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Surgical approach for the treatment of thymic carcinoma: 201 cases from a multi-institutional study

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ABSTRACT

Purpose: This study aimed to compare the outcomes of surgical approach (video-assisted thoracoscopic surgery [VATS] vs. sternotomy vs. thoracotomy) for the treatment of thymic carcinoma

Methods: We retrospectively reviewed 201 patients with pathologically proven thymic carcinoma who underwent surgical resection at four Korean institutions.

Results: From 2007 to 2013, 158 sternotomy, 33 VATS and 10 thoracotomy were conducted for thymic carcinoma. Open group underwent more preoperative biopsy (41.8% and 50% vs. 15.2%, P=0.012) and neoadjuvant treatment (22.2% and 30% vs. 0%, P=0.008) than VATS group. In preoperative imaging, tumor size of VATS group was smaller than sternotomy group (3.8±1.1 cm vs. 5.8±2 cm, P<0.05) and 91% of the VATS group was clinical tumor-node-metastasis (TNM) stage I. The lengths of chest tube and mechanical ventilation duration, postoperative hospital day and intensive care unit stay were shorter in VATS group than open group (P<0.001). The incidence of postoperative complications of VATS group was lower than sternotomy group (P=0.014). The 5-year overall survival of the sternotomy, VATS and thoracotomy group were 100%, 100% and 87.5%±11.7%, respectively (P=0.107). The 5-year recurrence-free survival rate was not significantly different between the groups (55.4%±4.5%, 67.9%±12.1%, and 87.5%±11.7%; P=0.131)

Conclusion: The VATS approach of surgical treatment for thymic carcinoma can be selectively employed in small (<5 cm) and TNM stage I tumor without compromise of oncologic outcome.

Keywords: Thymus neoplasms; Carcinoma; Thoracic surgery, video-assisted

INTRODUCTION

Thymic carcinoma is malignant tumor originating from the thymic epithelium, and it represents a very heterogeneous group of lesions with a wide spectrum of morphologic and prognostic features [1]. Thymic carcinoma is very rare, and only several studies on prognostic factors and treatments have been reported so far. According to most studies, surgical resection is the mainstay of treatment for thymic carcinoma [2-4].

Conventional transsternal approach has long been accepted as standard method of treatment for thymoma and thymic carcinoma. However, device developments and technological advances led to successful application of the minimally invasive approach for thymoma. Recently, minimally invasive procedure such as video-assisted thoracoscopic surgery (VATS) has been performed more frequently for resection of early-stage thymoma. Many literatures have reported the oncologic outcomes of VATS thymectomy for the treatment of thymoma. They showed that VATS thymectomy had less postoperative pain, the length of hospitalization and favorable oncologic outcomes [5-10]. In spite of the advantage of minimally invasive approach, the application of VATS for early-stage thymic carcinoma has controversy because of its poor prognosis and the lack of long-term data.

The present study was aimed to compare the outcomes of surgical approach (VATS vs. sternotomy vs. thoracotomy) for the treatment of thymic carcinoma.

METHODS

Study cohort

Korean Association for Research on the Thymus (KART) developed a multi-institutional database in 2014, and retrospectively collected the data of 1,663 patients with thymic epithelial tumor who underwent surgical treatment and biopsy between 2000 and 2013 at four Korean institutions. The KART database included patient characteristics, preoperative and pathologic tumor size, preoperative and final pathological Masaoka-Koga stage, pathological World Health Organization (WHO) classification, histologic type, type of resection, resection status, perioperative therapies, treatment, pattern of recurrence, and survival.

A total of 256 patients with pathologically proven thymic carcinoma underwent surgery. Among them, 201 patients underwent thymectomy via sternotomy (n=158), VATS (n=33), or thoracotomy (n=10). Patients who underwent diagnostic (n=17) or debulking surgery (n=8), operation for recurrence (n=16) and operation via other approach including transcervical, clamshell and sternotomy combined with thoracotomy (n=14) were excluded. We were classified histologic type according to latest WHO classification and thymic neuroendocrine tumors and type B3 thymomas were excluded.

This study was approved by Institutional Review Board of Samsung Medical Center (2017-03-006). Informed consent was waived by the board.

Statistical analysis

Continuous data are described by mean ± standard deviation and categoric data by frequencies and percentages. Comparison of preoperative baseline characteristics between three groups was analyzed by Kruskal-Wallis test for continuous variables, and the Pearson's chi-square and Fisher's exact tests for categorical variables, when appropriate.

The Kaplan-Meier method was used to analyze overall survival (OS) and recurrence-free survival (RFS). The log-rank test was used to assess the differences between survival rates. Univariate and multivariate Cox regression analyses were employed to evaluated OS and RFS prognostic factors. Chi-square test and Fisher's exact test, when appropriate, were used to evaluate the difference between groups. The statistical analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Patient characteristics

From January 2000 to December 2013, a total of 201 patients (158 sternotomy, 33 VATS, and 10 thoracotomy) were included in this study. Sex, age, smoking history, symptom, performance status, pulmonary function, body mass index, and comorbidity were not different between the groups. Open group including sternotomy and thoracotomy underwent preoperative biopsy and neoadjuvant treatment more frequently than VATS group. Baseline patient characteristics are summarized in Table 1.

Factors associated with undergoing VATS

Patients who underwent VATS had tumor less than 5 cm ($P<0.001$) and clinical tumor-node-metastasis (TNM) stage I International Association for the Study of Lung Cancer/International Thymic Malignancies Interest Group (IASLC/ITMIG) 8th edition ($P=0.001$). Furthermore, tumor without vascular invasion on preoperative computed tomography (CT) were

Table 1. Patient characteristics

Characteristic	Sternotomy (n=158)	VATS (n=33)	Thoracotomy (n=10)	P-value
Male sex	109 (69)	19 (57.6)	7 (70)	0.433
Age (yr)	57.7±10.6	60±11.7	59.2±8.1	0.497
Smoking history				0.551
None	73 (46.2)	20 (60.6)	5 (50)	
Ex-smoker	48 (30.4)	8 (24.2)	4 (40)	
Current smoker	37 (23.4)	5 (15.2)	1 (10)	
Symptom				0.188
None	89 (56.3)	25 (75.8)	5 (50)	
Chest pain	43 (27.2)	3 (9.1)	2 (20)	
Cough	13 (8.2)	2 (6.1)	1 (10)	
Face/arm swelling	3 (1.9)	0	0	
Dyspnea	9 (5.7)	2 (6.1)	2 (20)	
ECOG				0.283
0	127 (80.9)	28 (84.8)	7 (70)	
1	29 (18.5)	4 (12.1)	3 (30)	
2	1 (0.6)	0	0	
3 or 4	0	1 (3)	0	
FEV1 (% predicted)				0.557
≥80	110 (81.5)	21 (91.3)	7 (77.8)	
<80	25 (18.5)	2 (8.7)	2 (22.2)	
DLCO (% predicted)				0.847
≥80	62 (73.8)	10 (71.4)	5 (62.5)	
<80	22 (26.2)	4 (28.6)	3 (37.5)	
BMI (kg/m^2)	24±3.1	23.8±1.8	25.2±2.7	0.338
Comorbidity				
Diabetes	19 (12)	3 (9.1)	1 (10)	0.911
Hypertension	52 (32.9)	9 (27.3)	5 (5)	0.407
Chronic obstructive pulmonary disease	6 (3.8)	1 (3)	0	1.000
Autoimmune disease	1 (0.6)	1 (3)	0	0.383
Preoperative biopsy	66 (41.8)	5 (15.2)	5 (50)	0.012
Neoadjuvant treatment	35 (22.2)	0	3 (30)	0.008
Concurrent chemoradiation	5 (3.2)	0	0	
Chemotherapy	28 (17.7)	0	3 (30)	
Radiotherapy	2 (1.3)	0	0	
Response of neoadjuvant treatment				0.031
Partial response	21 (77.8)	0	2 (66.7)	
Stable disease	6 (3.8)	0	1 (33.3)	

Values are presented as number (%) or mean±standard deviation.
VATS, video-assisted thoracoscopic surgery; ECOG, European Cooperative Oncology Group; FEV1, forced expiratory volume in 1 second; DLCO, diffusing capacity of the lung for carbon monoxide; BMI, body mass index.

Table 2. Operative findings, procedures and pathologic findings

Variable	Sternotomy (n=158)	VATS (n=33)	Thoracotomy (n=10)	P-value
Extent				<0.001
Thymomectomy	17 (10.8)	19 (57.6)	5 (50)	
Partial thymectomy	7 (4.4)	7 (21.2)	1 (10)	
Total thymectomy	134 (84.8)	7 (21.2)	4 (40)	
Tumor size	6.4±2.3	4.6±1.8	3.9±2	<0.001
Lymph node dissection	80 (50.6)	8 (24.2)	6 (60)	0.015
Additional procedure	133 (84.2)	9 (27.3)	9 (90)	<0.001
Lung, wedge resection	92 (58.2)	5 (15.2)	5 (50)	<0.001
Lung, segmentectomy	2 (1.3)	0	1 (10)	0.209
Lung, lobectomy	5 (3.2)	1 (3)	2 (20)	0.079
Diaphragm, resection	2 (1.3)	0	1 (10)	0.209
Pericardium, resection	80 (50.6)	4 (12.1)	7 (70)	<0.001
Innominate vein, resection	46 (29.1)	0	2 (20)	<0.001
Phrenic nerve, resection	45 (28.5)	2 (6.1)	4 (40)	0.015
Operation time (min)	235 (115–736)	147 (99–196)	356 (305–408)	<0.001
Blood loss	350 (22–8,000)	135 (50–22)	825 (450–1,200)	<0.001
Transfusion	39 (24.8)	0	3 (30)	0.005
Pathologic TNM stage				<0.001
I	57 (36.1)	27 (81.8)	2 (20)	
II	10 (6.3)	1 (3)	1 (10)	
IIIA	43 (27.2)	0	2 (20)	
IIIB	11 (7)	1 (3)	0	
IVA	20 (12.7)	2 (6.1)	4 (40)	
IVB	17 (10.8)	2 (6.1)	1 (10)	
Subtype				0.861
Squamous cell carcinoma	119 (78.3)	29 (87.9)	9 (90)	
Lymphoepithelioma-like	6 (3.9)	0	0	
Sarcomatoid	3 (2)	0	0	
Mucoepidermoid	2 (1.3)	0	0	
Adenocarcinoma	3 (2)	0	0	
Clear cell carcinoma	1 (0.7)	0	0	
Not otherwise specified	11 (7.2)	4 (12.1)	0	
Complete resection				0.216
R0	128 (81)	32 (97)	7 (70)	
R1	29 (18.4)	0	3 (30)	
R2	1 (0.6)	1 (3)	0	

Values are presented as number (%) or median (range).
VATS, video-assisted thoracoscopic surgery; TNM tumor-node-metastasis.

subjected to VATS (P=0.049). Tumor location, size, TNM stage and invasion of surrounding tissue on preoperative CT image are described in Supplementary Table 1.

Surgical outcomes

The operation time of VATS was shorter than sternotomy and thoracotomy (P<0.001). The amount of blood loss and the

Table 3. Postoperative outcome

Variable	Sternotomy (n=158)	VATS (n=33)	Thoracotomy (n=10)	P-value
Mortality at 30 days	2 (1.3)	0	0	1.000
Chest tube duration (day)	5 (2–13)	2 (1–7)	1.5 (0–3)	<0.001
Ventilation duration (day)	0 (0–6)	0	1 (0–2)	<0.001
Intensive care unit stay (day)	1 (0–44)	0 (0–42)	0.5 (0–9)	<0.001
Hospital stay (day)	9 (3–63)	4 (2–158)	7 (4–19)	<0.001
Adjuvant therapy				0.350
None	30 (19)	10 (30.3)	3 (30)	
Chemotherapy	35 (22.2)	4 (12.1)	4 (40)	
Radiotherapy	73 (46.2)	15 (45.5)	3 (30)	
Concurrent chemoradiation	20 (12.7)	4 (12.1)	0	
Complications	44 (27.8)	3 (9.1)	0	0.014
Prolonged air leak (>5 days)	1 (0.6)	0	0	
Atelectasis	2 (1.3)	0	0	
Pneumonia	0	0	0	
Acute lung injury	1 (0.6)	0	0	
Pulmonary thromboembolism	1 (0.6)	0	0	
Re-intubation	1 (0.6)	0	0	
Chylothorax	2 (1.3)	1 (3)	0	
Arrhythmia	8 (5.1)	0	0	
Wound infection	1 (0.6)	0	0	
Bleeding	2 (1.3)	0	0	
Grade				0.134
I	11 (7)	2 (6.1)	0	
II	21 (13.3)	0	0	
III	10 (6.3)	0	0	
IV	2 (1.3)	1 (3)	0	

Values are presented as number (%) or median (range).
VATS, video-assisted thoracoscopic surgery.

incidence of transfusion were lower in the VATS group than in the open group (P<0.001 and P=0.005).

In terms of extent of resection, most of the sternotomy group underwent total thymectomy (P<0.001), and lymph node dissection was performed more frequently in open group (P=0.015). Furthermore, additional procedures including resection of lung, pericardium, innominate vein and phrenic nerve were conducted more frequently in open group (P<0.001). Complete resection was not different between the groups. Details are shown in Table 2.

One patient of sternotomy group was died within postoperative 30 days. The lengths of postoperative hospital stay (POHS), intensive care unit (ICU) stay and chest tube duration were shorter in the VATS group than in the open group (P<0.001). The incidence of postoperative complications of the VATS group was lower than those of open group (P=0.014). Details of the incidence of complications are shown in Table 3.

Survival and oncologic outcomes

The median follow-up duration was 50.3 months. The 5-year OS rates of the sternotomy and VATS group were 100%, while thoracotomy group was 87.5%±11.7% (P=0.107). The 5-year RFS rates were not significantly different between the groups (55.4%±4.5% for sternotomy group, 67.9%±12.1% for VATS group, 32.8%±18.3% for the thoracotomy group, P=0.131). These graphs are presented in Fig. 1.

In terms of recurrence patterns, local recurrence was not different between the groups, while the thoracotomy group

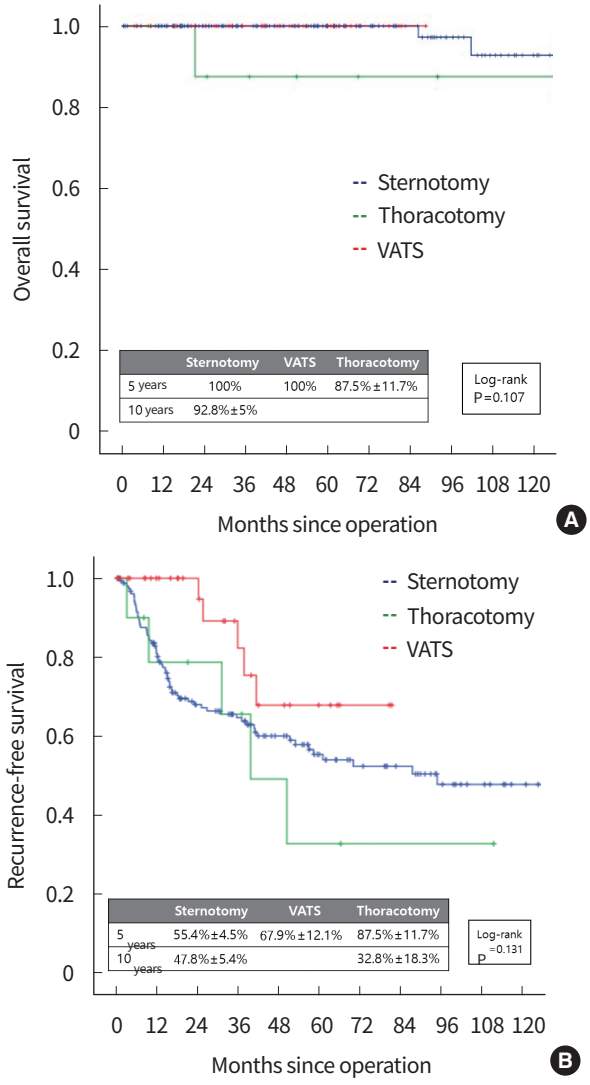

Fig. 1. Overall survival (A) and recurrence-free survival (B) of 201 patients. VATS, video-assisted thoracoscopic surgery.

Table 4. Pattern of recurrence

Variable	Sternotomy (n=158)	VATS (n=33)	Thoracotomy (n=10)	P-value
Site of recurrence				
Local	20 (33.9)	3 (60)	2 (40)	0.847
Regional	19 (32.2)	1 (20)	2 (40)	
Distant	20 (33.9)	1 (20)	1 (20)	

Values are presented as number (%).
VATS, video-assisted thoracoscopic surgery.

had more regional recurrence than the VATS group (30% vs. 3%, P=0.04). Details are shown in Table 4.

Table 5. Postoperative outcome of patients with tumor less than 5 cm and TNM stage I

Variable	Sternotomy (n=28)	VATS (n=27)	P-value
Extent			<0.001
Thymomectomy	2 (7.1)	16 (59.3)	
Partial thymectomy	0	5 (18.5)	
Total thymectomy	26 (92.9)	6 (22.2)	
Pathologic tumor size (cm)	4.7±1.7	4.2±1.6	0.182
Pathologic TNM stage			0.013
I	17 (60.7)	22 (81.5)	
II	2 (7.1)	0	
IIIA	6 (21.4)	0	
IIIB	0	1 (3.7)	
IVA	3 (10.7)	2 (7.4)	
IVB	0	2 (7.4)	
Concomitant procedure	21 (75)	7 (25.9)	<0.001
Lung, wedge resection	14 (50)	4 (14.8)	0.005
Lung, lobectomy	0	1 (3.7)	1.000
Pericardium, resection	12 (42.9)	3 (11.1)	0.008
Innominate vein, resection	8 (28.6)	0	0.004
Phrenic nerve, resection	3 (10.7)	2 (7.4)	1.000
Operation time (min)	175 (115–535)	102 (13–215)	<0.001
Blood loss (mL)	375 (0–2,000)	5 (0–400)	<0.001
Transfusion	3 (10.7)	0	0.236
Complete resection			0.491
R0	28 (100)	26 (96.3)	
R1	0	0	
R2	0	1 (3.7)	
Mortality at 30 days	0	0	1.000
Chest tube duration (day)	4 (2–13)	2 (1–7)	<0.001
Ventilation duration (day)	0 (0–2)	0	0.051
Intensive care unit stay (day)	1 (0–5)	0 (0–1)	<0.001
Hospital stay (day)	8 (3–20)	4 (2–13)	<0.001
Adjuvant therapy			0.755
None	7 (25)	10 (37)	
Chemotherapy	4 (14.3)	3 (11.1)	
Radiotherapy	14 (50)	10 (37)	
Concurrent chemoradiotherapy	3 (10.7)	4 (14.8)	

(Continued to the next page)

Table 5. Continued

Variable	Sternotomy (n=28)	VATS (n=27)	P-value
Complications	6 (21.4)	2 (7.4)	0.252
Prolonged air leak (>5 days)	0	0	
Atelectasis	0	0	
Pneumonia	0	0	
Acute lung injury	0	0	
Pulmonary thromboembolism	0	0	
Re-intubation	1	1	
Chylothorax	2	0	
Arrhythmia	2	0	
Wound infection	0	0	
Bleeding	0	0	
Others	1	1	
Grade			0.296
I	2	2	
II	3	0	
III	1	0	
IV	0	0	

Values are presented as number (%), mean ± standard deviation, or median (range).
TNM, tumor-node-metastasis; VATS, video-assisted thoracoscopic surgery.

Table 6. Pattern of recurrence of patients with tumor less than 5 cm and TNM stage I

Variable	Sternotomy (n=28)	VATS (n=27)	P-value
Site of recurrence			0.38
Local	2 (7.1)	3 (11.1)	
Regional	1 (3.6)	1 (3.7)	
Distant	5 (17.9)	1 (3.7)	

Values are presented as number (%).
TNM, tumor-node-metastasis; VATS, video-assisted thoracoscopic surgery.

Subgroup analysis for tumor less than 5 cm and clinical TNM stage I

A total of 55 patients (28 sternotomy and 27 VATS) had tumor less than 5 cm and clinical TNM stage I. The lengths of POHS, ICU stay and chest tube duration were shorter in the VATS group than in the sternotomy group (P<0.001). The incidence of postoperative complications of the VATS group did not differ from the sternotomy (P=0.252). Details are described in Table 5.

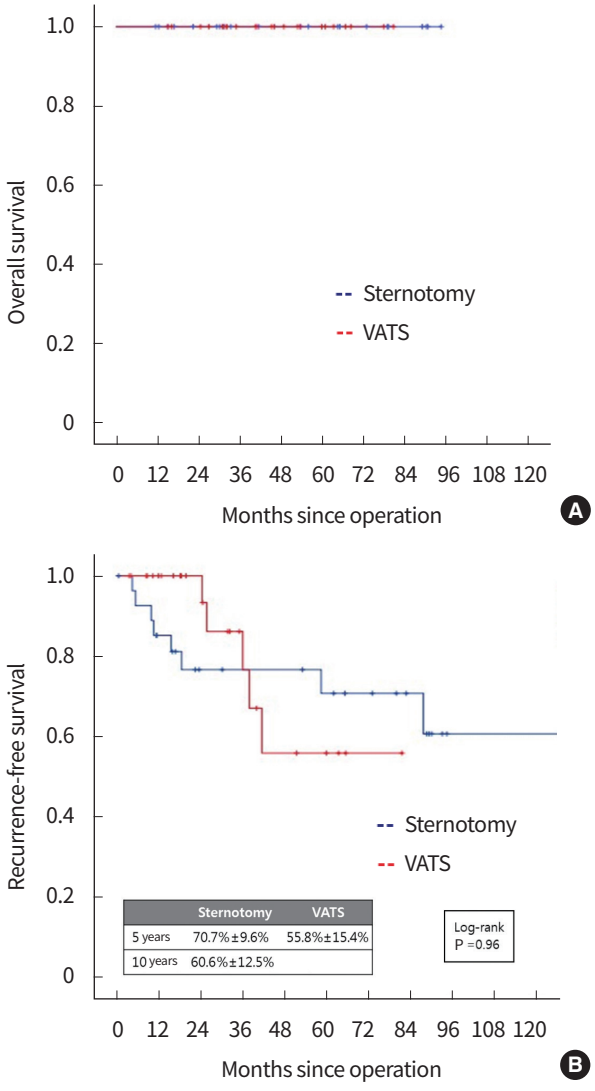

Fig. 2. Overall survival (A) and recurrence-free survival (B) of patients with tumor less than 5 cm and tumor-node-metastasis (TNM) stage I. VATS, video-assisted thoracoscopic surgery.

The 5-year OS rates of subgroup were 100% in both groups. The 5-year RFS rates of subgroup were not significantly different between the groups (70.7% ± 9.6% for sternotomy group, 55.8% ± 15.4% for VATS group, P=0.960). These graphs are illustrated in Fig. 2. The pattern of recurrence of subgroup was not different between the groups (Table 6).

Predictors of OS and RFS

The predictors of OS and RFS identified by univariable and multivariable analysis are listed in Tables 7, 8. In multivariable Cox regression analysis of prognostic factors, surgical approach was not significantly associated with OS (P=

Table 7. Cox regression analysis of prognostic factors of overall survival

Variable	Univariate			Multivariate		
	HR	95% CI	P-value	HR	95% CI	P-value
Sex	0.825	0.472–1.443	0.501			
Age	1.006	0.982–1.030	0.626			
Tumor size (CT)	1.045	0.914–1.195	0.522			
Clinical TNM stage			0.211			
I	Reference	Reference				
II	2.840	0.989–8.154				
III	1.591	0.747–3.390				
IV	1.253	0.665–2.360				
Clinical Masaoka-Koga stage			0.666			
I	Reference	Reference				
II	0.934	0.358–2.432				
III	1.280	0.657–2.494				
IV	1.482	0.711–3.091				
Neoadjuvant treatment						0.010
Chemotherapy	1.300	0.668–2.528	0.440	7.202	1.598–32.455	
Radiotherapy	5.987	1.441–24.883	0.014			
Concurrent chemoradiation	0.637	0.088–4.620	0.655			
Approach			0.089			0.138
Sternotomy	Reference	Reference		Reference	Reference	
VATS	0.565	0.138–2.317		0.614	0.140–2.689	
Thoracotomy	0.123	0.017–0.894		0.142	0.019–1.066	
Extent			0.8			
Thymomectomy	Reference	Reference				
Partial thymectomy	1.149	0.352–3.748				
Total thymectomy	1.273	0.620–2.615				
Pathologic TNM stage			0.004			0.238
I	Reference	Reference		Reference	Reference	
II	0.396	0.052–2.999		0.433	0.051–3.674	
III	1.609	0.821–3.155		1.232	0.497–3.053	
IV	2.981	1.546–5.750		2.125	0.832–5.429	
Subtype			0.743			
Squamous cell carcinoma	Reference	Reference				
Lymphoepithelioma-like	1.590	0.489–5.174				
Sarcomatoid	3.167	0.429–23.366				
Mucoepidermoid	1.114	0.152–8.173				
Adenocarcinoma	2.674	0.640–11.171				
Resection margin			0.214			0.55
R0	Reference	Reference		Reference	Reference	
R1	1.682	0.941–3.007		1.206	0.652–2.23	
Adjuvant therapy (%)						
Chemotherapy	1.211	0.681–2.153	0.514			
Radiotherapy	0.680	0.392–1.181	0.171			

HR, hazard ratio; CI, confidence interval; CT, computed tomography; TNM, tumor-node-metastasis; VATS, video-assisted thoracoscopic surgery.

Table 8. Cox regression analysis of prognostic factors of recurrence-free survival

Variable	Univariate			Multivariate		
	HR	95% CI	P-value	HR	95% CI	P-value
Sex	1.035	0.642–1.669	0.886			
Age	0.992	0.972–1.013	0.464			
Tumor size (CT)	1.071	0.964–1.19	0.203			
Clinical TNM stage			0.001			0.020
I	Reference	Reference		Reference	Reference	
II	5.092	2.234–11.607		3.749	1.418–9.912	
III	1.334	0.613–2.905		0.725	0.304–1.728	
IV	1.981	1.182–3.32		0.977	0.519–1.839	
Clinical Masaoka-Koga stage			<0.001			0.245
I	Reference	Reference		Reference	Reference	
II	2.066	0.797–5.357		1.452	0.487–4.329	
III	3.094	1.469–6.517		1.882	0.679–5.215	
IV	6.284	2.96–13.341		2.760	0.992–7.680	
Neoadjuvant treatment						
Chemotherapy	2.027	1.218–3.371	0.007	1.106	0.599–2.043	0.748
Concurrent chemoradiation	3.298	1.193–9.118	0.021	3.277	0.955–11.248	0.059
Approach			0.147			
Sternotomy	Reference	Reference				
VATS	0.427	0.171–1.062				
Thoracotomy	1.296	0.521–3.223				
Extent			0.764			
Thymomectomy	Reference	Reference				
Partial thymectomy	1.407	0.554–3.576				
Total thymectomy	1.089	0.582–2.039				
Pathologic TNM stage			<0.001			0.045
I	Reference	Reference		Reference	Reference	
II	1.517	0.507–4.542		1.070	0.304–3.761	
III	2.411	1.286–4.518		1.299	0.549–3.075	
IV	5.545	3.012–10.206		3.297	1.276–8.519	
Subtype			0.986			
Squamous cell carcinoma	Reference	Reference				
Lymphoepithelioma-like	0.749	0.183–3.066				
Adenocarcinoma	1.314	0.321–5.375				
NOS	0.602	0.189–1.921				
Resection margin			0.021			0.533
R0	Reference	Reference		Reference	Reference	
R1	1.897	1.1–3.27		0.819	0.438–1.532	
Adjuvant therapy (%)						0.248
Chemotherapy	1.702	1.033–2.804	0.037	1.386	0.796–2.413	
Radiotherapy	0.796	0.494–1.285	0.351			

HR, hazard ratio; CI, confidence interval; CT, computed tomography; TNM, tumor-node-metastasis; VATS, video-assisted thoracoscopic surgery; NOS, not otherwise specified.

0.138), although neoadjuvant radiotherapy was associated with poor OS (hazard ratio, 7.2; 95% confidence interval, 1.6 to 32.46; P=0.01). The multivariable Cox regression analysis for RFS showed pathologic TNM stage was a significant prognostic factor of RFS (P=0.045). However, VATS had not effect on either OR or RFS.

DISCUSSION

Thymic carcinomas are very rare, and most literatures about thymic carcinomas are retrospective, small-case, single-center studies. Only a few retrospective large-sample multicenter studies on long-term outcome of thymic carcinoma were reported in the United States (Surveillance, Epidemiology, and End Results database, n=290), Europe (European Society of Thoracic Surgeons database, n=229), Japan (Japanese Association for Research of the Thymus database, n=306), and China (Chinese Alliance for Research of Thymoma database, n=369) [2,11-13]. In Korea, the KART developed a multi-institutional retrospective database in 2014, and collected the data of thymic epithelial tumor, including thymic carcinoma.

In early stage thymic tumor, surgery for complete resection has remained the mainstay of curative treatment because complete resection was a significant prognostic factor in the many studies of thymic carcinoma [2,14]. Traditionally, this has been conducted with open procedures, especially median sternotomy. According to the European Society of Medical Oncology (ESMO) guidelines on thymic tumors, the standard surgical approach for resectable thymic epithelial tumor remains median sternotomy (grade IV, level A) [15]. More recently, due to the widespread use of VATS, there has been a progressive adoption of these techniques in surgery for thymic carcinoma. The ESMO guidelines suggest that minimally invasive surgery is an option for early stage tumor in the hands of appropriately trained surgeons. Several advantages of VATS for the treatment of thymic tumors have been known in a number of literatures in the last decade. VATS provide non inferior oncologic outcomes than open approach and is associated with shorter length of hospital stay, reduced blood loss and duration of chest tube [9,14-17]. Unfortunately, most of these literatures are retrospective studies and no randomized clinical study has been published because of the rarity of thymic tumor.

In the present study, most patients with thymic carcinoma who underwent VATS approach had tumor with less than 5 cm (mean tumor size, 3.8 ± 1.1 cm) and TNM stage I (90.9%). Therefore, we analyzed 55 patients (28 sternotomy and 27 VATS) who had tumor with less than 5 cm and clinical TNM stage I according to the approach of surgery. VATS was associated with shorter operation time, lower blood loss, reduced lengths of POHS, ICU stay, and chest tube duration. Furthermore, the 5-year OS and RFS rates and pattern of recurrence were not significantly different between the groups. Therefore, VATS can be applied to patients who had thymic carcinoma with less than 5 cm and clinical TNM stage I.

VATS was performed mostly in patients who did not confirm histology by preoperative biopsy according to our result. The National Comprehensive Cancer Network recommends that surgical biopsy should be avoided if a resectable thymic tumor is strongly suspected based on clinical and radiologic features [18]. However, histology of the thymic tumor is difficult to distinguish by imaging in case of small tumor with no lymphadenopathy [19]. In our series, although thymic tumor revealed to be thymic carcinoma (WHO type C) intraoperatively or postoperatively, VATS can be acceptable if complete resection was achieved.

The present study has limitations. First, the number of cases is small because of the rarity of thymic carcinoma, with only 201 cases over 7 years. Second, this is retrospective study, and selection bias exists. Surgeons would preferred VATS for less invasive tumor such as small size without invasion to innominate vein or great vessels on preoperative CT. Therefore, we analyzed subgroup who had tumor with less than 5 cm and TNM stage I. Third, the follow-up period after surgery is slightly insufficient. Because patients with thymic carcinoma have good prognosis, a follow-up time of 10 years or more may be necessary to identify substantial long-term outcomes. Fourth, surgical techniques, the degree of individual skills, and postoperative care of individual center could not be evaluated.

In conclusion, the VATS was applied for tumor less than 5 cm and TNM stage I. The VATS group had shorter duration of chest tube, mechanical ventilation, postoperative hospital day, and lower incidence of postoperative complication. The 5-year OS and RFS was not significantly different between the groups. Therefore, the VATS approach of surgical treatment for thymic carcinoma can be selectively employed in small and TNM stage I tumor without compromise of oncologic outcome.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was re-

ported.

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