Indian Journal of Thoracic and Cardiovascular Surgery (January–February 2021) 37(1):44–52
https://doi.org/10.1007/s12055-020-01023-x

ORIGINAL ARTICLE

Long-term outcome in mediastinal malignancies: video-assisted thoracoscopic versus open surgery

Huynh Quang Khanh[1] · Nguyen Van Khoi[1,2] · Nguyen Lam Vuong[2,3]

Received: 5 June 2020 / Revised: 20 July 2020 / Accepted: 24 July 2020 / Published online: 2 September 2020

Abstract

Purpose There are not many studies comparing long-term oncological outcomes between video-assisted thoracoscopic surgery (VATS) and open surgery for mediastinal malignancies. This study aimed to compare perioperative and long-term outcomes of these two techniques in the treatment of mediastinal malignancies.

Methods This is a retrospective study: patients with mediastinal malignancies underwent VATS or open surgery from 2010 to 2013 and were followed until 2019. The primary endpoints were long-term oncological outcomes, including tumor recurrence and mortality. Secondary endpoints were perioperative outcomes (operative duration, blood loss, pain, chest drainage duration, hospital length of stay, and complications).

Results There were 36 patients in the VATS group and 49 patients in the open group. The median follow-up duration was 90 months. VATS significantly reduced operation time (84.6 versus 124.8 min), blood loss (59.8 versus 235.2 ml), postoperative pain score (4.9 versus 6.7), the duration of chest tube drainage (2.1 versus 3.1 days), and postoperative hospital stay (5.2 versus 8.0 days). The two groups were comparable regarding the recurrence rate (2.4 versus 2.1/100 person-years) and mortality rate (0.8 versus 0.9/100 person-years).

Conclusion Compared with open surgery, VATS is less traumatic, reduces postoperative chest drainage, and shortens hospital stay with comparable long-term oncological outcomes. We advocate the VATS approach as a favored option for the resection of mediastinal malignancies.

Keywords Video-assisted thoracoscopic surgery · Thoracotomy · Sternotomy · Mediastinal tumor · Malignancy

Introduction

Mediastinal tumors include benign and malignant growths that form in either anterior, middle, or posterior mediastinum. Approximately one-third of all mediastinal tumors are malignant [1]. They are quite rare, which consist less than 1% of all types of cancer [2]. Mediastinal malignancies comprise a diverse group of tumors, including thymic cancers, lymphoma, teratoma, and several uncommon types of tumor. These tumors are usually diagnosed in patients aged 30 to 50 years and the thymoma is the most common type of mediastinal tumors reported in adults [1, 3, 4]. Surgery has been the primary treatment modality for most of mediastinal tumors [2, 3, 5]. The surgical options are thoracotomy, median sternotomy, and video-assisted thoracoscopic surgery (VATS). With the progress in the development of minimally invasive surgery, VATS has been widely used in the resection of mediastinal tumors [5–8]. However, the comparison of VATS versus traditional open surgery in patients undergoing resection for mediastinal malignancies remains deficient regarding long-term oncological outcome.

Aim of the study

This study was aimed to compare VATS with traditional open surgery in the treatment of mediastinal malignancies, with respect to perioperative and long-term oncological outcomes.

✉ Nguyen Lam Vuong
nguyenlamvuong@ump.edu.vn

[1] Department of Thoracic Surgery, Cho Ray Hospital, Ho Chi Minh City, Vietnam

[2] Department of Thoracic and Cardiovascular Surgery, Faculty of Medicine, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City, Vietnam

[3] Department of Medical Statistics and Informatics, Faculty of Public Health, University of Medicine and Pharmacy at Ho Chi Minh City, 217 Hong Bang, Ward 11, District 5, Ho Chi Minh City, Vietnam

Methods

Patients and study design

This is a retrospective study comparing outcomes in patients with mediastinal malignancies undergoing VATS resection versus open resection (through thoracotomy or median sternotomy). The patients were identified from our institutional database between 2010 and 2013, which is a tertiary referral center in Ho Chi Minh City, Vietnam. All patients received a multi-disciplinary consultation before surgery.

Inclusion criteria were based on preoperative clinical features and imaging findings, which include (1) radiological evidence of mediastinal tumor on computed tomographic (CT) imaging or magnetic resonance imaging (MRI), either in the anterior, middle, or posterior mediastinum; (2) no evidence of invasion to the heart, lungs, large blood vessels, trachea, and esophagus on CT or MRI images; (3) no suspicion of lymphoma; and (4) having no myasthenia gravis. Exclusion criteria were (1) tumors of the esophagus or the trachea; (2) metastasis of other cancers; and (3) pulmonary tuberculosis. All exclusion criteria were evident in postoperative pathological findings. Selection for eligible patients to undergo VATS or open surgery was based on the discussion between the surgical team and patients. All patients with postoperative pathological finding of mediastinal malignancies were followed up until December 2019 to investigate the long-term oncological outcome.

Operative techniques

All the operations were performed by a single main surgeon (HQK), who is a thoracic surgeon experienced in both VATS and open surgery. Complete resection of mediastinal tumors was performed in all cases. The VATS procedures were conducted with patients in the lateral position, under general anesthesia. Single lung ventilation was established via double-lumen endotracheal intubation. Three ports were used: one for a 10-mm 30° thoracoscope which was usually located at the midaxillary line in the fourth to eighth intercostal spaces; and two 10-mm ports for instrument manipulation were inserted using the triangle method. Care was taken to avoid injury to the phrenic nerve and other major organs. The thymic vein and other large vessels were sealed with ultrasonic scalpel or clamped with endoclippers. All resected specimens were placed in an endobag before retrieval. In case of difficulty in the dissection or removal of the tumor, one of the three ports was converted to a 4-cm transaxillary incision and the tumor was cut into pieces inside the endobag to facilitate the procedure. One 32F-sized chest tube was routinely retained after the operation. In the open resection group, mediastinal tumor was removed through a conventional thoracotomy or median sternotomy, depending on the location of the tumor. All patients with postoperative pathologies of lymphoma, sarcoma, teratoma, thymic carcinoma, other types of carcinoma, or Masaoka-Koga stage III–IV thymoma then received adjuvant chemotherapy or radiotherapy based on medical oncology consultation.

Study endpoints

Patients were followed up after discharge at 1 week; 1, 3, 6, 12 months; and then at 1-year intervals by outpatient clinical examination and chest X-ray. Unscheduled examination with chest CT scan was performed in cases with signs or symptoms suggestive of recurrence.

The primary endpoints were the long-term oncological outcomes, which included the recurrence-free and overall survival times during the follow-up period. Recurrence-free survival time was the length of time (in month) from surgery to either the time when patient was diagnosed of recurrent mediastinal tumor or the time of death from all cause (if no recurrence was observed). Overall survival time was the length of time (in month) from surgery to the time of death from all cause. If a patient did not experience any event (recurrence or death), these times were censored on the date of last follow-up.

Secondary endpoints were perioperative outcomes, which included the duration of operation, the amount of intraoperative blood loss, postoperative pain score, the duration of chest tube drainage, the length of postoperative hospital stay, and complications. The pain score was measured by the visual analog scale (VAS), which was marked by patients on a 10-cm line represented a scale from "no pain" to "worst pain," with a higher score representing worse pain. There was only one single measurement of pain score on the first postoperative day. The protocol for pain control was intravenous infusion of acetaminophen within the first 3 postoperative days, followed by oral acetaminophen until 1 week after discharge. Intravenous acetaminophen was provided in case of severe pain. The criteria for chest tube removal were (1) no blood or chylos fluid in the drain and no air leakage; (2) less than 200 ml of output in 24 h; and (3) fully expanded lung on chest X-ray examination. Patients were discharged after removal of chest tube, initiation of oral intake, and the absence of any other major complication. Excessive bleeding was defined when chest drainage was more than 200 ml per hour in 3 h or more than 1000 ml per 24 h along with decreased blood pressure and/or decreased hematocrit. Postoperative complication was defined as any complication occurred within 1 month after surgery.

Statistical analysis

All baseline characteristics and study outcomes were summarized by the two surgical groups. Comparison of variables between the two groups was performed using two-sided Fisher's exact test for categorical variables, two-sample *t* test for numeric variables with normal distribution, and Mann-

Whitney *U* test for numeric variables without normal distribution. Long-term outcomes were summarized by Kaplan-Meier estimates for the recurrence-free survival and overall survival and shown by the Kaplan-Meier curves for each group. In addition, we estimated the incidence rate of the long-term outcomes (recurrence and mortality) in each subgroup of age, gender, tumor size, tumor location, pathological finding, and surgical technique, to find potential factors related to the long-term outcomes. The differences in the incidence rate of the outcomes between the subgroups were tested by two-sided log-rank test. Statistical significance was determined when *P* value was less than 0.05. We also calculated the power of the results using the power calculation to test time-to-event outcome for equivalence study based on the primary endpoint (recurrence-free survival) [9]. All analyses were performed with the statistical software R version 3.6.1 (Austria).

Results

There were 246 patients with mediastinal tumors who were screened for eligibility at our institution from 2010 to 2013. Among those, 124 cases with benign tumors and 85 cases with malignant tumors underwent surgery. The malignant cases (36 cases in the VATS group, and 49 cases in the open group) were then followed up until December 2019 (Fig. 1). In the open group, 42 cases had a thoracotomy and 7 cases received a median sternotomy. Nine patients lost to follow-up (3 cases in the VATS group and 6 cases in the open group).

Baseline characteristics

Age, gender, American Society of Anesthesia (ASA) physical status classification, and comorbidities were not significantly different between the two groups (Table 1). The mean diameter of the tumors was lower in the VATS group compared with that in the open group (7.5 ± 2.3 vs. 8.4 ± 3.0 cm). A majority of the tumors were located in the anterior mediastinum (33 cases (91.7%) in the VATS group and 44 cases (89.8%) in the open group). More than half the cases were thymomas (26 cases (72.2%) in the VATS group and 27 cases (55.1%) in the open group). Thymic carcinoma occurred in 11 cases (3 (8.3%) in the VATS group and 8 (16.3%) in the open group). There were 9 cases with other

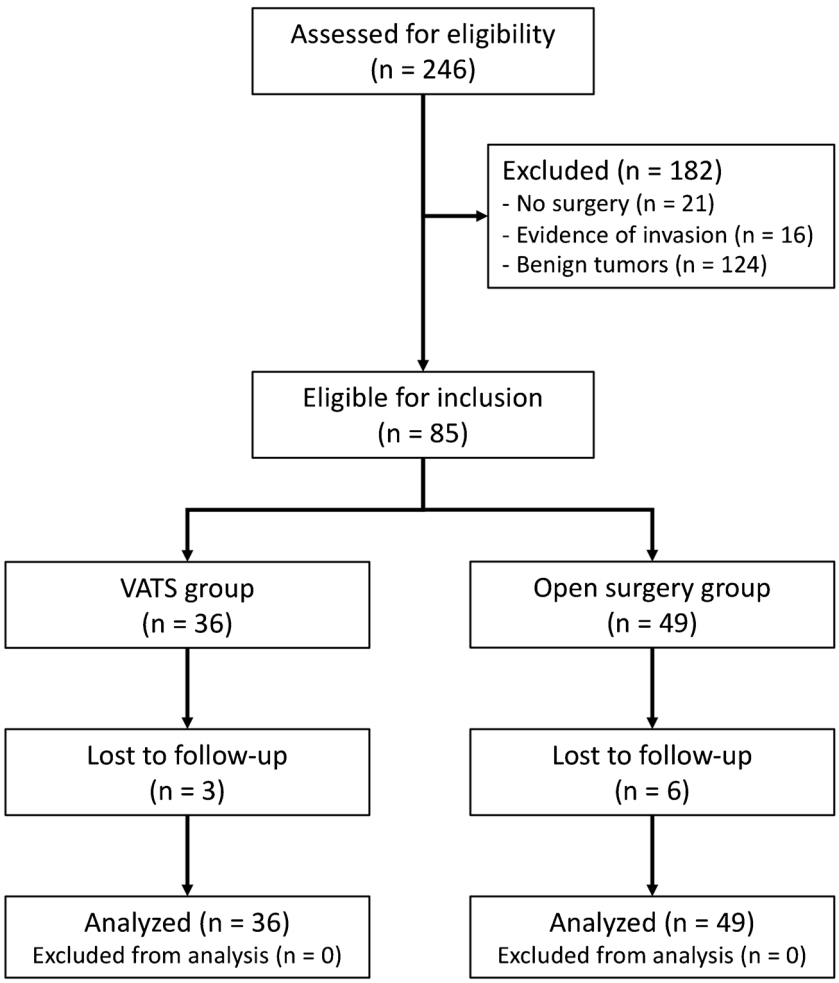

Fig. 1 Study flowchart of patients' enrollment and follow-up. VATS video-assisted thoracoscopic surgery

Table 1 Baseline characteristics of patients across treatment groups

Characteristics	VATS ($n = 36$)	Open ($n = 49$)	P
Age (years) (mean ± sd)	48.8 ± 13.2	48.5 ± 14.2	0.918[a]
Male (n (%))	15 (41.7)	23 (46.9)	0.664[b]
ASA physical status classification (n (%))			0.188[b]
I	8 (22.2)	4 (8.2)	
II	26 (72.2)	39 (79.6)	
III	2 (5.6)	5 (10.2)	
IV	0 (0.0)	1 (2.0)	
Comorbidities (n (%))			
Cardiovascular disease	4 (11.1)	2 (4.3)	0.396[b]
Respiratory disease	0 (0.0)	3 (6.1)	0.259[b]
Diabetes	2 (5.6)	0 (0.0)	0.163[b]
Tumor diameter (cm) (mean ± sd)	7.5 ± 2.3	8.4 ± 3.0	0.095[a]
Tumor location (n (%))			1.000[b]
- Anterior mediastinum	33 (91.7)	44 (89.8)	
- Middle mediastinum	2 (5.6)	3 (6.1)	
- Posterior mediastinum	1 (2.8)	2 (4.1)	
Pathological findings (n (%))			0.118[b]
- Thymoma	26 (72.2)	27 (55.1)	
- Thymic carcinoma	3 (8.3)	8 (16.3)	
- Lymphoma	5 (13.9)	4 (8.2)	
- Others	2 (5.6)	10 (20.4)	
+ Neuroendocrine carcinoma	0 (0.0)	3 (6.1)	
+ Adenocarcinoma	1 (2.8)	2 (4.1)	
+ Sarcoma	1 (2.8)	1 (2.0)	
+ Immature teratoma	0 (0.0)	1 (2.0)	
+ Germ cell tumor	0 (0.0)	1 (2.0)	
+ Large cell carcinoma	0 (0.0)	1 (2.0)	
+ Squamous cell carcinoma	0 (0.0)	1 (2.0)	
Adjuvant therapy (n (%))			0.104[b]
- None	26 (72.2)	25 (51.0)	
- Chemotherapy	7 (19.4)	13 (26.5)	
- Radiotherapy	3 (8.3)	11 (22.4)	
Follow-up duration (month) (median [IQR])	89.4 [80.8; 100.0]	91.1 [77.4; 105.4]	0.919[c]

ASA American Society of Anesthesia, *sd* standard deviation, *IQR* interquartile range, *VATS* video-assisted thoracoscopic surgery

[a] Two sample t test

[b] Fisher's exact test

[c] Mann-Whitney U test

types of carcinoma, 9 cases with lymphoma, 2 cases with sarcoma, and a case with teratoma. The lymphomas were diagnosed on post-operative histology and there was no pre-operative or intra-operative suspicion of lymphoma. The open group had higher percentage of adjuvant therapy (24 cases (49.0%) vs. 10 cases (37.8%)). The median (interquartile range) follow-up duration was 89.4 (80.8; 100.0) months for the VATS group and 91.1 (77.4; 105.4) months for the open group.

Perioperative outcomes

Five cases in the VATS group required a 4-cm transaxillary incision to facilitate the procedure. VATS was significantly better than the open surgery regarding the perioperative outcomes (Table 2). Compared with the open group, the VATS group required shorter operation time (84.6 ± 41.2 vs. 124.8 ± 50.8 min), had less intraoperative blood loss (59.8 ± 59.4 vs. 235.2 ± 307.7 ml), and reduced postoperative pain (pain score,

4.9 ± 1.4 vs. 6.7 ± 1.5). The VATS group also decreased postoperative chest tube drainage and hospitalization durations (chest drainage duration, 2.1 ± 0.3 vs. 3.1 ± 0.9 days; and postoperative hospital stay, 5.2 ± 1.4 vs. 8.0 ± 2.4 days). There were 7 (14.3%) postoperative complications in the open group: 5 patients had excessive bleeding (1 case required reoperation to stop bleeding) and 2 patients had postoperative atelectasis, while in the VATS group, no complication was observed.

Long-term oncological outcomes

During the follow-up period, 13 patients (15.3%) had recurrence of mediastinal tumors, including 1 case with thymoma, 2 cases with thymic carcinoma, 3 cases with lymphoma, and 7 cases with other types of cancer (Table 3). The number of recurrences was balanced (6 cases (16.7%) in the VATS group and 7 cases (14.3%) in the open group). Therefore, the two groups were not significantly different regarding the recurrence rate (2.4 vs. 2.1 per 100 person-years respectively, $p = 0.814$) (Table 3, Fig. 2). All the five deaths (5.9%) that occurred (2 cases (5.6%) in the VATS group and 3 cases (6.1%) in the open group) were related to recurrences. There was no significant difference in the mortality rate between the two groups (0.8 vs. 0.9 per 100 person-years, $p = 0.850$) (Table 3, Fig. 3). The hazard ratio (95% confidence interval) of the recurrence-free survival was 1.14 (0.38–3.39) when comparing VATS with the open group.

Additionally, we found that pathological finding was significantly related to the long-term outcomes (Table 3). Thymoma had the lowest rate of recurrence, followed by thymic carcinoma then lymphoma. Other types of cancer (e.g., sarcoma, teratoma, other carcinomas) had the worst prognosis with regard to both recurrence and mortality. Other characteristics (age, gender, tumor size, tumor location) had no significant association with the long-term outcomes.

Discussion

This study aimed to compare the short-term and long-term outcomes between VATS and traditional open surgery in patients with mediastinal malignancies. Our results suggest that VATS is feasible and safe in the treatment of mediastinal malignancies. Compared with traditional open surgery, VATS required significantly shorter duration of operation, postoperative chest tube drainage, and postoperative hospital stay. VATS also reduced postoperative pain and complications. The two procedures were similar regarding long-term outcomes (recurrence and mortality).

With the advantages of minimal invasiveness, VATS has been gaining popularity in recent years in the surgery of most of the thoracic disorders, including lobectomy for lung cancer, decortication for empyema, resection for esophageal cancer, thymectomy for thymoma and myasthenia gravis, lymph node dissection in several malignancies, and benign mediastinal tumors or cysts as well [10–27]. By reducing tissue damage, VATS also reduces postoperative complications, pain, and the risk of infection, in comparison with conventional open surgery [11, 12, 14–16, 19–21, 24, 28]. These advantages of VATS were confirmed in our study, which included a number of different types of mediastinal tumors. In addition, with rapid recovery, VATS can allow for early administration of adjuvant chemo-radiotherapy where required. There are other studies reporting similar advantages in perioperative outcomes with VATS for the resection of mediastinal tumors [7, 8, 14, 16, 17, 22, 23]. A limitation of VATS compared with open surgery is the limited vision and manipulation while

Table 2 Perioperative results across treatment groups

Characteristics	VATS ($n = 36$)	Open ($n = 49$)	P
Operation duration (min)	84.6 ± 41.2 70 [25; 180]	124.8 ± 50.8 120 [40; 270]	< 0.001[a]
Intraoperative blood loss (ml)	59.8 ± 59.4 50 [2; 200]	235.2 ± 307.7 150 [2; 1600]	< 0.001[a]
Postoperative pain score	4.9 ± 1.4 5 [2; 7]	6.7 ± 1.5 7 [3; 9]	< 0.001[a]
Chest tube drainage duration (day)	2.1 ± 0.3 2 [2; 3]	3.1 ± 0.9 3 [2; 7]	< 0.001[a]
Postoperative hospitalization duration (day)	5.2 ± 1.4 5 [3; 8]	8.0 ± 2.4 7 [5; 18]	< 0.001[a]
Complication (yes) (n (%))	0 (0.0)	7 (14.3)	0.019[b]
- Excessive bleeding	0	5	
- Postoperative atelectasis	0	2	

Summary statistic is absolute count (%) for categorical variables and mean ± sd and median [range] for continuous data

sd standard deviation; *VATS* video-assisted thoracoscopic surgery

[a] Mann-Whitney *U* test

[b] Fisher's exact test

Table 3 Prognostic factors for long-term outcomes

			Recurrence			Mortality		
Factor	*n*	Total time of follow-up (years)	Number of events	Incidence rate (per 100 person-years)	*P*	Number of events	Incidence rate (per 100 person-years)	*P*
Age group					0.243			0.500
- < 50 years	38	261.9	4	1.5		3	1.1	
- ≥ 50 years	47	322.5	9	2.8		2	0.6	
Gender					0.660			0.898
- Male	38	256.6	5	1.9		2	0.8	
- Female	47	327.9	8	2.4		3	0.9	
Tumor size					0.518			0.118
- < 9 cm	59	395.3	8	2.0		5	1.3	
- ≥ 9 cm	26	189.2	5	2.6		0	0.0	
Tumor location					0.555			0.442
- Anterior mediastinum	77	526.1	11	2.1		4	0.8	
- Middle/posterior mediastinum	8	58.3	2	3.4		1	1.7	
Pathological finding								
- Thymoma	53	381.1	1	0.3	Ref	0	0.0	Ref
- Thymic carcinoma	11	86.6	2	2.3	*0.036*	0	0.0	–
- Lymphoma	9	62.8	3	4.8	*<0.001*	0	0.0	–
- Others	12	54.0	7	13.0	*<0.001*	5	9.3	*<0.001*
+ Neuroendocrine carcinoma	3	19.9	1	5.0		0	0.0	
+ Adenocarcinoma	3	9.1	1	11.0		1	11.0	
+ Sarcoma	2	12.0	2	16.7		1	8.3	
+ Immature teratoma	1	2.5	1	40.0		1	40.0	
+ Germ cell tumor	1	2.1	1	48.0		1	48.0	
+ Large cell carcinoma	1	4.4	1	22.6		1	22.6	
+ Squamous cell carcinoma	1	4.0	0	0.0		0	0.0	
Surgical treatment					0.814			0.850
- VATS	36	254.3	6	2.4		2	0.8	
- Open	49	330.2	7	2.1		3	0.9	

P value is based on log-rank test. Significance is in italics

Ref reference group, *VATS* video-assisted thoracoscopic surgery

dissecting mediastinal tumors, especially when the tumor is adhered strongly to surrounding tissues, frequently seen in teratomas. In this study, we experienced a case of immature teratoma which was in the open surgery group. For benign mediastinal teratoma, a recent paper by Tian et al. with 108 cases favored VATS over traditional open surgery [22]. However, there is still a need for careful dissection, aspiration of the internal fluid, and at times conversion to mini-thoracotomy may be required in cases of large tumors, intra-operative excessive bleeding, or dense adhesions [23]. However, for mature cystic teratoma with malignant transformation, VATS should not be favored because of a high risk of complications.

Currently, because of the lack of evidence with regard to the long-term oncological efficacy, minimally invasive techniques have not been routinely recommended by guidelines for the treatment of mediastinal malignancies. Several studies reported similar overall survival, disease-free survival, and recurrence rates between VATS and open surgery in the treatment of thymic malignancies and teratoma [10, 29]. Similarly, our results showed that VATS and open surgery were comparable regarding the long-term oncological outcomes. With a 9-year follow-up period, the recurrence and mortality rates did not significantly differ between the two techniques. This might be due to the complete resection of all tumors in our study. Complete tumor resection is an

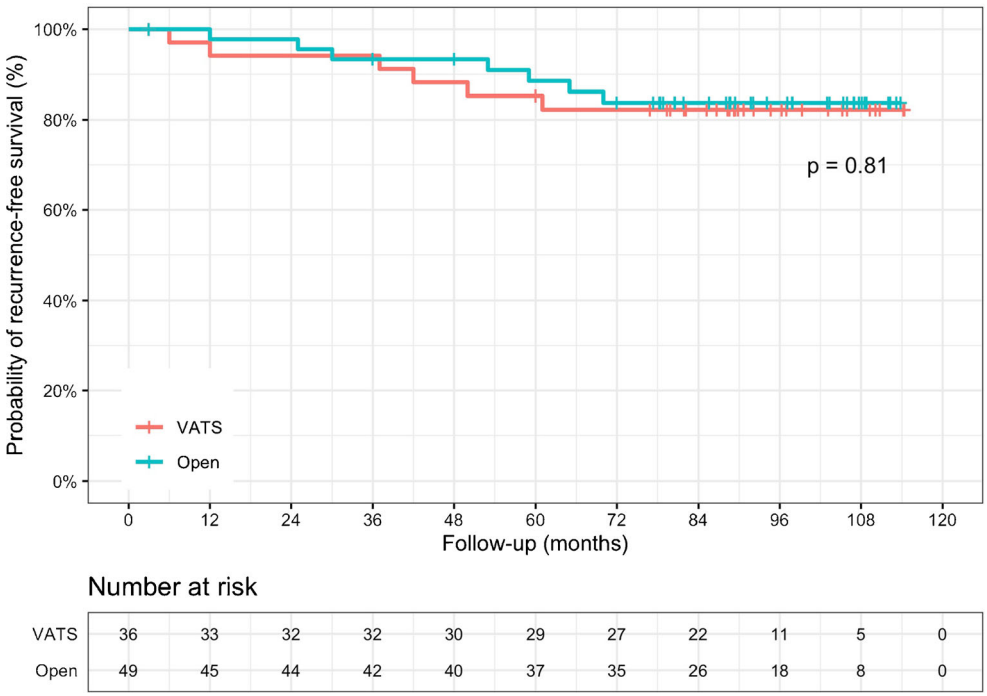

Fig. 2 Kaplan-Meier analysis of recurrence-free survival across treatment groups. VATS video-assisted thoracoscopic surgery

important indicator for long-term outcomes in the treatment of mediastinal malignancies and this could be achieved by either VATS or open technique. The power of the study for the primary endpoint (recurrence-free survival) was 0.8. In addition, we also found that the pathology of mediastinal malignancies was an important prognostic factor for patients. While thymic malignancies had good prognosis, other carcinomas, sarcoma, and teratoma were at a high-risk of recurrence and had worse mortality. Many novel techniques like single-port VATS and robotic surgery have been used to treat mediastinal tumors especially thymomas with good results [30, 31]. These techniques perhaps can also be applied for other mediastinal malignancies in the near future.

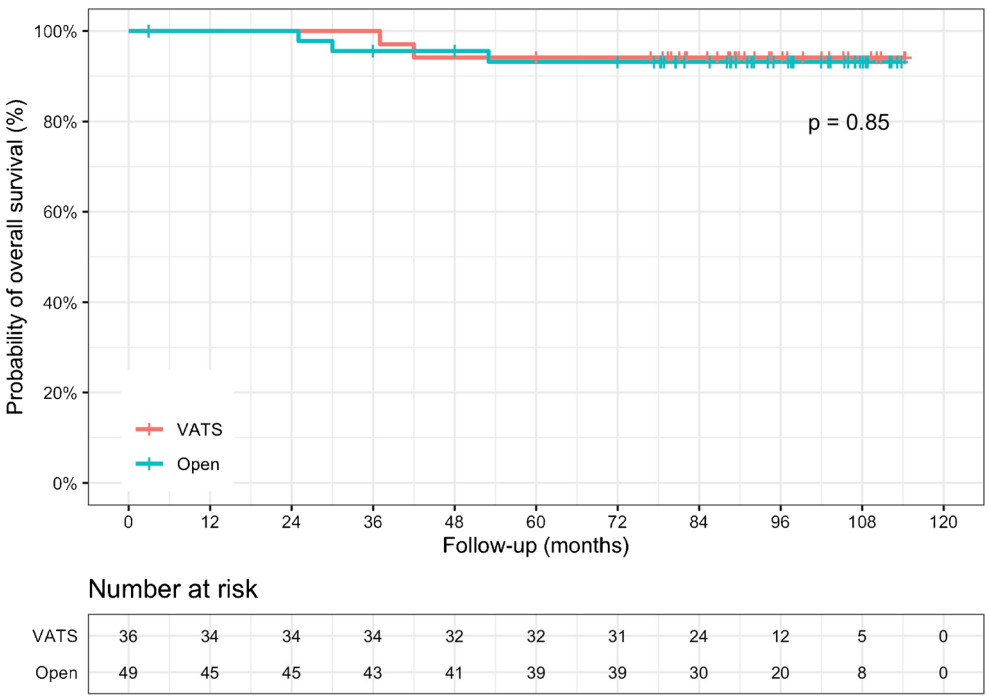

Fig. 3 Kaplan-Meier analysis of overall survival across treatment groups. VATS video-assisted thoracoscopic surgery

Limitations of the study

Firstly, the study has a relatively small sample size. Secondly, in the absence of randomization, selection bias cannot be ruled out which may have resulted in the imbalance between the two surgical groups with regard to the tumor size and pathological findings. This may have impacted the comparisons of the study endpoints. Also, the inclusion/exclusion criteria were limited to mediastinal tumors which were suitable for both VATS and open surgery; thus, our results could not be generalized to all mediastinal tumors especially those invading the surrounding tissues. Trucut biopsy was not available at our hospital when this study was performed; therefore, there were 9 cases of lymphoma who should not have undergone surgical resection.

Conclusion

Video-assisted thoracoscopic surgery is safe, feasible, and effective for the resection of mediastinal malignancies. Compared with traditional open approach, VATS is less traumatic with shorter operative duration, lower intraoperative blood loss, and lower postoperative pain and complication rate, and leads to reducing the duration of postoperative chest drainage and hospitalization. The two techniques are comparable regarding the long-term oncological and survival outcomes. Therefore, we advocate the VATS approach as a favored option for surgical resection of mediastinal malignancies.

Funding None

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of Cho Ray hospital, Ho Chi Minh City, Vietnam (No. 15C/2011/BV-HĐĐĐ, dated 09 March 2011).

Informed consent Consent to participate: Informed consent was obtained from all individual participants included in the study.

Consent to publish Patients signed informed consent regarding publishing their data and photographs.

References

1. Strollo DC, Rosado de Christenson ML, Jett JR. Primary mediastinal tumors. Part 1: tumors of the anterior mediastinum. Chest. 1997;112:511–22.
2. Cohen AJ, Thompson L, Edwards FH, Bellamy RF. Primary cysts and tumors of the mediastinum. Ann Thorac Surg. 1991;51:378–84.
3. Davis RD Jr, Oldham HN Jr, Sabiston DC Jr. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management, and results. Ann Thorac Surg. 1987;44:229–37.
4. Strollo DC, Rosado-de-Christenson ML, Jett JR. Primary mediastinal tumors: part II. Tumors of the middle and posterior mediastinum. Chest. 1997;112:1344–57.
5. Li WWL, van Boven WJP, Annema JT, Eberl S, Klomp HM, de Mol BAJM. Management of large mediastinal masses: surgical and anesthesiological considerations. J Thorac Dis. 2016;8:E175–84.
6. Demmy TL, Krasna MJ, Detterbeck FC, et al. Multicenter VATS experience with mediastinal tumors. Ann Thorac Surg. 1998;66:187–92.
7. Yuan ZY, Cheng GY, Sun KL, et al. Comparative study of video-assisted thoracic surgery versus open thymectomy for thymoma in one single center. J Thorac Dis. 2014;6:726–33.
8. Marshall MB, DeMarchi L, Emerson DA, Holzner ML. Video-assisted thoracoscopic surgery for complex mediastinal mass resections. Ann Cardiothorac Surg. 2015;4:509–18.
9. Chow S-C, Shao J, Wang H. Sample size calculations in clinical research (second edition). Chapman & Hall/CRC Biostatistics Series. 2008;177.
10. Shintani Y, Funaki S, Nakagiri T, et al. Experience with thoracoscopic resection for mediastinal mature teratoma: a retrospective analysis of 15 patients. Interact Cardiovasc Thorac Surg. 2013;16:441–4.
11. Wu X, He J, Jiang H, et al. Fully thoracoscopic versus conventional open resection for esophageal carcinoma: a perioperative comparison. Thorac Cancer. 2013;4:369–72.
12. Amer K, Khan AZ, Rew D, Lagattolla N, Singh N. Video assisted thoracoscopic excision of mediastinal ectopic parathyroid adenomas: a UK regional experience. Ann Cardiothorac Surg. 2015;4:527–34.
13. Harris CG, James RS, Tian DH, et al. Systematic review and meta-analysis of uniportal versus multiportal video-assisted thoracoscopic lobectomy for lung cancer. Ann Cardiothorac Surg. 2016;5:76–84.
14. Qi K, Wang B, Wang B, Zhang LB, Chu XY. Video-assisted thoracoscopic surgery thymectomy versus open thymectomy in patients with myasthenia gravis: a meta-analysis. Acta Chir Belg. 2016;116:282–8.
15. Yang YF, Dong R, Zheng C, et al. Outcomes of thoracoscopy versus thoracotomy for esophageal atresia with tracheoesophageal fistula repair: a PRISMA-compliant systematic review and meta-analysis. Medicine (Baltimore). 2016;95:e4428.
16. Yang Y, Dong J, Huang Y. Thoracoscopic thymectomy versus open thymectomy for the treatment of thymoma: a meta-analysis. Eur J Surg Oncol. 2016;42:1720–8.
17. Zhang W, Wei Y, Jiang H, Xu J, Yu D. Video-assisted thoracoscopic surgery versus thoracotomy lymph node dissection in clinical stage I lung cancer: a meta-analysis and system review. Ann Thorac Surg. 2016;101:2417–24.
18. Murakawa T, Sato H, Okumura S, et al. Thoracoscopic surgery versus open surgery for lung metastases of colorectal cancer: a multi-institutional retrospective analysis using propensity score adjustment. Eur J Cardiothorac Surg. 2017;51:1157–63.
19. Pan H, He J, Shen J, Jiang L, Liang W, He J. A meta-analysis of video-assisted thoracoscopic decortication versus open thoracotomy decortication for patients with empyema. J Thorac Dis. 2017;9:2006–14.
20. Reichert M, Posentrup B, Hecker A, et al. Thoracotomy versus video-assisted thoracoscopic surgery (VATS) in stage III

empyema-an analysis of 217 consecutive patients. Surg Endosc. 2018;32:2664–75.
21. Zhai B, Zhang Y, Chen Z, et al. Effect of video-assisted thoracoscopic surgery on pain stress indicators NO, IL-1β and IL-6 in the treatment of mediastinal tumor in children. Oncol Lett. 2020;19:3931–6.
22. Tian Z, Liu H, Li S, et al. Surgical treatment of benign mediastinal teratoma: summary of experience of 108 cases. J Cardiothorac Surg. 2020;15:36.
23. Pham LH, Trinh DK, Nguyen AV, et al. Thoracoscopic surgery approach to mediastinal mature teratomas: a single-center experience. J Cardiothorac Surg. 2020;15:35.
24. Da M, Peng W, Mo X, et al. Comparison of efficacy between video-assisted thoracoscopic surgery and thoracotomy in children with mediastinal tumors: 6-year experience. Ann Transl Med. 2019;7:653.
25. Wu S, Liang H, Liang W, et al. Single- versus two-port video-assisted thoracic surgery in mediastinal tumor: a propensity-matched study. J Thorac Dis. 2019;11:4428–35.
26. Tian Z, Sui X, Yang F, Wang J. Is video-assisted thoracoscopy a sufficient approach for mediastinal lymph node dissection to treat lung cancer after neoadjuvant therapy? Thorac Cancer. 2019;10:782–90.
27. Guo C, Xia L, Mei J, et al. A propensity score matching study of non-grasping en bloc mediastinal lymph node dissection versus traditional grasping mediastinal lymph node dissection for non-small cell lung cancer by video-assisted thoracic surgery. Transl Lung Cancer Res. 2019;8:176–86.
28. Khanh HQ, Quang NVD, Tien TQ, Vuong NL. Long-term oncological outcome in thymic malignancies: videothoracoscopic versus open thymectomy. Eur Surg. 2019;51:295–302.
29. Youssef SJ, Louie BE, Farivar AS, Blitz M, Aye RW, Vallieres E. Comparison of open and minimally invasive thymectomies at a single institution. Am J Surg. 2010;199:589–93.
30. Caronia FP, Fiorelli A, Arrigo E, Trovato S, Santini M, Lo Monte AI. Bilateral single-port thoracoscopic extended thymectomy for management of thymoma and myasthenia gravis: case report. J Cardiothorac Surg. 2016;11:153.
31. Na KJ, Kang CH. Robotic thymectomy for advanced thymic epithelial tumor: indications and technical aspects. J Thorac Dis. 2020;12:63–9.