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ORIGINAL ARTICLE

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THORACIC

Robotic-assisted versus video-assisted thoracoscopic surgery for thymic epithelial tumours, from the European Society of Thoracic Surgeons Database

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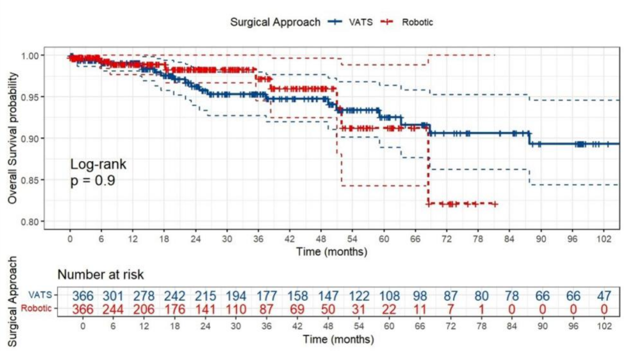
Robotic Assisted versus Video assisted Thoracoscopic surgery for Thymic Epithelial Tumours, from the European Society of Thoracic Surgeons Database

Summary

We assessed patients with thymic malignancy undergoing minimally invasive thymectomy (robot versus video-assisted) (899 patients, median age 55). Robot-assisted surgery had lower odds of incomplete resection (R1) but no difference in overall or disease-free survival was seen between techniques.



VATS: Video-assisted thoracoscopic surgery.

Abstract

OBJECTIVES: Minimally invasive thymectomy is an accepted approach for early-stage thymic epithelial neoplasia, reducing pain and length of stay compared with open surgery. In this study, we compare robotic and video-assisted thymectomy to assess pathological resection status, overall and disease-free survival.

†The first two authors are joint first authors and contributed equally to this study.
‡ESTS Thymus Collaborative Steering Group Author Model is available in the Acknowledgements section.
§The last two authors are joint senior authors and contributed equally to this study.

METHODS: Data were retrieved from the European Society of Thoracic Surgeons prospectively maintained thymic database. Eighty-two international centres were invited to participate in the ESTS registry. Thirty-seven centres agreed to take part. We included all patients who had undergone complete thymectomy for malignancy through a minimally invasive approach and excluded patients in whom complete data were not available.

RESULTS: Between October 2001 and May 2021, a total of 899 patients with thymic malignancy underwent minimal access surgical resection and were included in the study. A propensity matched analysis was conducted with interrogation of 732 patients. Median age was 55 years, and 408 (56%) patients were female. Propensity matched was performed with 1:1 matching for surgical approach (video assisted = 366, robot assisted = 366). Robot-assisted surgery conferred significantly lower odds of incomplete resection (R1; 0.203 95% CI 0.13–0.317; $P < 0.001$). However, there was no difference in terms of overall and disease-free survival between the 2 techniques.

CONCLUSIONS: In this analysis, after adjusting for thymoma stage, the odds of incomplete surgical resection were higher in patients undergoing video-assisted surgery than robotic. However, there was no difference in overall or disease-free survival. With data maturation and increased follow-up, this would need repeat analysis and perhaps may provide more credence to the concept of a prospective randomized study to compare outcomes in thymic epithelial neoplasia by surgical approach with a standardized pathological work-up.

Keywords: Thymoma • Robot-assisted thoracic surgery • Video-assisted thoracic surgery • Minimally invasive surgery • Thymectomy • Survival

ABBREVIATIONS

RATS	Robotic-assisted thoracic surgery
R0	Margin negative
R1	Microscopically margin positive
R2	Macroscopically margin positive
TNM	Tumour-node-metastasis
WHO	World Health Organization
VATS	Video-assisted thoracoscopic surgery

INTRODUCTION

Early-stage thymoma can be treated with radical surgery with a 5-year survival >95%, and a risk of recurrence for stage I or II thymoma of 4–14% [1]. Traditionally, open surgery was the approach of choice for thymectomy, with a move towards minimally invasive video-assisted surgery in the last 20 years. Minimally, invasive surgery is now an accepted approach for early-stage thymic epithelial neoplasia and is associated with reduced pain, length of scar, complications and length of stay compared with open surgery [2–4].

Recently, robotic-assisted thoracic surgery (RATS) has been introduced, with a growing interest and increased uptake worldwide. Early reports of a randomized trial for lobectomy showed robotic-assisted surgery to be associated with better patient reported health-related quality of life at 12 weeks than video-assisted surgery (VATS) and improved lymph node clearance [3]. However, evidence comparing video-assisted to robotic-assisted thymectomy is limited, with retrospective cohort studies providing the standard for comparison. A recent meta-analysis of 7 publications including 994 patients (RATS = 428, VATS = 566) found no statistically significant difference in terms of operative time, blood loss, complications and resection status [5]. Another meta-analysis of 1418 patients (RATS = 688, VATS = 730) reported less blood loss, lower chest drainage, shorter length of stay and fewer post-operative complications in those undergoing robotic surgery [6]. However, data are limited as to whether video- or robotic-assisted surgery is superior in terms of resection status, disease-free and overall survival.

In this paper, we review the European Society of Thoracic Surgery prospectively maintained database to compare operative and survival outcomes for patients undergoing RATS versus VATS thymectomy.

METHODS

Data were retrieved from the European Society of Thoracic Surgeons (ESTS) prospectively maintained thymic database [7]. This database is a satellite database of the ESTS registry collecting patients with thymic tumors (thymomas, thymic carcinomas and neuroendocrine thymic tumors) among the ESTS Institutions. The history and development of the database has been previously well-described [7]. Eighty-two international centres were invited to participate in the ESTS registry with their most recent follow-up data. Thirty-seven centres agreed to take part, and 26 subsequently contributed to the registry with their follow-up data. The remaining 11 hospitals were excluded owing to incompleteness of data (Supplementary Material, Fig. S1). In each centre, data were submitted by the researcher who is committed as per the institutional agreement to collaborate in the study. Patients are carefully screened prior to being offered a minimally invasive procedure and not all patients having VATS or RATS resection are entered into the ESTS thymic database.

Inclusion criteria

We included all patients who had undergone complete thymectomy for malignancy through a minimally invasive approach and excluded patients in whom complete data were not available.

Exclusion criteria

Patients undergoing surgery prior to 2001 were excluded due to historical differences in thymic pathology reporting. Five cases with no recorded pathological diagnosis were excluded from the analysis.

Outcome measures

Our primary outcome measures were overall and disease-free survival (the length of time after primary treatment ends, in this case surgery, that the patient survives without any signs or symptoms of cancer recurrence). We also assessed secondary measures such as operative factors (conversion rate, pathological resection status and intraoperative blood loss) and short-term outcomes such as length of stay in hospital. Patient characteristics, operative, histological, and overall and disease-free survival data were collected. All patients were followed up until 2024.

Data collection and synthesis process

Data have been collected and synthesized as per the ESTS database protocol [7]. Within the cohort numerous approaches have been described particularly for the VATS group. The RATS group were overall more standardized with a 3–4 port approach (+/− assistant port) and use of the Da Vinci X or Xi model. The majority of the VATS/RATS procedures (>90%) were carried out unilaterally according to tumour laterality. Less than 5% were carried out from the subxiphoid approach (all VATS) and for myasthenic patients in the VATS cohort ($n = 8$), a bilateral approach was adopted. All centres participating in the database and who had performed RATS operations had been fully proctored by experienced robotic surgeons endorsed by the respective medical technology company. All pathological assessments were largely standardized between centres in accordance with the 2015 WHO Classification but most recently updated and conformed to the 2021 iteration [8, 9].

Statistical analysis

Continuous data will be reported as mean with standard deviation (SD) or median with interquartile range (IQR) as appropriate to the data distribution, and categorical data as counts and percentages. The data were explored using cross-tabulations with the outcome and exposure variables, and continuous data explored graphically using histograms. For categorical variables, we reported counts and percentages. For continuous data, group comparison was carried out using a Student's *t*-test or Mann–Whitney test depending on the distribution of data. Normality was assessed using Shapiro-Wilk testing. Group differences for categorical data were assessed using the chi-squared test of independence or Fisher's exact test for low frequencies.

Propensity score matching was used to estimate the effect of surgical approach on various intra- and post-operative parameters (continuous and binary outcome modelling). The propensity scores were estimated using logistic regression based on Age, Sex, BMI, Comorbidities, Neoadjuvant treatment requirement, subtype of approach (unilateral, bilateral, laterality (left or right), subxiphoid and number of incisions), the year and era of approach, clinical and pathological Masaoka-Koga stage, postoperative chemo- or radiotherapy, clinical TNM stage, pathological TNM stage, the presence of autoimmune conditions including Myasthenia Gravis, final pathological diagnosis including WHO classification and tumour size. One-to-one nearest neighbour matching was used. Seven hundred and thirty-two patients from the original 899 patients cohort were matched according to surgical approach used (RATS or VATS). Good balance was achieved between the VATS and RATS groups, with all standardized mean differences below 0.2 after matching, all standardized mean differences for squares and 2-way interactions between covariates were <0.15, indicating adequate balance. Caliper matching (0.2 times the standard deviation of the logit of the propensity score) was used as per Austin [10]. Figures 1 and 2 show the balance of covariates before and after matching. All patients within the range of propensity scores where both treated and control subjects exist were included in the analysis.

To estimate the effect of surgical approach on outcomes, logistic and linear regression modelling were used according to data distribution of the outcome variable with surgical approach use as the exposure, along with covariates and their interaction as predictors. For time-to-event data, Kaplan–Meier curves were estimated for treated and untreated samples in the propensity-matched cohort. Survival comparison between groups of patients was performed by the log-rank test with stratification by pairs for overall survival. For disease-free survival, we used the Gray estimator for competing risks with stratification by pairs. Covariate adjusted survival analyses were performed to estimate the relative effect of treatment on the hazard of outcome using a Cox proportional hazards model. We included full matching weights in the estimation. The comparisons () function in the *marginaleffects* package was used to perform g-computation in the matched sample to estimate the average treatment effect of the treated population (ATT). A cluster-robust variance was used to estimate its standard error with matching stratum membership as the clustering variable.

All analyses were conducted using R 4.2.3 and the *MatchIt*, *cobalt*, *sandwich*, *survival*, *survminer*, *lmtest*, *cmprsk*, *survRM2* and *marginaleffects* packages [11–18].

RESULTS

Patient characteristics

Between October 2001 and May 2021, 899 patients underwent minimal access complete thymectomy at 26 international centres for suspected thymic epithelial malignancy. Supplementary Material, Fig. S1 shows a flowchart for the study recruitment. Following 1:1 propensity matching, 732 matched patients were included in the final analysis.

The median age was 55 (43–80), with an overall female preponderance (56%). Five hundred and thirty-three patients (59%) underwent video-assisted surgery and 366 (41%) robotic assisted in the overall unmatched cohort. Table 1 details the number of patients from each institution contributing to the paper. We have included patient characteristics, staging distribution and histopathological data stratified by surgical approach in the overall unmatched cohort for transparency (Tables 2–4).

There was no difference between the 2 groups in terms of age ($P = 0.38$), body mass index ($P = 0.09$), IASLC stage distribution ($P = 0.55$) or WHO histological classification ($P = 0.61$) between the 2 groups. The median size of tumour size in VATS and RATS, respectively was 48 mm (23–79) and 45 mm (18–80), P = NS. The distribution of propensity scores and covariate balance is shown in Figs 1 and 2, respectively. After matching, all covariates demonstrated an absolute standardized mean difference of <0.1 apart from tumour size (0.12) indicating good matching.

Operative data

Estimation of the average treatment effect in the treated (ATT) showed that the RATS approach had a marginally shorter operative time (−7.68 min), albeit insignificant ($P = 0.094$; Table 5).

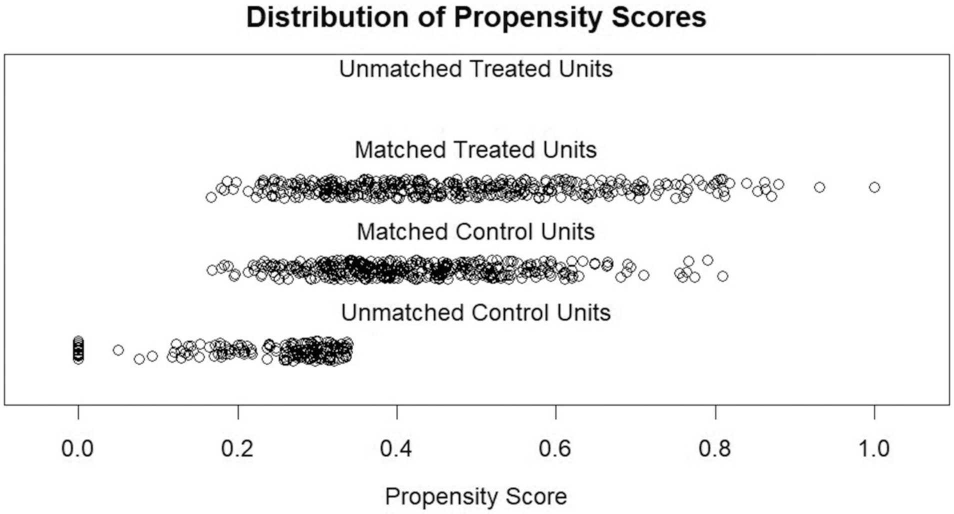


Figure 1: Distribution of propensity scores in the matched and unmatched dataset.

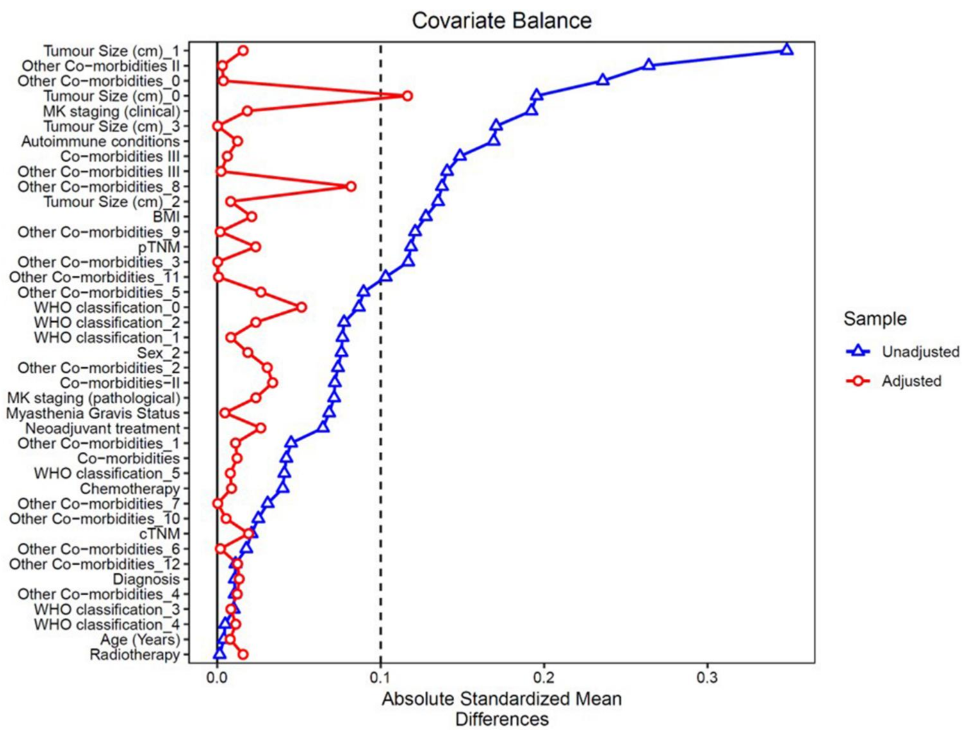


Figure 2: Covariate balance with differences in absolute mean standardized differences between matched and unmatched cohorts.

Intra-operative blood loss was also less in the RATS group (−23.6mls); however, this was also not statistically significant ($P = 0.128$). Odds of conversion was lower in the RATS group (OR 0.671 95% CI 0.244–1.84) which again was not significant ($P = 0.439$) (Table 5).

Resection status

A complete pathological resection with clear (R0) margin was achieved in 341 (94.7%) VATS cases and 360 (98.3%) RATS cases. The RATS approach was associated with a significantly lower odds of incomplete resection (0.227 95% CI 0.09–0.551; $P < 0.001$) (Table 5). Patients with R1/2 resections were managed according to the ESMO guidelines [19], and hence some were referred for further adjuvant treatment, usually radiotherapy; however, this was appropriately matched for in the quasi experimental propensity scoring. Within the overall cohort, alongside complete thymectomy 23 patients (12—VATS, 11—RATS) required concomitant resection of a combination of the lung, pericardium or phrenic nerve. These were matched accordingly (1:1) in the analysis cohort.

Postoperative outcomes

There was 1 intraoperative death due to bleeding, in a patient undergoing robotic thymectomy. More patients in the robotic

Table 1: Participating centres

Centre	$n = 732$ (100%)	Centre	$n = 732$ (100%)
Alexandrov national Centre, Belarus	180 (24.6)	Azienda University Hospital, Italy	14 (1.9)
Montreal University Hospital, Canada	75 (10.2)	Thoracic Oncology Centre, Switzerland	13 (1.9)
Saine Marguerite Hospital, France	55 (7.5)	Monza University Hospital, Italy	10 (1.4)
Poznan University, Poland	53 (7.2)	Cerrapasa Medical Faculty, Istanbul	9 (1.2)
University of Essen, Germany Karl Landsteiner Institute, Vienna, Austria	74 (10.1)	Delmenhorst Hospital, Germany	6 (0.8)
Royal Papworth Hospital, UK	43 (5.9)	Maggiore Hospital, Italy	5 (0.7)
Salamanca University Hospital, Spain	30 (4.1)	La Sapienza University Hospital, Italy	6 (0.8)
University Hospital Antwerp, Belgium	29 (3.9)	Ramon y Cajal Hospital, Spain	4 (0.5)
Azienda Hospital, Italy	29 (3.9)	Complejo Hopital, Spain	5 (0.7)
Instituto Europeo Di Oncologia, Italy	26 (3.6)	Luz Hospital, Portugal	3 (0.4)
University Hospital Parma, Italy	19 (2.6)	University Hospital Assiut, Egypt	1 (0.1)
Guy's Hospital, UK	23 (3.1)	St James's Hospital, Ireland	1 (0.1)
Misericordia de Porto, Brazil	19 (2.6)		

Table 2: Patient characteristics and comorbidities

	VATS, $n = 528$ (100%)	RATS, $n = 366$ (100%)
Age (SD)	61 (12)	60 (13)
BMI (SD)	27 (5)	26 (5)
Coronary artery disease (%)	82 (15)	45 (12)
Previous cardiac surgery (%)	5 (1)	5 (1)
Hypertension (%)	120 (22)	108 (29)
Arrhythmia (%)	20 (4)	16 (4)
Cardiac failure (%)	11 (2)	4 (1)
Insulin-dependent diabetes (%)	125 (23)	82 (22)
Creatinine >2 mg/dl (%)	32 (6)	29 (8)
Previous stroke/TIA (%)	54 (10)	27 (7)
Chronic kidney disease (%)	56 (11)	41 (11)
Chronic obstructive pulmonary disease (%)	9 (2)	7 (2)
Gastric ulcer (%)	25 (5)	15 (4)
Gastro-oesophageal reflux (%)	93 (17)	45 (12)
Liver disease (%)	10 (2)	–
Connective tissue disease (%)	17 (3)	16 (4)
Myasthenia Gravis (%)	9 (2)	7 (2)
Previous malignancy (%)	14 (3)	8 (2)

BMI: body mass index (kg/m^2); RATS: robotic-assisted thoracic surgery; VATS: video-assisted thoracic surgery.

Table 3: IASLC/ITMIG pre-operative stage distribution

	VATS, $n = 528$ (100%)	RATS, $n = 366$ (100%)
I	472 (89)	304 (83)
II	37 (7)	38 (10)
IIIA	15 (3)	19 (5)
IIIB		
IVA	2 (0.5)	5 (2)
IVB	2 (0.5)	

IASLC: international association for the study of lung cancer; ITMIG: international thymic malignancy interest group; RATS: robotic-assisted thoracic surgery; VATS: video-assisted thoracic surgery.

Table 4: WHO histological subtype

Subtype	VATS, $n = 528$ (100%)	RATS, $n = 366$ (100%)
A	93 (18)	48 (13)
AB	229 (43)	176 (48)
B1	75 (15)	60 (16)
B2	71 (13)	49 (14)
B3	42 (8)	16 (4)
C	11 (2)	11 (3)
Other: NET	7 (1)	6 (2)

Chi-squared P-value 0.61; NET: neuroendocrine tumour; RATS: robotic-assisted thoracic surgery; VATS: video-assisted thoracic surgery.

group had post-operative pneumonia (3.8% vs 0.5% in the VATS group), and more patients in the VATS group had a phrenic nerve injury (3% vs 1%). There was no significant difference in post-operative length of stay between the treatment arms, although the raw data favoured the RATS arm (−0.51 days, 95% CI −1.12 to 0.0974 days, $P = 0.099$) (Table 5).

Survival analysis

The median duration of follow-up was 50 months in the VATS group (IQR 12–66) compared to 40 months in the RATS group (IQR 24–58). By the end of follow-up, 19 patients (5.2%) had died in the VATS arm and 9 (2.5%) in the RATS. There was 1 intraoperative death due to bleeding in a patient treated with robotic resection. Three deaths in the VATS group were due to cancer recurrence, and 1 in the RATS group. The log-rank test showed no difference in overall survival between the 2 groups ($P = 0.903$). At the end of follow-up, 30 patients (4.1%) experienced a recurrence; 18 (4.9%) in the VATS arm and 12 (3.3%) in the RATS arm. The cumulative incidence function for relapse over time in the presence of competing events such as mortality showed no difference in recurrence rates by surgical approach (Gray estimate 0.199, $P = 0.655$) (Fig. 3). Restricted mean survival time analysis (truncated to 1200 days) demonstrated no

Table 5: Operative parameters and early post-operative outcomes analysed by weighted univariate modelling

Variable	Average treatment effect on treated	Standard error	95% confidence interval	P-value
Operative time (min)	−7.68	4.58	−16.7 to 1.3	0.094
Intra-operative blood loss (ml)	−23.6	15.5	−53.9 to 6.77	0.128
Length of stay (days)	−0.51	0.31	−1.12 to 0.0974	0.099
Pathological resection status	0.227 (odds ratio)		0.09 to 0.551	**<0.001**[a]
Conversion to open	0.671 (odds ratio)		0.244 to 1.84	0.439

[a]Values in bold indicates $P<0.05$.

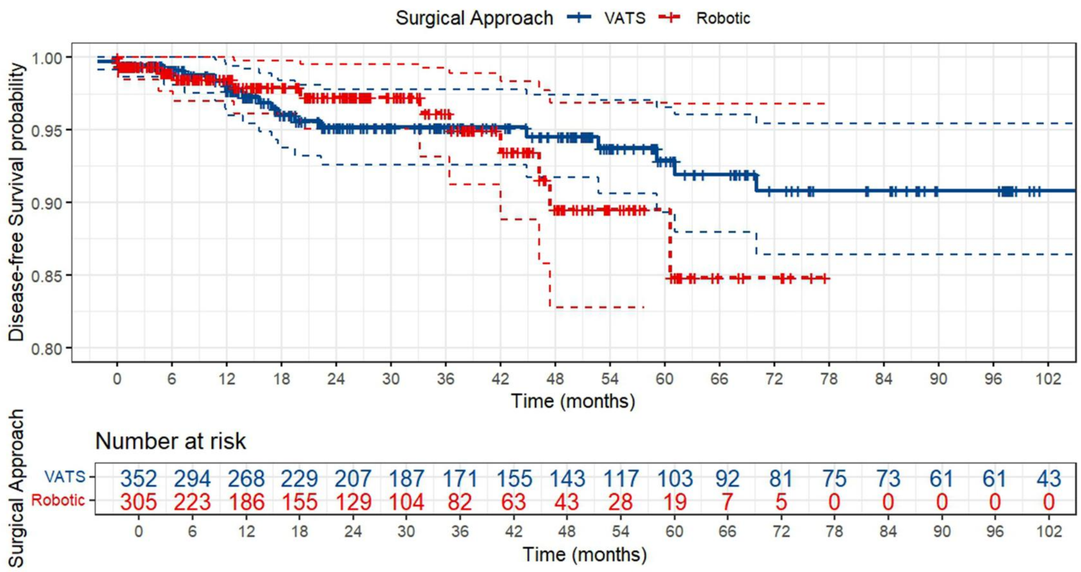


Figure 3: Kaplan–Meier curve for disease-free survival between RATS and VATS arms. RATS: robotic-assisted thoracic surgery; VATS: video-assisted thoracic surgery.

significant difference in average overall or disease-free survival times for either surgical approach (Table 6). Cox proportional hazards modelling for mortality and recurrence were not significant between surgical groups; HR 0.95 (0.399–2.26) and 1.27 (0.579–2.77), respectively (Table 7).

DISCUSSION

Minimally invasive thoracic surgery for management of thymectomy is an accepted and often preferred approach for early-stage thymic epithelial neoplasia, reducing pain and length of stay compared with open surgery [20]. However, there is limited evidence as to which surgical approach, VATS or RATS is superior in terms of pathological resection, recurrence and survival.

Worldwide, the most employed minimal access approach is VATS, with a large body of data to testify feasibility, safety and equivalent oncological outcomes to open surgery [21]. However, in recent years there has been increasing uptake of robotic techniques for thoracic surgery, with evidence of an advantage for operating in anatomically difficult regions [22].

Robotic surgeons argue that robotic systems allow unparalleled access to the anterior mediastinum, with improved instrument control and accuracy of dissection [23]. VATS surgeons maintain that they achieve equal resection margins with less cost involved, and the added benefit that in some cases, the VATS approach only requires a single incision, reducing pain and improving cosmesis [24].

A recent meta-analysis has shown VATS and RATS thymectomy to be equivalent in terms of operative outcomes [5], and another showing RATS to have superior outcomes in terms of intraoperative blood loss, complication rates and reduced length of stay [6]. Our study did not demonstrate statistically significant superiority of RATS in this regard, in fact we noted a higher post-operative rate of pneumonia in RATS patients compared with VATS. These patients were significantly comorbid however (COPD, diabetes and history of stroke or renal failure) which is likely to be more contributory than the actual access approach.

Data relating minimal access surgical approach to resection status, disease-free and overall survival is currently limited [25–27]. In our study, there was a significant difference in the rates of complete pathological resection. VATS surgery had an odds ratio for R1/R2 resection of 4.93 after adjusting for covariates in the matched dataset.

The Da-Vinci robotic system (Intuitive Surgical Inc., Sunnyvale, CA, USA) is currently the most adopted robotic system worldwide and may allow improved intraoperative vision thanks to high magnification and high-definition 3D cameras [22]. The improved visualization compared with hand-held VATS systems, as well as improved access via wristed

Table 6: Restricted mean survival time analysis up to 1200 days between surgical groups

Variable	Approach	RMST (days)	Standard Error	95% confidence interval	*P*-value
Overall survival (days)	VATS	1166.8	9.4	1148.3–1185.4	0.198
	RATS	1182.5	7.8	1167.3–1197.8	
Disease-free survival (days)	VATS	1160.2	10.9	1138.9–1181.5	0.471
	RATS	1171.1	10.5	1150.4-–1191.7	

RATS: robotic-assisted thoracic surgery; VATS: video-assisted thoracic surgery.

Table 7: Weighted cox-proportional hazards analysis for overall and disease-free survival (RATS versus VATS)

Variable	Hazard ratio	Standard error	95% confidence interval	*P*-value
Overall survival (days)	0.95	0.442	0.399–2.26	0.908
Disease-free survival (days)	1.27	0.399	0.579–2.77	0.553

RATS: robotic-assisted thoracic surgery; VATS: video-assisted thoracic surgery.

instruments may account for the increased number of completely resected specimens.

Despite the difference in resection status, there was no difference in either survival or recurrence by surgical approach. The analysis was limited by low follow-up duration, with a median follow-up of 50 months in the VATS group (IQR 12–66) and 40 months in the RATS group (IQR 24–58). In thymic malignancy, relapse often occurs after an extended period has elapsed from initial surgery [28], and further review of this database is required in the future to assess if the differences in resection status transpire into a survival or recurrence difference.

This is a long interval dataset from 2001 to 2021, and as a result there may be inherent lead time and treatment biases over time. We did account for the year and era of resection (in 5-year increments) in the propensity matching, nonetheless. We did not see any major differences in outcome between either technique over time. The most significant time-dependent phenomenon we encountered was related to the need for pre-operative biopsy which was pursued more aggressively in the earlier experience of this series but gradually declined over time as radiology was relied upon to diagnose thymic tumours pre-operatively.

This study is limited by its retrospective nature, and low numbers of events (recurrence/death). Whilst the 2 cohorts seem well matched in baseline characteristics, histology and stage distribution, there is a risk with all observational studies and data registries of selection bias and unaccounted confounding. Participation in the ESTS registry is voluntary, and therefore a bias may be present due to self-selection of contributors. The overall follow-up duration could still be longer, and this is an important consideration in a disease process which can recur 10–15 years post-operatively. With data maturation overall and disease-free survival analysis will likely need to be repeated to ensure the trends observed are preserved over time. Complete reliable and long-term follow-up data are a significant challenge for data registries, and therefore only centres who were able to provide accurate follow-up data were included in the study.

Whilst we have found a significant difference in resection status, due to the limitations of a data registry, a recommendation for preferring one or the other cannot be made. This study does, however, create an argument for the need of a prospective randomized study comparing RATS and VATS thymectomy, as well as reviewing selection criteria for minimally invasive surgery. Given the indolent nature of thymic cancer, a prospective study represents a significant challenge in terms of time and resources. In view of the rarity of thymic disease and the intrinsic difficulties of a prospective study, our data add to a growing body of evidence testifying to the safety and applicability of robotic thymic resection. With ongoing innovation in the field, as exemplified by the recent Korean experience of the single-port robotic approach in thymic resection [29], data will continue to be added to the literature and with maturation over time, we will be able to see if outcomes remain equivocal between different minimally invasive techniques.

CONCLUSION

In this multicentre international observational study, video-assisted thymectomy was associated with significantly higher odds of incomplete tumour resection compared with robotic assisted surgery. There was 1 intraoperative death in the RATS group due to bleeding. There was no difference in overall survival or disease-free survival in this cohort, with data maturation and increased follow-up, this would need repeat analysis and perhaps may provide more credence to the concept of a prospective randomized study to compare outcomes in thymic epithelial neoplasia by surgical approach with a standardized pathological work-up and thus delineate the optimal minimal access approach in this condition.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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DATA AVAILABILITY

All data are available upon reasonable request from the corresponding author.

ETHICAL STATEMENT

Local IRB ethical consent was waived for this study given that there was no direct patient contact (01.08.23).

Author contributions

Akshay J. Patel: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Software; Supervision; Validation; Writing—original draft; Writing—review & editing. **Alexander Smith:** Conceptualization; Data curation; Methodology; Writing—original draft. **ESTS Thymus Collaborative Steering Group:** Data curation. **Enrico Ruffini:** Conceptualization; Data curation; Methodology; Writing—review & editing. **Andrea Bille:** Conceptualization; Data curation; Writing—review & editing.

Reviewer information

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REFERENCES

[1] Detterbeck FC, Parsons AM. Thymic tumors. Ann Thorac Surg 2004;77:1860–9.
[2] 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.
[3] Patel YS, Baste JM, Shargall Y, Waddell TK, Yasufuku K, Machuca TN et al Robotic lobectomy is cost-effectiveeffective andand provides comparable health utility scores toto video-assistedassisted lobectomy: early results of the RAVAL trial. Ann Surg 2023;278:841–9.
[4] Patel YS, Hanna WC, Fahim C, Shargall Y, Waddell TK, Yasufuku K et al RAVAL trial: protocol of an international, multi-centered, blinded, randomized controlled trial comparing robotic-assisted versus video-assisted lobectomy for early-stage lung cancer. PLoS One 2022;17:e0261767.
[5] O'Sullivan KE, Kreaden US, Hebert AE, Eaton D, Redmond KC. A systematic review and meta-analysis of robotic versus open and video-assisted thoracoscopic surgery approaches for lobectomy. Interact Cardiovasc Thorac Surg 2019;28:526–34.
[6] Shen C, Li J, Li J, Che G. Robot-assisted thoracic surgery versus video-assisted thoracic surgery for treatment of patients with thymoma: a systematic review and meta-analysis. Thorac Cancer 2022;13:151–61.
[7] Ruffini E, Falcoz PE, Guerrera F, Filosso PL, Thomas P, Novoa N et al The European Society of Thoracic Surgeons (ESTS) thymic database. J Thorac Dis 2018;10:S3516–S20.
[8] Marx A, Chan JKC, Coindre JM, Detterbeck F, Girard N, Harris NL et al The 2015 world health organization classification of tumors of the thymus: continuity and changes. J Thorac Oncol 2015;10:1383–95.
[9] Marx A, Chan JKC, Chalabreysse L, Dacic S, Detterbeck F, French CA et al The 2021 who classification ofof tumors ofof thethe thymus andand mediastinum: wwhat is new inin thymic epithelial, germ cell, andand mesenchymal tumors? J Thorac Oncol 2022;17:200–13.
[10] Austin PC. Optimal caliper widths for propensity-score matching when estimating differences in means and differences in proportions in observational studies. Pharm Stat 2011;10:150–61.

[11] MatchIt: getting started [Internet]. https://cran.r-project.org/web/packages/MatchIt/vignettes/MatchIt.html (11 March 2024, date last accessed).
[12] Zeileis A, Lumley T, Graham N, Koell S. Sandwich: robust covariance matrix estimators [Internet] 2023. https://cran.r-project.org/web/packages/sandwich/index.html (11 March 2024, date last accessed).
[13] Estimation of RMST differences in 2 arms at a single time point [Internet]. https://cran.r-project.org/web/packages/simtrial/vignettes/rmst.html (12 August 2024, date last accessed).
[14] cmprsk package—RDocumentation [Internet]. https://www.rdocumentation.org/packages/cmprsk/versions/2.2-12 (12 August 2024, date last accessed).
[15] Survminer R package: Survival Data Analysis and Visualization—Easy Guides—Wiki—STHDA [Internet]. http://www.sthda.com/english/wiki/survminer-r-package-survival-data-analysis-and-visualization (20 August 2019, date last accessed).
[16] ggkm: Kaplan-Meier Survival Plot in emilelatour/laviz: What the Package Does [Internet]. https://rdrr.io/github/emilelatour/laviz/man/ggkm.html (4 March 2021, date last accessed).
[17] lmtest package—RDocumentation [Internet]. https://www.rdocumentation.org/packages/lmtest/versions/0.2-2 (11 March 2024, date last accessed).
[18] Arel-Bundock V, Diniz MA, Greifer N, Bacher E. Marginaleffects: predictions, comparisons, slopes, marginal means, and hypothesis tests [Internet]. 2024. https://cran.r-project.org/web/packages/marginaleffects/index.html (11 March 2024, date last accessed).
[19] Girard N, Ruffini E, Marx A, Faivre-Finn C, Peters S, ESMO Guidelines Committee. Thymic epithelial tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2015;26 Suppl 5:v40–55.
[20] Fok M, Bashir M, Harky A, Sladden D, DiMartino M, Elsyed H et al Video-assisted thoracoscopic versus robotic-assisted thoracoscopic thymectomy: systematic review and meta-analysis. Innov Phila Pa 2017; 12:259–64.
[21] Ng CSH, Wan IYP, Yim APC. Video-assisted thoracic surgery thymectomy: the better approach. Ann Thorac Surg 2010;89:S2135–2141.
[22] Bodner J, Augustin F, Wykypiel H, Fish J, Muehlmann G, Wetscher G et al The da Vinci robotic system for general surgical applications: a critical interim appraisal. Swiss Med Wkly 2005;135:674–8.
[23] Cerfolio RJ, Bryant AS, Minnich DJ. Starting a robotic program in general thoracic surgery: why, how, and lessons learned. Ann Thorac Surg 2011; 91:1729–36; discussion 1736–7.
[24] Li J, Qi G, Liu Y, Zheng X, Zhang X. Meta-analysis of subxiphoid approach versus lateral approach for thoracoscopic thymectomy. J Cardiothorac Surg 2020;15:89.
[25] Huang J, Rizk NP, Travis WD, Riely GJ, Park BJ, Bains MS et al Comparison of patterns of relapse in thymic carcinoma and thymoma. J Thorac Cardiovasc Surg 2009;138:26–31.
[26] Blumberg D, Port JL, Weksler B, Delgado R, Rosai J, Bains MS et al Thymoma: a multivariate analysis of factors predicting survival. Ann Thorac Surg 1995;60:908–13; discussion 914.
[27] Smith A, Cavalli C, Harling L, Harrison-Phipps K, Routledge T, Pilling J et al Impact of the TNM staging system for thymoma. Mediastinum 2021;5:32.
[28] Margaritora S, Cesario A, Cusumano G, Lococo F, Porziella V, Meacci E et al Single-centre 40-year results of redo operation for recurrent thymomas. Eur J Cardio-Thorac Surg Off J Eur Assoc Cardio-Thorac Surg 2011;40:894–900.
[29] Park SY, Lee JH, Kim YH, Kim HK. Multi-institutional surgical outcomes of robotic single-port surgery: a Korean experience. Ann Cardiothorac Surg 2023;12:41–5.

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