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SHORT COMMUNICATION

Survival outcomes after minimally invasive thymectomy for early-stage thymic carcinoma

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Abstract

Minimally invasive surgery (MIS) has occasionally been used for selected patients with thymoma, but there is little information on the MIS approach for thymic carcinoma. The aim of this study was to evaluate survival outcomes after MIS for early-stage (Masaoka stage I–II) thymic carcinoma and thymic neuroendocrine carcinoma. A retrospective chart review of the cases recorded in our multi-institutional database was performed to identify patients who underwent resection for thymic carcinoma between 1995 and 2017. MIS thymectomy was performed in 17 cases (VATS, $n=14$; RATS, $n=3$. male, 41%; median age, 72 years). The median follow-up period was 32.7 (range 7.4–106) months. The five-year overall survival and relapse-free survival rates were 84.4% and 77.8%, respectively. The present study demonstrated encouraging preliminary results regarding MIS for the treatment of early-stage thymic carcinoma and thymic neuroendocrine carcinoma. Further studies with a larger sample size are required to evaluate the indications for this surgery.

Keywords Thymic carcinoma · Minimally invasive surgery · Survival

Thymoma and thymic carcinoma are rare malignancies of the mediastinum [1]. Patients undergoing resection of thymoma have a 5-year overall survival (OS) rate of approximately 90% [2, 3], while that for thymic carcinoma is only approximately 55% [4]. Thymic carcinomas are more aggressive tumors and their worse prognosis in comparison to thymomas is due to frequent metastasis to regional lymph nodes and extrathoracic sites [4]. Thus, survival after the complete resection of thymic carcinoma is more favorable than that after incomplete resection or surgical biopsy [5].

To the best of our knowledge, it is unknown whether a minimally invasive approach results in acceptable long-term survival in patients undergoing surgical resection of early-stage (Masaoka stage I or II) thymic carcinoma. Recently, minimally invasive surgery (MIS), including video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracoscopic surgery (RATS), has been used for the treatment of thymoma, although MIS is not routinely recommended due to a lack of long-term data [6, 7]. The feasibility of MIS for thymic carcinoma and thymic neuroendocrine carcinoma is uncertain because these tumors have a significantly worse oncological prognosis and a higher incidence of lymph node and distant metastasis in comparison to thymoma [8]. Thus, the purpose of this study was to evaluate the survival

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outcomes after MIS for early-stage thymic carcinoma and thymic neuroendocrine carcinoma.

This study was approved by the Kyoto University Hospital Institutional Review Board (IRB) and the IRBs at Nishi-Kobe Medical Center, Tenri Hospital, Kitano Hospital, Nagara Medical Center, and Otsu Red Cross Hospital, all of which waived the need for consent for this study. A retrospective chart review was performed to identify patients who underwent thymectomy with curative intent for thymic carcinoma or neuroendocrine carcinoma in the databases of the above six hospitals between May 1995 and July 2017. Patients were classified into the MIS group if resection was performed via VATS or RATS. VATS was performed by a unilateral or bilateral approach with three or four ports and a 10 mm and 30-degree thoracoscope. RATS was performed by a unilateral approach in view of tumor locations with three to four ports under carbon dioxide insufflation. The selection of the MIS approach was at the discretion of the attending surgeon in patients with early-stage tumors on preoperative radiological staging [chest and abdominal computed tomography (CT), and positron emission tomography (PET)-CT]. Patients were classified into the open group if resection was performed via sternotomy or thoracotomy.

The patients' background information (age and sex), intraoperative and perioperative data (surgical approach, extent of resection, completeness of resection, postoperative complications, drainage duration, postoperative hospital stay, postoperative mortality, and postoperative radiotherapy), pathological information (histology, maximum diameter of the specimen, lymph node metastasis, pathological Masaoka stage, and pathological TNM classification based on the Eighth Edition of the International Union for Cancer Classification for thymic epithelial tumor), and follow-up information (relapse site, treatment for relapse, and cause of death) were included in the analysis. Overall survival (OS) was calculated from the date of surgery until death or the last clinic visit. Relapse-free survival (RFS) was calculated from the date of surgery to the time of recurrence, death, or the last clinic visit if the patient remained recurrence free. The diagnosis of relapse was confirmed radiologically (CT with or without PET). RFS and OS were analyzed using the Kaplan–Meier method. All analyses were performed using the JMP® 13 software program (SAS Institute Inc., Cary, NC, USA).

Seventeen patients who underwent MIS were identified (VATS, $n=14$; RATS, $n=3$). The median follow-up period was 32.7 (range 7.4–106) months. A preoperative biopsy of thymic malignancy was not attempted in any case because all of the tumors were deemed resectable. The characteristics of these patients are shown in Table 1. A unilateral approach was adopted in 5 cases (29%, VATS 3; RATS 2), and a bilateral approach was adopted in 12 cases (71%). Total thymectomy (by bilateral VATS) was performed in 8 cases (47%), and partial thymectomy with resection of the tumor was performed in 9 cases (53%). Two patients (12%) underwent wedge resection of the lung. The pathological diagnosis was early-stage thymic carcinoma in 13 patients (76%), 4 (24%) of whom had pathological Masaoka stage III disease (all pathological stage IIIA). Complete resection was performed in 14 cases (82%) and a positive margin was found in 3 (pericardium, lung, and unknown, respectively). The 5-year OS and RFS rates were 84.4% and 77.8%, respectively (Fig. 1a, b).

Table 1 Patient characteristics

Item	($n=17$)
Median age (range)	72 (52–86)
Male gender	7 (41%)
Unilateral approach	5 (29%)
Pathological Masaoka stage I–II/III	
Partial thymectomy	7 (41%)/2 (12%)
Total thymectomy	6 (36%)/2 (12%)
Additional resection	2 (12%)
Tumor size	
Mean ± SE (mm)	26.9 ± 4.4
< 50 mm/≥50 mm	15 (88%)/2 (12%)
Histology	
Sq	8 (47%)
NETT	2 (12%)
Sq + NETT	1 (6%)
Others	5 (29%)
Unknown	1 (6%)
Pathological Masaoka stage	
I/II/III	1 (6%)/12 (70%)/4 (24%)
Lymph node metastasis	
No/not available	16 (94%)/1 (6%)
Surgical margin status	
R0/R1	14 (82%)/3 (18%)
Postoperative complication	1 (6%)
Drainage duration (days, $n=15$)	
Median (range)	2 (1–4)
Postoperative hospital stay (days, $n=15$)	
Median (range)	6 (3–50)
Postoperative mortality	0 (0%)
PORT	8 (47%)
Interval from surgery to PORT (days, $n=7$)	
Median (range)	29 (14–59)

MIS minimally invasive surgery, *SE* standard error, *Sq* squamous cell carcinoma, *NETT* neuroendocrine thymic tumor, *PORT* postoperative radiotherapy

Patients who underwent open thymectomy (median sternotomy or open thymectomy) for preoperative and pathological Masaoka stage I–II were compared to those who underwent MIS (Supplemental Table, Supplemental Figs. 1 and 2). The 5-year OS rates of patients with clinical early-stage tumors after open surgery and MIS were 72.9% and

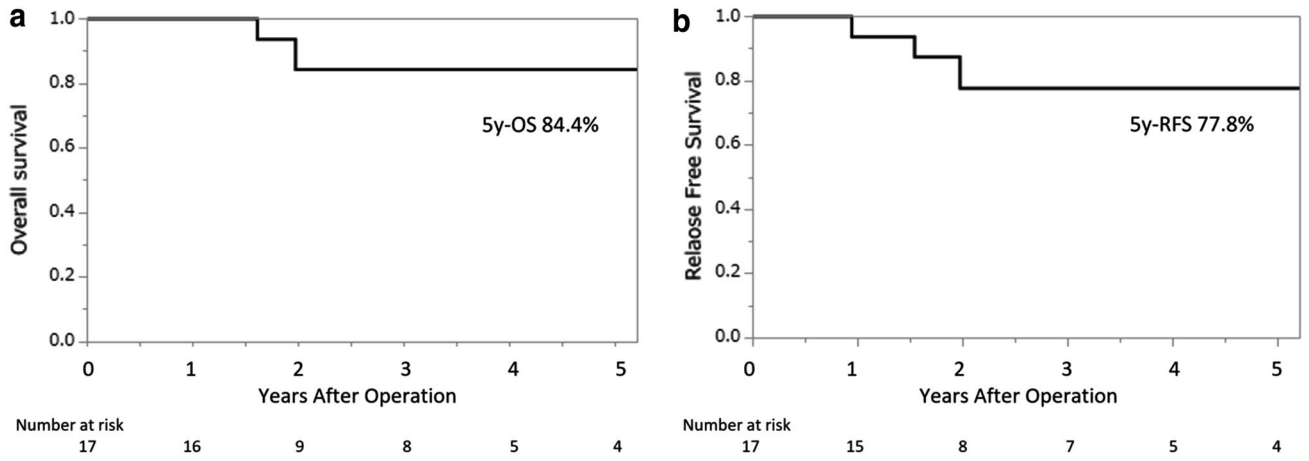

Fig. 1 **a** Overall survival (OS) curve after minimally invasive thymectomy. **b** Relapse-free survival (RFS) curve after minimally invasive thymectomy

80.8%, respectively, while the 5-year RFS rates were 60.0% and 72.5%. In contrast, the 5-year OS rates of patients with pathological early-stage tumors after open surgery and MIS were 83.3% and 80.2%, respectively, and the 5-year RFS rates were 88.9% and 80.2%.

To our knowledge, this is the first report to describe the survival outcomes after MIS thymectomy for thymic carcinoma and thymic neuroendocrine carcinoma. VATS is a less invasive approach for patients with thymic malignancies [9–12]. Although there have been no data from studies that were limited to thymic carcinoma, the advantage of MIS may also apply to patients with early-stage thymic carcinoma. Our major finding is that MIS thymectomy may be an acceptable approach for early-stage thymic carcinoma, as well as thymoma. The open approach is a time-honored procedure for the resection of thoracic malignancies, whereas there is a dearth of data for the MIS approach. Complete resection is the most critical prognostic factor for long-term survival in patients with thymic carcinoma [5], and complete resection was achieved in 82% of our patients. In our study, 76% of MIS the patients were diagnosed with pathological Masaoka stage I–II disease. An early Masaoka stage is a good prognostic factor and 5-year OS and RFS were 80% and 85%, respectively [13]. Thus, an early Masaoka stage may contribute to good survival in MIS. In our study, the 5-year OS rate of patients undergoing MIS for early-stage thymic carcinoma was 80.2%, showing favorable long-term survival in these patients. Although the WHO classification was associated with survival [14], our data suggested that an MIS approach is reasonable in selected patients with early-stage thymic carcinoma (previously WHO type C, Supplemental Fig. 3). We intentionally did not compare MIS with an open approach for thymic carcinoma because there is presumably a bias between these groups. For example, there was a tendency toward older age and early thymic carcinoma in the MIS group. The reason for the older age was unclear, while the tendency toward early-stage disease would be attributed to an anatomical reason, as was reported in a previous study [12]. We hypothesize that the tendency toward older age reflected each surgeon's preference. The favorable survival outcomes after MIS suggest that this surgery may be acceptable in selected patients; however, it should be noted that the results from the present study are preliminary. Furthermore, it is difficult to comment on when to convert to open thoracotomy. Due to the lack of robust statistical analyses, we should keep the discussion open. Our limited experience suggests that MIS may be associated with favorable survival in patients with thymic carcinoma, which may mean that conversion to open thoracotomy or sternotomy is not always necessary, even if an intraoperative frozen section shows thymic carcinoma or neuroendocrine carcinoma. Rather, we should convert to open without hesitation when it is necessary to secure negative margins.

The present study is associated with several limitations, including the retrospective design, the short follow-up period and the small sample size, which influenced the power of the study. We were unable to include standardized uptake values from positron emission tomography to evaluate the possibility of thymic carcinoma preoperatively, and a unilateral MIS approach cannot evaluate pleural dissemination on the opposite side. Thus, further prospective studies in more patients and the accumulation of more data are required. Despite these limitations, the present study demonstrated encouraging preliminary results regarding the performance of MIS for the treatment of early-stage thymic carcinoma and thymic neuroendocrine carcinoma.

Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest in association with the present study.

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