Intermediate-term oncologic outcomes after video-assisted thoracoscopic thymectomy for early-stage thymoma

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Objective: To evaluate the impact on patient survival of video-assisted thoracoscopic surgery (VATS) thymectomy for the treatment of early-stage thymoma, by comparing the intermediate-term oncologic outcomes with outcomes after open thymectomy.

Methods: Eighty-two patients who underwent complete resection of a Masaoka stage I or II thymoma between November 1998 and December 2011 were reviewed.

Results: The patients included 32 men and 50 women (median age, 57 years; range, 20-90 years), of whom 44 had stage I thymoma and 38 had stage II thymoma. Seventy-one patients underwent VATS, of whom 4 (5.6%) underwent conversion to open thymectomy; the remaining 11 patients underwent planned open thymectomy. Thirty-six patients underwent total thymectomy and 46 underwent partial thymectomy. Operative mortality was nil. The tumor stage, tumor size, and proportion of patients who underwent total thymectomy were not significantly different between the open and VATS thymectomy groups. The median follow-up period was 49 months (VATS, 48 months; open, 52 months). There was a significant difference between the 2 groups for the estimated 5-year overall survival (VATS, 97.0%; open, 79.5%; $P = .041$) but not in the estimated 5-year recurrence-free survival.

Conclusions: Our findings indicate that the intermediate-term oncologic outcomes after VATS thymectomy for early-stage thymoma are as favorable as outcomes after open thymectomy. Further follow-up is still required to evaluate the long-term outcomes after VATS thymectomy. (J Thorac Cardiovasc Surg 2014;148:1230-7)

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Supplemental material is available online.

Complete resection is the most important aspect of treatment to prolong survival in patients with any stage of thymoma.[1-4] In stage I or II (early-stage) thymoma, thymectomy usually achieves complete resection of the tumor, resulting in favorable oncologic outcomes.[1-5] Independently of the favorable outcomes after open thymectomy, advances in both equipment and expertise for video-assisted thoracoscopic surgery (VATS) have expanded the use of VATS thymectomy for the treatment of early-stage thymoma over the past 2 decades.[6-10] However, few data have been published regarding the long-term oncologic outcomes (10 years or longer) of VATS thymectomy compared with open thymectomy. Although many reports have suggested that VATS thymectomy for early-stage thymoma is technically feasible and safe, long-term follow-up data are not yet available.[7-10]

The appropriate extent of thymectomy for complete resection of thymoma also remains unclear. Many investigators recommend complete resection of the thymoma with complete resection of the thymus, even in patients without myasthenia gravis (MG) and without evidence of involvement of the rest of the thymus.[1,11] However, it is not clear whether total thymectomy (TTx) results in a better prognosis than tumor resection alone (thymomectomy).[2,3,8,9] Nakagawa and colleagues[3] studied a series of 126 patients, and found no difference in survival between patients who underwent TTx and those who underwent thymomectomy. Although some studies have reported on short-term outcomes after VATS partial thymectomy (PTx) for early-stage thymoma without MG, the long-term oncologic outcomes of this procedure remain unclear.[8,9]

This article presents our single-center experience of the surgical treatment of early-stage thymoma over a 13-year period. VATS was the most common surgical approach, and VATS PTx was performed more frequently than VATS TTx. The aim of this study was to evaluate the impact

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Abbreviations and Acronyms

CT = computed tomography
MG = myasthenia gravis
MRI = magnetic resonance imaging
OS = overall survival
PTMG = postthymectomy myasthenia gravis
PTx = partial thymectomy
RFS = relapse-free survival
TTx = total thymectomy
VATS = video-assisted thoracoscopic surgery

on patient survival of VATS thymectomy for the treatment of early-stage thymoma by analyzing intermediate-term oncologic outcomes. Outcomes after PTx in patients with thymoma who did not have clinical signs or laboratory evidence of MG were also evaluated.

MATERIALS AND METHODS

Our experience of the surgical treatment of stage I and II thymoma at the Department of Chest Surgery, Osaka Police Hospital, between November 1998 and December 2011 is reviewed. The study was approved by the institutional review board of Osaka Police Hospital. The preoperative diagnosis of noninvasive thymoma was based on computed tomography (CT) and/or magnetic resonance imaging (MRI) findings, without biopsy, according to the criteria previously described.[12,13] The final diagnosis of thymoma was based on histologic examination findings during and after surgery. Frozen section examination of the resected specimen was performed during surgery in all cases to ensure clear surgical margins. The Masaoka staging system[14] was used to define stage I and II thymoma. The World Health Organization classification system[15,16] was used to classify tumors according to histologic subtype A, AB, B1, B2, or B3. Patients with advanced-stage disease or with type C or carcinoid tumors were treated differently and were excluded from this study.

Patient Characteristics

Among the 105 patients who underwent complete resection of a thymic epithelial tumor during the study period, 82 had stage I or II thymoma. The process of patient selection is shown in Figure E1. All patients had a single mass in the thymus on imaging examinations, with no evidence of multifocal tumor. These 82 patients included 32 men and 50 women (mean age, 57 years; range, 20-90 years), of whom 44 had stage I thymoma and 38 had stage II thymoma. Thirty-six patients underwent TTx and 46 underwent PTx. VATS thymectomy was planned in 71 patients and open thymectomy in 11 patients. Of the 71 VATS procedures, 67 were completed as planned, and 4 were converted to open resection. Twenty-nine patients (35%) had coexisting MG. The patient characteristics are shown in Table 1.

Surgical Approaches and Procedures

The criteria for selecting the surgical approach were as follows. VATS thymectomy was planned if the tumor characteristics on CT and/or MRI were noninvasive, and open thymectomy was planned if tumor invasion of the great vessels or the pericardium was suspected or could not be excluded. VATS thymectomy was converted to open thymectomy via median sternotomy if there were severe adhesions that were difficult to distinguish from vascular or pericardial invasion, or if there was bleeding from a major vessel that could not be controlled by compression. TTx was performed according to the extended thymectomy criteria described by Masaoka and colleagues,[17] and involved en bloc resection of the thymus with the perithymic adipose tissues between the phrenic nerves and from the diaphragm to the thyrothymic lamina. PTx was usually subtotal thymectomy, but included a variety of procedures ranging from hemi- to subtotal[8] thymectomy, depending on the size and location of the tumor. The decision to perform TTx was based on the presence of MG, regardless of the surgical approach.

Details of Video-Assisted Thoracoscopic Thymectomy

During unilateral or bilateral VATS thymectomy, the thymus including the thymoma was resected as previously described.[8,18] Briefly, the patient was placed in the supine position under general anesthesia, and the trachea was intubated with a double-lumen tube. Three ports were placed between the anterior and midaxillary lines on the side of operation. For the bilateral approach, these ports were placed on each side when entering the respective hemithorax. The perithymic tissues and thymoma were bluntly dissected and excised, using a 30° angled 5-mm-diameter telescope and surgical instruments. The thymic veins were meticulously dissected and divided using an ultrasonically activated device or a bipolar vessel-sealing system. For TTx, a cervical incision or chest wall lifting method[18] was not always required. After resection, 1 of the ports was enlarged to allow extraction of the specimen in a plastic bag. In some patients with a bulky tumor, the specimen was extracted through a subxiphoid incision. TTx was performed via a subxiphoid approach with a sternum-lifting method (Laparolift and Laparofan system; Origin Medsystems, Menlo Park, Calif) as previously described[19] from 1998 to 2007, and via a transthoracic approach from 2008 to 2011.

Collection of Data

Data on patient demographics, tumor characteristics, tumor stage, presence of MG, extent of thymectomy, surgical approach, duration of operation, surgical complications, and adjuvant therapy were collected. The Osserman score and Myasthenia Gravis Foundation of America grade were recorded in patients with MG before and after surgery. CT was performed every 6 months after surgery for the first year and yearly thereafter, to screen for signs of disease recurrence.

Statistical Analysis

The primary end point was overall survival (OS) and the secondary end point was relapse-free survival (RFS). Statistical analyses were performed according to the intention-to-treat principle. The actuarial OS and RFS curves were calculated using the Kaplan-Meier method, and differences between survival curves were analyzed using the log-rank test. Patients were censored for OS at the time of the last follow-up. RFS was defined as the time from thymectomy to the detection of relapse. Patients who died of non−thymoma-related causes with no evidence of relapse were censored at the time of death. Patient characteristics were compared between the open and VATS thymectomy groups and between the TTx and PTx groups using the χ^2 test for categorical variables and the Student t test for continuous variables. The mean values were compared between subgroups using one-way analysis of variance. The Cox proportional hazards model was used for multivariate analyses of prognostic factors.

RESULTS

Tumor Characteristics in Patients Who Underwent Open Versus Thoracoscopic Thymectomy

There were no significant differences between the open and VATS thymectomy groups in terms of age, male/female ratio, proportions who underwent TTx and adjuvant radiotherapy, or proportion with improvement of MG after