

Original Article

Association Between Pleural Breach and Perioperative and Long-Term Outcomes after Thymectomy for Myasthenia Gravis: A Two-Center Retrospective Study

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Cite this article as: Nabi MS, Sarwar Z, Shamshad R, Iftikhar H. Association between pleural breach and perioperative and long-term outcomes after thymectomy for myasthenia gravis: a two-center retrospective study. *Thorac Res Pract.* [Epub Ahead of Print]

ABSTRACT

OBJECTIVE: Thymectomy is an established treatment for myasthenia gravis and thymic tumors. This study evaluated the impact of pleural breach on perioperative pleural-related morbidity and long-term neurologic and oncologic outcomes following thymectomy.

MATERIAL AND METHODS: A retrospective multicenter review of 455 patients who underwent thymectomy between January 2005 and December 2024 was conducted at Services Hospital and Surgimed Hospital, Lahore, Pakistan. Patients underwent either a partial transsternal thymectomy (n = 273) or a video-assisted thoracoscopic surgery (VATS) thymectomy (n = 182). The primary outcome was pleural-related postoperative morbidity. Secondary outcomes included neurologic remission, recurrence-free survival (RFS), postoperative complications, and hospital stay.

RESULTS: Pleural breach occurred in all VATS cases and incidentally in 29 (10.6%) transsternal cases. VATS thymectomy was associated with lower blood loss ($P < 0.001$) and shorter hospital stay ($P < 0.001$), but with longer operative time ($P < 0.001$). Pleural-related complications were more frequent following pleural breach, but were generally transient and were managed conservatively. On multivariable analysis, pleural breach independently predicted pleural-related morbidity [odds ratio (OR): 2.6, $P = 0.006$]. The combined proportion of patients achieving complete stable remission, pharmacologic remission, or clinical improvement exceeded 90%. Neurologic remission and 5-year RFS were comparable between groups ($P = 0.612$ and $P = 0.538$, respectively).

CONCLUSION: Pleural breach during thymectomy was independently associated with increased transient pleural-related postoperative morbidity (OR: 2.6). However, these complications were generally self-limited and managed conservatively. Long-term neurologic remission and RFS were comparable between surgical approaches, but these findings should be interpreted cautiously given the retrospective observational design.

KEYWORDS: Myasthenia gravis, thymectomy, pleural integrity, video-assisted thoracoscopic surgery, partial transsternal approach, recurrence-free survival

Received: 07.03.2026

Revision Requested: 27.06.2026

Last Revision Received: 02.08.2026

Accepted: 03.08.2026

Epub: 09.10.2026

INTRODUCTION

Myasthenia gravis (MG) is an antibody-mediated disorder of the neuromuscular junction. Surgical removal of the thymus (thymectomy) is an established therapeutic option for patients with thymoma and for selected patients with non-thymomatous generalized MG.¹ Recent literature on thoracoscopic procedures highlights that prolonged air leak (PAL) and pleural-space complications are important contributors to postoperative morbidity after pleura-entering thoracic operations. By contrast, pleura-sparing transsternal thymectomy avoids intentional pleural violation but is more invasive to the chest wall and the sternum. Comparative studies and meta-analyses published in the last ten years have examined short-term perioperative outcomes and longer-term neurologic (remission/improvement) and oncologic outcomes after open, video-assisted thoracoscopic surgery (VATS), and robotic thymectomy. The completeness of mediastinal fat clearance remains a critical determinant of long-term neurologic remission and recurrence for both thymomatous and non-thymomatous indications.²⁻¹²

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Despite increasing adoption of minimally invasive thymectomy, the independent clinical impact of pleural breach during thymectomy remains insufficiently characterized. Most comparative studies evaluate outcomes according to surgical approach rather than actual pleural integrity status. Because pleural violation may influence postoperative pulmonary morbidity independently of operative technique, further evaluation is warranted. We hypothesized that pleural breach increases short-term pleural morbidity without adversely affecting long-term neurologic or oncologic outcomes. The present study, therefore, aimed primarily to assess the association between pleural breach and pleural-related postoperative morbidity following thymectomy and, secondarily, to compare neurologic and oncologic outcomes between transsternal and VATS approaches. Because long-term neurologic remission and oncologic control are more strongly influenced by the completeness of resection, mediastinal fat clearance, tumor biology, and MG severity than by pleural integrity itself, long-term outcomes in the present study were analyzed as exploratory secondary endpoints rather than as direct mechanistic consequences of pleural breach.

Few large-scale, long-term reports from South Asia describe the outcomes of different thymectomy approaches for symptomatic MG. This is the first South Asian study specifically evaluating actual pleural integrity rather than the surgical approach alone. Regional retrospective series from Pakistan and neighboring countries report remission and improvement rates that are broadly comparable to international experience.^{10,13} Presenting a twenty-year (2005–2024), two-center experience from Services Hospital and Surgimed Hospital, Lahore, Pakistan, will therefore add important local data on surgical details, perioperative complications, and long-term neurologic outcomes among symptomatic MG patients managed in a tertiary care setting.

MATERIAL AND METHODS

Study Design and Setting

This was a retrospective multicenter cohort study conducted at the Department of Thoracic Surgery, Services Hospital, and Surgimed Hospital in Lahore, Pakistan. The study included all consecutive patients who underwent thymectomy for MG or thymic pathology between January 2005 and December 2024.

Main Points

- Video-assisted thoracoscopic surgery (VATS) thymectomy demonstrated significantly longer operative time, reduced blood loss, and longer hospital stay compared with partial transsternal thymectomy.
- Neurologic outcomes, including complete stable remission and pharmacologic remission, were comparable between VATS and transsternal approaches in patients with myasthenia gravis.
- Pleural breach during VATS thymectomy did not negatively impact long-term recurrence-free survival when meticulous surgical technique and postoperative care were applied.

The study protocol was approved by the Institutional Review Board/Ethics Committee of the Services Institute of Medical Sciences (SIMS), Services Hospital, Lahore, Pakistan (approval no.: IRB/2025/1693/SIMS, date: 07/11/2025). Given the retrospective nature of the study and the use of anonymized clinical data, the institutional review board waived the requirement for written informed consent.

Patient Selection

All adult patients (≥ 18 years) who underwent complete thymectomy via either partial transsternal (open) or VATS approach were included. A total of 497 patients were identified. Forty-two patients with incomplete clinical records, prior mediastinal surgery, palliative resection, or follow-up shorter than 12 months were excluded. A total of 455 patients met the inclusion criteria and formed the final study cohort.

The diagnosis of MG was based on compatible clinical features, electrophysiologic testing (including repetitive nerve stimulation and/or single-fiber electromyography, particularly in seronegative patients or diagnostically uncertain cases), and positive serum acetylcholine receptor (AChR) antibody assays. Thymic tumors were diagnosed histopathologically according to World Health Organization (WHO) classification and staged using the Masaoka–Koga system.

Preoperative Evaluation and Optimization

All patients underwent standard preoperative evaluation, including chest computed tomography (CT) with contrast, pulmonary function testing, and neurology consultation for MG management. Preoperative optimization protocols remained institutionally standardized throughout the study period and included neurologic assessment, adjustment of anticholinesterase therapy, corticosteroid optimization, respiratory physiotherapy, and selective use of plasmapheresis or intravenous immunoglobulin for patients with advanced Myasthenia Gravis Foundation of America (MGFA) class (III–V) or bulbar symptoms.

Surgical Techniques

Two primary surgical approaches were employed:

• Partial Transsternal Thymectomy (Pleura-sparing)

The procedure was performed via upper/partial median sternotomy, with en bloc removal of the thymic gland, anterior mediastinal fat, and pericardiophrenic tissue, extending bilaterally to the phrenic nerves. The mediastinal pleura was preserved whenever feasible.

• VATS Thymectomy (Pleura-Breaching)

Conducted using a triportal or biportal technique under single-lung ventilation. Both phrenic nerves were identified and preserved. The mediastinal pleura was routinely opened to permit complete dissection of thymic and perithymic fat. Carbon dioxide insufflation (6–8 mmHg) was employed to enhance mediastinal exposure. One or two chest drains were placed at the end of the procedure.

All surgeries were performed by consultant thoracic surgeons experienced in both open and minimally invasive approaches. The choice of approach was determined by tumor characteristics, MG severity, and surgeon preference.

Pleural Integrity Assessment

Pleural integrity status (breached vs. intact) was recorded intraoperatively. Any pleural rent or intentional entry during VATS was categorized as “breached”. Postoperative pleural complications, including pneumothorax, effusion, PAL and empyema, were prospectively documented and graded according to the Clavien–Dindo classification.

Histopathological Examination

Resected specimens were analyzed by specialized pathologists. Histological subtypes (thymoma, thymic hyperplasia, or normal thymus) and tumor staging were performed using the Masaoka–Koga system, which remained the institutional standard throughout the study period. Margin status (R0/R1/R2) was verified in all thymoma cases. Thymoma staging was incorporated into subgroup and survival analyses.

Outcomes

The primary outcome of the study was pleural-related postoperative morbidity, defined as the occurrence of any of the following: pleural effusion requiring prolonged drainage, pneumothorax, PAL, empyema, or prolonged chest drainage (>5 days). Secondary outcomes included overall postoperative complications, neurologic outcomes according to MGFA-Post-Intervention Status (PIS) criteria, recurrence-free survival (RFS), operative parameters, and length of hospital stay.

Postoperative Care and Follow-Up

All patients were extubated in the operating room or in the early postoperative period unless extubation was delayed because of respiratory weakness or myasthenic crisis. Respiratory failure was defined as the requirement for prolonged postoperative mechanical ventilation (>48 hours), reintubation, or the development of postoperative myasthenic crisis requiring ventilatory support. Patients received standard postoperative analgesia, chest physiotherapy, and gradual resumption of anticholinesterase therapy. Pleural drains were removed when pleural drainage output was <100 mL/24 h and no air leak was present. Postoperative complications and 30-day mortality were recorded. Neurologic outcomes were assessed at 3 months, 6 months, and annually thereafter in collaboration with the neurology department. Clinical improvement and remission were defined according to the MGFA-PIS criteria. Long-term RFS was measured from the date of thymectomy to the date of documented tumor recurrence or the last follow-up. Patients without recurrence at the time of the last clinical follow-up were right-censored in Kaplan–Meier analyses. Follow-up continued until recurrence, death, or last available follow-up.

Statistical Analysis

Demographic data, preoperative variables, intraoperative details, and postoperative outcomes were retrieved from operative logs and electronic records. Normality of continuous variables was

assessed using the Shapiro–Wilk test. Normally distributed variables were compared using Student’s *t*-test, whereas non-normally distributed variables were analyzed using the Mann–Whitney *U* test. Categorical variables were compared using χ^2 or Fisher’s exact test as appropriate. Multivariable logistic regression analysis was performed to identify independent predictors of pleural-related morbidity. Variables with $P < 0.10$ in univariate analysis and clinically relevant covariates were entered into the model; these included age, MGFA class, presence of thymoma, Masaoka–Koga stage, operative period, operative duration, and pleural breach status. RFS, defined by tumor recurrence only, was evaluated using Kaplan–Meier analysis and Cox proportional hazards regression. Hazard ratios (HR) with 95% confidence intervals (CI) were reported. Statistical significance was defined as $P < 0.05$. The statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 455 patients with symptomatic MG underwent thymectomy between January 2005 and December 2024. Of these, 273 (60.0%) underwent partial transsternal pleura-sparing thymectomy (group A), and 182 (40.0%) underwent VATS thymectomy (group B). To account for temporal bias, the study period was stratified into early (2005–2014) and late (2015–2024) eras. VATS thymectomy was more frequently performed during the later period. Despite shorter hospital stays and lower blood loss in the later era, long-term neurologic and oncologic outcomes remained comparable after adjustment for the operative period. The mean age of the entire cohort was 35.8 ± 11.6 years (range: 18–69 years), with no significant age difference between the partial transsternal (36.4 ± 12.1 years) and VATS (34.9 ± 10.8 years) groups ($P = 0.214$). Females predominated in both groups (overall, 62.4%; $P = 0.376$). The mean duration of MG symptoms before surgery was 18.7 ± 10.3 months, similar between groups ($P = 0.451$). According to the MGFA clinical classification, 47.3% of patients had Class II disease, 35.6% had Class III disease, and 8.4% had Class IV–V disease, with no intergroup differences. AChR antibodies were detected in 82.6% of patients; while 5.5% were muscle-specific kinase-positive and 11.9% were seronegative. Preoperative immunotherapy included anticholinesterase agents in all patients, corticosteroids in 71.4%, and plasmapheresis in 22.2%. Chest CT revealed thymoma in 126 patients (27.7%): 77 (28.2%) in group A and 49 (26.9%) in group B ($P = 0.763$). Pulmonary function (forced vital capacity % predicted) averaged $78.9 \pm 9.8\%$ in the transsternal group and $80.3 \pm 10.1\%$ in the VATS group ($P = 0.172$) (Table 1).

The median operative times with interquartile range (IQR) were 125 (90–140) minutes for transsternal thymectomy and 142 (100–160) minutes for VATS thymectomy ($P < 0.001$). Median blood loss was 230 mL (IQR: 180–300) for the transsternal approach and 140 (100–180) mL for VATS ($P < 0.001$). Patients were further stratified by actual pleural status (breached versus intact), irrespective of surgical approach. Pleural-related complications, including prolonged drainage and pleural effusion, were significantly more common in patients with pleural breach whereas neurologic remission and RFS were not significantly influenced by pleural integrity status. The median

duration of chest drainage was 3 days (IQR: 2–5) in group A and 4 days (IQR: 3–6) in group B ($P = 0.008$). The median hospital stay was significantly longer for transsternal patients (6 days; IQR: 5–7) than for VATS patients (4 days; IQR: 3–5) ($P < 0.001$) Table 2.

Intraoperative complications were rare; the most common was small vessel injury (0.9%), and none required conversion from VATS to an open approach. There was no intraoperative mortality.

Table 1. Baseline demographic and clinical characteristics (n = 455)

Variable	Overall (n = 455)	Partial transsternal (n = 273)	VATS (n = 182)	P value
Age (years, mean $\pm$ SD)	35.8 $\pm$ 11.6	36.4 $\pm$ 12.1	34.9 $\pm$ 10.8	0.214
Female sex, n (%)	284 (62.4)	165 (60.4)	119 (65.4)	0.376
MG duration (months, mean $\pm$ SD)	18.7 $\pm$ 10.3	19.1 $\pm$ 10.9	18.0 $\pm$ 9.6	0.451
MGFA classification, n (%)				
Class I	40 (8.8)	23 (8.4)	17 (9.3)	0.538
Class II	215 (47.3)	132 (48.4)	83 (45.6)	
Class III	162 (35.6)	98 (35.9)	64 (35.2)	
Class IV–V	38 (8.4)	20 (7.3)	18 (9.9)	
AChR antibody positive, n (%)	376 (82.6)	224 (82.1)	152 (83.5)	0.691
MuSK-positive, n (%)	25 (5.5)	14 (5.1)	11 (6.0)	0.742
Seronegative MG, n (%)	54 (11.9)	35 (12.8)	19 (10.4)	0.468
Preoperative corticosteroid therapy, n (%)	325 (71.4)	198 (72.5)	127 (69.8)	0.531
Preoperative plasmapheresis/IVIG, n (%)	101 (22.2)	63 (23.1)	38 (20.9)	0.587
Thymoma on CT, n (%)	126 (27.7)	77 (28.2)	49 (26.9)	0.763
Masaoka–Koga stage (thymoma patients only), n (%)				
Stage I	66 (52.4)	34 (44.2)	32 (65.3)	0.041
Stage II	42 (33.3)	28 (36.4)	14 (28.6)	
Stage III	14 (11.1)	11 (14.3)	3 (6.1)	
Stage IV	4 (3.2)	4 (5.1)	0 (0.0)	
FVC (% predicted, mean $\pm$ SD)	79.5 $\pm$ 9.9	78.9 $\pm$ 9.8	80.3 $\pm$ 10.1	0.172
Operative era, n (%)				
Early era (2005–2014)	198 (43.5)	156 (57.1)	42 (23.1)	<0.001
Late era (2015–2024)	257 (56.5)	117 (42.9)	140 (76.9)	

Masaoka–Koga staging percentages were calculated among thymoma patients only (n = 126)
 MGFA: Myasthenia Gravis Foundation of America, AChR: acetylcholine receptor, MuSK: muscle-specific kinase, IVIG: intravenous immunoglobulin, FVC: forced vital capacity, VATS: video-assisted thoracoscopic surgery, MG: myasthenia gravis, SD: standard deviation, CT: computed tomography

Table 2. Procedural details of thymectomy

Parameter	Partial transsternal (n = 273)	VATS (n = 182)	P value
Operative time (min) median (IQR)	125 (90–140)	142 (100–160)	<0.001
Blood loss (mL) median (IQR)	230 (180–300)	140 (100–180)	<0.001
Pleural breach, n (%)	29 (10.6)	182 (100)	-
Intentional pleural breach, n (%)	0 (0)	182 (100)	<0.001
Incidental pleural breach, n (%)	29 (10.6)	0 (0)	<0.001
Chest drain insertion, n (%)	29 (10.6)	182 (100)	<0.001
Duration of chest drainage (days) median (IQR)	3 (2–5)	4 (3–6)	0.008
Hospital stay (days) median (IQR)	6 (5–7)	4 (3–5)	<0.001
Intraoperative complications, n (%)	3 (1.1)	1 (0.5)	0.482

Intentional pleural breach refers to a planned pleural entry during VATS thymectomy. An incidental pleural breach refers to an unintended violation of the pleura during transsternal thymectomy. In the transsternal group, chest drainage duration refers only to the 29 patients who required chest drain placement following an incidental pleural breach

VATS: video-assisted thoracoscopic surgery, IQR: interquartile range, min: minute

Overall, postoperative complications occurred in 63 patients (13.8%) (Table 3). The most frequent complications were transient respiratory failure in 25 patients (5.5%), pleural effusion requiring prolonged drainage for more than 3 days in 13 patients (2.9%), PAL for more than 5 days in 11 patients (2.4%), wound infection in 9 patients (1.8%), and postoperative bleeding requiring re-exploration in 5 patients (1.1%). Respiratory complications were more common with the VATS approach (7.1%) than with the transsternal approach (4.4%), although this difference was not statistically significant ($P = 0.187$). Wound complications were significantly higher in the transsternal group (2.9% vs. 0.5%, $P = 0.046$). The 30-day mortality was 0.7% ($n = 3$); all deaths occurred in the transsternal group and were due to myasthenic crisis and sepsis ($P = 0.265$).

Histopathologic examination showed thymic hyperplasia in 248 (54.5%), normal thymus in 81 (17.8%), and thymoma in 126 (27.7%). Among thymomas, the WHO subtypes were A (10.3%), AB (25.4%), B1 (30.2%), B2 (23.0%), B3 (8.7%), and C (2.4%). The distribution of histologic types differed significantly between surgical groups ($P = 0.006$). Among thymoma patients, Masaoka–Koga stage I disease was present in 52.4%, stage II in 33.3%, stage III in 11.1%, and stage IV in 3.2%. Early-stage disease (stage I–II) predominated in the VATS cohort, whereas advanced-stage thymomas were more frequently managed through transsternal thymectomy. Complete (R0) resection was achieved in 119 of 126 thymoma patients (94.4%). R1 resection occurred in 6 patients (4.8%), and R2 resection occurred in 1 patient (0.8%). R1/R2 resections were more common in advanced-stage thymomas managed by transsternal thymectomy (Table 4).

Table 3. Postoperative complications and 30-day mortality

Complication	Partial transsternal (n = 273)	VATS (n = 182)	P value
Respiratory failure	12 (4.4)	13 (7.1)	0.187
Pleural effusion	7 (2.6)	6 (3.3)	0.662
Prolonged air leak (for >5 days)	5 (1.8)	6 (3.3)	0.303
Wound infection	8 (2.9)	1 (0.5)	0.046
Re-exploration for bleeding	4 (1.5)	1 (0.5)	0.376
30-day mortality	3 (1.1)	0 (0.0)	0.265

VATS: video-assisted thoracoscopic surgery

Table 4. Histopathologic and oncologic outcomes

Variable	Overall	Partial transsternal (n = 273)	VATS (n = 182)	P value
Histopathology, n (%)				
Thymic hyperplasia	248 (54.5)	159 (58.2)	89 (48.9)	0.006
Normal thymus	81 (17.8)	36 (13.2)	45 (24.7)	
Thymoma	126 (27.7)	77 (28.2)	49 (26.9)	
WHO thymoma subtype, n (%)				
Type A	14 (10.3)	8 (10.3)	6 (10.4)	0.999
Type AB	32 (25.4)	20 (25.6)	12 (25.0)	
Type B1	37 (30.2)	23 (29.5)	14 (31.3)	
Type B2	29 (23.0)	18 (23.1)	11 (22.9)	
Type B3	11 (8.7)	7 (9.0)	4 (8.3)	
Type C	3 (2.4)	2 (2.6)	1 (2.1)	
Masaoka–Koga stage, n (%)				
Stage I	66 (52.4)	34 (44.2)	32 (65.3)	0.041
Stage II	42 (33.3)	28 (36.4)	14 (28.6)	
Stage III	14 (11.1)	11 (14.3)	3 (6.1)	
Stage IV	4 (3.2)	4 (5.1)	0 (0.0)	
Resection status, n (%)				
R0 resection	119 (94.4)	74 (94.9)	45 (93.8)	0.723
R1 resection	6 (4.8)	4 (5.1)	2 (4.2)	
R2 resection	1 (0.8)	1 (1.3)	0 (0)	
Mean follow-up duration (months)	58±27			
VATS: video-assisted thoracoscopic surgery. WHO: World Health Organization				

The median follow-up was 84 months, and data were available for 409 patients. At the last follow-up, complete stable remission (CSR) was achieved in 142 (34.7%); pharmacologic remission (PR) in 94 (23.0%); improvement in 133 (32.5%); and unchanged or worsened status in 40 (9.8%). Patients with MGFA class I–II demonstrated significantly higher rates of CSR than patients with MGFA class III–V ($P < 0.05$). Time-to-remission analysis demonstrated no significant difference between surgical approaches. Remission or improvement rates (CSR + PR + improved) were 91.9% in the partial transsternal group and 93.3% in the VATS group ($P = 0.612$). At last follow-up, need for ongoing immunosuppressive therapy was lower in the VATS group (27.4% vs. 34.1%, $P = 0.164$). Among thymoma patients, recurrence occurred in 11 (8.7%) patients—eight after partial transsternal thymectomy and three after VATS thymectomy ($P = 0.298$) (Table 5).

Univariate analysis identified pleural breach ($P = 0.004$), operative time (per 10-min increase; $P = 0.012$), and presence of thymoma ($P = 0.047$) as significant predictors of postoperative pleural complications (effusion, air leak, or prolonged drainage). In multivariable logistic regression analysis, pleural breach [odds ratio (OR): 2.6, 95% CI: 1.3–5.1, $P = 0.006$] and longer operative time (OR: 1.9, $P = 0.018$) remained independent predictors (Table 6).

Follow-up was available for 409 patients (89.9%) at a mean duration of 58 ± 27 months. Among thymoma patients, recurrence occurred in 11 (8.7%): 8 in the partial transsternal group and 3 in the VATS group ($P = 0.298$). The median follow-up among thymoma patients was 56 months in the transsternal group and 64 months in the VATS group. Kaplan–Meier analysis demonstrated comparable RFS between surgical approaches, with 5-year RFS rates of 92.1% for partial transsternal thymectomy and 94.3% for VATS thymectomy (log-rank $P = 0.538$). Kaplan–Meier curves were generated, with numbers at risk and recurrence events for each subgroup displayed beneath the curves (Figure 1).

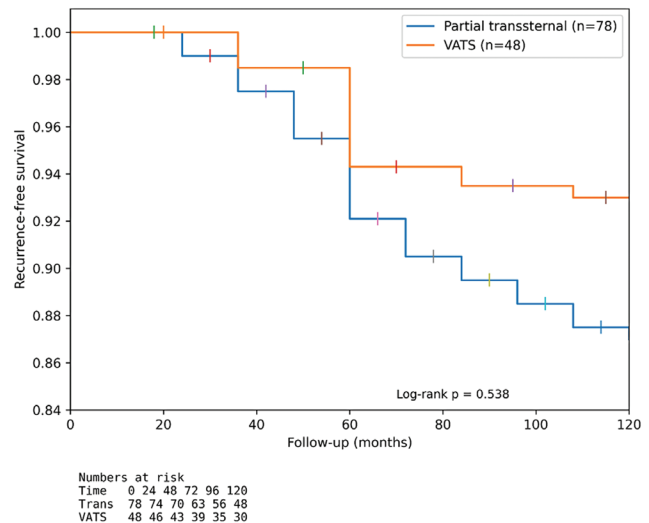


Figure 1. Kaplan–Meier RFS curve

RFS: recurrence-free survival, VATS: video-assisted thoracoscopic surgery

Among thymoma patients, Cox proportional hazards analysis demonstrated that advanced Masaoka–Koga stage (III–IV) and incomplete resection (R1/R2) were independently associated with significantly worse RFS (HR: 3.94, 95% CI: 1.42–10.87, $P = 0.008$; HR: 4.76, 95% CI: 1.61–14.03, $P = 0.004$, respectively). WHO B2/B3/C histology was also associated with an increased risk of recurrence (HR: 2.21, 95% CI: 1.03–4.74, $P = 0.041$). In contrast, surgical approach (VATS vs. transsternal), pleural breach status, and age were not significantly associated with RFS (Table 7).

DISCUSSION

The present 20-year, multicenter retrospective cohort study evaluated perioperative and long-term neurologic outcomes following partial transsternal (pleura-sparing) and VATS (pleura-breaching) thymectomy in patients with MG.

Table 5. Long-term neurologic and oncologic outcomes after thymectomy

Outcome	Overall (n = 409/455)	Partial transsternal (n = 250/273)	VATS (n = 159/182)	P value
Complete stable remission, n (%)	142 (34.7%)	88 (35.2%)	54 (34.0%)	0.798
Pharmacologic remission, n (%)	94 (23.0%)	56 (22.4%)	38 (23.9%)	0.725
Improved, n (%)	133 (32.5%)	88 (35.2%)	45 (28.3%)	0.147
Unchanged/worsened, n (%)	40 (9.8%)	18 (7.2%)	22 (13.8%)	0.028

VATS: video-assisted thoracoscopic surgery

Table 6. Predictors of pleural-related morbidity (logistic regression)

Variable	Univariate P value	Multivariate OR (95% CI)	P value
Pleural breach	0.004	2.6 (1.3–5.1)	0.006
Operative time (per 10 min increase)	0.012	1.9 (1.1–3.3)	0.018
Thymoma present	0.047	1.5 (0.9–2.8)	0.074
Age (increase per year)	0.288	-	-
Male sex	0.402	-	-

CI: confidence interval, min: minute, OR: odds ratio

Table 7. Cox proportional hazards analysis for recurrence-free survival in thymoma patients

Variable	HR	95% CI	P value
VATS vs. transsternal approach	0.81	0.24–2.71	0.538
Pleural breach	1.12	0.41–3.08	0.826
Masaoka–Koga stage III–IV	3.94	1.42–10.87	0.008
R1/R2 resection	4.76	1.61–14.03	0.004
WHO B2/B3/C subtype	2.21	1.03–4.74	0.041
Age (per year increase)	1.02	0.98–1.05	0.317

Cox proportional hazards regression was performed in thymoma patients (n = 126). Recurrence-free survival was defined as the interval from thymectomy to documented tumor recurrence or last follow-up. Variables included in the multivariable model were selected based on clinical relevance and prior oncologic literature. Advanced Masaoka–Koga stage and incomplete resection were independently associated with poorer recurrence-free survival

HR: hazard ratio, CI: confidence interval, VATS: video-assisted thoracoscopic surgery, WHO: World Health Organization

Our findings demonstrate that both surgical approaches provide comparable long-term neurologic improvement and RFS. The present findings should be interpreted in light of the nonrandomized retrospective design. Surgical approach selection was influenced by tumor characteristics, disease severity, operative era, and surgeon preference, introducing potential selection bias despite multivariable adjustment. Accordingly, the observed perioperative advantages of VATS thymectomy may partly reflect differences in case selection rather than operative technique alone. These results align with the international literature comparing neurologic outcomes between open and minimally invasive thymectomy when performed with comparable mediastinal clearance. The landmark Myasthenia Gravis Thymectomy Trial (MGTX) randomized controlled trial (2016) established the benefit of extended transsternal thymectomy in improving MG symptom control and reducing corticosteroid requirements.¹ Although the overall neurologic remission and improvement rates in our cohort exceeded 90%, direct comparison with the MGTX trial should be interpreted with caution because the outcome measures differed fundamentally. The MGTX trial assessed neurologic efficacy using quantitative endpoints, including the Quantitative MG score, prednisone requirements, and time-weighted clinical outcomes, whereas the present study evaluated postoperative neurologic status according to the MGFA-PIS classification. Furthermore, our reported rate represents the combined proportion of patients achieving CSR, PR, or clinical improvement, rather than complete remission alone. Differences in study design, follow-up duration, patient selection, and outcome definitions therefore preclude direct comparison of remission rates between the two studies. Since then, several comparative and meta-analytic studies have confirmed that VATS and robotic-assisted thymectomy achieve similar rates of clinical remission and improvement, with superior perioperative recovery metrics.^{14–17} In our series, the 5-year RFS was 92.1% for the partial transsternal group and 94.3% for the VATS group (log-rank $P = 0.538$), consistent with reported survival rates in large contemporary cohorts.^{15,18,19}

Our findings highlight the clinical relevance of pleural integrity during thymectomy. The pleura-sparing partial transsternal approach avoids pleural entry and thus minimizes postoperative air-leak risk; it is inherently more invasive to the chest wall, requiring a partial sternotomy and a longer recovery. Conversely, VATS thymectomy, by design, breaches the pleura and necessitates chest drainage; however, the minimal chest wall trauma translates into shorter hospitalization and faster rehabilitation. In our cohort, pleural breach was associated with a higher incidence of transient postoperative effusion (2.9%) and minor air leak (2.4%), both of which resolved with conservative management. These findings are comparable to those of other reports.^{16,20,21}

Although chest drainage duration was longer in the VATS cohort, hospitalization remained shorter overall, likely reflecting reduced chest wall trauma, earlier postoperative mobilization, and institutional practice favoring discharge with a chest drain once patients were clinically stable. By contrast, recovery following partial sternotomy required longer inpatient observation. An additional consideration is the potential influence of institutional and surgeon learning-curve effects. Over the 20-year study period, increasing experience with thoracoscopic thymectomy, improvements in perioperative care, refinement of anesthetic techniques, and advances in thoracoscopic instrumentation may have contributed to improved perioperative outcomes independent of the surgical approach. Although the operative era was incorporated into multivariable analyses, residual temporal confounding likely persists. In terms of operative efficiency, the mean operative time was marginally longer in the VATS group.²² However, blood loss was substantially lower, and the average length of hospital stay was nearly two days shorter than in the open group, an observation echoed in meta-analyses, which established minimally invasive thymectomy as a less morbid alternative to transsternal surgery without compromising oncologic or neurologic outcomes.^{17,23}

Histopathologic analysis in our cohort revealed thymoma in 27.7% of patients, thymic hyperplasia in 54.5% of patients, and a normal thymus in 17.8% of patients. This distribution closely mirrors global data, where thymoma accounts for 30–40% of surgical MG cases.^{14,24} Both surgical approaches achieved complete (R0) resection in >94% of thymoma cases. Recurrence occurred predominantly in patients with advanced Masaoka–Koga stage and incomplete (R1/R2) resection. Recurrence rates were substantially higher following incomplete resection than after R0 resection, emphasizing that completeness of resection is a principal determinant of long-term oncologic outcome. Multiple comparative and meta-analytic studies have demonstrated comparable clinical and oncologic outcomes between minimally invasive and open thymectomy, with VATS and robotic approaches offering superior perioperative recovery.^{15,25–29}

Postoperative pulmonary complications, particularly respiratory failure, occurred more frequently in patients with advanced MGFA grades (III–IV). This trend has been similarly described in large institutional series from East Asia, where postoperative myasthenic crisis remains a key determinant of morbidity.¹⁹ In our study, the overall 30-day mortality was 0.7%, comparable

to international reports ranging from 0% to 2% in modern series.^{17,21,23} The slightly higher rate of respiratory failure in the VATS group may reflect routine single-lung ventilation and patient selection rather than the thoracoscopic approach itself, given that the difference was not statistically significant. From a regional perspective, data on thymectomy outcomes for MG from Pakistan and South Asia remain limited. Local single-center reports describe remission and improvement rates of 75–85% following thymectomy.¹⁰ Our 20-year institutional experience provides data from tertiary public-sector and private settings, demonstrating that favorable outcomes can be achieved despite resource limitations. Within the limitations of retrospective analyses and the potential for selection bias, both approaches demonstrated acceptable long-term neurologic and oncologic outcomes in appropriately selected patients. The pleura-breaching nature of minimally invasive thymectomy carries manageable pulmonary sequelae and does not adversely affect long-term remission or recurrence rates. As thoracoscopic and robotic platforms become more accessible in South Asian centers, their adoption may further improve patient recovery without compromising clinical efficacy.

Study Limitations

This study has several limitations. First, its retrospective nonrandomized design introduces inherent selection bias, particularly because the selection of the surgical approach was influenced by tumor characteristics, disease severity, surgeon preference, and operative era. Second, the study spans nearly two decades, during which perioperative care, surgical expertise, and minimally invasive techniques evolved substantially, potentially contributing to temporal bias. Third, formal propensity-score matching was not performed; however, multivariable adjustment was undertaken to reduce confounding. Fourth, the duration of neurologic follow-up was not uniform across patients. No formal pre-study sample size calculation was performed because of the retrospective nature of the study. Standardized postoperative pain assessment was not uniformly available throughout the study period; therefore, comparative pain outcomes between approaches could not be reliably evaluated.

CONCLUSION

Pleural breach during thymectomy was associated with increased transient postoperative pleural-related morbidity, particularly prolonged drainage and minor pleural-space complications. However, when complete resection was achieved, long-term neurologic remission and RFS appeared comparable across surgical approaches. These findings should be interpreted cautiously, given the retrospective design, potential selection bias, and temporal confounding related to evolving experience with minimally invasive techniques.

Ethics

Ethics Committee Approval: The study protocol was approved by the Institutional Review Board/Ethics Committee of the Services Institute of Medical Sciences (SIMS), Services Hospital, Lahore, Pakistan (approval no.: IRB/2025/1693/SIMS, date: 07/11/2025).

Informed Consent: Given the retrospective nature of the study and the use of anonymized clinical data, the institutional review board waived the requirement for written informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.S.N., Z.S., R.S., H.I., Concept: M.S.N., Design: M.S.N., Z.S., Data Collection or Processing: M.S.N., Z.S., R.S., H.I., Analysis or Interpretation: Z.S., Literature Search: R.S., H.I., Writing: Z.S., R.S., H.I.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Declaration on the use of Artificial Intelligence (AI): The authors declare that artificial intelligence (AI)-based tools were used solely to assist in improving the clarity and correctness of the English language during the preparation of this manuscript. All data, results, and conclusions presented in this manuscript are entirely the authors' own work. As English is not the authors' first language, AI was employed only for grammar refinement and language editing. The authors thoroughly reviewed, verified, and approved all text corrected or suggested by AI tools to ensure accuracy and integrity.

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