. [21] and Ponseti et al. [22] reported that ectopic thymic tissues exist and possibly represent local recurrence (Figure 1). Scelsi et al. [23] also reported that remnants of the thymus may remain in extrathymic fat (pretracheal, anterior mediastinal, and costophrenic areas) and therefore recommended extended thymectomy. Removal of all ectopic thymic tissue is difficult, but at least the extrathymic fat must be resected.

Extended Thymectomy refers to *en bloc* resection from the superior to inferior pole of the thymus with the thymoma, including pretracheal fatty tissues and lymph nodes. The resection extends inward from the bilateral phrenic nerves, including the mediastinal pleura, and upward from costophrenic areas, including the fatty tissue; the pericardial leaves are also removed. The resection limits are the lower portion of the thyroid (top), pericardiophrenic fat (bottom), phrenic nerve (side), and pericardium (back). The resection include the cervical fat, perithymic fat, aortocaval groove fat, aortopulmonary window fat, and pericardiophrenic fat. However, Nakagawa et al. [24]

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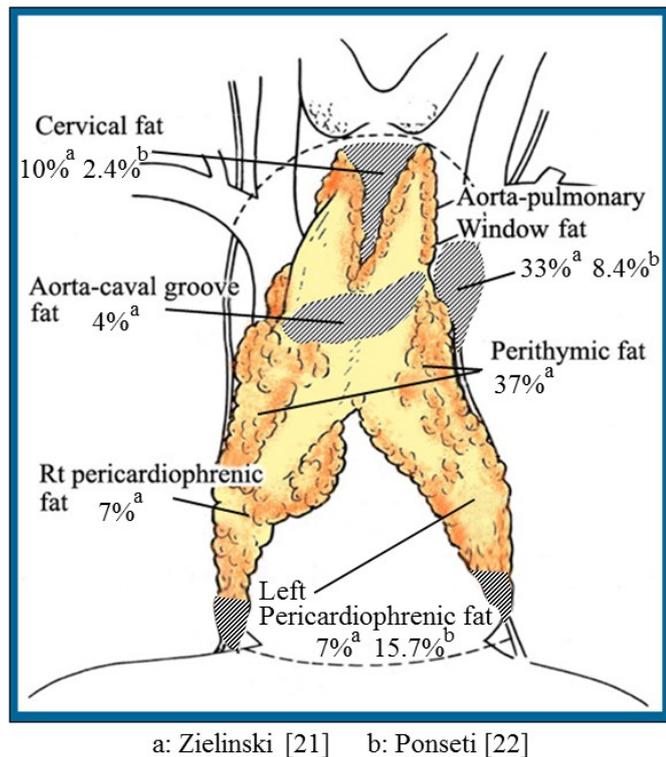


Figure 1. Distribution and percentages of ectopic thymic tissue.

Rt- Right, ^aFrom Zielinski et al. [21], ^bFrom Ponseti et al. [22]

reported that there was no significance different in prognosis between thymomectomy (resection of thymoma with partial thymectomy) group and a thymothymomectomy (resection of thymoma with total thymectomy) group for stage I nonmyasthenic thymoma during open surgery. So, Extended Thymectomy may be needed for early-stage Thymoma with myasthenia gravis, but whether this procedure is needed for early-stage nonmyasthenic thymomas is controversial.

Technical problems of VATS complete resection of thymoma

The thymus is located in the anterior mediastinum immediately behind the sternum. The bilateral innominate veins, superior vena cava, and pericardium are located toward the back and the mediastinal pleura, bilateral intrathoracic arteries and veins, phrenic nerves, and lungs are located laterally. The most difficult point of thymectomy is the extent of excision required within the narrow working space. The surgeon must also be aware of the above-mentioned vessels and nerves near the thymus, especially the bilateral brachiocephalic veins, intrathoracic arteries and veins, thymic veins and arteries, and superior vena cava. The lungs and pericardium are also located in close proximity to the thymus, and the thymoma is sometimes firmly adherent to or invades the lung and/or pericardium. Each of these conditions contributes to the technical difficulty of VATS thymectomy in patients with thymomas.

History of VATS thymectomy

Throughout the history of developing various thoracoscopic approaches to the thoracic cavity, Landreneau et al. [25] were the first to report an approach from the left side of the thoracic cavity in 1992 and Yim et al. [26] from the right side of the thoracic cavity in 1995. Roviario et al. [27] described a bilateral approach in 1993. Takeo et al. [28] reported a combined transcervical/subxiphoid and bilateral

thoracic cavity approach in 2001, Mantegazza et al. [29] reported a cervical and bilateral approach in 2003, and Hsu et al. [30] reported a subxiphoid right-sided approach in 2004.

Recent advances in thoracoscopic technology have encouraged surgical experts to extend new approaches to more extensive procedures, including the treatment of thymic tumors. Several approaches have been established following these efforts. Several sternum-lifting methods (Figure 2) and several approaches to the tumor have been used to solve the problems associated with the narrow working space while maintaining a safe surgical environment.

Several one-sided approaches [31-37] have been described, as have unilateral and bilateral approaches [38-41], a transcervical approach [42,43], bilateral access with an optional cervical incision [32], and a combined transcervical/subxiphoid and bilateral approach [35]. Finally, investigators have performed VATS thymectomy involving the combination of several approaches with or without sternum-lifting methods. Figure 3 shows the advantages and disadvantages of each approach with respect to anatomical difficulties.

The transcervical method is an easy approach with respect to the location of the pretracheal fat and brachiocephalic vein, but it is difficult to resect large tumors or reach the lower portions of the thymus and pericardiophrenic fat. The incision for this method is long and located at the neck; a special apparatus is necessary. The mid-sternum technique can be used to easily approach the tumor, but it is difficult to distinguish the upper portion of the tumor from the brachiocephalic vein. Additionally, this method is a difficult and dangerous approach within the thoracic space, even if thoracoscopy is used.

The trans-subxiphoid method provides easy access to the lower portion of the mediastinum but makes it difficult to resect the upper portion of the thymus and fat tissue. Resection of the thymic veins is also difficult using this method because the forceps lie parallel to the veins; thus, a special apparatus is required.

Sternum-lifting methods avoid these disadvantages, but whether these lifting methods are necessary remains unclear. We do not believe that a lifting method is necessary when thymectomy is the only procedure performed in a patient with a thymoma. When complete resection of thymoma is performed, however, a lifting method could be useful to secure the working space and maintain a safe surgical environment.

Indications for VATS thymectomy

Thoracoscopic resection of bulky or invasive thymomas remains technically challenging and controversial [44,45]. No consensus regarding the tumor size limit for VATS thymectomy has been established. Most investigators agree that the procedure is technically feasible for thymomas up to 5 cm in diameter [32,39,44,46,47]. We believe that the most important criteria for selecting VATS thymectomy depend more on the lack of tumor invasion to the great veins and pericardium than on the tumor size alone. The imaging characteristics that indicate tumor invasion have been widely studied [48,49] and should be considered when selecting a surgical approach. Finally, VATS thymectomy should be indicated in patients with a Masaoka early-stage thymoma.

Current state of VATS thymectomy compared with trans-sternal thymectomy

We found several major series that reported the outcomes of VATS thymectomy for treatment of thymoma [36,38,41,44]. VATS thymectomy for early stage thymoma appears safe and feasible. This

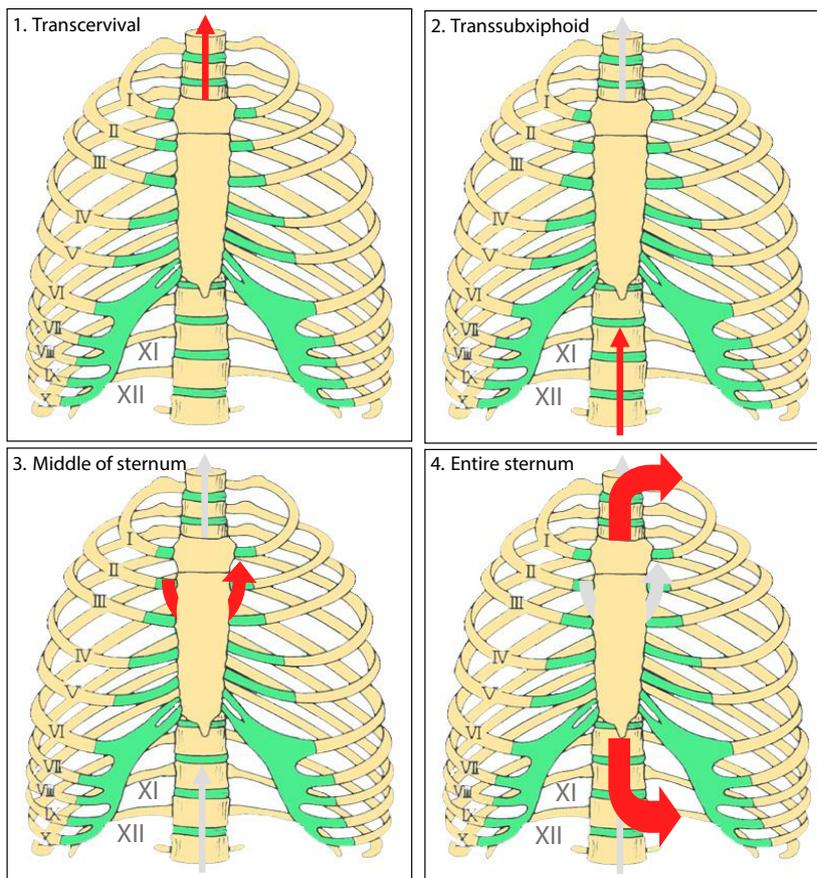


Figure 2. Several sternum-lifting methods

Approach	Working space	Vessel			Nerves		Lung	Pericardium	Tumor resection	Anatomical problem
		Brachiocephalic vein	Intrathoracic vein and artery	Thymic vein and artery	Phrenic nerve	Recurrent nerve (left)				
Trans-cervical	Limited	Possible	Possible	Possible and partially difficult	Difficult	Good	Impossible	Difficult	Limited to small tumor	Impossible to resect large tumor; impossible to approach lower portions of thymus
One-sided trans-intrathoracic	Limited but same side: good Other side: limited	Possible and partially difficult	Same side: good Other side: difficult	Possible and partially difficult	Same side: good Other side: difficult	Impossible	Good	Good	Needed intercostal thoracotomy; postoperative pain	Impossible to resect cervical portion; difficult to approach another part of the thymus
Bilateral trans-intrathoracic	Good	Possible	Good	Good	Good	Impossible	Good	Good	Needed intercostal thoracotomy; postoperative pain	Difficult to resect cervical portion
Trans-subxiphoid	Limited	Possible and partially difficult	Possible and partially difficult	Possible and partially difficult	Possible and partially difficult	Impossible	Possible	Possible	No need for thoracotomy	Difficult to resect cervical fat portion completely; difficult to approach the upper portion of the left innominate vein
Our method [33]	Good	Good	Good	Good	Good	Good	Good	Good	No need for thoracotomy	No problems

Figure 3. Advantages and disadvantages of each approach

technique is associated with a shorter hospital stay and has oncological outcomes comparable with those of trans-sternal thymectomy [31,34–38,40,41,47].

The completeness of resection of early stage thymomas with VATS thymectomy or trans-sternal thymectomy seems to be equally good [32,38,41,44]. VATS thymectomy is not yet recommended in the NCCN guidelines because the long-term prognosis has not been evaluated. However, several studies have found no difference in the short-term [33,38,47], mid-term [34,40,41], and long-term prognoses [50,51] between VATS and trans-sternal thymectomy. Because port-site recurrence in association with VATS thymectomy has been reported [52], surgeons must take care to avoid contact between the tumor surface and port tracts during this procedure to prevent tumor cell implantation.

Required standard for long-term prognosis of VATS thymectomy

Three factors are important when considering the long-term prognosis: the overall survival rate, disease-free survival (DFS) rate, and recurrence rate. Among series investigating open surgery in >200 patients with stage I and II disease, the 5-year overall survival rate was 89-100% and 71-98%, respectively, and the 10-year overall survival rate was 80-100% and 60-98%, respectively [53,54]. Several studies involving >100 patients found that the average 10-year DFS rate for stage I and II disease was 92% and 87%, respectively [56-59].

Several authors have reported that during open surgery for treatment of thymoma, an average of 38% (range, 19-58%) of deaths were related to the primary tumor, 9% (range, 2-19%) to postoperative causes, 22% (range, 16-27%) to myasthenia gravis, 9% (range, 2-19%) to other autoimmune diseases, and 29% (range, 8-47%) to unrelated causes (including other cancers) [53,56-59]. Patients rarely die of a thymoma-related cause. Hence, the DFS rate may be a better measure than the overall survival rate when determining the effectiveness of a surgical treatment.

Verley and Hollmann [60] reported that the mean time to recurrence following open surgery is 10 years in patients with a stage I thymoma and 3 years in patients with a stage II, III, or IV thymoma. A postoperative observation period of at least 10 years is needed for patients with a stage I thymoma. It is possible that overall survival and DFS rates of 15 years after VATS thymectomy for treatment of early stage thymoma will be recommended. However, because thymomas are rare tumors, it is needed to evaluate the long-term oncological outcomes of VATS thymectomy for early stage thymoma in national registries and randomized controlled trials.

Conclusion

If VATS thymectomy can be performed to the same extent as surgery with a trans-sternal incision, the functional and cosmetic advantages for the patient are unquestionable. Complete resection, defined as resection of all thymic tissue along with the thymoma itself, is also necessary for patients with a clinical early stage thymoma. VATS thymectomy could therefore be indicated in patients with a clinical early stage thymoma.

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Conflict of interest

Authors declare no conflicts of interest.

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