2772-9931
https://doi.org/10.1016/j.atssr.2024.10.011

Mediastinum & Esophagus: Short Report

Outcome of Robotic-Assisted Resection of Large Primary Thymic Tumors: A Single High-Volume Institutional Experience

Abigail Fong, MD,[1,*] Inderpal Sarkaria, MD,[1,*] Nicholas Baker, MD,[1] Neil Christie, MD,[1] Sangmin Kim, MD,[1] Rajeev Dhupar, MD,[1] Ryan Levy, MD,[1] Omar Awais, MD,[1] James Luketich, MD,[1] Arjun Pennathur, MD,[1] and Matthew Schuchert, MD[1]

ABSTRACT

BACKGROUND The role of robotic-assisted resection for large primary thymic malignant tumors is uncertain. This study compares outcomes of robotic-assisted resection by tumor size.

METHODS Robotic resections for anterior mediastinal masses were identified from an institutionally maintained database and were retrospectively analyzed. Cases were stratified by tumor size. Data points collected included patient demographics, tumor characteristics, and perioperative outcomes.

RESULTS From 2014 to 2022, 67 robotic-assisted mediastinal resections were performed for primary thymic malignant tumors. The average tumor size was 5.6 cm (range, 0.7-14.0 cm). The median length of stay was 3 days (range, 1-73 days). The median operative time was 186 minutes (range, 69-644 minutes). Tumors ≤4 cm (n = 21; 31%) vs >4 cm (n = 46; 69%), trended toward a shorter median operative time (157 minutes vs 208 minutes; $P = .06$), length of stay (2 days vs 3.5 days; $P = .18$), and lower positive margins (21 [100%] R0 resections in the ≤4-cm group vs 40 [87%] R0 resections in the >4-cm group; $P = .09$). There was no difference in major complications (2 [9.5%] vs 3 [2.5%]; $P = 1.0$).

CONCLUSIONS Robotic-assisted resection can be safe and effective for primary thymic malignant tumors. Concern regarding increased rates of positive margins vs an open approach for large tumors remain. Although a robotic approach for larger tumors may spare selected patients the morbidity of an open procedure without compromising outcomes, a low threshold should exist for conversion to open surgery.

(Ann Thorac Surg Short Reports 2025;3:352-356)

Mediastinal masses account for a small portion, approximately 3%, of thoracic lesions.[1] Anterior mediastinal malignant diseases include thymomas, thymic carcinomas, germ cell tumors and lymphomas. For primary thymic malignant diseases, such as thymomas and thymic carcinomas, surgery remains the mainstay of treatment for resectable lesions.[2] Minimally invasive approaches to thymectomy have been steadily adopted, including video-assisted thoracoscopic surgery (VATS) and robotic-assisted thoracoscopic surgery (R-VATS) approaches.

Robotic surgery has significant appeal in anterior mediastinal mass resections because of improved visualization, instrument flexibility, precision, and control of the operative field afforded the surgeon. Robotic surgery has become

Accepted for publication Oct 21, 2024.
*Drs Fong and Sarkaria are co-first authors.
[1]Department of Cardiothoracic Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania
Address correspondence to Dr Fong, Department of Cardiothoracic Surgery, University of Pittsburgh, 200 Lothrop Street, Pittsburgh PA 15213; email: ajbfong@gmail.com.

the approach of choice in many centers, especially for smaller tumors. Whether this approach is appropriate for extralarge mediastinal tumors remains in question. The purpose of this study was to examine outcomes of robotic-assisted primary thymic tumor resection at the University of Pittsburgh Medical Center (Pittsburgh, PA), a high-volume thoracic surgery center.

IN SHORT

- For <4-cm tumors, low complication rates, short median LOS, and a minimal positive margin rate support robotic surgery as a standard of MIS intervention.
- Robotic mediastinal resections can be safe for large primary thymic malignant tumors for experienced surgeons in a high-volume center; however, concerns regarding increased positive margin rates vs open approaches remain and require further study.

MATERIAL AND METHODS

An Institutional Review Board-approved (REN17030025) retrospective review was performed of robotic-assisted anterior mediastinal resections in our institution from 2014 to 2022. Data were gathered on these patients, including demographics such as age, sex, race, Charlson Comorbidity Index (CCI), tumor histologic type, tumor size, perioperative outcomes such as operative time, length of stay (LOS), complications, and positive margins. Data were stratified by pathologic diagnosis to identify a group of primary thymic malignant tumors. Outcomes for our cohort were examined and compared by tumor size. Statistical analysis was performed using the χ^2 test, the Fisher exact test, the Wilcoxon rank sum test, the Mann-Whitney test, and *t*-tests as appropriate.

RESULTS

A total of 67 primary thymic malignant tumors were identified at our institution between 2014 and 2022. The mean cohort age at the time of surgery was 61 years (range, 31-85 years). Of these patients, 35 (52%) were female and 58 (87%) were White. The average CCI was 4.6 (Table 1).

Most of the tumors were thymomas (61; 91%). Other pathologic types included thymic squamous cell carcinoma (5; 7%) and thymic small cell carcinoma (1; 1%). The average tumor size was 5.6 cm (range, 0.7-14.0 cm) (Table 1). For thymomas, 14 (23%) were Masaoka-Koga stage I, 40 (66%) were stage IIA, 4 (7%) were stage IIB, and 3 (5%) were stage III. The median follow-up was 13.1 months.

The median operative time was 186 minutes (range, 69-644 minutes). The median LOS was 3 days (range, 1-73 days). LOS was affected by patients with myasthenia gravis (9; 13%). Three patients had stays >40 days related to a preoperative myasthenic crisis that extended their stay preoperatively and postoperatively. These critically ill patients were managed in a multidisciplinary fashion using ventilatory support, plasmapheresis, and medical optimization. They underwent surgery after aggressive, prolonged efforts failed to resolve their myasthenic crisis or with active tumor growth.

A total of 11 (16%) patients had concurrent resections, including wedge resection or lobectomy, phrenic nerve resection, pericardial resection, or vascular resection (Table 2). Three of the lung resections were for unrelated lung masses, and 6 patients had positive margins. Of these 6 patients, 4 had grossly negative margins intraoperatively by the surgeon's assessment. Frozen section was used liberally at the surgeon's discretion, and results were negative in all positive margin cases assessed. One patient (with thymic squamous cell carcinoma of 7.7 cm) was unable to complete resection because of an unanticipated extent of disease and an inability to tolerate single-lung ventilation or pulmonary resection required for complete resection, thus resulting in R2 resection. One patient had a grossly fully resected specimen that fractured during extraction; therefore, pathologic examination was unable to assess the true margin. This was believed to be a clinically negative margin intraoperatively by the surgeon. A total of 5 (7%) patients had major complications (Clavien-Dindo grade III-V), including respiratory failure or reintubation, empyema requiring drainage, non-ST-segment elevation myocardial infarction with readmission and mortality, and additional chest tube placement for pneumothorax.

The cohort was then stratified by tumor size. When comparing the group with tumors $\leq$ 4 cm (n = 21) vs those the tumors >4 cm (n = 46), we found no difference in age (*P* = .51), sex (*P* = .59), CCI (*P* = .52), or histologic type (*P* = .3 7) between the groups (Table 1). We found no difference in complication rate (2 [9.5%] in the $\leq$4-cm group vs 3 [6.5%] in the >4-cm group; *P* = 1). A shorter median operative time of 157 minutes was observed in the $\leq$4-cm group vs 208 minutes in the >4-cm group (*P* = .006). No statistically

TABLE 1 Demographics

Demographics	Cohort (N = 67)	≤4 cm (n = 21)	>4 cm (n = 46)	P	≤7 cm (n = 48)	>7 cm (n = 19)	P
Age, y (mean)	61 (31–85)	62.3	60.4	.51	63.4	61.7	.98
Sex							
Female	35 (52.2)	12 (57.1)	23 (50)	.59	29 (60)	6 (32)	.03
Male	32 (47.8)	9 (42.9)	23 (50)	...	19 (40)	13 (68)	
Race							
White	58 (86.6)	17 (81.0)	41 (89)	.45	41 (85.4)	17 (89.5)	.66
African American	7 (10.4)	4 (19.0)	3 (6.5)	...	6 (12.5)	1 (5.3)	...
Asian	0 (0)	0 (0)	0 (0)	...	0 (0)	0 (0)	...
American Indian	0 (0)	0 (0)	0 (0)	...	0 (0)	0 (0)	...
Native Hawaiian/Pacific Islander	2 (3)	0 (0)	2 (4.3)	...	1 (2.1)	1 (5.3)	...
CCI (mean)	4.6	4.8	4.5	.52	4	5	.74
Tumor size, cm	5.6 (0.7–14)	3.3	6.4	...	4.4	8.0	...
Histologic type							
Thymoma	61 (91.0)	18 (85.7)	43 (93.5)	.42	44 (91.7)	17 (89.5)	.73
Thymic squamous cell carcinoma	5 (7.5)	2 (9.5)	3 (6.5)	...	3 (6.3)	2 (10.5)	...
Thymic small cell carcinoma	1 (1.5)	1 (4.8)	0 (0)	...	1 (2.1)	0 (0)	...
LVI	5 (7)	2 (9.5)	3 (2.5)	.65	4 (8.3)	1 (5.3)	...
TNM stage							1
I	45 (67.2)	16 (76.2)	29 (63.0)	.05	32 (66.7)	13 (68.4)	...
II	15 (22.4)	3 (14.3)	12 (26.1)	...	13 (27.1)	2 (10.5)	.2
III	5 (7.5)	0 (0)	5 (10.9)	...	2 (4.2)	3 (15.8)	...
IV	2 (3.0)	2 (9.5)	0 (0)	...	2 (4.2)	0 (0)	...
WHO class							
A	11 (16.4)	3 (14.3)	11 (23.9)	.34	5 (10.4)	6 (31.6)	...
AB	22 (32.8)	4 (19.0)	22 (47.8)	...	17 (35.4)	5 (26.3)	.14
B1	11 (16.4)	3 (14.3)	11 (23.9)	...	7 (14.6)	4 (21.1)	...
B2	15 (22.4)	6 (28.6)	15 (32.6)	...	13 (27.1)	2 (10.5)	...
B3	2 (3)	2 (9.5)	2 (4.3)	...	2 (4.2)	0 (0)	...
C	0 (0)	0 (0)	0 (0)	...	0 (0)	0 (0)	...
Masaoka stage							
I	14 (20.9)	3 (16.7)	11 (25.6)	.52	8 (18.2)	6 (35.3)	...
II	44 (65.7)	15 (83.3)	29 (67.4)	...	34 (77.3)	10 (58.8)	.25
III	3 (4.5)	0 (0)	3 (7.0)	...	2 (4.5)	1 (5.9)	...
IV	0 (0)	0 (0)	0 (0)	...	0 (0)	0 (0)	...

Values are n (%), mean, median (range), or *P*. CCI, Charlson Comorbidity Index; LVI, lymphovascular invasion; TNM, Tumor, Node, Metastasis; WHO, World Health Organization.

significant difference in LOS was noted (median 2 days for the ≤4-cm group vs 3.5 in the >4-cm group; $P = .18$). Of note, no positive margins were found in the ≤4-cm group (0, 0%), whereas 6 (5%) of the >4-cm group had positive margins ($P = .09$) (Table 2).

When comparing tumors ≤7 cm (n = 48) withs extralarge tumors >7 cm (n = 19), no difference was seen in age ($P = .98$), CCI ($P = .74$), or histologic type ($P = 1$). More female patients were identified in the ≤7-cm group (29; 60%) vs the >7-cm group (6; 31.5%) ($P = .03$). No difference was seen in complication rate, with 3 (6.3%) major complications in the ≤7-cm group and 2 (10.5%) in the >7-cm group ($P = .62$). Three (6%) of the ≤7-cm group and 3 (16%) of the >7-cm group had positive margins ($P = .34$). Shorter operative time was seen in the ≤7-cm group, with a median time of 159 minutes vs 268 minutes in the >7-cm group ($P < .001$). LOS was shorter in the ≤7-cm group, with a median 2.5 days vs 4 days in the >7-cm group ($P = .05$) (Table 2).

COMMENT

Minimally invasive surgery (MIS) resections have become a standard approach to small thymic tumors in many centers. The National Comprehensive Cancer Network (NCCN) guidelines on thymic cancers state, "Minimally invasive procedures are not routinely recommended due to the lack of long-term data. However, minimally invasive procedures may be considered for clinical stage I-II if all oncologic goals can be met as in standard procedures, and if performed in specialized

TABLE 2 Outcomes

Outcomes	Cohort (N = 67)	≤4 cm (n = 21)	>4 cm (n = 46)	P	≤7 cm (n = 48)	>7 cm (n = 19)	P
Length of stay, D	3 (1–73)	2	3.5	.18	2.5	4	.98
Operative time, min	186 (96–664)	157	208	.006	159	268	.03
Margins							
R0	61 (91.0)	21 (100)	40 (87.0)	.09	45 (93.8)	16 (84.2)	.34
Positive margins	6 (9.0)	0 (0)	6 (13.0)	...	3 (6.3)	3 (15.8)	...
Positive lymph nodes	2 (3.0)	2 (9.5)	0 (0)	.09	2 (4.2)	19 (100)	1
Recurrence	0 (0)	0 (0)	0 (0)	1	0 (0)	0 (0)	1
Median follow-up, mo	13.1	3.6	17.4	.02	12.4	19.2	.18
Complications grade III–V	5 (7.5)	2 (9.5)	3 (6.5)	1	3 (6.3)	2 (10.5)	.62
Concurrent PROCEDURES	11 (16.4)	1 (4.8)	10 (21.7)	.15	4 (8.3)	7 (36.8)	.009
Wedge resection or LOBECTOMY	9 (13.4)	1 (4.8)	8 (17.4)	...	4 (8.3)	5 (26.3)	...
Phrenic NERVE	2 (3.0)	0 (0)	2 (4.3)	...	1 (2.1)	3 (15.8)	...
Pericardium	4 (6.0)	0 (0)	4 (8.7)	...	1 (2.1)	3 (15.8)	...
Innominate VEIN	1 (1.5)	0 (0)	1 (2.2)	...	0 (0)	1 (5.3)	...

Values are median (range), n, n (%), and *P*.

centers by surgeons with experience in these techniques."[2] Previous studies compared VATS thymectomy with transsternal thymectomy and found VATS thymectomy to be a safe and effective alternative to open surgery, with decreased LOS, blood loss, and morbidity.[3,4] Additionally, previous literature supports comparable rates of R0 resections in MIS and open thymectomies for stage I or II thymic malignant tumors, with open surgery rates of R0 resections varying from 85% to 100%.[3,5,6]

Much of the literature on MIS thymectomies uses <3 cm or <5 cm as a cutoff size guideline for MIS resection of thymic masses.[7,8] Other investigators have opined that size is not the main issue, but rather vessel invasion is the only hard contraindication to an MIS approach.[9] Larger tumors are still often approached by sternotomy, with the role of MIS approaches still in question.

Although there was a heterogeneity of study comparisons, including both benign and malignant entities, overall studies investigating robotic thymectomy found the procedure to have comparable or improved safety and efficacy compared with open and VATS procedures.[4,8] A recent metaanalysis, including several of these studies, similarly found R-VATS thymectomy to be comparable to the VATS approach, and with lower LOS, complications, and positive margins compared with open surgery.[6] Several studies looked more specifically at early-stage, smaller anterior mediastinal tumors and found favorable results with shorter LOS in R-VATS vs VATS resections and comparable complications and recurrences.[7,10]

This study's findings were in concurrence with the previous literature regarding short LOS (median 3 days) and low complication rate (7%) in R-VATS thymectomies. Although previous studies often included larger masses, the numbers of large masses were low, not specifically investigated, and the studies were therefore unable to draw more than anecdotal conclusions of efficacy for very large masses.

Our study looked specifically at extralarge resections (>7 cm). The specimens were extracted by placement into a specimen bag and extension of 1 of the port sites to a size able to accommodate the specimen. In patients with larger masses, surgical "shingling" of the access incision rib without rib spreading was performed to avoid tumor fracture during extraction. Although LOS and operative time were longer in the extralarge mass group, they remains within range of those seen in other studies and showed no differences in complications. Of the 6 positive margins seen in the study, all but 1 were grossly fully resected and had negative frozen sections where evaluated, 3 were found in masses 4 to 7 cm, and 3 were found in masses >7 cm. No difference was seen in positive margins between our groups; however, the trend toward significance and distribution of all the positive margins in >4-cm mass resections is concerning. Our study was underpowered to investigate this finding fully, and further study is warranted. The rates of margin positivity of larger masses with open surgical approaches are also poorly understood.

Although an open approach may not have changed the resected margin given microscopic invasion of tumor (grossly resected in 5 of 6 positive margin cases, and negative frozen section where assessed), it may have prevented tumor fragmentation on extraction that could obscure true specimen margins. Whether this clinical measure justifies the additional morbidity of a sternotomy is an area of debate. Ultimately, using MIS vs open surgery for large thymic masses becomes a judgment that is based on surgeon experience, comfort level, and patient tumor characteristics. Surgeons should have a low threshold to convert to open surgery if it is the more appropriate means of adhering to oncologic principles and achieving a safe outcome with negative tumor margins.

Our institutional experience demonstrates that robotic surgical resection can be safely performed for selected large primary thymic malignant tumors. For smaller tumors <4 cm, low complication rates, short median LOS, and nearly absent positive margin resections support robotic surgery as a standard of MIS intervention for these tumors. Our study included a large series of primary thymic malignant tumors and reported on outcomes of robotic resection by tumor size, particularly in extralarge thymic malignant tumors.

STUDY LIMITATIONS. This study was a retrospective single-arm, single-institution, nonrandomized study and was subject to the selection and cause-effect biases of such reports. The cohort was limited to the surgical population, and the sample size was limited. Additionally, surgical techniques and the learning curve effect may vary among attending physicians over the time course of the study. This study was performed at a high-volume center with experienced robotic surgeons, and this may limit generalizability to the greater community.

CONCLUSION. For smaller <4-cm primary thymic malignant tumors, low complication rates, short median LOS, and a minimal positive margin rate support robotic surgery as a standard of MIS intervention for this group with experienced surgeons in a high-volume center. For extralarge (>7-cm) masses, we found that LOS and operating room time were longer, although rate of complications were comparable. Trends seen in positive margins in larger masses remain concerning. A low threshold for conversion to open surgery should exist, with the preservation of the oncologic principles of the operation remaining the critical priority. Further work is necessary to identify factors that could predict complications or positive margins in these patients.

The authors wish to acknowledge Kristine Ruppert for assistance with biostatistics and Summer Mazur for assistance with database management.

FUNDING SOURCES

This project was supported by the National Institutes of Health (grant number UL1TR001857). Internal departmental funding was provided by the University of Pittsburgh Medical Center. All other authors declare that they have no funding sources.

DISCLOSURES

Inderpal Sarkaria reports a relationship with Intuitive Surgical that includes: consulting or advisory; with Medtronic that includes: consulting or advisory; with CMR that includes: consulting or advisory; with Stryker that includes: consulting or advisory; with OTL that includes: consulting or advisory; with Active Surgical that includes: consulting or advisory; with VTI that includes: consulting or advisory; with AMSI that includes: consulting or advisory; and with VAIM-IS that includes: consulting or advisory. All other authors declare that they have no conflicts of interest.

REFERENCES

1. Aroor AR, Rama Prakasha S, Seshadri S, Teerthanath S, Raghuraj U. A study of clinical characteristics of mediastinal mass. *J Clin Diagn Res*. 2014;8:77-80. https://doi.org/10.7860/JCDR/2014/7622.4013

2. NCCN guidelines. Thymomas and thymic carcinomas. National Comprehensive Cancer Network. 2023. Accessed August 21, 2024. https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf

3. Friedant AJ, Handorf EA, Su S, Scott WJ. Minimally invasive versus open thymectomy for thymic malignancies: systematic review and meta-analysis. *J Thorac Oncol*. 2016;11:30-38. https://doi.org/10.1016/j.jtho.2015.08.004

4. Weksler B, Tavares J, Newhook TE, Greenleaf CE, Diehl JT. Robot-assisted thymectomy is superior to transsternal thymectomy. *Surg Endosc*. 2012;26:261-266. https://doi.org/10.1007/s00464-011-1879-7

5. Fang W, Yao X, Antonicelli A, et al. Comparison of surgical approach and extent of resection for Masaoka-Koga stage I and II thymic tumours in Europe, North America and Asia: an International Thymic Malignancy Interest Group retrospective database analysis. *Eur J Cardiothorac Surg*. 2017;52:26-32. https://doi.org/10.1093/ejcts/ezx042

6. O'Sullivan KE, Kreaden US, Hebert AE, Eaton D, Redmond KC. A systematic review of robotic versus open and video assisted thoracoscopic surgery (VATS) approaches for thymectomy. *Ann Cardiothorac Surg*. 2019;8:174-193. https://doi.org/10.21037/ACS.2019.02.04

7. Marulli G, Rea F, Melfi F, et al. Robot-aided thoracoscopic thymectomy for early-stage thymoma: a multicenter European study. *J Thorac Cardiovasc Surg*. 2012;144:1125-1132. https://doi.org/10.1016/j.jtcvs.2012.07.082

8. Wilshire CL, Vallières E, Shultz D, Aye RW, Farivar AS, Louie BE. Robotic resection of 3 cm and larger thymomas is associated with low perioperative morbidity and mortality. *Innovations (Phila)*. 2016;11:321-326. https://doi.org/10.1097/IMI.0000000000000295

9. Wei B, Cerfolio R. Robotic thymectomy. *J Vis Surg*. 2016;2:136-136. https://doi.org/10.21037/jovs.2016.07.17

10. Ye B, Tantai JC, Li W, et al. Video-assisted thoracoscopic surgery versus robotic-assisted thoracoscopic surgery in the surgical treatment of Masaoka stage I thymoma. *World J Surg Oncol*. 2013;11:1-5. https://doi.org/10.1186/1477-7819-11-157