

AB001. Robot-assisted thoracic surgery for thymic epithelial tumors: a real-world study of 143 cases

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Background: Robot-assisted thoracoscopy (RATS) is rapidly emerging as the preferred approach for the resection of thymic epithelial tumors (TETs). Current challenges include exploring the significance of RATS in locally advanced disease and maximum resectable tumor size. The purpose of this article is to analyze perioperative results and findings from a large center for robot-assisted surgery.

Methods: This single-center analysis was conducted on the basis of a prospectively assembled database including all robot-assisted surgeries. Patients' medical and surgical records as well as radiologic and pathologic findings were reviewed and analyzed.

Results: One hundred forty-three patients underwent RATS for the resection of histologically confirmed TET between 2018 and 2024, including 130 (90.9%) patients with thymoma and 13 (9.1%) patients with thymic carcinoma. Concomitant myasthenia gravis was present in 28 (19.6%) patients. The median tumor size was 54 mm [interquartile range (IQR), 35.5–75 mm]. Masaoka-Koga stage I was diagnosed in 63 patients (44.1%), stage II in 39.9%, stage III in 11.2% and stage IV in 4.9%. The median operating time was 96.5 min (IQR, 81–152 min). Combined additional resections including lung, pericardium or major vessels were performed in 44 (30.8%) patients. Controlled conversion occurred in 6 patients (4.2%)

without any emergency conversion. R0 resection was achieved in 134 (93.7%) patients. The median postoperative stay was 4 days (IQR, 3–6 days) with a median duration of chest tube of 2 days (IQR, 1–3 days). Postoperative complications occurred in 28 (19.6%) patients, of which 7 (4.9%) were classified as major complications according to Clavien-Dindo grade III–IV. Postoperative complications occurred significantly more frequently in patients who also underwent resection of lung tissue, vessels or pericardium [odds ratio (OR) = 2.87; 95% confidence interval (CI): 1.09–7.58; P=0.03]. Concomitant autoimmune disease or tumor size over 50 mm did not predict complications. There was no 90-day mortality. Median follow-up time was 16.1 months with 94.3% recurrence-free survival at 2 years.

Conclusions: Robot-assisted resection of thymic epithelial tumors is feasible and safe. Combined additional resections are a significant predictor of postoperative complications. In view of the challenges posed by locally advanced TET, collaborative efforts should be encouraged to facilitate multicenter cooperation and generate robust evidence on RATS in this context.

Keywords: Thymoma; robotic; surgery

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AB002. Histopathological heterogeneity in resected thymomas

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Background: Morphologic heterogeneity in thymomas depends on histopathological patterns and sampling techniques. There is a lack of knowledge about the incidence and potential impact of heterogeneous thymomas on the disease burden. The primary aim of this study is to investigate the incidence and patient characteristics of thymomas with heterogeneous histopathology.

Methods: All patients who underwent a thymomectomy between 2012 and 2024 in the Maastricht University Medical Center (MUMC) were included and retrospectively analyzed. Thymomas were histologically classified by the 5th edition of the World Health Organization of thymic epithelial tumors. The Masaoka-Koga staging system and 9th TNM classification reported tumor invasion. All thymomas were postoperatively evaluated by the same senior pathologist. After fixation, regular sampling of the specimen is performed, with at least one block per cm of tumor and generous sampling of close margins. The definition of heterogeneous thymoma is based on histologically proven heterogeneity in resected thymoma. Components of mixed histopathology were noted in percentages. Patients with a biopsy were excluded from this

study. Pearson's Chi-squared test was considered statistically significant in case $P < 0.05$.

Results: Morphological heterogeneity was observed in 81 of the 206 included patients (39.3%). The majority of the heterogeneous thymomas were type A–B2 (43.2%) and type B2–B3 (30.9%). Heterogenic thymomas were more frequently observed in non-steroid using patients (34.2% *vs.* 1.8%, $P < 0.001$). The B3-component was $\geq 50\%$ in 100% of A–B3 thymomas. The B2 component was $\geq 50\%$ in 68.6% of A–B2 thymomas. Adjuvant postoperative radiotherapy (PORT) was performed less in heterogeneous thymomas compared to homogenous thymomas (12.3% *vs.* 25.6%, $P = 0.02$), and most diverse in heterogeneous B3-thymomas compared to homogeneous B3-thymomas (29.0% *vs.* 73.0%, $P < 0.001$). No significant differences in gender, age, tumor size, or presence of myasthenia gravis were found in patients with homogeneous versus heterogeneous thymomas.

Conclusions: Morphological tumor heterogeneity was found in 39.3% of the resected thymomas. Neglecting the involvement of aggressive thymoma subtypes might have an impact on decisions regarding treatment, such as PORT. Future research is necessary to analyze the consequences of thymoma heterogeneity on recurrence and survival rates. Development of guidelines with sampling recommendations may help identify heterogeneous thymomas.

Keywords: Thymoma; heterogeneity; histopathology

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AB003. Optimizing postoperative proton radiotherapy in thymic epithelial tumors: added value of breath hold?

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Background: Postoperative radiotherapy for thymic epithelial tumors (TETs) is indicated for more advanced/aggressive disease or incomplete resection. At Maastrro, postoperative proton therapy is guided by the Dutch model-based approach to minimize the estimated risk of heart toxicity, pneumonitis, and dysphagia. Inspiratory breath hold (BH) may increase lung volume and alter heart positioning, potentially improving dose distributions. This study aimed to evaluate whether BH could enhance proton therapy planning for TET patients.

Methods: Since BH computed tomography (CT) scans were unavailable for TET patients, we used data from 10 lymphoma patients. The free breathing (FB) clinical target volumes (CTVs) were derived from matched TET patients using deformable image registration. To generate a BH CTV, the 50% exhalation phase and the BH CT were deformably registered. The FB CTV was copied to the BH CT, adapted to anatomy and checked for consistency and comparable volume. For each patient two intensity-modulated proton therapy plans were made: one based on an average FB 4D-CT and another on the BH CT, using

the same beam setup. Both were optimized to deliver 45 GyRBE over 25 fractions, with robust optimization considering 5 mm setup and 3% range uncertainties. Plans were compared by analyzing mean doses to the heart (MHD), lungs (MLD), and esophagus (MED).

Results: The impact of BH on normal tissues varied among patients (*Figure 1*): 1/10 patients showed a MHD reduction >1 GyRBE, and 1/10 had a MED reduction >1 GyRBE. However, in three patients, normal tissue doses increased by >0.5 GyRBE with BH. While individual reductions up to -0.8 GyRBE (MLD), -1.3 GyRBE (MHD), and -2.0 GyRBE (MED) were observed with BH, overall differences from FB plans were not statistically significant: -0.1 ± 0.5 GyRBE (MLD), -0.1 ± 0.7 GyRBE (MHD), and -0.3 ± 0.7 GyRBE (MED).

Conclusions: The benefits of intensity-modulated proton therapy with BH for TET patients are anatomy-dependent. Although most patients showed minimal change, about 10% experienced notable dose reductions, which may be clinically meaningful for long-term survivors.

Keywords: Postoperative radiotherapy; thymic epithelial tumor (TET); proton radiotherapy; breath hold

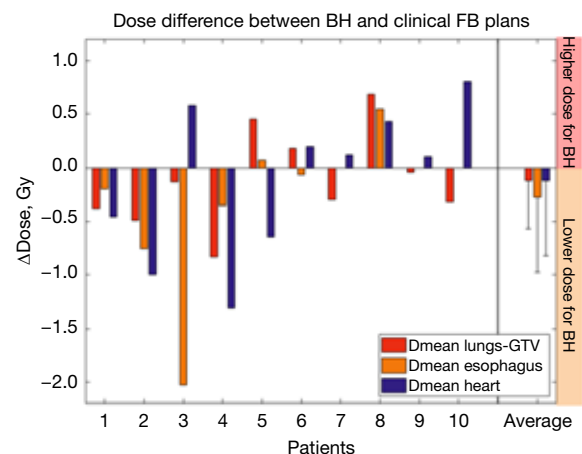


Figure 1 Dose difference between BH and clinical FB plans. BH, breath hold; FB, free breathing.

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AB004. Optimizing surgical strategies in mediastinal tumor resections through comparative analysis of hemi-clamshell and sternotomy techniques

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Background: Anterior mediastinal tumors near critical vascular structures present significant surgical challenges. Traditional median sternotomy, often complicated by limited access and visibility, can impede complete tumor excision. Conversely, the hemi-clamshell incision has shown potential in reducing surgical trauma and enhancing visibility, thereby improving resection outcomes. This study compares the perioperative outcomes of the hemi-clamshell technique with those of conventional median sternotomy.

Methods: This retrospective study from January to December 2023 involved fourteen patients, equally divided

between those undergoing mediastinal tumor resections via hemi-clamshell or conventional sternotomy. We evaluated perioperative parameters such as surgery duration, intraoperative blood loss, hospital stay, complication rates, and tumor dimensions.

Results: The hemi-clamshell group had marginally longer surgery times, averaging 188.57 ± 42.92 minutes compared to 177.29 ± 36.88 minutes for the sternotomy group. However, it significantly reduced intraoperative blood loss, averaging 192.86 ± 94.22 versus 264.29 ± 182.67 mL for sternotomy. Tumor sizes were similar between groups, measuring 6.929 ± 3.09 cm for hemi-clamshell and 7.36 ± 2.72 cm for sternotomy. Hemi-clamshell patients also had shorter postoperative hospital stays, averaging 6.29 ± 1.50 days compared to 8.86 ± 1.86 days for sternotomy (*Figure 1*). In terms of complications categorized as Grade II, the hemi-clamshell group had two patients with manageable complications, one with pneumonia and another with both pneumonia and a surgical site infection. In comparison, five patients in the sternotomy group experienced complications, including two with pneumonia and three with arrhythmias, all of which were managed medically.

Conclusions: Both hemi-clamshell and sternotomy techniques are effective for mediastinal tumor resections. However, the hemi-clamshell approach offers significant advantages in reducing intraoperative blood loss and shortening recovery times, suggesting better patient outcomes. It also has a lower complication rate, highlighting its safety profile. Tailored surgical planning, considering individual patient conditions, is recommended. Further research with larger cohorts is needed to confirm these findings and refine surgical practices for complex mediastinal tumors.

Keywords: Hemi-clamshell; mediastinal tumor; perioperative outcome

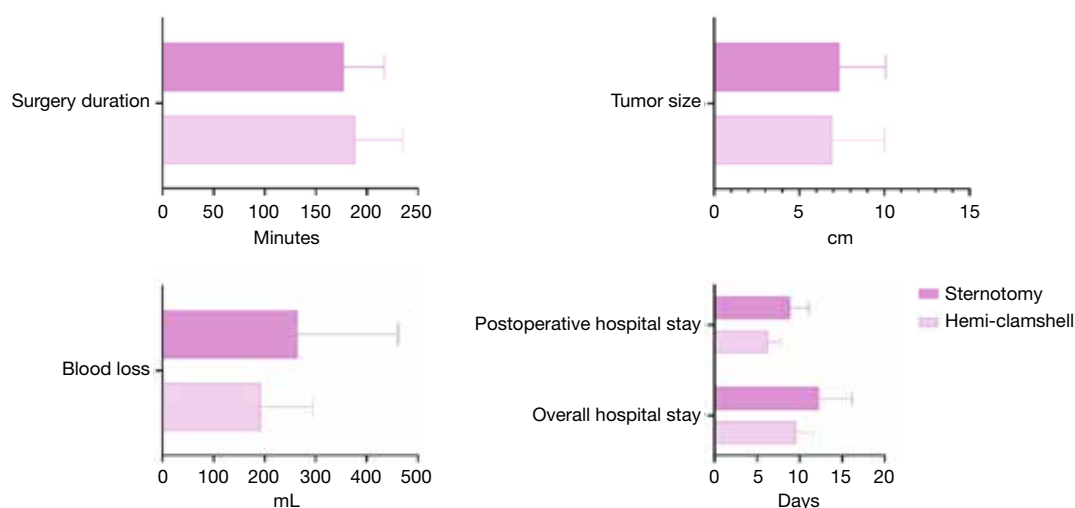


Figure 1 Comparison of perioperative parameters between the sternotomy and hemi-clamshell approaches. Bar graphs show mean $\pm$ standard deviation for surgery duration (minutes), tumor size (cm), blood loss (mL), postoperative hospital stay (days), and overall hospital stay (days).

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AB005. Metaplastic thymoma of the mediastinum—a clinicopathological report of three cases

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Background: Metaplastic thymoma (MT) is an exceptionally rare, biphasic epithelial tumor of the thymus, officially designated by the World Health Organization in 2004. It is characterized histologically by intermixed epithelioid and spindle cell components and harbors a unique YAP1-MAML2 gene fusion, distinguishing it from other thymoma subtypes which typically carry GTF2I mutations. Fewer than 100 cases have been documented in the English literature, often presenting as incidental anterior mediastinal masses in asymptomatic middle-aged women.

Case Description: We present three cases of MT to enrich the current understanding of this rare entity. The first case involved a 47-year-old woman with non-specific symptoms and a 6.5-cm anterior mediastinal mass, managed successfully with bilateral video-assisted thoracoscopic thymectomy followed by radiotherapy, with no recurrence at 11 years. The second case was an asymptomatic 37-year-old woman with a 3.1-cm lesion detected during routine health screening. She underwent curative resection without adjuvant therapy and remains disease-free at 2 years. The third case involved a 56-year-old woman with long-standing chest tightness and a 10-cm anterior mediastinal tumor, excised via median sternotomy with no evidence of recurrence at 2 years postoperatively. Pathologically, all three tumors displayed the characteristic biphasic morphology of MT. Immunohistochemistry revealed expression of epithelial markers (CK AE1/AE3, p40, p63), and fluorescence *in situ* hybridization confirmed MAML2 rearrangement. RNA sequencing identified in-frame YAP1-MAML2 fusions in two cases.

Conclusions: MT typically presents as a well-circumscribed anterior mediastinal mass in asymptomatic middle-aged women and demonstrates excellent outcomes with complete surgical resection. The presence of YAP1-MAML2 fusion serves as a valuable diagnostic marker. Our cases contribute further to the limited pool of documented MTs, supporting its indolent behavior and favorable prognosis.

Keywords: Thymoma; case report; mediastinum

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AB006. Postoperative complications and early recurrence in surgically treated thymoma: a single-centre retrospective study

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Background: Thymoma is a rare mediastinal tumour with variable postoperative outcomes. The impact of surgical approach, margin status, and adjuvant therapies on recurrence remains debated. Our aim is to explore factors associated with postoperative complications, hospital stay, and early recurrence in surgically treated thymoma patients.

Methods: We retrospectively analysed 41 patients who underwent thymoma resection between 2020 and 2024. Data included surgical approach [video-assisted thoracoscopic surgery (VATS) *vs.* open], margin status, tumour size, Masaoka-Koga (MK) stage, tumor-node-metastasis (TNM) stage, World Health Organization (WHO) histological subtype, neoadjuvant therapy, postoperative radiotherapy (RT), postoperative complications, and early recurrence. Early recurrence was defined as histologically confirmed tumour relapse within 2 years (730 days) following surgery. Statistical analyses included chi-square tests, Fisher's exact test, and univariate logistic regression.

Results: Of 41 patients, 35 (85.4%) underwent open surgery and 6 (14.6%) had VATS. There was no significant

difference in hospital stay between VATS (median 2 days) and open surgery (median 4 days, $P=0.25$). Postoperative complications occurred in 10 patients (24.4%), including 6 minor and 4 major events, and were associated with a significantly longer hospital stay (mean increase 9.12 days, $P<0.001$). Surgical approach was not associated with complications ($P=0.63$). Early recurrence occurred in 2 patients (4.9%), both following R1 resection (8.0%, 2/25) with none in R0 resection (0/16, $P=0.25$).

Recurrence was more frequent in patients receiving postoperative RT (15.4% *vs.* 0%, $P=0.04$) or neoadjuvant therapy (50% *vs.* 2.6%, $P=0.003$), although this likely reflects selection for more advanced disease. Both recurrences occurred in tumours ≥ 5 cm, WHO subtype B1/B2, MK stage II–IV, and TNM stage IIIA/IVA, although statistical significance was limited. In univariate analysis, postoperative RT remained significantly associated with recurrence ($P=0.03$).

Conclusions: Surgical approach did not impact hospital stay or complication rates. Early recurrence was rare and occurred only in patients with larger tumours, incomplete resection, advanced stage, and adjuvant therapy, reflecting aggressive disease. Multicentre studies are needed to validate these findings and guide optimal adjuvant therapy in thymoma management.

Keywords: Thymoma; surgery; complications; recurrence; radiotherapy (RT)

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AB007. The impact of immunological indicators on the prognosis of thymectomy in patients with thymoma-associated myasthenia gravis

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Background: Extensive research has illuminated the complex landscape of immunological disparities in patients suffering from thymoma-associated myasthenia gravis (MG), a condition marked by considerable fluctuations in immune system markers. The intricate relationship between these immunological aberrations and the therapeutic efficacy of thymectomy remains an area ripe for investigation, underscoring the necessity of this study to unravel the potential impact of specific immunological markers on the postoperative prognosis of MG in individuals afflicted with thymoma. This study aims to identify preoperative immunological markers—including T-cell subsets, immunoglobulins, and complement components—predictive of long-term outcomes in thymoma-associated MG patients undergoing thymectomy.

Methods: We embarked on a comprehensive retrospective analysis encompassing a cohort of 163 patients diagnosed with MG, all of whom underwent thymectomy at our institution within the period from January 2011 to December 2022. The methodological core of our investigation centered around the deployment of Kaplan-Meier survival analysis coupled with Cox proportional hazards modeling. This dual analytical framework enabled us to dissect the nuanced relationship between a predefined set of immunological markers—namely, TH17 cells, Treg cells, CD4⁺ T cells, CD8⁺ T cells, and a range of immunoglobulins [immunoglobulin G (IgG), immunoglobulin A (IgA), immunoglobulin M (IgM), and immunoglobulin E (IgE)], along with C-reactive protein

(CRP), complement C3, and complement C4—and the subsequent prognostic landscape post-thymectomy.

Results: Among the patients participating in this study, 88 achieved sustained relief after surgery, while 68 patients experienced unchanged, recurrent, or aggravated symptoms of MG after surgery, including a history of recurrence; Another 7 patients died due to MG, with an average follow-up period of 68.2 months. Through univariate and multivariate regression analysis, we found a significant correlation ($P < 0.001$) between the decrease in complement C3 levels and the inability of patients to achieve sustained relief of MG symptoms after surgery. And the level of T cells in the body immunological indicators such as IgG are not associated with prognosis.

Conclusions: The study conclusively underscores the prognostic valor of complement C3 levels in shaping the long-term therapeutic trajectory of patients with thymoma-associated MG undergoing thymectomy. Lower C3 levels as a predictive marker for a heightened risk of postoperative MG symptom exacerbation heralds the potential of complement C3 as an instrumental prognostic tool.

Keywords: Immunological indicators; thymoma; myasthenia gravis (MG)

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AB008. Analysis of natural development and changes of thymic cysts on imaging

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Background: Currently, the understanding of thymic cysts among thoracic surgeons remains inconsistent. This study aimed to conduct a comprehensive follow-up on patients with thymic cysts to analyze their natural progression and imaging changes, as well as identify factors influencing the advancement or regression of these cysts.

Methods: Retrospective analysis was performed on patients with unoperated thymic cysts or those who had been operated in our department from 2014 to 2023. The follow-up time of patients was required to be at least 6 months and the patients were confirmed as thymic cysts by computed tomography (CT) + magnetic resonance imaging (MRI). Baseline patient data were collected for analysis. Univariate and multivariate Cox regression analyses were performed to assess factors affecting changes in thymic cyst size. Patients were categorized into progressive and regressive groups based on doubling time to determine optimal follow-up intervals.

Results: Compared to the stable group, most individuals in the progressive group exhibited long T1 and T2 MRI signals, initial volumes exceeding 1 cm³, and initial locations adjacent to the midline or left side of the thymus gland (Figure 1). The results from univariate Cox regression analysis indicated that middle-aged [hazard ratio (HR) =0.30, 95% confidence interval (CI): 0.12–0.73, P=0.008; median =54.00 years, range, 45.00–59.00 years] and elderly (HR =0.33, 95% CI: 0.13–0.85, P=0.02; median =65.00 years, range, 60.00–79.00 years) cohorts had more favorable prognoses than younger individuals; additionally, symptomatic patients demonstrated better outcomes compared to asymptomatic ones (HR =0.44, 95% CI: 0.22–0.88, P=0.02; median =26.00, range 0.00–52.00). In multivariate Cox regression analysis, those with initial volumes greater than 1 cm³ showed improved prognosis relative to those with volumes ≤1 cm³ (HR =3.96, 95% CI: 1.34–11.66, P=0.01; median =1.40 cm³, range, 0.13–37.70 cm³), while symptomatic individuals also fared better than their asymptomatic counterparts (HR =0.28, 95% CI: 0.11–0.69, P=0.006; median =26.00, range 0.00–52.00). The median doubling time for the progressive cohort was recorded at 35.41 (10.13–120.05) months, whereas it was noted at 19.49 (1.76–59.05) months for those experiencing regression.

Conclusions: The prognosis of young patients and patients with initial volume ≤1 was worse. Patients with symptoms have a better prognosis than those without symptoms. The best follow-up time for patients with unoperated thymic cysts was 13.72 months (about 1 year).

Keywords: Thymic cyst; developmental changes; progression-free rate; doubling time case report

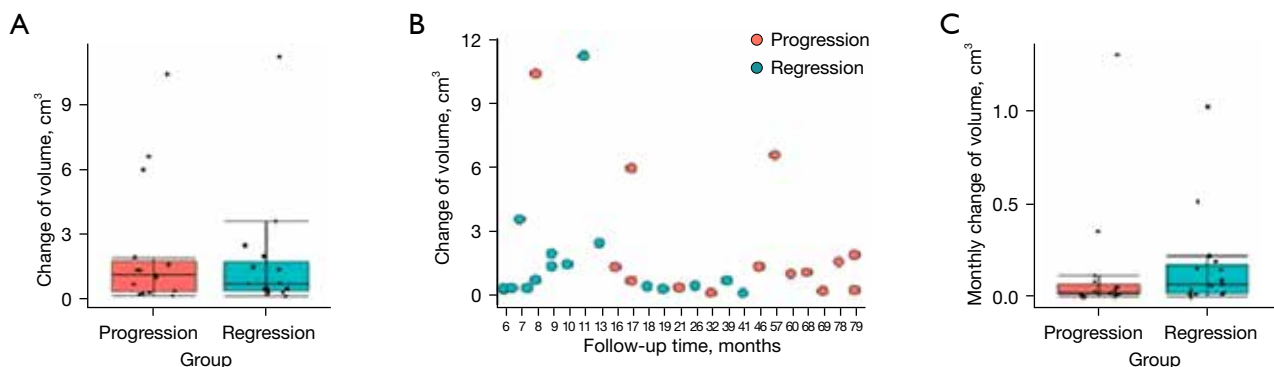


Figure 1 Changes of cysts in patients with thymic cysts. (A) The range of cyst volume changes in the enlarged and reduced cyst groups; (B) the range of increased or decreased cyst volume independent of follow-up time; (C) the average monthly volume change between the two groups.

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by the Tianjin Medical University General Hospital (The registration number of the ethics board has not been officially issued yet) and individual consent for this retrospective analysis was waived.

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AB009. Review of case characteristics and exploration of mechanisms of thymoma shrinkage after glucocorticoid therapy

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Background: Thymomas are frequently associated with autoimmune diseases. For such patients, stabilizing the autoimmune condition prior to surgery is essential to avoid complications. Glucocorticoids (GCs) are the first-line therapy for autoimmune diseases, and clinical observations suggest that GC treatment may reduce thymoma size, facilitating surgical resection. This study aims to investigate the mechanism underlying GC-induced thymoma shrinkage through case analysis and *in vitro* experiments.

Methods: We retrospectively analyzed 12 patients with thymic disease and autoimmune disorders treated at our center between January 2020 and December 2024. Data were collected on tumor volume reduction following GC therapy, including mean reduction rate and duration of hormone use. Comparisons were made with thymoma patients without GC treatment (including those with concurrent myasthenia gravis and pure thymoma cases). Recombinant glucocorticoid receptor alpha (GR α) expression levels were measured in thymoma tissues from GC-treated patients, and the relationship between GR α and the Nuclear Factor kappa-light-chain-enhancer of activated B cells/B-cell lymphoma-2 (NF- κ B/Bcl-2) pathway was analyzed in thymoma cells.

Results: The mean duration of GC therapy in this cohort was 2.2 months, with an average reduction of 53.29% in the maximum cross-sectional area of the thymoma. This significant shrinkage did not increase surgical complications. Furthermore, no tumor recurrence was observed during

follow-up, and all patients achieved stable control of their autoimmune disease. Pathological examination confirmed that these cases were predominantly type B2 and/or B3 thymomas. Compared to untreated patients (including those with concurrent myasthenia gravis and pure thymoma cases), GC-treated patients exhibited higher GR α expression in thymoma tissues. *In vitro* experiments demonstrated that the NF- κ B/Bcl-2 pathway is present in thymoma cells and regulated by GCs. GC treatment upregulated glucocorticoid receptor (GR) expression while increased GR α levels suppressed downstream NF- κ B and Bcl-2 expression.

Conclusions: These findings highlight the beneficial role of preoperative GC therapy in thymoma patients with autoimmune diseases. GCs modulate the thymoma microenvironment and induce apoptosis via the GR α -NF- κ B/Bcl-2 pathway, offering a novel clinical strategy for managing these patients.

Keywords: Thymoma; autoimmune disease; glucocorticoids (GCs); glucocorticoid receptor (GR)

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AB010. A phase 1 trial of PRTH-101, a monoclonal antibody targeting discoidin domain receptor 1 (DDR1), alone or in combination with pembrolizumab, for the treatment of thymic malignancies

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Background: There are no Food and Drug Administration (FDA)-approved therapies for recurrent/metastatic thymic epithelial cancers (TECs) and current treatments with chemotherapy and immunotherapy leave considerable room for improvement. Discoidin domain receptor 1 (DDR1) is a collagen receptor expressed on tumor epithelial cells. DDR1 binding to collagen surrounding tumor cells results in highly aligned collagen fibers, and exclusion of cluster of differentiation 8 (CD8)⁺ T cells from the tumor (i.e., immune exclusion), precluding an effective anti-tumor response. High DDR1 expression has been observed in

TECs and other epithelial tumor types. Furthermore, published data suggest that high DDR1 expression is associated with poor prognoses and lack of response to immunotherapies. The purpose of this article is to describe the results of PRTH-101 treatment in thymic cancer patients in our ongoing clinical trial.

Methods: PRTH-101 is a humanized monoclonal antibody that blocks the interaction of collagen with the extracellular domain of DDR1; it is being tested in a phase 1 clinical trial (PRTH-101-0001) as a single agent (phase 1a) and in combination with pembrolizumab (phase 1b). PRTH-101 doses up to 1,600 mg have shown no dose-limiting toxicities alone or together with pembrolizumab. Clinical, pharmacokinetic, and target engagement data from 56 patients have informed a recommended phase 2 dose of 1,200 mg, which is being tested in phase 1c, with or without pembrolizumab.

Results: To date, 16 TEC/thymoma patients have been treated with PRTH-101 at doses of 240 to 1,600 mg, 10 of whom have also received pembrolizumab; 14 had previously progressed on immunotherapy. Of seven patients in phase 1a and phase 1b who stayed on trial for more than one cycle, median progression-free survival (mPFS) is >7.7 months (2 ongoing) [>9.8 months mPFS for thymoma (1 ongoing); >6.6 months mPFS for TEC (1 ongoing)]. PFS was observed in patients receiving PRTH-101 alone or with pembrolizumab, irrespective of programmed death-ligand 1 (PD-L1) status. One previously untreated patient with metastatic TEC receiving 1,200 mg PRTH-101 with pembrolizumab, has an ongoing partial response, despite a PD-L1 combined positive score <1%. Six patients (of seven) are ongoing in phase 1c.

Conclusions: DDR1 and PD-L1 expression data, combined with PFS data, suggest that PRTH-101 contributes to or is responsible for observed PFS in these patients. The data support further clinical evaluation of PRTH-101 alone and in combination with pembrolizumab for patients with recurrent/metastatic TEC.

Keywords: PRTH-101; discoidin domain receptor 1 (DDR1); programmed death-ligand 1 (PD-L1); phase 1; pembrolizumab

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Monopteros Therapeutics, Navire Pharma Inc., Nimbus Therapeutics, NGM Biopharmaceuticals, OBI Pharma, OncoResponse Inc., Pfizer, Revolution Medicines, Step Pharmaceuticals, Symphogen, Tachyon Therapeutics, Teon Therapeutics, Tyligand Bioscience, Vincerox Pharma, Vividion Therapeutics, ZielBio Inc and Zymeworks Inc. DS is staff of NEXT Oncology. R.E.S. received consulting fees from AstraZeneca, Janssen Oncology/Johnson and Johnson, Sanofi Aventis, GlaxoSmithKline, Illumina, G1 Therapeutics, Daiichi Sankyo, Lilly Oncology, Amgen, Gilead Sciences, GE Healthcare, AbbVie, IDEology Health, BeiGene, Inhibrx, Boehringer Ingelheim, Rigel, Pfizer and Natera, and received payment or honoraria from Targeted Oncology, Curio Science, Illumina, OncLive and PRIME Education. R.E.S. also received support for attending meetings and/or travel from HotSpot Therapeutics, and received Funding for Investigator-initiated trial from Merck and AstraZeneca. She also participation on DSMB. A.P. has held Equity in C2i Genomics, Khora, OneCell, XGenomes, Cadex, and Parithera. In the last 36 months, she received consulting fees from Zola, CVS, Phesi, Xilio, 3T Biosciences, Do More Diagnostics, Summit Therapeutics, Pfizer, Regeneron, GSK, Foundation Medicine, Careset, Value Analytics Labs, Naterara, Adroya, Astra Zeneca, Scare, Hookipa, Guardant, Abbvie, Seagen, Mirati, Takeda, PMV, Kahr, Sirtex, Eli Lilly, Merck, Amgen, Delicate, Exact, Caris, BMS, Incyte, Phesi, Neogenomics, J & J, Exact Third Rock Ventures, MPM Capital, and Science For America. She receives fees from Up to Date. She has received travel fees from Karkinos Healthcare. She has received research funding to the Institution from PMV Pharmaceuticals, BMS, Mirati, Erasca, Genentech, Daiichi Sankyo, Syndax, Revolution Medicine and Parthenon. JB received grants from Abbvie, Astellas, Atreca, Bayer, Dragonfly, I-Mab, Lilly, Incyte, EMD Serono, Pfizer, BMS, Tyra, Totus, Sumitomo Dainippon Pharma Oncology, 23 and me, parthenon/Incendia, hiberCell, ribosciences, NCI, BMS and Clasp, and received consulting fees from EMD Serono 3/25, 4/25*, Ipsen 5/25*, Merck, Sharp, Dohme, Merus, Bms, Mekanistic, Agenus (pending), Astellas, Amplia, Taiho*, Regeneron 1/25, Beigene 1/25 and ALX Oncology 6/25. J.B. received support for attending meetings and/or travel from Ipsen and EMD Serono, and participation on a Data Safety Monitoring Board or Advisory Board of Astra Zeneca, I-SPY and Novocure. G.T.C. is a former employee of Incendia Therapeutics and may be named as an inventor on a methods-of-use patent for PRTH-101 with Incendia

Therapeutics; G.T.C. previously held stock options from Incendia Therapeutics (no longer holds any). A.M. and I.W. are employees of Incendia Therapeutics and have received support for attending meetings as well as stock options from Incendia Therapeutics. T.S., S.M., and J.P.E. are employees of Incendia Therapeutics, have received support for attending meetings and/or travel, hold stock options from Incendia Therapeutics, and may be named as inventors on a methods-of-use patent for PRTH-101 with Incendia Therapeutics. A.S. received grants from LAM Therapeutics, Roche, Astra Zeneca, Boehringer Ingelheim, Astellas Pharma, Incyte, Novartis, AbbVie, Ignyta, Takeda, MacroGenics, CytomX Therapeutics, Astex Pharmaceuticals, Bristol-Meyers Squibb, Loxo, Gritstone, Plexxikon, Amgen, Daiichi Sankyo, ADCT, Janssen Oncology, Rubius, Synthekine, Mersana, Blueprint Medicines, Regeneron, Alkermes, Black Diamond Therapeutics, Nalo Therapeutics, Scorpion Therapeutics, ArriVent Biopharma, Revolution Medicines, Prelude Therapeutics and Lilly, received consulting fees from Incyte, Amgen, Novartis, Mirati Therapeutics, Gritstone Oncology, Jazz Pharmaceuticals, Takeda, Janssen Research & Development, Mersana, Daiichi Sankyo/Astra Zeneca, Regeneron, Lilly, Black Diamond Therapeutics, Sanofi, ArriVent Biopharma, Synthekine, GSK, CRISPR Therapeutics, Revolution Medicines, Astra Zeneca/MedImmune, Merck, Bristol-Meyers Squibb and Blueprint Medicines, and received honoraria from CytomX Therapeutics, Merck, Takeda, Amgen, Janssen Oncology, Novartis, Bristol-Meyers Squibb, Bayer, Prelude Therapeutics, AbbVie and Astellas Pharma. A.S. is staff of NEXT Oncology. The authors have no other conflicts of interest to declare.

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appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by Salus IRB (registration numbers IRB00006833, IRBI00006834, IRB00009473, IRB00013027, and IRB00013544), MD Anderson IRB (registration number IRB00000121), Vanderbilt Human Research Protection Program, Health Sciences Committee 3 IRB (registration number IRB00002125), Providence St. Joseph Health IRB (registration numbers IRB00012388, IRB00012541, IRB00012389, IRB00012390, IRB00012391, IRB00012392, IRB00012393, IRB00012882, and IRB00012964), Mass General Brigham IRB (registration numbers IRB00012706 and IRB00012707), and WCG IRB (registration number IRB00000533) and informed consent was obtained from all individual participants.

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AB011. Robot-assisted subxiphoid approach for resection of a giant cervicothoracic junction tumor: a case report

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Background: The cervicothoracic junction (CTJ) is an anatomically complex region marking the transition from cervical to thoracic structures. It encompasses several critical neurovascular elements. Resection of tumors in this region is particularly challenging when lesions are large, poorly defined, and closely adherent to adjacent structures. Conventional cervical or unilateral thoracic approaches often provide limited and asymmetrical exposure. In contrast, the subxiphoid approach offers superior visualization and bilateral access to the anterior mediastinum and thoracic inlet, particularly when combined with robotic assistance, particularly when combined with robotic assistance, offers superior visualization and bilateral access to the anterior mediastinum and thoracic inlet.

Case Description: A 56-year-old woman presented with

a 1-month history of chest tightness. Contrast-enhanced computed tomography revealed an 8.0 cm × 3.5 cm mass at the cervicothoracic junction, demonstrating indistinct planes of separation from adjacent structures (*Figure 1A*). A robot-assisted subxiphoid resection was performed using the da Vinci Xi system. As shown in *Figure 1B*, a 3-cm vertical incision was made below the xiphoid process, through which a wound protector with a sealed access cap was inserted. This access system accommodated multiple trocars: one served as the robotic camera port, while the others allowed for assistant instrumentation. Additional robotic trocars were inserted bilaterally beneath the costal margins and connected to the robotic operating arms. The intraoperative findings revealed that the tumor tissue was densely adherent to the innominate vein (*Figure 1C*). To optimize the surgical field, carbon dioxide insufflation was used to establish an artificial pneumothorax, effectively expanding the retrosternal space. This technique, combined with the articulation and precision of robotic instrumentation, enabled excellent visualization without the need for sternal retractors. Finally, the tumor was completely excised without intraoperative complications, and vital structures were preserved (*Figure 1D*). Estimated blood loss was 50 mL. Postoperatively, the patient ambulated on day 2, had chest drains removed on day 3, and was discharged on postoperative day 5 without complications.

Conclusions: Robot-assisted subxiphoid resection is a safe and effective technique for managing large tumors at the cervicothoracic junction. It provides excellent exposure and operative control in anatomically constrained regions, while minimizing surgical trauma and promoting early recovery.

Keywords: Case report; cervicothoracic junction tumor (CTJ tumor); robot-assisted thoracic surgery; subxiphoid approach

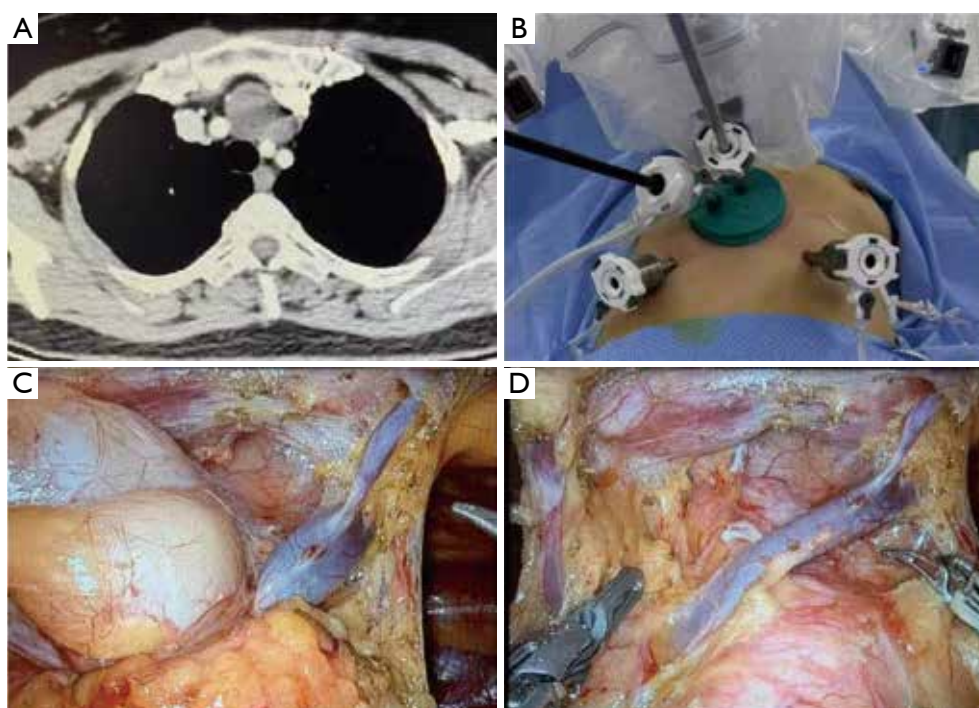


Figure 1 Patient's clinical case data. (A) Preoperative contrast-enhanced CT scan of the patient; (B) the robotic trocar was positioned in the subxiphoid location; (C) location of the tumor during the operation; (D) exposure of the upper mediastinal anatomy following total tumor removal. CT, computed tomography.

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obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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AB012. Short-term outcome of robotic subxiphoid-optical thymectomy for malignant thymic epithelial tumors

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Background: Robotic thymectomy has been accepted as a minimally invasive surgery for thymic epithelial tumors (TETs). Two main different approaches via subxiphoid or lateral access into anterior mediastinum have been reported. We review our standard procedure of robotic subxiphoid-optical thymectomy (RST) and aim to show the technical advantages of the fine surgical field of view in total thymectomy and combined resection of neighboring structures for malignant TETs.

Methods: Under spine position, only robotic scope is inserted via subxiphoid port without wound retractable device and Maryland-type dissectors are applied via bilateral 6th intercostal spaces on mid-clavicular line. An assist port is placed at the right 3rd intercostal space on anterior axillar line for artificial CO₂ insufflation using AirSeal® (Figure 1). RST was indicated in 54 anterior mediastinal lesions and 28 TETs cases are investigated.

Results: Pathological diagnoses are 26 thymomas [World Health Organization (WHO) type A 6, AB 7, B1 2, B2 8, B3 2, micronodular 1] and 2 thymic squamous cell carcinomas. Pathological staging was Masaoka stage I 6, II 20, III 2, and TNM stage I 26, II 1, III 1 patients. Myasthenia gravis (MG) is associated in 4 patients and 2 patients showed the elevation of serum anti-acetylcholine antibody without MG symptom. We experienced one Morvan syndrome and one Good syndrome with pure red cell aplasia cases. Total and subtotal thymectomies were performed in 27 and 1 patients, respectively. A combined resection of the innominate vein with the phrenic nerve was performed in a thymic carcinoma, and a partial pericardium resection

was experienced in a B2 invasive thymoma. The median operative and console durations were 177 and 115 minutes, respectively. Neither open median sternotomy conversion nor transfusion was observed. One patient with pericardial resection showed post-pericardiotomy syndrome requiring readmission. No recurrent case was found in the short-term follow-up with the median of 2 years.

Conclusions: RST is a safe and useful procedure applicable to extended resection for TETs. The excellent surgical field of view from subxiphoid scope and exquisite manipulation could realize the similar procedure to the median sternotomy approach.

Keywords: Robotic surgery; thymic epithelial tumor (TET); thymectomy

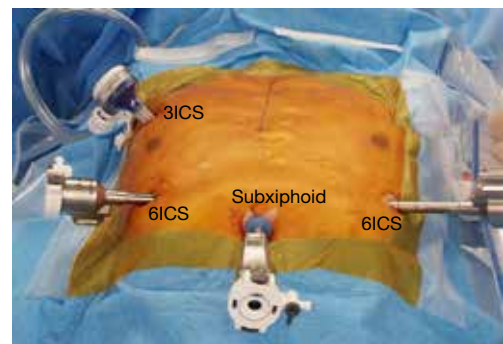


Figure 1 Ports placement in robotic subxiphoid-optical thymectomy. ICS, intercostal space.

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and its subsequent amendments. The study was approved by the institutional ethics board of Kyoto Prefectural University of Medicine (No. ERB-C-2718-1) and individual consent for this retrospective analysis was waived.

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AB013. A pivotal phase 2 trial to compare PRTH-101, a monoclonal antibody targeting discoidin domain receptor 1 (DDR1), in combination with an immune checkpoint inhibitor (ICI) and ICI alone, for the treatment of recurrent or metastatic thymic epithelial carcinoma (TEC)

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Background: PRTH-101 is a humanized monoclonal that blocks the interaction of collagen with the extracellular domain of discoidin domain receptor 1 (DDR1) and has been studied in a phase 1, all-comers clinical trial (NCT05753722). In that trial, patients with thymic carcinoma or thymoma were treated with PRTH-101 alone or in combination with pembrolizumab. We observed stable disease, one confirmed partial response, multiple minor RECIST improvements, and improved quality of life in patients across all tumor types. Based on these results, a world-wide registrational trial is planned, to be initiated in 2026, enrolling patients ≥ 12 years old with recurrent or metastatic thymic epithelial carcinoma (TEC). The objective of this article is to describe the planned phase 2 pivotal study.

Methods: This open-label trial is a two-cohort trial. Cohort 1 will enroll ~ 45 immune checkpoint inhibitor (ICI)-refractory patients for treatment with PRTH-101 plus pembrolizumab. The sample size provides 90% power with a one-sided $\alpha = 0.05$ to detect a difference between the hypothesized null median progression-free

survival (mPFS) of 3 months and target mPFS of 6 months. Cohort 2 will enroll ~ 84 ICI-naïve patients randomized 1:1 to a pembrolizumab alone group and a PRTH-101 plus pembrolizumab group. The sample size provides 80% power with a one-sided $\alpha = 0.05$ and hazard ratio of 0.05, assuming an interim analysis for futility and efficacy when half of the expected 73 progression-free survival (PFS) events have occurred. Primary objectives are PFS, safety, and tolerability. Secondary objectives will assess pharmacokinetics and anti-drug antibodies. Exploratory endpoints include tumor evaluation by magnetic resonance imaging (MRI) and fluorodeoxyglucose positron emission tomography (FDG-PET), analyses of efficacy by expression of programmed death-ligand 1 (PD-L1) and DDR1, and assessment of health-related quality-of-life. There will be two planned data cut offs (DCOs) for the primary endpoint of PFS: for futility (DCO1), to occur when approximately 30% of PFS events have been observed in cohort 2; and a final analysis (DCO2) to occur when approximately 73 PFS events in Cohort 2 have been observed.

Discussion: The design allows for comparison of the efficacy of PRTH-101 plus pembrolizumab and pembrolizumab alone in ICI-naïve patients, and for evaluation of PRTH-101 benefit when added with pembrolizumab in patients previously refractory to immune checkpoint inhibitors. Trial sub-analyses may identify patients most likely to benefit from treatment with PRTH-101 alone or in combination with pembrolizumab.

Trial Registration: Pending.

Keywords: PRTH-101; discoidin domain receptor 1 (DDR1); programmed death-ligand 1 (PD-L1); pivotal; pembrolizumab

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of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study will be conducted in accordance with the Declaration of Helsinki and its subsequent amendments. Relevant institutional ethics approval and informed consent has not been obtained as the trial registration is still pending.

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AB014. Autoreactome analysis reveals novel autoantibodies in thymoma-associated myasthenia gravis

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Background: Thymomas are unique among neoplasms for their strong association with a number of autoantibody-mediated diseases with upwards of half of patients having acetylcholine receptor antibody-positive myasthenia gravis (thymoma-associated MG, TAMG). The majority of thymomas have a deficiency in the autoimmune regulator (AIRE) protein, a key factor in maintaining central immune tolerance, which suggests a general propensity to autoantibody formation. The propensity to produce autoantibodies against striated muscle proteins, ryanodine receptor, and potassium channels has been documented, however, the scope of the autoantibodies has not been fully assessed. The objective of the study was to determine an autoantibody profile in TAMG patients. We utilized a broad-based approach to interrogate this question.

Methods: Eighteen control and 43 sera from patients with TAMG from George Washington and Indiana Universities were used to assess the autoreactome using molecular indexing by self-assembly to assess over 16,000 full-length proteins and nearly 400,000 peptide sequences for autoreactive antibodies.

Results: Controls and TAMG subjects demonstrated a wide variation in autoreactivity from 62 to 623 protein directed autoantibodies with no clear differences among individuals. No uniformity was observed across individuals for a protein target. However, a subpopulation of TAMG subjects had high levels of antibodies directed against a range of interferons. Within this group of patients, all had antibodies towards TRIM46 and P2X4 receptor. TRIM46 is a known paraneoplastic antigen in neurological disease,

but not previously identified in thymoma. TRIM46 and P2RX4 receptor are linked to T cell signaling or differentiation. There was no association with thymoma World Health Organization (WHO) classification or other patient characteristics.

Conclusions: The presence of these autoantibodies would indicate disrupted immune tolerance mechanisms in TAMG patients, particularly those affecting antigen processing and regulatory T-cell function driven by autoantibody formation. P2X4 receptor is a purinergic and ligand-gated ion channel, which, when activated, leads to interferon secretion. If the P2X4 receptor antibodies activate lead to high, localized levels of interferons, then an interferonopathy supportive for autoreactivity would be expected.

Keywords: Thymoma; myasthenia gravis (MG); autoimmunity; interferons; P2X4 receptor

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AB015. Perioperative outcomes and surgical strategies in malignant anterior mediastinal tumors

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Background: Malignant mediastinal tumors, despite their low incidence, often present with aggressive histology and challenging anatomical features. This study evaluated perioperative outcomes associated with different surgical approaches and explored tumor-related factors impacting surgical complexity.

Methods: A retrospective review was conducted of 27 patients with histologically confirmed malignant anterior mediastinal tumors who underwent surgical resection at our institution. Surgical approaches included open surgery (n=10), video-assisted thoracoscopic surgery (VATS, n=12), and robotic-assisted surgery (n=5). A comparative analysis was undertaken of perioperative factors such as operative

duration, blood loss, intensive care unit (ICU) admission, tumor dimensions, multiorgan resection, and post-surgical complications. A correlation analysis was carried out to examine the relationship between tumor size and surgical burden

Results: Squamous cell carcinoma was the most common subtype (26%), followed by thymic carcinoma, sarcomas, mesothelioma, lymphoma, and undifferentiated malignancies. Compared to VATS (93.5±80.8 mL; 112.5±39.0 min) and robotic surgery (68.6±30.2 mL; 171.4±82.9 min), open surgery resulted in greater blood loss (640.0±940.4 mL) and longer operative time (214.5±129.5 min). ICU admission was required in 30% of open cases, but in none of the minimally invasive cases. Tumor size (mean 6.9±2.7 cm) was moderately correlated with blood loss (r=0.51) and ICU admission (r=0.37), with a weaker correlation to operative time (r=0.11) (*Figure 1*). Postoperative complications occurred in 33% of patients, mostly pneumonia (19%) and arrhythmia (10%), all Clavien-Dindo grade I or II. No perioperative mortality was observed.

Conclusions: Malignant mediastinal tumors are histologically diverse and often involve complex anatomical relationships. Tumor size significantly influences surgical difficulty and risk. While minimally invasive approaches like VATS offer benefits in recovery, surgical strategy should be individualized. Robotic-assisted surgery, offering both minimally invasive access and oncologic precision, may play an increasingly important role in future mediastinal tumor management.

Keywords: Anterior mediastinal tumor; perioperative outcomes; surgical approach

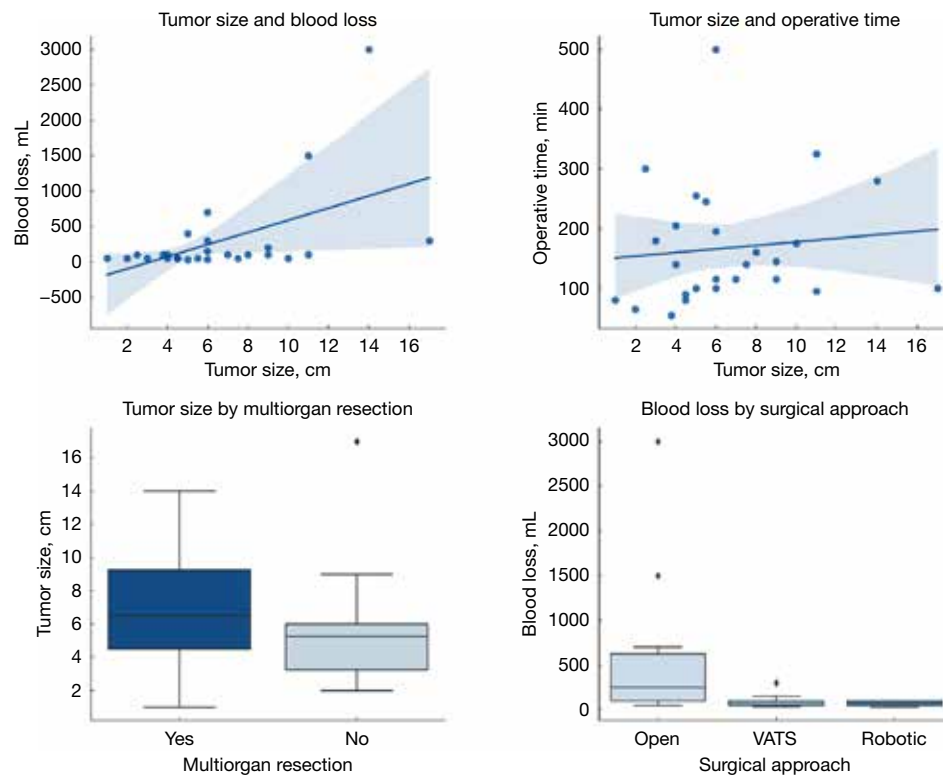


Figure 1 Associations between tumor size, surgical complexity, and intraoperative metrics. Top: scatter plots showing correlations between tumor size and blood loss (left) and operative time (right). Bottom: box plots comparing tumor size with multiorgan resection (left) and blood loss across surgical approaches (right). VATS, video-assisted thoracoscopic surgery.

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by the institutional ethics committee of Harbin Medical University Cancer Hospital (No. 2020-50-IIT) and individual consent for this retrospective analysis was waived.

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AB016. Towards understanding mechanisms of thymectomy benefit for myasthenia gravis

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Background: The MGTX trial demonstrated therapeutic benefit of thymectomy for myasthenia gravis (MG), however, the biological mechanisms contributing to this benefit remain unclear with the standard explanation being limited to removal of a site of autoantibody production. To evaluate the systemic change in the peripheral circulation, we assessed whole blood transcriptional profile for mechanisms underlying the effect of extended transsternal thymectomy (ETTX) in MG.

Methods: We utilized whole blood RNA samples collected during the MGTX trial and applied generalized linear mixed models and differential gene expression. Our goal was to identify gene expression patterns and biochemical pathways associated with ETTX. We correlated transcriptional profile to quantitative MG (QMG) and area under the QMG over time analysis (AUQMG).

Results: Filtering the genes based on the prevalence and variation, 3,175 genes were included in the analysis. At the false discovery rate (FDR) of 0.05, 222 genes were identified as differentially expressed in ETTX subjects compared to those receiving prednisone only. Sorted by gene ratio, top pathways were focal adhesion, cell-substrate junction, ribosome structure, secretory granule membrane, regulation of cell-cell adhesion and specifically immune response-regulating cell surface receptor signaling pathways. We detected 151 genes upregulated in association with higher QMG scores. The greatest increases involved *DEFA3*, *CYP4F3*, *LTF*, *HLA.C_3*, *AHSP*, and *KRT*. These genes enrich for immune response-activating signaling, mononuclear cell differentiation, GTPase regulator activity,

immune response-regulating cell surface receptor signaling, lymphocyte differentiation, and leukocyte cell-cell adhesion. For area under the quantitative myasthenia gravis time curve (AUQMG), 307 genes were differentially expressed with 109 genes upregulated in association with higher AUQMG. Among these, *CD69*, *SNORD17*, *RPS7*, *NIBAN3*, and *RPS27* showed the highest expression levels. These genes enrich for regulation of protein catabolic process, immune response-activating signaling, viral process, ubiquitin-like protein ligase binding, and macroautophagy pathways.

Conclusions: Our initial findings—set to expand in the coming months—reveal that ETTX modulates distinct transcriptional programs and biochemical pathways involved in immune signaling, ribosomal function, and cellular metabolism. These insights shed light on the broader molecular mechanisms driving the therapeutic effects of ETTX, extending beyond the traditional view of thymectomy as merely the removal of an antibody-producing site.

Keywords: Thymectomy; treatment-response; myasthenia gravis (MG); RNASeq

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Footnote

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identified samples (091222) and informed consent was obtained from all individual participants.

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AB017. Clinicopathologic features, treatment outcomes, and survival in thymic neuroendocrine tumors: a 25-year single-center experience

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Background: Thymic neuroendocrine tumors (TNETs) are rare, aggressive neoplasms with limited prospective data guiding optimal management. We aimed to analyze clinicopathologic features, treatment outcomes, and survival of TNET patients treated at a single comprehensive cancer center over 25 years.

Methods: A retrospective review of 19 adult patients with TNETs diagnosed between 2000 and 2024 was conducted. Demographic, clinical, histological, treatment, and survival data were collected from medical records. Survival outcomes, including overall survival (OS), disease-free survival (DFS), and progression-free survival (PFS), were analyzed using the Kaplan-Meier method.

Results: The median age at diagnosis was 52 years (range, 24–73 years), with 12 patients (63.2%) being male. Atypical carcinoid was the most common histological subtype, diagnosed in 10 patients (52.6%), followed by large cell neuroendocrine carcinoma in 6 patients (31.6%). Symptoms were reported in 73.7% of patients at diagnosis, with dyspnea and chest pain being the most common manifestations. Paraneoplastic syndromes were observed

in 26.3% of cases, with clinically confirmed Cushing's syndrome in 15.8%. Treatment modalities and outcomes are summarized in *Table 1*. Curative intent treatment was performed in 9 patients (47.4%), whereas 10 patients (52.6%) received palliative treatment. Radical surgery was attempted in 8 patients. Complete (R0) resection was achieved in 2 cases (22.2%), while microscopic residual disease (R1) was present in six cases. Postoperative radiotherapy was administered to 7 patients, with doses ranging from 4,600 to 6,000 cGy. Adjuvant chemotherapy, consisting of a cisplatin-etoposide regimen, was used in 3 patients. Among patients treated with palliative intent, 8 received systemic chemotherapy, mainly based on cisplatin-etoposide combinations, and 2 patients received best supportive care. During follow-up, disease recurrence was observed in 4 (44.4%) of the 9 patients initially treated with curative intent. Of these, one patient underwent salvage radical-intent therapy, while three patients received palliative treatment following recurrence. In the group of patients who received palliative treatment, disease progression occurred in 8 patients (80%). After progression, 7 patients received further active palliative therapy, whereas one patient was managed exclusively with best supportive care. Post-progression radiotherapy was administered to 3 patients, and 4 patients received chemotherapy. For the entire cohort, the median OS was 127 months [95% confidence interval (CI): 33–170]. In the curatively treated group, the median PFS was 90 months (95% CI: 42–90), and the median OS was 170 months (95% CI: 127–170). Among patients treated with palliative intent, the median PFS was 11 months (95% CI: 3–105), and the median OS was 33 months (95% CI: 2–65).

Conclusions: TNETs are aggressive tumors associated with high rates of recurrence and progression despite multimodal treatment strategies. Complete surgical resection remains the cornerstone of curative therapy. Palliative treatment yields poor long-term outcomes, highlighting the urgent need for new therapeutic approaches and prospective studies to improve survival in this rare entity.

Keywords: Thymic neuroendocrine tumors (TNETs); thymic carcinoids; surgery; survival outcomes; recurrence

Table 1 Treatment modalities and outcomes in patients with thymic neuroendocrine tumors

Variable	Values
Primary treatment intent	
Curative	9 (47.4)
Palliative	10 (52.6)
Surgical treatment	
Surgery performed	8 (42.1)
Complete resection (R0)	2 (25.0)
Microscopic residual disease (R1)	6 (75.0)
Adjuvant therapy after surgery	
Radiotherapy	7 (36.8)
Chemotherapy (PE regimen)	3 (15.8)
Palliative systemic treatment	
Systemic chemotherapy	8 (80.0)
Recurrence/progression	
Recurrence after curative therapy	4 (44.4)
Salvage radical treatment after recurrence	1 (11.1)
Progression after palliative therapy	8 (80.0)
Salvage palliative treatment after progression	7 (70.0)
Survival outcomes	
PFS for curatively treated patients (months)	90 [42–90]
OS for curatively treated patients (months)	170 [127–170]
PFS for palliatively treated patients (months)	11 [3–105]
OS for palliatively treated patients (months)	33 [2–65]

Data are presented as n (%) or median [95% CI]. CI, confidence interval; OS, overall survival; PE regimen, cisplatin/etoposide regimen; PFS, progression-free survival.

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AB018. Targeted biologics for treating thymoma associated myasthenia gravis: a multicenter retrospective study

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Background: Thymoma-associated myasthenia gravis (TAMG) is frequently resistant to conventional treatment and portends poorer prognosis. Targeted biologic therapies have been implemented for treating generalised myasthenia

gravis (MG), evidence for their long-term safety and efficacy in TAMG remains scarce. To investigate the long-term safety and efficacy of targeted biologics in patients with TAMG, we conducted this real-world study.

Methods: In this multicenter, retrospective real-world study, we enrolled TAMG patients treated with maintenance targeted biologic therapy at six neuromuscular centers in China from May 2023 to May 2024. Therapies comprised the anti-CD20 monoclonal antibody (rituximab), the C5 inhibitor (eculizumab), and the neonatal Fc receptor (FcRn) antagonist (efgartigimod). Survivors were followed for at least 1 year, while all deaths were captured regardless of follow-up duration. Stable treatment was defined as rituximab at least once every 6 months, or efgartigimod/eculizumab at least once per month. The primary outcome was the proportion achieving minimal symptom expression (MSE). Secondary outcomes included rates of adverse events (AEs), myasthenic crises (MC) or impending crises, and mortality.

Results: Twenty-two patients (mean age 50.3±12.8 years; median disease duration 12.5 months) were analyzed over a mean follow-up of 13.0±5.5 months. Thymectomy was performed in 95.5% of cases, with 59.1% receiving adjuvant chemoradiotherapy. Biologic therapy commenced perioperatively in 18.2%, and 81.8% initiated treatment amid acute exacerbations or crises. Histopathology was dominated by World Health Organization (WHO) type B2 thymoma (40.9%) with Masaoka stage IV (54.5%). After treatment, fell markedly (13.14±5.83 to 3.35±4.66 at 1 year), and median daily steroid dose declined from 45 to 10 mg (*Figure 1A*). MSE was achieved in 40.9%, lasting on average 230 days. AEs occurred in 59.1%, chiefly infections (50.0%). Both MC (from 63.6% to 22.7%) and impending crisis (from 18.2% to 0%) rates declined. At 1 year, 16 patients (72.7%) attained “Improved” or “Minimal manifestations”, while 5 patients (22.7%) died during follow-up (*Figure 1B*).

Conclusions: Maintenance targeted biologic therapy substantially improves clinical outcomes, reduces steroid burden and lowers the risk of MC or impending crisis in TAMG, with an acceptable safety profile. These findings support its long-term use in this challenging population.

Keywords: Thymoma; myasthenia gravis (MG); biologics; minimal symptom expression (MSE)

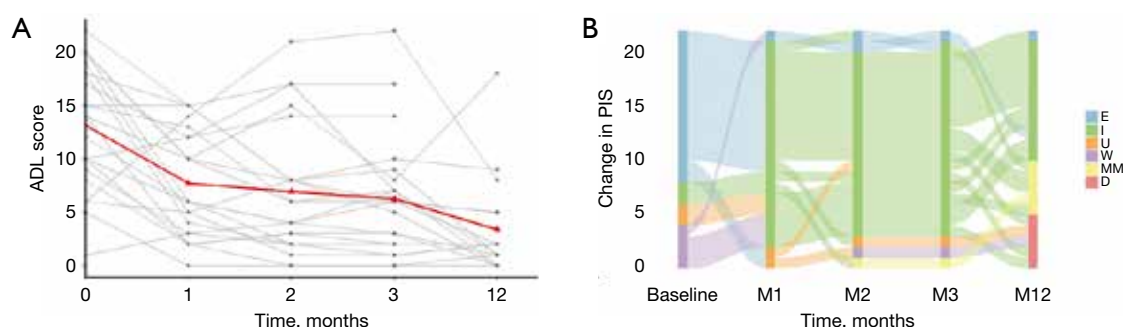


Figure 1 Efficacy of targeted biologics in patients with TAMG. (A) The changes in ADL score. (B) The changes in PIS. The PIS includes E, I, U, W, MM, and D. ADL, activities of daily living; D, died; E, exacerbation; I, improved; MM, minimal manifestations; PIS, post-intervention status; TAMG, thymoma-associated myasthenia gravis; U, unchanged; W, worse.

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Footnote

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and its subsequent amendments. The study was approved by the institutional ethics committee of Huashan Hospital (No. KY2020-999) and informed consent was obtained from all individual participants.

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AB019. Machine learning models from FDG PET/CT for predicting recurrence in thymomas

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Background: An accurate pre-operative strategy is fundamental for patients' risk stratification and prognostication in order to choose the appropriate treatment for patients with thymomas. This study aimed to develop machine learning (ML) models to predict recurrence in patients with thymomas using conventional and radiomic signatures extracted from fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT).

Methods: A total of 50 patients (25 males, 25 females; mean age 63.3 years) who underwent FDG PET/CT before surgery between 2012 and 2022 were retrospectively analyzed. Radiomic analysis was performed using free-from-recurrence (FFR) status as a reference. A total of 856 radiomic features (RFs) were extracted from PET and CT datasets following IBSI guidelines, and robust RFs were selected. The dataset was split into training (70%) and validation (30%) sets. Two ML models (PET- and CT-based, respectively), each with three classifiers—Random Forest (RF), Support-Vector-Machine (SVM), and Decision Tree,

were trained and internally validated using RFs and clinical-metabolic signatures.

Results: A total of 50 regions of interest (ROIs) were selected and segmented. Height patients had recurrence (FFR 1), whereas 42 did not (FFR 0). Forty-three robust RFs were selected from the CT dataset and 16 from the PET dataset, predominantly wavelet-based RFs. Additionally, three metabolic PET parameters [i.e., relative PET (rPET), quantitative PET (qPET), and tumor-to-mediastinum (T/M) ratio] were selected and included in the PET model: tumor SUVmax/LiverSUVmax (rPET), tumor SUVpeak/LiverSUVmean (qPET), and the ratio between the SUVmax of thymomas and the SUVmean of aortic arc (T/M). Both the CT and PET models successfully discriminated FFR after surgery, with the CT Model slightly outperforming the PET Model across different classifiers. The performance metrics of the RF classifier for the CT and PET models were area under the curve (AUC) =0.970/0.949, accuracy =0.880/0.840, precision =0.884/0.842, recall =0.880/0.846, specificity =0.887/0.839, sensitivity =0.920/0.844, true-positive =81.8%/83.3%, true-negative =92.9%/84.6%, respectively (Figure 1).

Conclusions: ML-models trained on PET/CT radiomic features show promising results for predicting recurrence in patients with thymomas, which could be potentially applied in clinical practice for a better personalized treatment strategy.

Keywords: Thymomas; fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT); recurrence; radiomics; machine learning (ML)

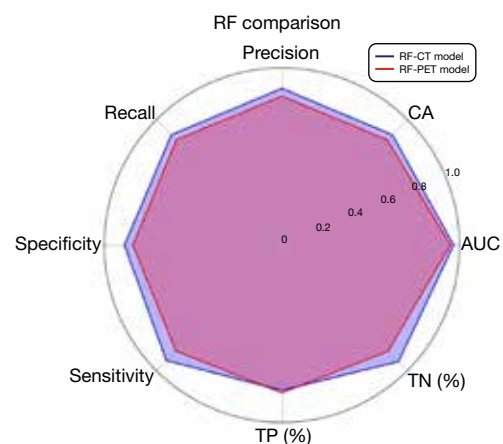


Figure 1 Radial plot of RF learner performances scores of ML models. AUC, area under the curve; CT, computed tomography; ML, machine learning; PET, positron emission tomography; RF, Random Forest; TN, true-negative; TP, true-positive.

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of Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan (study identification: INT121/24) and individual consent for this retrospective analysis was waived.

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AB020. Salvage surgery following definitive chemoradiotherapy and immune checkpoint inhibitor therapy for locally advanced thymic carcinoma: a case report

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Background: Thymic carcinoma is a rare malignancy with a poor prognosis. Complete surgical resection is a favourable prognostic factor and is recommended whenever possible. Platinum-based chemotherapy or lenvatinib is the current standard treatment for unresectable thymic carcinomas; however, its efficacy remains limited. The efficacy of immune checkpoint inhibitors is currently under investigation. Here, we present a case of salvage surgery

after immune checkpoint inhibitor therapy for an initially unresectable, locally advanced thymic carcinoma.

Case Description: The patient was a 67-year-old woman. Computed tomography showed a 4.7-cm anterior mediastinal mass compressing the aortic arch and left main pulmonary artery (*Figure 1A*), along with enlargement of the anterior mediastinal lymph nodes. It was diagnosed as an unresectable thymic epithelial tumour, cStage IVa (T4N0M0), because the tumour was suspected to have invaded the left main pulmonary artery. Thoracoscopic biopsy confirmed the diagnosis of squamous cell carcinoma with high programmed cell death-ligand 1 (PD-L1) expression (90–100%). After chemoradiotherapy (carboplatin, paclitaxel, and radiation at 60 Gy), the patient received eight courses of durvalumab. Without any significant immune-related adverse events, the primary tumour size reduced to 4.2 cm (*Figure 1B*), and the anterior mediastinal lymph nodes resolved after two and a half years of treatment. Salvage surgery was performed via a posterolateral incision without invasion of the great vessels. The operative time was 285 minutes, and blood loss was 95 mL. The final pathological stage was ypStage IIIA (T3N0M0) with an Ef1b–2. The patient was discharged uneventfully on postoperative day 9. The patient remained disease-free for 1 year and 8 months after salvage surgery.

Conclusions: Complete resection with salvage surgery was performed after definitive chemoradiotherapy, followed by treatment with immune checkpoint inhibitors. Salvage surgery following immune checkpoint inhibitor therapy may be an option for treating thymic carcinomas with high PD-L1 expression.

Keywords: Thymic carcinoma; thymic epithelial tumor; immune checkpoint inhibitors; salvage surgery; case report

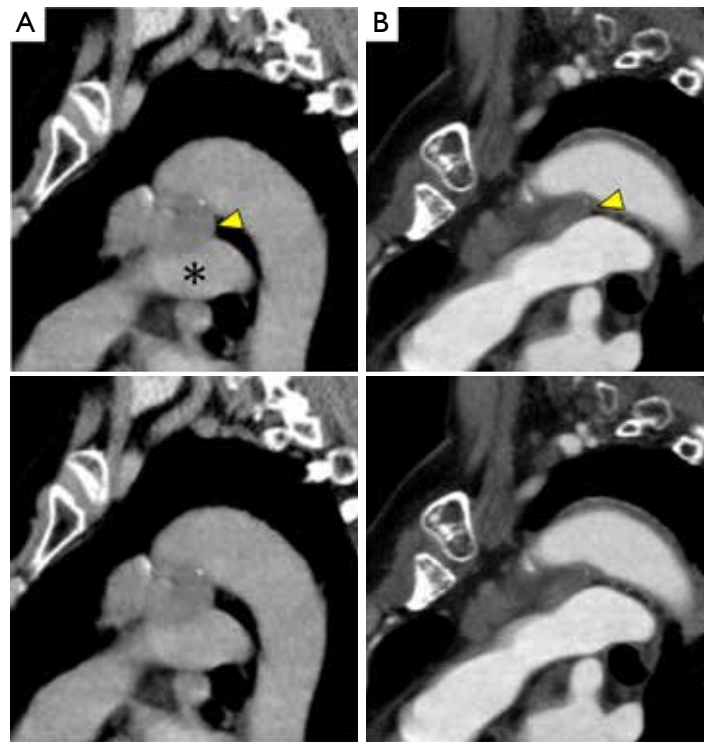


Figure 1 Radiographic findings. (A) Computed tomography findings before treatment. Chest computed tomography findings show a 4.7-cm mass in the anterior mediastinum (arrowhead), which is suspected to have invaded the left main pulmonary artery (asterisk). (B) Computed tomography findings after immune checkpoint inhibitor therapy. The anterior mediastinal tumour is reduced to 4.2 cm (arrowhead), with no obvious invasion into the great vessels.

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obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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AB021. A single-arm, multicenter, phase II trial of glucocorticoids induction followed by surgery for advanced thymomas with type B component

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Background: Glucocorticoid was reported to be effective in thymomas, especially thymomas with type B component. This prospective, single arm, phase II trial aims to further study the efficacy and safety of glucocorticoids induction for patients with advanced thymomas.

Methods: Patients with previously treated potentially unresectable tumor-node-metastasis (TNM) (8th) stage III–IVa, histologically confirmed thymomas with type B component were considered eligible for this trial. Enrolled patients would accept high-dose glucocorticoids induction (methylprednisolone 1 g ivgtt d1–3, Q1W, 2 courses; or prednisone 1 mg/kg orally for 2 months) and subsequent surgery. The primary end point was objective response rate to glucocorticoids.

Results: From Jan 2023 to Oct 2024, a total of 30 patients were enrolled including 8 (26.7%) with stage III diseases and 22 (73.3%) with stage IV diseases. The objective response rate was 53.3% with 16 cases of partial response. The rest 14 (46.7%) had stable diseases. No one had progressed disease. No severe adverse event developed during induction. All patients received surgery with complete resection of the tumor. Two cases of air-leak and one case of pneumonia were recorded after surgery.

Conclusions: Glucocorticoid is effective and safe for the

treatment of advanced thymomas. It might be a choice of induction therapy before surgery and further research is required.

Keywords: Thymoma; glucocorticoid; induction; surgery

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Footnote

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Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at <https://med.amegroups.com/article/view/10.21037/med-25-ab021/coif>). The authors have no conflicts of interest to declare.

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AB022. Retrospective evaluation of cardiac toxicity during irradiation of thymic malignancies

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Background: Cardiac toxicities of thymic irradiations are relatively unknown because of to the rarity of the indication but are very important to study due to the long overall survival of this population. The objective of this study is to evaluate the occurrence of cardiac events in patients irradiated for thymic malignancies, in relation to the doses delivered to the cardiac structures.

Methods: All patients treated with radiotherapy for thymic tumors between 2012 and 2024 in the Department of Radiotherapy of the CHU de Bordeaux were retrospectively included. We collected the doses received by the heart, coronary arteries and by the pericardium (V30, V40, V45 and V50) by performing a specific pericardial contour defined as an internal expansion of 3 mm from the cardiac contour. More specific structures were analyzed a posteriori according to the post-therapeutic toxicity.

Results: Of the 52 patients identified, 43 were included in the final analysis (9 patients excluded because irradiated outside the thymic compartment). The majority of tumors were thymomas (58%) or squamous cell carcinomas (30%). Before treatment, 79% of patients had at least one cardiovascular risk factor. Radiotherapy was adjuvant in 88% of cases (positive margins: 60%) with a median dose of 53.2 [45–66] Gy. Exclusive radiotherapy with concomitant chemotherapy was performed in 7% of patients {median dose of 51 [50–66] Gy}, and palliative intent in 2 patients. Nine patients (21%) presented with a cardiac event: 2 arrhythmias, 1 valvular pathology, 1 infarction, 2 proven pericardial toxicities and 3 atypical chest pain possibly of pericardial origin. Doses received by conduction nodes

or pathological valve structures in affected patients were less than 15 Gy making the imputability to radiotherapy uncertain. The patient who required inter-ventricular coronary angioplasty had received the prescription dose of 50 Gy in the artery. In patients with a pericardial or related event, the doses received by the pericardium were significantly higher than in the population without the event: V30Gy at 20.2% *vs.* 10.8%, V40Gy at 15.4% *vs.* 8.2%, V45Gy at 11.2% *vs.* 7%, V50Gy at 8.3% *vs.* 5%, and mean cardiac dose at 14.4 *vs.* 10.3 Gy.

Conclusions: Radiotherapy of thymic tumors can induce cardiac toxicity, particularly pericardial toxicity, which appears to be correlated with the dose received by the heart and pericardium. This can lead to personalized reinforced cardiac follow-up for identified persons at risk.

Keywords: Radiation oncology; thymus malignancies; cardiac toxicities

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments and approved by the regional ethics committee board, the CER of Bordeaux with the following registration number: CER-BDX 2025-292. Individual consent for this retrospective analysis was waived.

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AB023. Thymic epithelial tumors and immune system: a particular relationship still to be clarified

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Background: Thymic epithelial tumors (TETs) are rare cancers of the thymus, frequently associated with autoimmune diseases (ADs), including myasthenia gravis (24.5–44%). The correlation between TETs and autoimmunity still remains unknown. We aim to evaluate the autoantibody profile of patients affected by TETs before surgery in order to assess the presence of differences in patients with or without ADs, even in a subclinical setting.

Methods: We have prospectively enrolled patients affected by TETs and thymic hyperplasia (TH), including age- and sex-matched healthy donors (HDs) as control group. The tests performed were: antinuclear antibodies (ANA), extractable nuclear antigens (ENA), rheumatoid factor (RF), anti-acetylcholine receptor (AChR) and anti-muscle specific kinase (MuSK) immunoglobulin G (IgG), anti-SSA antibodies, anti-SSB, anti-Smith (Sm), anti-ribonucleoprotein (RNP), anti-topoisomerase (Scl-70) and anti-Jo1 anti-cyclic-citrullinated peptide (CCP), anti-neutrophil cytoplasmic antibodies (ANCA) and anti-

myeloperoxidase and proteinase 3 (MPO-PR3) antibodies, dsDNA antibodies, thyroglobulin antibodies (TGAb), anti-thyroid peroxidase antibodies (TPOAb) and anti-TSH receptor (TRAb).

Results: From 2020 to date, a total of 171 patients (100 thymomas, 14 thymic carcinomas, 27 THs, and 30 HDs) were enrolled. Among 141 patients with TETs and TH, 28 patients (19.8%) had an overt AD at time of surgery, including myasthenia gravis in 17 patients (60.7%). Notably, the presence of at least one autoantibody positivity was also detected in 69 patients without overt ADs (61.4%) at much higher frequency compared with 30 HDs (23.3%). In patients without overt AD we found AChR positivity in 22 patients (19.4%), TGAb positivity in 12 (11.1%), and TPOAb positivity in 18 (16.2%). Moreover, in the absence of an overt AD, the highest percentage of positivity for autoantibody tested was observed in patients with Thymoma B1 (57%) and B2 (55%).

Conclusions: The pathophysiological links between TETs and autoimmunity still remains unclear. Indeed, while a pre-existing autoimmune condition does not constitute a risk for AD relapse after surgery, the impact of surgical resection on AD flares is unpredictable. In our series we observed several autoantibody positivities despite the absence of overt ADs, suggesting a higher percentage of patients potentially carrying an autoimmune disorder clinically unrecognized when affected by TETs and TH.

Keywords: Thymic tumors; autoimmune diseases (ADs); surgery

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional ethics committee board of IRCCS

Humanitas Research Hospital (No. ONC/OSS-01/2020) and informed consent was obtained from all individual participants.

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AB024. MIST: a weakly supervised deep learning system for multicenter diagnosis of mediastinal tumors

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Background: Mediastinal tumors represent a distinct group of thoracic diseases, with a rising global incidence and generally poor prognosis. Clinical diagnosis remains challenging due to the complex anatomical structure of the mediastinum and the often ambiguous boundaries between different pathological subtypes. The objective of this study is to develop and validate a high-performance deep learning diagnostic system—Mediastinal tumor Identification with weakly Supervised Training (MIST)—that can accurately and automatically identify mediastinal tumors from chest computed tomography (CT) scans

using multicenter data.

Methods: The MIST system was trained using a dataset comprising 1,173 cases of mediastinal tumors with ten pathological subtypes, collected from a high-volume medical center in China. The system processes chest CT scans as input. It first applies a pretrained segmentation model to roughly localize tumor regions within the mediastinum. Then, imaging features are extracted using BiomedCLIP, a multimodal biomedical foundation model. These features are subsequently aggregated by the Transformer based Correlated Multiple Instance Learning (TransMIL) approach to assess tumor malignancy and predict specific pathological subtypes (*Figure 1A*). MIST's generalizability was evaluated using an external validation cohort of 227 cases from five independent medical centers (*Figure 1B*).

Results: MIST demonstrated strong performance in 5-fold cross-validation on the training set, achieving an average area under the curve (AUC) of 0.741 ± 0.045 for malignancy classification and a macro-average AUC of 0.760 ± 0.004 for multiclass subtype classification. In the external validation cohort, MIST maintained comparable performance, with an AUC of 0.818 [95% confidence interval (CI): 0.744, 0.883] for malignancy detection and a macro-average AUC of 0.763 (95% CI: 0.715, 0.807) for subtype classification (*Figure 1C*). The detailed classification performance is shown in the confusion matrix (*Figure 1D*). The system achieved a top-1 accuracy of 0.194 (95% CI: 0.145, 0.247) and a top-3 accuracy of 0.480 (95% CI: 0.419, 0.542).

Conclusions: MIST enables accurate identification of both the malignancy and pathological subtypes of mediastinal tumors, with robust generalization across external multicenter datasets. This weakly supervised, foundation model-based approach holds promise for improving diagnostic accuracy and efficiency in clinical settings.

Keywords: Mediastinal tumors; deep learning; weakly supervised learning; subtype prediction; multicenter study

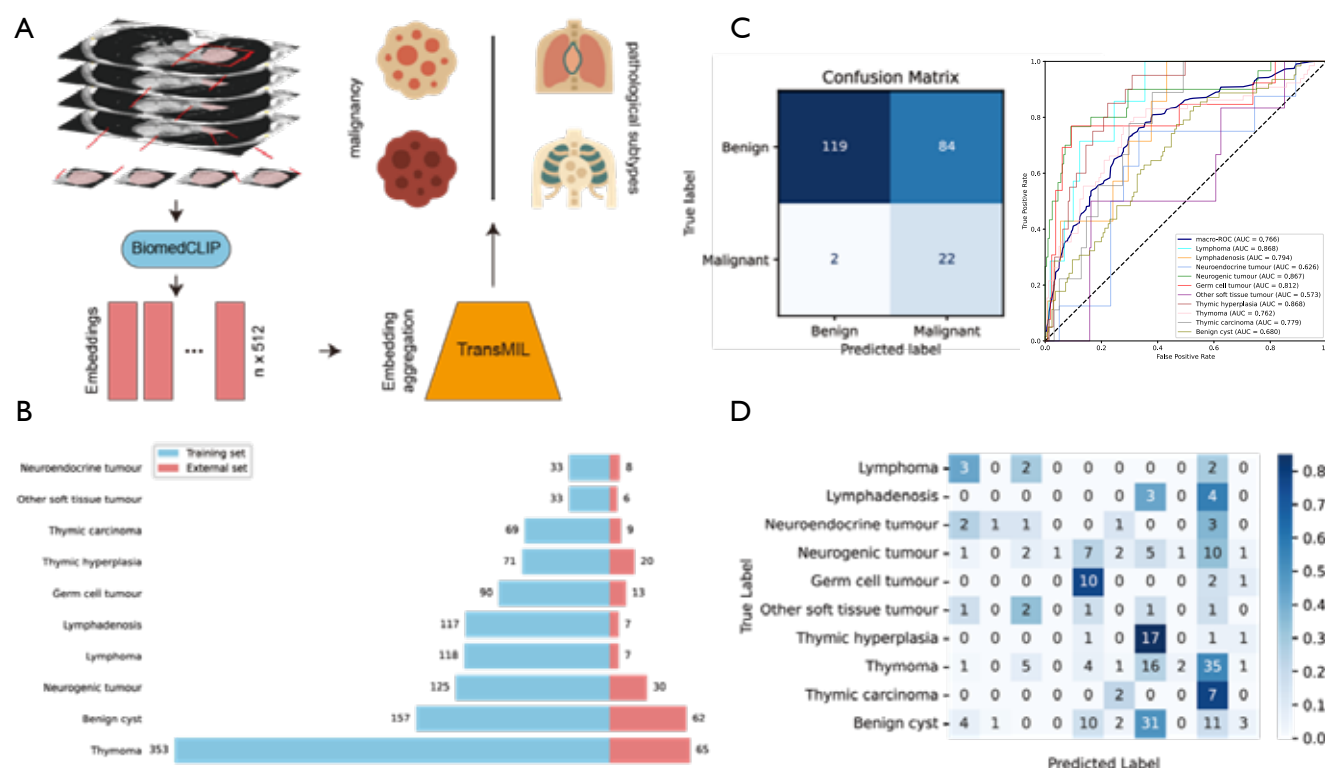


Figure 1 Overview and performance of the MIST system. (A) The overall workflow of the MIST diagnostic system. Slices from chest CT scans are processed by the BiomedCLIP model to extract image features (embeddings). These features are then aggregated by the TransMIL model to predict both malignancy and specific pathological subtypes. (B) The distribution of 10 pathological subtypes across the training set (n=1,173) and the external validation set (n=227). (C) Performance evaluation on the external validation set. The confusion matrix (left) illustrates the performance of binary malignancy classification. The ROC curves (right) show the performance for multiclass subtype classification, with corresponding AUC values for each subtype. (D) A detailed confusion matrix for the 10-class pathological subtype classification on the external validation set. AUC, area under the curve; CT, computed tomography; MIST, Mediastinal tumor Identification with weakly Supervised Training; TransMIL, Transformer based Correlated Multiple Instance Learning; ROC, receiver operating characteristic.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional Ethics Committee of the National Center for Respiratory Medicine/The First Affiliated Hospital of Guangzhou Medical University (Oct 12, 2020; Institutional Review Board number: 2020 No.138) and individual consent for this retrospective analysis was waived. Approval from the Ethics Committee of Sichuan Cancer Hospital was waived, as the study involved retrospectively collected medical images that had been anonymized prior to data processing.

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AB025. When the thymus crosses the line: an unusual case of lung-infiltrating endobronchial thymoma – a case report

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Background: Thymomas typically demonstrate an indolent growth pattern, showing a non-infiltrative behaviour and displacing adjacent structures, even when they reach a great size. However, high-grade thymomas may invade the capsule and directly extend into neighbouring organs. Airway involvement is exceedingly rare, with only a few cases documented in the literature.

Case Description: We report an uncommon case of invasive thymoma with endobronchial growth in a 75-year-old female. The patient initially presented with hemoptysis. Chest computed tomography imaging revealed a calcified mass in the anterior mediastinum with invasion of the left

upper pulmonary lobe. Due to the extent of bronchial obstruction to a subsegmental bronchus of the left upper lobe, the radiological findings were initially interpreted as being most consistent with a primary lung neoplasm. Flexible bronchoscopy confirmed the presence of a polypoid lesion originating from the subsegmental bronchus of the left upper lobe (*Figure 1*). Histopathological examination of endobronchial biopsies revealed a B2 thymoma. Following multidisciplinary evaluation and staging investigations that excluded distant metastases, the patient was initially referred for neoadjuvant chemotherapy due to suspected involvement of the left main pulmonary artery and mediastinal lymph nodes. However, owing to significant toxicity after the first cycle, an upfront surgical approach was considered more appropriate. The patient subsequently underwent an *en-bloc* extended thymectomy with left upper lobectomy via a left posterolateral thoracotomy. Histopathological analysis of the surgical specimen confirmed tumour invasion into the pulmonary parenchyma and the bronchial lumen. All surgical margins, including the bronchial stump, were negative, and no lymph node metastases were identified [pT3N0, stage IIIa according to the 9th dedicated tumor-node-metastasis (TNM) classification, although the latest system does not yet consider bronchial involvement]. The postoperative course was uneventful, and the patient was discharged on postoperative day 6. She was subsequently enrolled in a pulmonary rehabilitation program to support recovery. Adjuvant radiotherapy targeting the anterior mediastinum was administered without complications. Follow-up bronchoscopies showed no abnormalities, and the patient remains disease-free on initial post-surgical surveillance imaging.

Conclusions: In conclusion, this rare case of invasive thymoma with endobronchial involvement emphasises the significance of prompt diagnosis, effective multidisciplinary treatment, and successful surgical management, leading to a favourable post-treatment outcome.

Keywords: Thymoma; airway invasion; multimodality treatment; case report

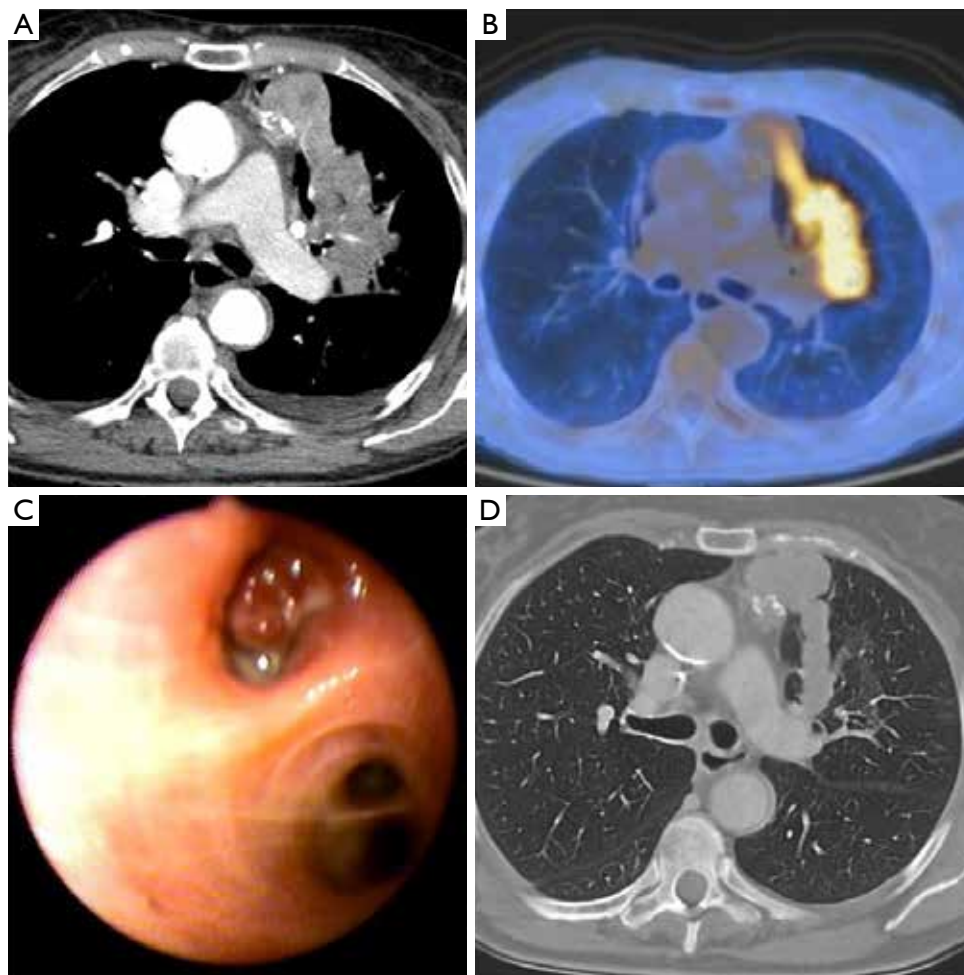


Figure 1 Thymoma with infiltration of the lung and peripheral airways. (A) First CT scan showing a neoplasm infiltrating the airways and occluding a subsegmental branch of the left upper lobe, resulting in distal atelectasis; (B) PET scan demonstrating radiotracer uptake in the lesion; (C) flexible bronchoscopy revealing occlusion of a subsegmental branch of the left upper lobe; (D) preoperative CT scan. CT, computed tomography; PET, positron emission tomography.

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of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration and its subsequent amendments. Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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AB026. Contralateral pleura-sparing modified subxiphoid approach for robotic thymectomy: operative results, and advantages in metachronous lung cancer resection

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Background: Robotic thymectomy for thymic epithelial tumors (TETs) yields favorable perioperative results and effective disease control. The lateral approach is commonly employed for robot-assisted thymectomy, while the subxiphoid approach offers another option for robotic thymectomy. However, the subxiphoid approach necessitates bilateral pleural resection, which may lead to unfavorable conditions, such as bilateral pneumothorax and the bilateral dissemination of tumors. To mitigate this risk, we utilize the subxiphoid method along with three additional robotic ports on the hemithorax, referred to as the “modified subxiphoid approach”. We aimed to assess the clinical outcome and the advantage of this procedure using our clinical data.

Methods: We retrospectively reviewed patients who underwent modified subxiphoid robotic thymectomy for TETs at Nishi-Kobe Medical Center from September 1, 2019, to December 31, 2024. We evaluated the surgical results and elucidated the cases that underwent lung cancer resection after thymectomy.

Results: A total of 21 patients were eligible for this study. The mean age was 65.3 [44–81] years. The breakdown of diseases is as follows: thymoma without myasthenia gravis (MG), 15; thymoma with MG, 4; and thymic cancer, 2. The mean tumor diameter was 44.6 [13–100] mm. The operative side was right in 13 cases and left in 8 cases. No major morbidity occurred. R0 resection was achieved in 20 cases.

A microscopic positive margin was found in the largest tumor case, which recurred 36 months later as ipsilateral pleural disseminations. No other recurrences or patient deaths occurred during the follow-up (median 24 months, range, 6–65 months). The 3-year recurrence-free survival rate was 85.7%. Lung cancer was detected in 3 cases after thymectomy, with ipsilateral lung resection performed in 1 case and contralateral lung resection in 2 cases. Adhesion to the vascular was found in the ipsilateral case, while no adhesion was found in the contralateral cases. In the case of the patient with MG who underwent contralateral lung resection, the operative findings revealed a complete resection of the contralateral thymus, except for the fat above the diaphragm.

Conclusions: The contralateral pleura-sparing modified subxiphoid approach is an acceptable and safe method, particularly given the advantage of metachronous lung resection. A large tumor should be avoided due to the risk of unresectability and recurrence.

Keywords: Robotic thymectomy; contralateral pleura-sparing modified subxiphoid approach; metachronous lung resection

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AB027. Surgery for *de novo* stage IVa thymomas: time to broaden our horizons?—a single-centre retrospective analysis

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Background: *De novo* stage IVa thymomas, characterised by plural or pericardial dissemination at diagnosis, pose significant management challenges. The purpose of this article is to describe our experience with a two-step surgical strategy in the management of *de novo* stage IVa thymomas, and to evaluate its impact on oncological outcomes.

Methods: Clinical and oncological data were retrospectively collected for all patients with pleural *de novo* stage IVa thymoma, classified according to the 9th tumor-node-metastasis (TNM) staging system, who underwent surgical treatment at the University Hospital of Pisa between January 2005 and December 2024. Variables included clinical and surgical characteristics, histological subtype [per

World Health Organization (WHO) classification], and adjuvant treatments. Overall survival (OS) and disease-free survival (DFS) were analysed, stratifying patients based on surgical timing: single-step surgery (primary tumour and metastases treated simultaneously) versus two-step surgery (procedures performed 3–6 months apart).

Results: Thirty patients (14 males, 16 females; median age 47 years, range 29–82 years) were included, 13 (43.3%) of whom had myasthenia gravis. All patients had pleural dissemination at diagnosis: 33% had a single metastasis, while one-third of patients had more than 10 implants. Neoadjuvant chemotherapy was administered in 63.3% of cases when judged potentially resectable. Nineteen patients (63.3%) underwent single-step surgery with radical intent on the primary tumour and pleural metastases. Eleven patients (36.7%) underwent two-step surgery, with the first procedure addressing the primary tumour, with a lower rate of post-operative complications and an earlier discharge, followed by a second operation targeting pleural metastases. The most common histological subtypes were B3 (36.7%), B2 (23.3%), and combined B2/B3 (23.3%). Twenty-five patients received adjuvant therapy, 8 of whom were prior to the second surgical procedure.

During follow-up, recurrence occurred in 22 patients without differences between the two groups ($P=0.95$), while eleven patients (36.6%) died. OS ($P=0.41$) and DFS ($P=0.98$) were comparable across groups, irrespective of the timing of complete surgical resection (primary tumour, metastases, or both) and surgical strategy (*Figure 1*).

Conclusions: Managing *de novo* stage IVa thymomas usually requires a multimodal approach. Given the typically indolent behavior of the disease, a two-step surgical strategy does not compromise the oncological outcomes, compared to single-step surgery, but may reduce the post-operative complication rate.

Keywords: Thymoma; *de novo* stage IVa; multimodality treatment; thymic surgery; two-step surgery

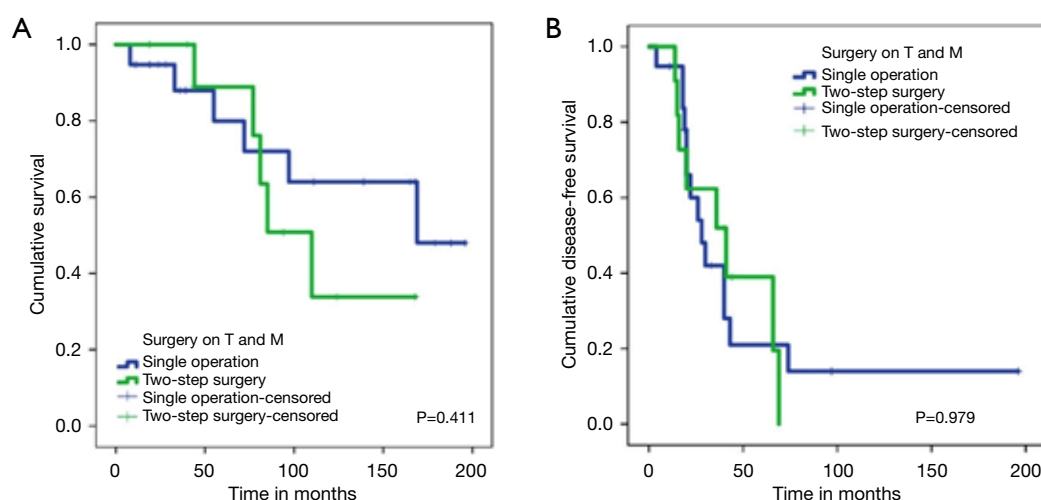


Figure 1 Kaplan-Meier analysis of survival curves for patients with de novo stage IVa thymomas. (A) Overall survival curves stratified according to the timing of surgical resection; (B) disease-free survival curves stratified according to the timing of surgical resection. M, metastasis; T, tumor.

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AB028. Good's syndrome and infections in a large retrospective cohort of thymoma

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Background: Good's syndrome (GS) was reported as immunodeficiency associated with thymoma and hypogammaglobulinemia. The co-existence of recurrent infections may significantly impact the quality of life and overall survival. However, these have rarely been studied in large cohorts. The study aims to report the prevalence of GS and infections in patients with thymoma and its impact on the survival.

Methods: This is a large retrospective cohort study of patients with pathologically diagnosed thymoma from Huashan Hospital, Fudan University, between May 2010 and November 2024. GS was defined as hypogammaglobulinemia with thymoma.

Results: From 1,001 patients with thymoma we have reviewed, we finally enrolled 158 cases who had peripheral immune profile evaluations. The prevalence of GS was 45.6% (72/158) while the infections were reported in 43.69% (69/158). The mortality in patients with GS was 15.28% (11/72) and 8.14% (7/86) in the non-GS group, respectively. In addition, the proportion of patients with infections was higher in the GS group (50% versus 32.72%, $P=0.04$). Regarding all pathogens identified from this cohort ($n=121$), bacteria account for the majority (52.07%, 63/121), followed by the fungus (34.71%, 42/121) and virus (13.22%, 16/121). The overall survival of 20 years was worse in patients with infections compared with those without infections [hazard ratio (HR) = 6.365, $P<0.001$]. Patients with single paraneoplastic syndrome (PNS) had better survival outcome after 20 years than that with multiple PNS

($P<0.001$). However, there is no significant difference in 10-year overall survival between GS and non-GS group.

Conclusions: A substantial proportion of thymoma patients had GS and infections, which significantly impacts their survival. Early detection and intervention are essential for improving prognosis and long-term survival.

Keywords: Good's syndrome (GS); infections; thymoma

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Footnote

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AB029. Eculizumab as a new option for perioperative treatment in thymoma-associated myasthenia gravis: a prospective case series

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Background: Eculizumab in patients with thymoma-associated myasthenia gravis (TAMG) for perioperative treatment have not been evaluated. The aim of this study is to explore the perioperative efficacy and safety of eculizumab in patients with TAMG.

Methods: This is a single-centre observational prospective study. Patients were stratified into two groups with conventional immunotherapies, including corticosteroid, with (n=10) or without eculizumab as an add-on (n=15). The clinical outcomes, surgical outcomes, MG-activities of daily living (ADL), Myasthenia Gravis Foundation of America-quantitative MG (QMG), Manual Muscle Test (MMT), were compared between groups. Immune profiling and adverse events were also assessed pre-thymectomy and post-thymectomy. The intercostal muscle was collected and stained for C5b-8/9 to evaluate the membrane attack complex (MAC) deposition.

Results: Both groups exhibited significant postoperative

reductions in QMG, MMT and ADL scores compared to preoperative baseline levels. Eculizumab group presented earlier improvement for Δ QMG (median 8.5 *vs.* -1.0, $P<0.001$), Δ MMT (6.0 *vs.* -3.0, $P=0.001$), and Δ ADL (5.0 *vs.* -3.5, $P=0.001$) at 1 week. The relative superiority in clinical scores was consistent through week 2. For eculizumab group, the percentages of CD3⁺CD4⁺T helper cells significantly declined from 41.17% $\pm$ 7.98% to 30.39% $\pm$ 8.12% ($P=0.003$), CD3⁺T lymphocytes significantly declined from 74.21% $\pm$ 8.91% to 67.82% $\pm$ 11.39% ($P=0.045$). In contrast, there were no significant changes in CD3⁺CD8⁺T and CD19⁺B lymphocytes. The retrospective analysis revealed an increase in the expression of C5b-8/9 in patients with TAMG, as compared with healthy controls ($P=0.04$).

Conclusions: This small case series highlights the use of eculizumab in TAMG as a rapid symptom-control treatment during the perioperative period. Future prospective cohort studies with a large sample size are expected to validate these findings, particularly for those TAMG with moderate to severe myasthenia before thymectomy.

Keywords: Thymoma; perioperative; eculizumab

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AB030. Clinical significance of SUVmax as a predictor of pathological invasion and prognostic factor in advanced thymic epithelial tumors requiring a combined resection of adjacent organs and dissemination

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Background: Thymic epithelial tumors (TETs) are rare and heterogeneous malignancies. Because they are surrounded by vital mediastinal structures, achieving complete (R0) resection and determining the extent of lymph node dissection are often challenging in advanced cases. Therefore, accurate preoperative assessment of tumor invasiveness is of critical importance for treatment planning. The maximum standardized uptake value (SUVmax) has been reported to correlate with biological aggressiveness and tumor progression in various malignancies. However, its clinical significance in TETs remains insufficiently clarified, and the association with tumor size has also been scarcely investigated. This study aimed to evaluate the clinical utility of SUVmax as a predictor of pathological invasion and a prognostic factor in advanced TETs requiring combined resection of adjacent organs or management of dissemination.

Methods: A multicenter retrospective study was conducted, comprising 102 patients with TETs, requiring combined resections of adjacent organs or pleural disseminations, from January 2000 to November 2024. Among these, 53 patients with available SUVmax data were included. Receiver operating characteristic (ROC) curves were used to determine optimal SUVmax and tumor size cut-offs for predicting advanced pathological stage (Masaoka stage III/IV) and nodal metastasis. Logistic regression identified factors associated with pathological invasion. Progression-free survival (PFS) was analyzed using Kaplan-Meier methods (log-rank test) and Cox hazard model.

Results: Twenty-five thymomas and 27 thymic carcinomas or thymic neuroendocrine tumors were analyzed. The median SUVmax and tumor size were 5.3 [interquartile range (IQR), 3.8–8.4] and 5.5 (IQR, 5.5–8.0) cm, respectively. Pathological staging revealed 2 stage I, 9 stage II, 29 stage III, 4 stage IVa, and 9 stage IVb cases. Both SUVmax and tumor size were significant predictors of advanced stage and nodal involvement. ROC analysis identified SUVmax cut-offs of 4.7 for advanced disease [area under the curve (AUC) =0.685, sensitivity 71.4%, specificity 63.6%] and 6.1 for nodal involvement (AUC =0.765, sensitivity 77.8%, specificity 68.2%). Tumor size cut-offs were 5.6 cm for both events. Combination of SUVmax (≥ 4.7 or ≥ 6.1) and tumor size (≥ 5.6 cm) stratified risk: rates of advanced disease were 45.5%, 80.0%, and 100% ($P < 0.001$) and nodal involvement rates were 0%, 15.0%, and 46.2% ($P = 0.001$) for patients with 0, 1, and 2 risk factors, respectively. During a median follow-up of 34 months, 15 disease progressions/relapses were observed. High SUVmax (≥ 6.1) was associated with significantly worse PFS compared

to low SUVmax (<6.1) ($P<0.001$; 5-year PFS, 41.9% *vs.* 77.5%; hazard ratio 4.53, 95% confidence interval: 1.53–13.4). No significant interactions were found between SUVmax and tumor size, stage, or histology.

Conclusions: SUVmax is a valuable indicator of pathological invasion along with tumor size and may guide surgical decision-making and nodal dissection strategy. Furthermore, SUVmax serves as a prognostic factor in advanced TETs.

Keywords: Thymic epithelial tumor (TET); maximum standardized uptake value (SUVmax); pathological invasion; nodal metastasis; prognostic factor

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AB031. Global patterns and trends in thymic epithelial tumors incidence: worldwide healthcare disparity on detection

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Background: Thymic epithelial tumors (TETs) are a group of rare thoracic malignancies with undefined global epidemiology. We aim to comprehensively characterize global patterns of TET incidence, explore their relationship with disease detection disparities, and thereby advance understanding and management of these malignancies.

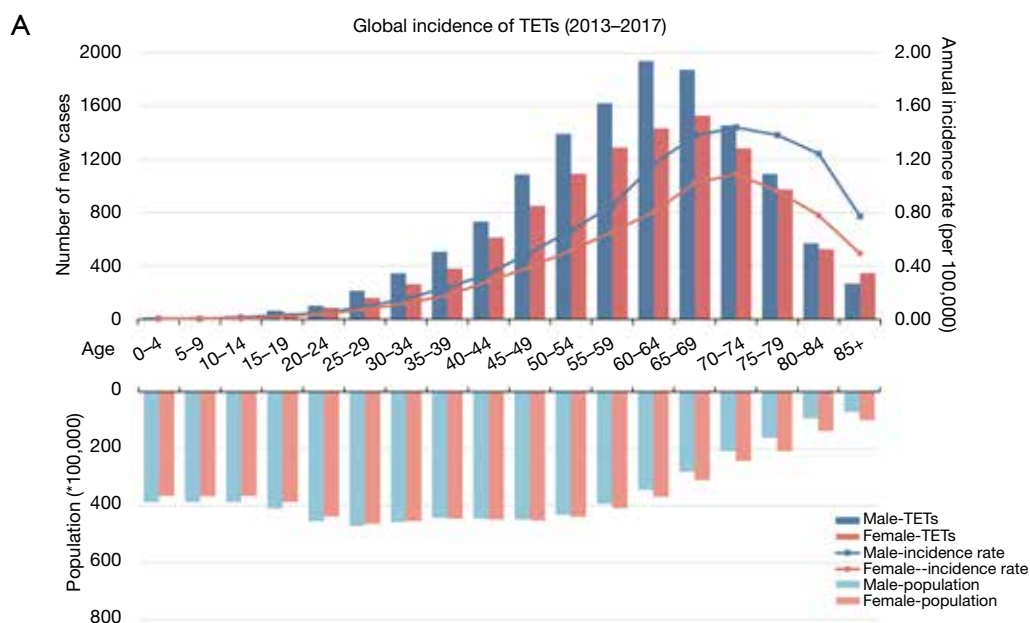
Methods: Data were obtained from successive volumes of Cancer Incidence in Five Continents. Age standardized incidence rate (ASR) and average annual percentage change (AAPC) were calculated by age, sex, region, country, and

Human Development Index (HDI) level.

Results: Globally, there were 25,473 cases of TETs among 1.27 billion people between 2013 and 2017, with an ASR of 0.26 per 100,000. From 1988 to 2017, the incidence of TETs has been gradually increasing worldwide (AAPC: 3.13). Most cases (70.2%) were diagnosed in people aged 50–79 years, and males had a higher incidence than females (Figure 1). There were significant ethnic differences in incidence, with Asian and Pacific Islanders having the highest ASR, followed by black people and then white people. There were large disparities in the incidence both between and within countries, which were found to be associated with HDI. In particular, the incidence of the same ethnicity was higher in high HDI countries than in low HDI countries. Most countries with high HDI had experienced a substantial increase in incidence, especially after 2003. However, the change in incidence was less pronounced in countries with relatively low HDI.

Conclusions: This study provides a comprehensive global prevalence landscape of TETs, revealing marked variations in incidence across demographic, geographic, and temporal dimensions. In addition to inherent ethnic difference, these variations are closely associated with disparities in disease detection. This study highlights the need for greater attention to these rare malignancies and socio-economic inequities in healthcare.

Keywords: Thymic epithelial tumors (TETs); global prevalence; healthcare disparity



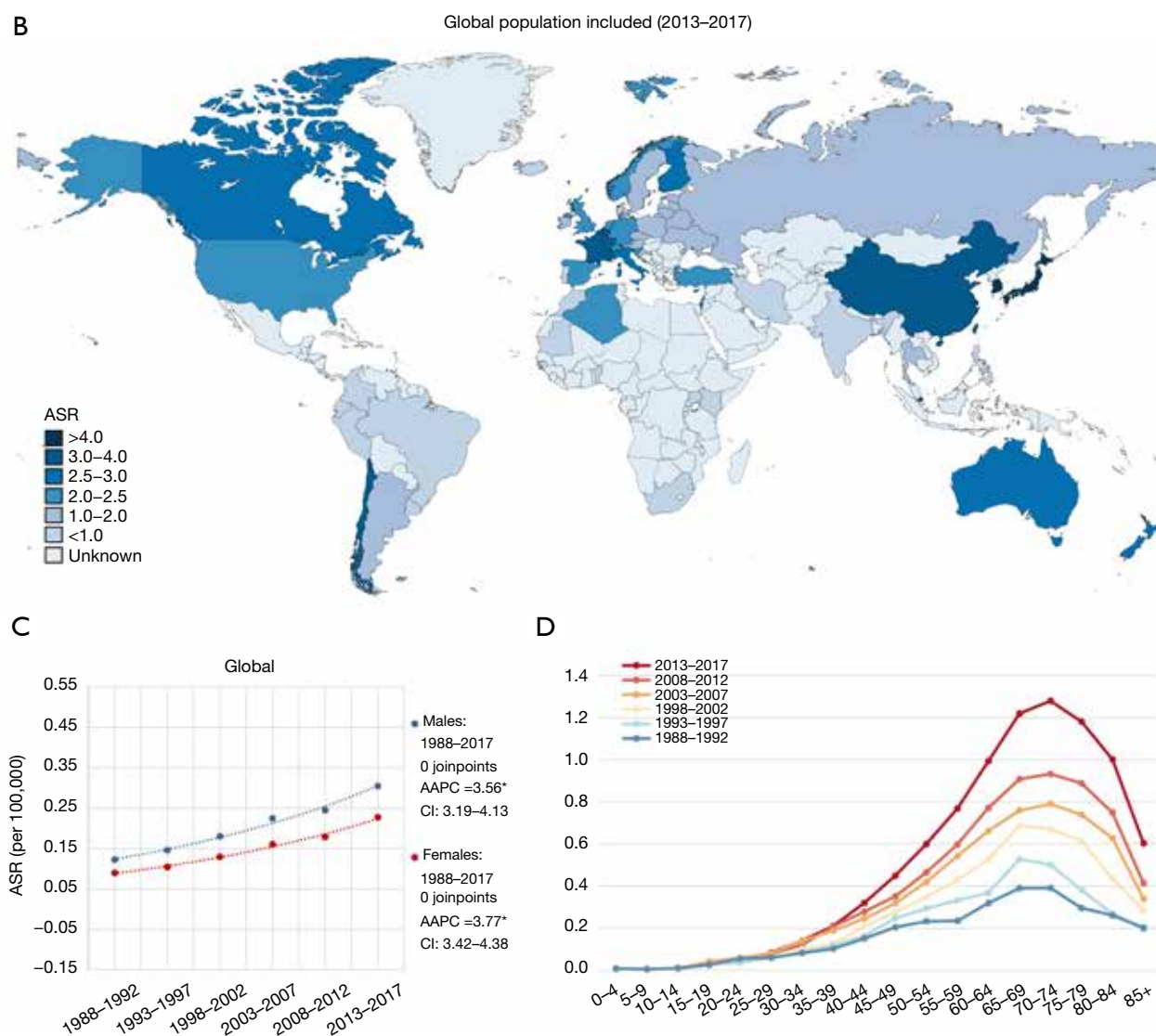


Figure 1 Global epidemiological landscape of thymic epithelial tumors. (A) Age-sex distribution of cases and annual incidence rates, 2013–2017; (B) maps of age-standardized incidence rates by country, 2013–2017; (C) temporal trends in age-standardized incidence rates, 1988–2017; (D) age-specific incidence trends by quinquennium, 1988–2017. AAPC, average annual percentage change; ASR, age standardized incidence rate; CI, confidence interval; TETs, thymic epithelial tumors.

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appropriately investigated and resolved. The data used in this study are publicly available and this article does not contain any studies with human or animal subjects. We did not require ethics approval to analysis these data sets.

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AB032. Central pathology review of thymic tumors: updated analysis of diagnostic concordance in the French RYTHMIC cohort—a retrospective study

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Background: Thymic epithelial tumors (TETs) are rare malignancies with variable histological subtypes and clinical behavior. Accurate classification of histotype and stage is

essential for guiding postoperative radiotherapy (PORT) and systemic therapy. A previous national study conducted by the RYTHMIC network (France) on cases diagnosed from 2012 to 2016 identified a 6% rate of major diagnostic discrepancies between local and expert pathology reviews (Molina *et al.*, *Eur J Cancer* 2021). A follow-up study was conducted to assess the frequency and clinical relevance of such discrepancies in a larger cohort.

Methods: This retrospective study included all patients with suspected or confirmed TETs discussed at the RYTHMIC national tumor board between January 2017 and December 2023. Expert pathology review was conducted by at least two specialized pathologists. Diagnoses were classified according to World Health Organization (WHO) 2015 criteria and Masaoka-Koga (MK) staging. Discordances between initial and expert diagnoses were recorded for histotype and/or stage, and categorized as minor or major based on potential clinical impact. Cases were considered non-evaluable when either the initial diagnosis or the expert review lacked sufficient material or contextual data (e.g., biopsy-only samples, absence of operative reports) to reliably assess the histotype and/or MK stage.

Results: A total of 1,334 cases were reviewed. Initial and central diagnoses were concordant in 623 cases (46.7%). Discordances were observed in 415 cases (31.1%), of which 323 (24.2%) were minor and 92 (6.9%) were major. In addition, 296 cases (22.2%) were classified as non-evaluable. Among the 92 major discordances, 59 (64.1%) would have altered the indication for PORT, 7 (7.6%) would have changed systemic therapy or follow-up, and 23 (28.2%) involved a diagnosis outside the TET spectrum (e.g., lymphoma, metastatic carcinoma, thymic hyperplasia).

Conclusions: This updated analysis confirms the continued relevance of expert pathology review in TETs. Although major discrepancies remained at a similar rate to the previous study, most had significant therapeutic consequences. The presence of misdiagnoses outside the TET spectrum underscores the need for systematic expert validation. Given the rate of discordance, future integration of AI-based classification systems may offer complementary support in the diagnosis of TETs.

Keywords: Thymic epithelial tumors (TETs); central pathology review; diagnostic discordance

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Commission Nationale de l'Informatique et des Libertés (CNIL, No. 916181, 24 May 2016). In accordance with French law, individual consent for this retrospective analysis was waived, and patient non-opposition was systematically sought by the treating physician.

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AB033. Thymic cancer in France: a comprehensive analysis of incidence based on French National Healthcare Data—a retrospective observational study

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Background: Thymic epithelial tumors (TETs) are rare malignancies with an estimated incidence of 0.18 cases per 100,000 person-years in the European Union. Comprehensive national data remain limited. This study aimed to evaluate the epidemiology, clinical characteristics, and associated conditions of TETs in France.

Methods: A retrospective cohort was extracted from the French National Health Data System (SNDS), which covers over 99% of the population and integrates health insurance and hospital data. Patients hospitalized with a primary diagnosis of malignant thymic neoplasm (ICD-10 code

C37) between 2015 and 2019 were included. Demographic and clinical data were collected. Incidence rates were based on the first hospitalization and expressed as the mean number of new cases per year divided by the average French population during the study period.

Results: A total of 2,205 patients were identified, 42.1% female, with a median age of 64 years. The mean annual incidence was 0.71 per 100,000 persons, markedly higher than previous reports. Autoimmune conditions were present in 15.8% of patients, including myasthenia gravis (13%), aplasia (1%), and systemic lupus erythematosus (1.2%). These preceded TET diagnosis in 22 patients (1%), occurring on average 17.7 months before diagnosis (median: 25 months before), and occurred concurrently or within 2 years after in 221 patients (10%), with a mean delay of 15.4 months (median: 2). A total of 326 patients (14.8%) received immunoglobulin therapy. We assessed second primary malignancies, excluding thoracic tumors (C33, C34, C38, C39) and unspecified secondary cancers (C76–C80) to avoid overlap. Still, 719 patients (32.6%) had additional malignancies, mainly male genital (C60–C63, 118 cases) and hematologic (C81–C96, 110 cases). There were 430 hospitalizations for other cancers in the 2 years preceding TET diagnosis, increasing from 8 per month at 24 months before diagnosis to 42 in the month immediately prior to TET diagnosis. In the 2 years after diagnosis, 850 hospitalizations occurred, including 210 (24.7%) in the first 3 months and 75 (8.8%) in month 2.

Conclusions: This nationwide study shows a higher incidence of TETs than previously reported, with expected rates of autoimmune disease and a surprisingly high frequency of secondary malignancies despite limited follow-up.

Keywords: Thymic epithelial tumors (TETs); incidence; National Health Data

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extraction on the Health Data Hub online platform (No. F20230616142940).

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AB034. Weakly supervised artificial intelligence-based subtyping of thymic epithelial tumors using H&E whole slide images

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Background: Thymic epithelial tumors (TETs) are rare neoplasms classified by the World Health Organization (WHO) into thymomas (A, AB, B1, B2, B3) and thymic carcinomas (TCs). Due to overlapping histopathological features, accurate differentiation is challenging, leading to diagnostic variability among pathologists. This study aimed to develop a diagnostic tool to support precise subtyping, reduce ambiguity, improve treatment strategies, and ultimately enhance patient outcomes.

Methods: Our study utilized an in-house Erasmus Medical

Center (EMC) dataset of 669 patients diagnosed by eight pathologists and an external Lyon dataset of 97 patients. After excluding cases with less than 70% agreement within the pathologist panel and irrelevant thymoma types (n=510), 159 EMC cases remained. Tumor areas were annotated, and 512×512-pixel tiles were taken at 10x magnification using QuPath. To reduce staining differences, Vahadane's stain normalization method was used (see *Figure 1*). The dataset was divided at the patient level, resulting in 76 EMC cases and 12 Lyon cases for training, while 83 EMC cases and 85 Lyon cases were used for testing. After preprocessing, two separate AI models were developed: the first was designed to generate additional labels, while the second, built on the VGG16 architecture, was used to classify the subtypes A, AB, B1, B2, B3, and TC. To ensure the reliability of the results, stratified 3-fold cross-validation was employed.

Results: The model achieved an area under the curve (AUC) of 1 and a balanced accuracy (BAcc) of 0.97±0.02 on the validation set. On the 70–100% consensus test set, it recorded an AUC of 0.91±0.01 and BAcc of 0.78±0.03, while the 100% consensus test set yielded an AUC of 0.98±0.01 and BAcc of 0.89±0.01. On the external dataset, it reached an AUC of 0.93±0.01 and BAcc of 0.76±0.04. Grad-CAM visualizations showed subtype-specific patterns, although distinguishing group B remained challenging.

Conclusions: The model demonstrated robust accuracy in distinguishing between TET subtypes in both external and internal dataset, thereby providing substantial support to pathologists and facilitating informed treatment decisions. Nonetheless, similar to the difficulties faced by pathologists, the model's efficacy was compromised in ambiguous cases characterized by mixed histological features. In future work, we will evaluate its performance on additional external.

Keywords: Thymic epithelial tumors (TETs); histopathology; subtyping; artificial intelligence classification (AI classification); deep learning

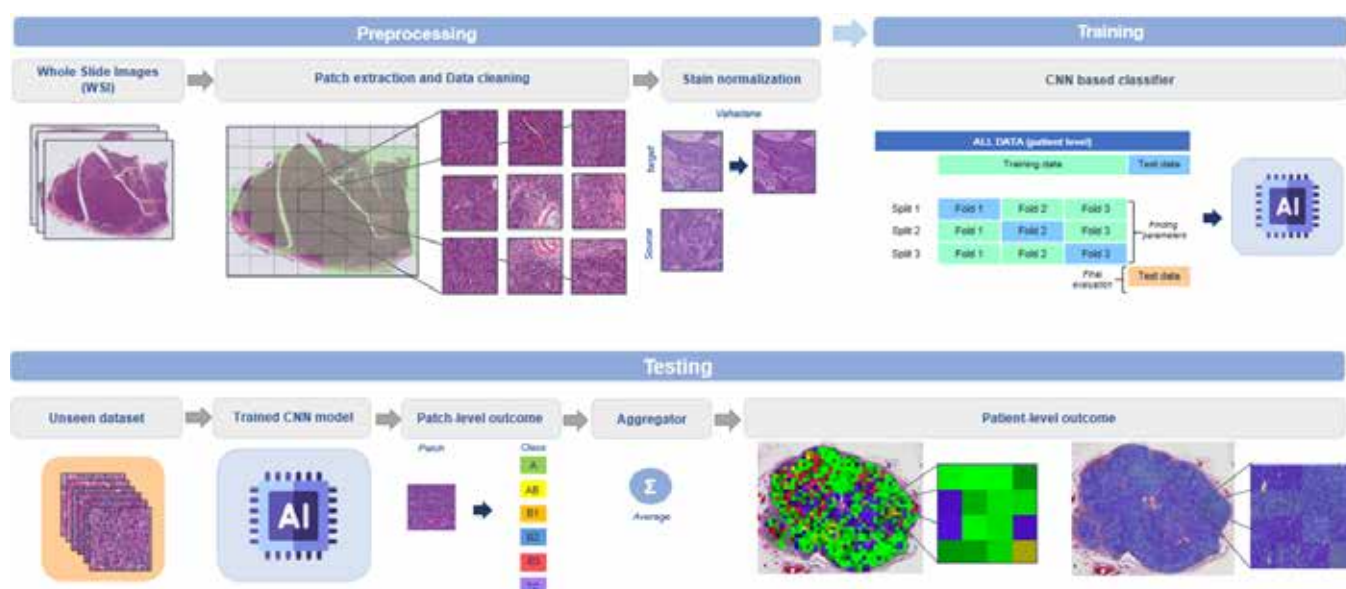


Figure 1 Workflow for histological image preprocessing, CNN training, and patient-level evaluation. CNN, convolutional neural network.

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AB035. PD-1 checkpoint inhibitors exhibit significant antitumor activity in patients with Masaoka stage IV thymoma: a case report

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Background: Thymoma is a relatively rare tumor originating from the thymic epithelial cells, with a low incidence rate, accounting for approximately 0.2% to 1.5% of all malignant tumors. The primary treatment for thymoma is surgical resection, and early-stage or localized tumors can often be cured through surgery. For locally advanced or invasive thymomas, a multidisciplinary approach centered on surgery is typically adopted. Neoadjuvant chemotherapy before surgery or adjuvant radiotherapy after surgery can improve outcomes. For patients who are not candidates for surgery, chemoradiotherapy is an alternative. Some cases may involve targeted therapy or immunotherapy.

The treatment plan must be tailored based on the tumor stage, pathological type, and individual patient factors, and the overall prognosis is relatively favorable.

Case Description: A 40-year-old female presented with an anterior mediastinal mass incidentally detected during routine health screening 4 months prior. Contrast-enhanced computed tomography (CT) revealed a heterogeneous anterior mediastinal mass (maximum diameter: 5.2 cm) with radiologic features suggestive of thymic malignancy (Masaoka-Koga stage IVa), accompanied by multiple metastatic nodules along the left pleura. Ultrasound-guided core needle biopsy performed on 2024-11-05 confirmed histopathological diagnosis of type B3 thymoma. Following three cycles of CAP regimen (cyclophosphamide 500 mg/m² + doxorubicin 50 mg/m² + cisplatin 50 mg/m²), serial imaging surveillance demonstrated stable disease (SD) (*Figure 1A-1F*). Therapeutic strategy was subsequently escalated to second-line therapy comprising albumin-bound paclitaxel (260 mg/m²), carboplatin [area under the curve (AUC) 5], and programmed death-1 (PD-1) inhibitor (200 mg q3w). Post two treatment cycles, CT confirmed partial response (PR) (*Figure 1G-1I*). The treatment course was notable for grade 1 diarrhea (CTCAE v5.0) managed effectively with symptomatic intervention. No immune-related adverse events (irAEs) or hematologic toxicity ≥ grade 2 were observed during immunotherapy.

Conclusions: PD-1 checkpoint inhibitors exhibit significant antitumor activity in patients with type B3 Masaoka stage IV thymoma.

Keywords: Thymoma; PD-1 checkpoint inhibitors; partial response (PR); case report

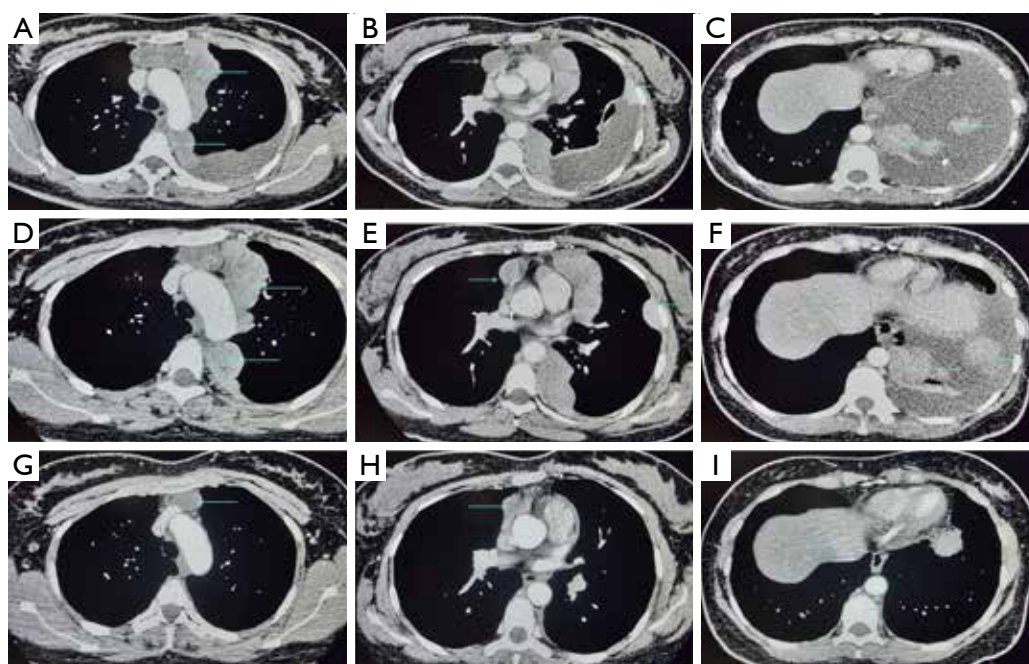


Figure 1 CT images demonstrate the course of treatment for type B3 thymoma. (A-C) Upon initial diagnosis, CT imaging revealed metastatic thymoma invading the chest wall and diaphragm accompanied by massive pleural effusion. (D-F) Serial clinical evaluations following three cycles of CAP chemotherapy regimen demonstrated SD status. (G-I) Subsequent therapeutic modification to albumin-bound paclitaxel combined with carboplatin and PD-1 inhibitor immunotherapy resulted in PR after two treatment cycles, as evidenced by radiological reassessment. CT, computed tomography; CAP, cyclophosphamide + doxorubicin + cisplatin; PD-1, programmed death-1; PR, partial response; SD, stable disease.

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None.

Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Declaration of Helsinki and its subsequent amendments. Written informed consent

was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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AB036. Trends in thymic epithelial tumor patients in the Netherlands: a population-based study

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Background: Thymic epithelial tumors (TETs) are rare tumors and the provided care is not standardized. This study describes the population of TET patients in the Netherlands, diagnosed between 2017 and 2023, registered

by the Dutch Cancer Registry (NKR). The aim of this study was to analyze changing care patterns for TET patients and differences between high- and low-volume centers regarding surgery and outcome.

Methods: All patients with a new diagnosis of TET between 2017 and 2023 were selected from the NKR database. Data on patient characteristics, staging, treatment and survival were collected and analyzed. Chi-squared test and log-rank test was used to determine differences between high- and low-volume centers. High-volume center was defined as >10 TET surgeries a year.

Results: In total, 965 patients were included. The crude incidence rate of TETs was 7.3/1,000,000. This was 6.1/1,000,000 for thymoma and 1.2/1,000,000 for thymic carcinoma. The mean age was 62.1 years with SD 13.2 and the male:female ratio was 1.15. Surgery was performed in 721 (74.7%) patients, 154 (16%) patients had radiotherapy and 163 (16.9%) patients had chemotherapy. The most commonly used chemotherapy regimen consisted of doxorubicin with cyclophosphamide and cisplatin. In 90 patients no treatment was given for various reasons. Surgery was performed in 25 centers throughout the Netherlands; two were high-volume centers. The number of incomplete resections (R1 and R2) was significantly lower in high-volume centers (9.8%) than in low-volume centers (17.4%) ($P=0.02$) (*Table 1*). Survival was significantly higher when resection was complete ($P=0.01$). Median survival was not reached, 5-year survival was 89% in R0, 82% in R1 and 73% in R2 resections.

Conclusions: This study describes the population of TET patients in the Netherlands and changing care patterns. The number of incomplete resections was significantly lower in high-volume hospitals compared to low-volume. Moreover, complete resection was associated with improved survival. Therefore, centralization of TET care is recommended.

Keywords: Thymic epithelial tumor (TET); thymoma; epidemiology

Table 1 Patient characteristics and outcome high- vs. low-volume centers

Table 2. Patient characteristics and outcome in high- vs. low-volume centers				
Variables	Total (n=965)	Surgical patients		High- vs. low-volume (P)
		High-volume centers [n=257 (35.7%)]	Low-volume centers [n=462 (64.3%)]	
Patient characteristics				
Mean age (years) (SD)	62±13.2			
Gender (M/F)	513/452			
TNM				
1	616 (63.8)	199 (77.4)	366 (79.2)	
2	41 (4.2)	10 (3.8)	25 (5.4)	
3a	77 (8.0)	22 (8.6)	30 (6.5)	
3b	18 (1.9)	5 (1.9)	4 (0.9)	
4a	88 (9.1)	16 (6.2)	25 (5.4)	
4b	96 (9.9)	4(1.6)	6 (1.3)	
Unknown	29 (3.0)	1(0.0)	6 (1.3)	
Resection outcome				
R0	555 (77.2)	222 (86.4)	323 (69.9)	<0.01
R1	78(10.8)	20 (7.8)	58 (12.6)	<0.01
R2	15 (2.1)	5 (1.9)	10 (2.2)	0.2
Unknown	81 (11.3)	10 (3.9)	71 (15.4)	

Data are presented as mean ± standard deviation or n (%). F, female; M, male; TNM, tumor-node-metastasis.

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by the institutional ethics board of the Netherlands Comprehensive Cancer Organization (IKNL) (No. 24-00396). Because this is a database study with anonymous non-traceable data, individual consent was not indicated.

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AB037. The safety of surgery plus hyperthermic intrathoracic chemotherapy perfusion in patients with IVa thymic epithelial tumors

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Background: In thymic epithelial tumors (TETs) with pleural dissemination, namely stage IVa TETs, hyperthermic intrathoracic chemotherapy perfusion (HITHOC) has been used to augment the effect of local control by surgery. This study aimed to re-examine the safety features surgery plus HITHOC in stage IVa TETs.

Methods: Patients with stage IVa TETs were prospectively enrolled in this study at Shanghai Chest Hospital. Procedure included surgical resection of anterior mediastinal lesion and all visible pleural lesions, followed by HITHOC. Perfusion was performed using 120–150 mg/m² of cisplatin at a set temperature of 45 Celsius for 60 minutes.

Results: From January 2024 to March 2025, a total of 86 patients were enrolled in this study. All the patients complete this procedure. Thirty-six (41.9%) patients were *de novo* stage IVa TETs, 21 (24.4%) had concurrent Myasthenia Gravis, 28 (32.6%) patients received minimally invasive surgery, and the median surgery duration was 230 [110–585] minutes. The first 10 patients received a dosage of 150 mg/m² of cisplatin. One experienced grade 3 hepatotoxicity and the other one experienced grade 4 nephrotoxicity. The followed 76 patients received a dosage of 120 mg/m² of cisplatin. No cases of grade 3 or higher hepatotoxicity or nephrotoxicity were observed. There was no evidence of myelosuppression associated with HITHOC in any of the patients. The remaining most common postoperative complication was vomiting, which could possibly be related to anesthetic agents. There were no perioperative deaths in these patients.

Conclusions: Surgical resection plus HITHOC with a dosage of 120 mg/m² of cisplatin showed good safety features. Long-termed oncological outcomes need further follow-up.

Keywords: Thymic epithelial tumor (TET); pleural dissemination; surgical resection; hyperthermic intrathoracic chemotherapy perfusion (HITHOC)

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the ethics board of Shanghai Chest Hospital (No. IS24110) and informed consent was obtained from all individual participants.

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AB038. A 10-year retrospective review of recurrent thymomas: a single-centre experience

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Background: Thymomas are the most common anterior mediastinal tumours, however, overall incidence remains rare. Because of their rarity and low malignant potential, recurrence of thymomas is rarer still. Data on long-term outcomes thus remains limited. We present a single-centre review of recurrent thymoma cases over 10-years. Our objective is to assess the clinical characteristics, management, and long-term outcomes of recurrent thymoma, with a focus on recurrence patterns, histological changes, and the role of surgical intervention in recurrent disease.

Methods: Retrospective review was conducted using prospectively collected data of all patients diagnosed with recurrent thymomas at our centre between January 2014 and December 2024. A total of 77 patients underwent surgical treatment for thymoma. Of these, 10 patients had recurrence. While 3/10 opted for and remain under active surveillance, 7/10 underwent further surgery for recurrence. Data including demographic characteristics, presence of paraneoplastic disorders, initial and recurrent tumour histology [World Health Organization (WHO) classification], timing and location of recurrence, and clinical outcomes were analyzed.

Results: Equal gender-distribution was noted (5 males: 5 females). Myasthenia gravis was diagnosed in 5/10. Mean age at time of recurrence was 58.3 years. The median time to recurrence was 9.8 months (but ranged up to 192 months). All recurrences were picked up on follow-up cross-sectional imaging and multidisciplinary team (MDT) discussion. Histology from original surgery showed complete

macroscopic resection (R0/R1) in 8/10 patients. However, the majority of them were noted to have advanced stage (stage III/IV) thymomas on initial histology. Of 7 patients who underwent further surgery, 2 patients had different WHO grade on recurrent histology: one had a recurrence of B3 in a previously predominant B2 tumour, while another had a recurrence of B2 thymoma in a previously type A thymoma. The average length of stay following recurrence operation was 4.06 days. Despite the complexity of re-interventions, there was no peri-operative mortality. Unfortunately, 1 patient passed away from unrelated cause.

Conclusions: Although historically we follow-up thymomas for 10 years, our experience with recurrent thymomas over a decade supports the need for lifelong surveillance, as recurrence may emerge years after initial resection in these indolent tumours. In addition, imaging follow-up allows early detection and possible further surgical intervention. Where surgical resection is feasible, we would advocate proceeding with the goal of achieving complete excision of recurrent disease. Nonetheless, MDT discussion and individualized multimodality treatment/surveillance are crucial for optimizing long-term outcomes in these rare advanced recurrent thymomas.

Keywords: Thymoma; recurrent thymoma; thymectomy; rare tumours

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The collection of thymic samples was conducted for clinical care (for diagnosis and/or treatment). The use of clinical, radiological and laboratory data from the patients for research falls under an existing wider study that includes patients with autoimmune neurological conditions and those associated

with malignancies. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by Yorkshire & The Humber - Leeds East Research Ethics Committee (16/YH/0013) and individual consent for this retrospective analysis was waived.

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AB039. Survival of Danish patients with thymic epithelial tumors: a nationwide cohort study

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Background: Knowledge of prognostic factors for survival of patients with thymic epithelial tumors (TETs) is not yet implemented in clinical practice. The aim of this study is to report the overall survival (OS) of TET patients and prognostic value of baseline characteristics to enable the incorporation of prognostic factors in treatment and surveillance design.

Methods: The study cohort was comprised by 282 Danish TET patients diagnosed between January 1st, 2015, and December 31st, 2020. Data from baseline and patient follow-ups were collected from online medical records and included disease characteristics, vital status, and cause of death. Prognostic factors for OS were identified using the Cox-proportional hazards model.

Results: Thymoma, thymic carcinoma (TC), and thymic neuroendocrine tumor (NET) comprised respectively 85%, 14%, and 1.4% of the TETs diagnosed in the cohort. During the period of follow-up (mean 72 months; range 44 to 115 months) 65 patients deceased resulting in an OS of 77% with a 5-year OS of 75.6%. TET-specific deaths were the most common cause of death accounting for 42% of the deaths in the cohort. In the multivariate analysis, both increasing age and advanced tumor/lymph node/metastasis (TNM) stage (III or IV) were negative independent prognostic factors of OS.

Conclusions: We report an improved OS of Danish TET patients compared to the OS reported in previous population-based studies, thus supporting increasing trend in the incidence of early stage TETs and improved survival of TET patients suggested in re-cent literature. Still, TET specific death was the most common cause of death in the cohort, thereby highlighting the potential fatality of TETs and supporting the need for surveillance of TET patients.

Keywords: Survival; prognostic factors; population-based; mortality; thymic epithelial tumors (TETs)

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study is conducted in compliance with the guidelines of the Danish National Medical Research Ethics Committee, and required no approval from the ethics committee as no additional tests or investigations are done in the patients whose data are included in this study.

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AB040. Subclinical myasthenia gravis after thymectomy: a 20-year retrospective cohort study

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Background: Subclinical myasthenia gravis (subMG) is characterized by circulating anti-acetylcholine receptor antibodies (anti-AChR-ab) without clinical symptoms of myasthenia gravis (MG). Previously, we reported a 10.8% incidence of sMG in 102 patients with resected thymoma. The current study aims to assess the incidence and clinical course of sMG in a larger thymoma cohort following thymectomy.

Methods: We retrospectively analyzed 248 consecutive patients who underwent robotic-assisted thoracoscopic

surgery for thymoma at the Maastricht University Medical Center+ between 2004 and 2024. Anti-AChR-ab was found positive in cases of >0.25 nmol/L measured by radioimmunoassay. Inclusion criteria were total thymectomy for thymoma, age ≥ 18 years, and a minimum follow-up of 6 months. MG symptoms were classified using the Myasthenia Gravis Foundation of America (MGFA) system. A neurologist specialized in neuromuscular disorders was consulted pre-thymectomy in patients with MG or subMG. Pearson's chi-squared and Fisher's exact test were statistically significant in the case $P < 0.05$.

Results: Anti-AChR-ab were analyzed in 228 thymoma patients (91.9%) pre-thymectomy and 6 patients post-thymectomy (*Figure 1*). Symptomatic MG was observed in 129 patients (52.0%). The development to symptomatic MG was observed in 14 patients (53.8%), although the median follow-up was also significantly longer in patients who developed symptomatic MG compared to subMG patients who did not develop symptoms (58.0 vs. 26.0 months, $P = 0.02$). The most frequent time of development of symptomatic MG was directly after thymectomy (3 patients) and between 12 and 24 months of follow-up (6 patients). Ten subMG patients required cholinesterase inhibitors or immunosuppressive therapy. Five patients died during follow-up, including two from myasthenic crisis.

Conclusions: The incidence of subMG among patients with thymoma was 10.5%. A substantial proportion (54%) progressed to symptomatic MG over time, with peak incidences directly after thymectomy and between 12–24 months of follow-up post-thymectomy, underscoring the need for prolonged attention for developing MG symptoms and thorough pre-operative assessment. Further research is necessary to investigate the mechanisms of subMG and the development of symptomatic MG post-thymectomy. Specific guideline recommendations could help clinicians with the surgical, oncological, and neurological workup of patients with subMG.

Keywords: Subclinical myasthenia gravis (subMG); thymoma; thymectomies; anti-acetylcholine receptor antibodies (anti-AChR-ab)

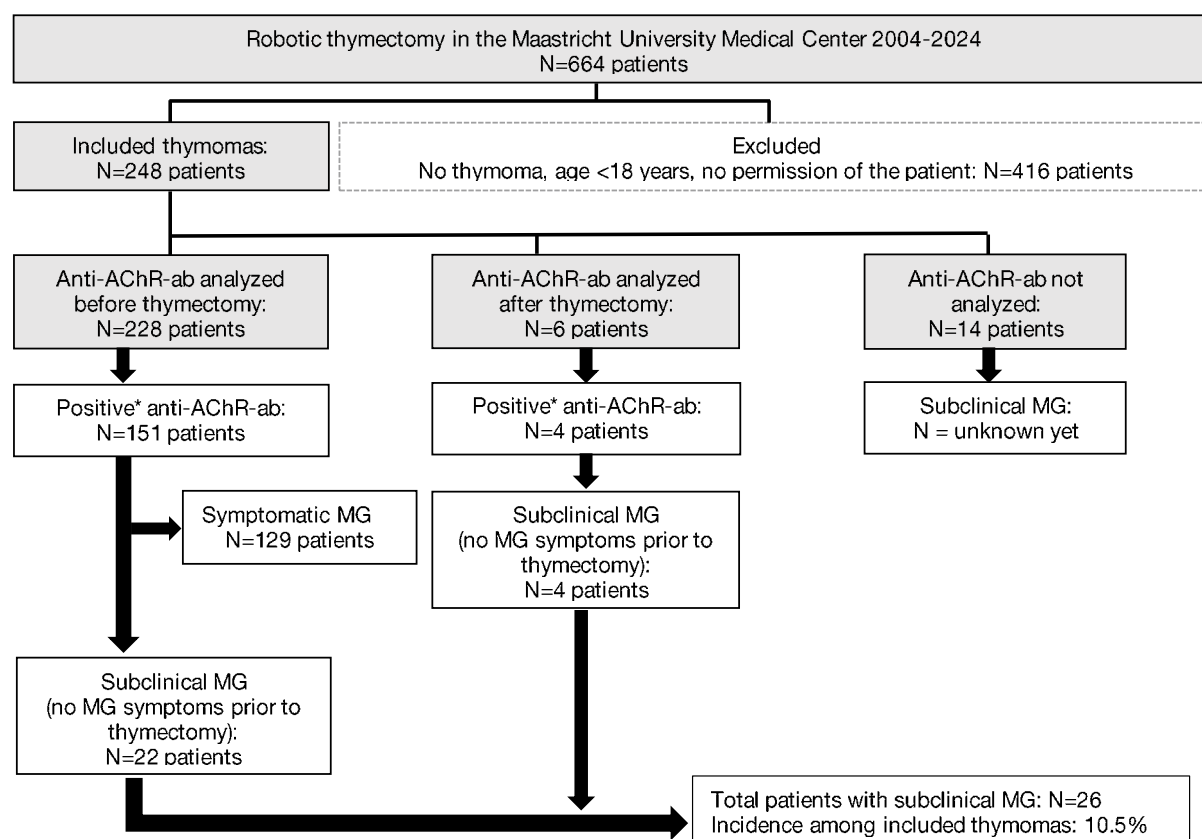


Figure 1 Flowchart and patient characteristics subclinical myasthenia gravis. *, positive anti-AChR-ab are considered in case >0.25 nmol/L measured by radio immune assay. Anti-AChR-ab, anti-acetylcholine receptor antibodies; MG, myasthenia gravis.

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histopathological classification and recurrence prediction of thymic epithelial tumor. But this project is not related to the current abstract. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the ethics board of Maastricht University Medical Center+, Maastricht, the Netherlands (No. 2018-0491, 2018-0491-A-11), and individual consent for this retrospective analysis was waived.

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AB041. Treatment response after induction therapy in unresectable thymic tumors: TYME database analysis

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Background: Induction therapy (IT) in unresectable thymic tumours (UTTs) is an option to downstage the tumour and to obtain a complete resection as well as a better outcome.

Which patients benefit from IT is still a matter of debate. This study aims to investigate treatment response (TR) after IT and potential prognostic factors among Italian patients with UTTs.

Methods: Clinicoradiological, histopathological, molecular, oncological and surgical features of 76 UTTs (clinical-TNM-stage II–IV) undergoing IT from 01/2002 to 12/2024 were retrospectively collected from the large multicentric database within the Italian collaborative group for ThYmic MalignanciEs (TYME).

Results: Mean age and male/female ratio were 52 years and 45/31, respectively. World Health Organization (WHO) histology was thymoma in 62 (82%), thymic carcinoma in 12 (16%) and neuroendocrine neoplasia in 2 (3%) patients. According to 8th tumor-node-metastasis (TNM), pathological stage distribution was: stage I 6%, IIA 5%, IIB 8%, III 51%, IVA 19% and IVB 11%. The most administered IT regimen was cisplatin plus doxorubicin plus cyclophosphamide (PAC) in 61% of cases; adjuvant radiotherapy was performed in 68% of patients. According to Response Evaluation Criteria in Solid Tumours (RECIST) criteria, 67% patients achieved partial response (responders) and 33% stable/progressive disease (non-responders). Extended mediastinal resection with or without reconstruction was the most common surgical procedure (61%), through sternotomy (36%), thoracotomy (33%) and hemi-clamshell incision (19%). Radical R0 resection was achieved in 76% of cases. Median follow-up time from surgery was 2.8 years, with a 5-year overall survival (OS) and 5-year recurrence-free survival (RFS) of 92% and 31%, respectively (*Figure 1*). Compared to non-responders, responders had a more aggressive histology (24% *vs.* 16%), higher clinical TNM stage (84% *vs.* 71%), underwent mainly PAC scheme (65% *vs.* 37.5%) and achieved better radicality (78% *vs.* 68%). At multivariable analysis, physical status according to American Society of Anesthesiologists (ASA) score was the most important prognosticator of response after IT (“*P*=0.02”).

Conclusions: the TYME database analysis confirms a potential role for IT in UTTs. Due to high rate of non-responders, efforts should be made to investigate further multimodal treatments to improve response rate and resectability in this subset. Physical status according to ASA score seems a prognostic factor of TR in UTTs undergoing IT.

Keywords: Thymic tumors; induction therapy; response

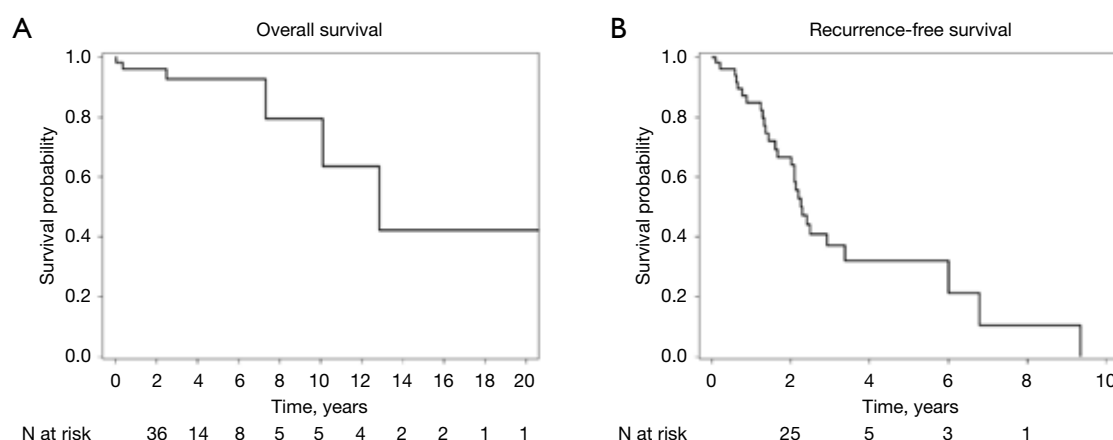


Figure 1 Overall survival (A) and recurrence-free survival (B) in unresectable thymic tumors after induction therapy plus surgery.

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AB042. Robotic-assisted surgery for large thymomas: preliminary results on feasibility and safety in a single center experience

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Background: Thymic tumor size has been frequently considered a factor limiting the indication for minimally invasive surgery. Robotic-assisted thoracic surgery (RATS) has been mainly offered to patients with limited thymoma up to 4 cm. However, considering increasing experience in the field and improved technical skills, RATS has proved to allow safe resection of larger lesions. To date, RATS thymectomy for large and advanced thymomas remains controversial and there is no a general consensus. The present retrospective study aims to evaluate the feasibility and the safety of RATS thymectomy for the treatment of large thymomas.

Methods: Between May 2021 and February 2025, 88 consecutive patients underwent RATS thymectomy in the Division of Thoracic Surgery of Sant'Andrea Hospital, Sapienza University of Rome, Italy. Patients older than 18 years old, with histology of thymoma, both myasthenic and non-myasthenic, with lesions larger than 5 cm were included (*Figure 1*), with a final sample of 70 patients. Data on lesions side, dimensions, associated resections, time of surgery, complications, conversion rate, final pathology, length of stay, adjuvant therapy and survival, were retrospectively analyzed.

Results: Mean tumor size in the study cohort was 6.69 ± 1.92 cm (range, 5–10 cm). Five patients (7.14%) presented with myasthenia. The mean operative time excluding docking-

undocking time was 52.31 ± 16.52 minutes. Associated resections were 11 (15.71%): 3 pericardium portion, 3 pleura nodules, 4 lung resections, and 1 anonymous vein. No conversion rate was described and only 4 minor complications (atrial fibrillation, pleura effusion) were reported. Five patients received R1 resections and 3 of them underwent adjuvant radiation. A total of 7 patients (10%) received post-operative radiation. At the median follow-up of 36 months, no mortality was described.

Conclusions: Previous studies reported that the optimum diameter of resected thymomas was 4 cm, thus aiming to reduce the risk of capsule rupture during excision. According to our results, larger thymomas were successfully excised using RATS. Most of them (42.86%) were classified as Masaoka stage I, followed by 32.85% showing microscopic invasion. Importantly, no capsule ruptures were observed at pathology. Follow-up data showed excellent overall survival. Based on our preliminary results, RATS can be considered safe and feasible for large thymomas.

Keywords: Robotic-assisted thoracic surgery (RATS); thymoma; thymectomy



Figure 1 CT scan of a large thymoma. CT, computed tomography.

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AB043. Comparative analysis of surgical approaches and optimal resection extent in thymoma treatment

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Background: The optimal minimally invasive surgical approach and resection extent for thymoma remain controversial. This study aims to evaluate the prognostic impact and safety profiles of different surgical approaches and resection extents in thymoma management.

Methods: A retrospective cohort analysis included patients undergoing thymectomy for thymoma at Xuanwu Hospital, Capital Medical University (January 2014–March 2021). Patients were stratified by surgical approach and resection extent. Clinical outcomes, operative parameters, complications, and long-term follow-up data were analyzed.

Results: Among 209 patients, surgical approaches included unilateral intercostal (n=134, 64.1%), subxiphoid (n=53, 25.4%), and bilateral intercostal (n=22, 10.5%). Baseline characteristics were comparable across groups. The subxiphoid approach demonstrated superior outcomes, including reduced intraoperative blood loss, shorter postoperative hospitalization, lower complication rates, and no chest tube drainage. Although subxiphoid and bilateral intercostal approaches initially required longer operative times, surgical efficiency improved with surgeon experience. Both subxiphoid and bilateral intercostal approaches demonstrated similar rates of ectopic thymic tissue identification. In subclinical myasthenia gravis patients (asymptomatic thymoma with seropositivity for pathogenic antibodies), extended thymectomy demonstrated equivalent perioperative safety to conventional thymectomy. Long-term follow-up demonstrated that extended thymectomy significantly reduced the risk of neurological symptom

recurrence in subclinical myasthenia gravis patients.

Conclusions: The subxiphoid approach optimizes perioperative recovery as a minimally invasive strategy, while extended thymectomy improves neurological outcomes in subclinical myasthenia gravis. These findings underscore the importance of tailored surgical strategies in thymoma management.

Keywords: Thymoma; surgical approach; extended thymectomy; surgical outcomes

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AB044. Late thymoma occurrence after thymectomy for thymic hyperplasia: case reports of our experience

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Background: Thymic hyperplasia (TH) is a rare condition, often diagnosed following the onset of myasthenia gravis (MG) symptoms. The standard treatment involves surgical thymectomy. However, in multiple cases, MG symptoms persist despite surgery. To date, no cases of thymoma occurrence have been reported following thymectomy performed for TH.

Cases Description: Patient A, a 46-year-old woman, underwent thymectomy in 1999 due to symptoms of MG. Histopathological examination revealed TH. Next, she received medical treatments for MG. In 2018, due to an exacerbation of myasthenic symptoms, a chest computerized tomography (CT) scan revealed a large, irregular soft tissue mass in the anterior mediastinum (62 mm × 22 mm × 67 mm), with pericardial infiltration. Biopsy of the lesion confirmed a World Health Organization (WHO) type A thymoma, stage III according to the Masaoka staging system. A 68Ga-DOTATOC positron emission tomography (PET) scan demonstrated focal tracer uptake (standardized uptake value, SUVmax 3.8), and the patient

was initiated on octreotide long-acting release (LAR), 30 mg every 28 days. She remains on this treatment, with imaging studies showing stable disease. Patient B, a 41-year-old man, underwent thymectomy in 1994 for MG, with histologic confirmation of TH. In 2013, he experienced right-sided chest pain. CT-scan revealed pleural lesions, and video-assisted thoracoscopic surgery (VATS) biopsy confirmed a WHO type B2 thymoma. He performed ¹⁸F-fluorodeoxyglucose positron emission tomography (¹⁸FDG-PET) with mediastinal (SUVmax 7.2) and multiple pleural uptakes (stage IV A Masaoka). Therefore, he received six cycles of chemotherapy with the cisplatin, doxorubicin and cyclophosphamide schedule (PAC schedule), achieving a partial response. ¹⁸FDG-PET was negative for residual disease, but Octreoscan revealed focal tracer uptake (SUVmax 4.2). Octreotide LAR (30 mg every 28 days) was initiated, with stable disease until 2018, when progression was noted on CT. Consequently, he was candidate for oral therapy with etoposide (50 mg/day, 3 weeks on, 1 week off) administered until 2021. Due to further progression, Octreotide LAR was reintroduced and is currently ongoing. He remains on this treatment, with latest imaging studies showing stable disease (*Figure 1*).

Conclusions: These cases suggest the possibility of delayed thymoma development even after thymectomy for histologically confirmed TH. Further data are required to confirm this observation. Close and prolonged monitoring of patients undergoing thymectomy is recommended, particularly in the presence of recurrent or worsening myasthenic symptoms.

Keywords: Case report; thymic hyperplasia (TH); myasthenia gravis (MG); occurrence

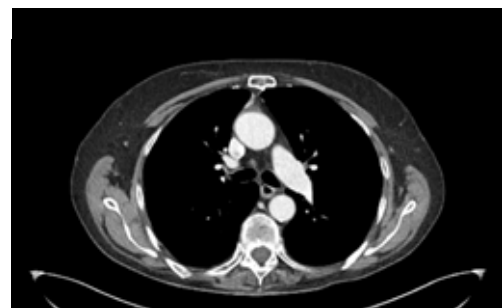


Figure 1 Patient B, latest CT-scan showing stable disease. CT, computerized tomography.

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was obtained from the patients for publication of this case report and accompanying image. A copy of the written consent is available for review by the editorial office of this journal.

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AB045. Are complement inhibitors safe for thymoma-associated myasthenia gravis patients?—a literary review and case report

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Background: Thymoma-associated myasthenia gravis (TAMG) occurs in about 30% of patients affected by thymic epithelial tumors (TETs) and leads to a suboptimal response to treatment. Myasthenia gravis (MG) is a chronic autoimmune disease caused by acetylcholine receptor (AChR) generally and other autoantibodies reacting against the neuromuscular junction. The complement system plays an important role in the pathogenesis of MG. AChR antibodies [immunoglobulin G (IgG) oligomers] in MG can activate the complement cascade binding C1q; consequently, complement inhibitors, such as eculizumab, are now available for treatment in MG refractory to standard treatment. Before starting treatment with complement inhibitors, it is mandatory to be vaccinated against *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae* type B. Limited data are available regarding TAMG: the most significant study is a real-world cohort presented by Lei Jin, and sporadic case reports. In the phase III, randomized, double-blind, placebo-controlled REGAIN study patients with a history of thymoma or

thymic neoplasm were excluded. Conversely, Lei Jin's study involving eculizumab included 42 seropositive AChR antibodies patients with refractory MG, but only 22 patients were included. Two patients reported coronavirus disease 19 (COVID-19) and herpes labialis infection, while four patients died from respiratory or circulatory failure linked to thymoma metastasis.

Case Description: We reported our experience with a young patient who underwent thymectomy diagnosed with stage IV thymoma type B2, with lung and pleural metastasis (pT3 pNx M1a) and a higher frequency of myasthenic crisis. Cisplatin, adriamycin and cyclophosphamide (PAC schedule) were administered for six cycles. Good's syndrome (GS) was diagnosed based on low levels of B lymphocytes and Immunoglobulins. MG was treated with corticosteroids, pyridostigmine, immunoglobulins and plasmapheresis. The patient was included in an experimental protocol involving complement inhibitors for the treatment of refractory MG. After two months from the initiation of treatment, the patient experienced severe lung infections with exacerbation of myasthenic symptoms and subsequently died.

Conclusions: Further studies are needed in patients with myasthenia and TETs with associated immunopathies, particularly GS. Antibacterial prophylaxis, vaccinations, monitoring of C-reactive protein, white blood cell count, immunoglobulins and the diagnosis of refractory MG are mandatory prior to starting treatment with complement inhibitors.

Keywords: Case report; thymomas; myasthenia gravis (MG); Good's syndrome (GS); complement inhibitors

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AB046. Robotic resection of thymoma recurrence with intra thoracic phrenic nerve reconstruction using a sural nerve graft: a case report

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Background: Radical resection of extensive or recurrent thymoma may require phrenic nerve resection which can be associated with significant respiratory morbidity. This study aims to demonstrate the feasibility of nerve reconstruction using a sural nerve graft by total robotic approach which has never been reported before.

Case Description: This case involved a 75-year-old male patient who underwent thymomectomy 5 years earlier in a different hospital. After 5 years, a local recurrence was evident exactly on the location of the left phrenic nerve at the level of the right ventricular outflow tract. Radical resection was deemed possible only if the phrenic nerve was excised together with the mass. To this end, we used our standardized three-port robotic-assisted thoracoscopic surgery (RATS) approach using the DaVinci Xi system (Intuitive surgical Inc., Sunnyvale, CA, USA) from the left mid-axillary intercostal plane and added a 12-mm assistant port. After careful introduction of the camera trocar, CO₂ insufflation was started and the other trocars and instruments are introduced by sight. After dissection of the

initially adhesive plain between the mediastinal pleura and the pericardium, the part of the pericardium overlaying the right ventricular outflow tract up to the level of the aortic arch was clear and the phrenic nerve was visible. The mass was located directly on the phrenic nerve and as expected no surgical plain with safe oncological margins could be achieved. There were no signs of growth into the pericardium or lung parenchyma. The phrenic nerve was transected caudally and cranially 3 cm from the mass and removed en-bloc with the recurrence within an endobag. The distal end of the sural nerve was anastomosed to the proximal end of the phrenic nerve due to the direction of development of the fascicles. A single 7-0 Prolene Suture (Ethicon Inc., New Jersey, US) was attached to this distal end before introduction in the thorax, to facilitate the first anastomosis and avoid the need for an additional instrument to present the graft. Each anastomosis was made by four single 7-0 Prolene epineural sutures using the Black Diamond micro forceps (Intuitive surgical Inc., Sunnyvale, CA, USA) (*Figure 1*).

Conclusions: The sural nerve is a preferred donor graft for reconstruction due to its well tolerated morbidity, ease of harvesting, multiple fascicles, and available length. Total robotic reconstruction is technically feasible and preferred in a minimal invasive approach. The postoperative course was uneventful and the patient was discharged after 3 days. Histopathological analysis revealed a B2 thymoma (World Health Organization).

Keywords: Case report; phrenic reconstruction; nerve; sural; thymoma

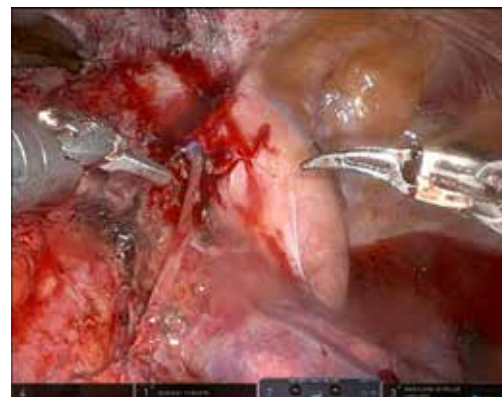


Figure 1 Intra-operative view of reconstructed phrenic nerve through sural nerve interposition.

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AB047. Mixed type A thymoma and micronodular thymoma with lymphoid stroma: a case report of an unusual tumor and literature review

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Background: Micronodular thymoma with lymphoid stroma (MNTLS) is a rare subtype of thymoma and accounts for only 1–5% of all thymoma. Though the histogenesis of MNTLS is not yet elucidated, it is postulated that type A thymoma and MNTLS shared a common histogenesis with suspected medullar origin. To date, only five cases of mixed thymoma composed of type A thymoma and Micronodular thymoma has been adequately described in the literature.

Case Description: A 76-year-old woman presented with a mediastinal mass incidentally found on routine chest radiograph during a regular health check-up. There was no evidence of myasthenia gravis. On further evaluation by chest computed tomography, an 8.3 cm mediastinal mass was identified in the left anterior mediastinum. The mass had a lobulated contour, suggested a thymic epithelial tumor. He received extended thymectomy via median sternotomy. On cut sections, the tumor measured 9 cm × 7 cm and was enclosed by a thin fibrous capsule. On histological examination, two different types of thymoma were noted, showing partly infiltrative growth into the fibrous capsule. Large nodules seen were composed of epithelial cells with sparse lymphocytes. Spindled tumor

cells arranged in short fascicles. These characteristics, together with positivity for cytokeratin, were compatible with type A thymoma. The type A area showing gradual transition into the rest of the tumor, which harbored a mixture of epithelial and lymphoid components. Epithelial tumor nodules were segregated by lymphoid stroma. Tumor cells were strongly positive for cytokeratin. Lymphoid stroma was positive for CD1a. The patient was diagnosed ultimately with mixed type A thymoma and MNTLS.

Conclusions: In the present case, epithelial components of type A thymoma and MNTLS showed similar histologic and immunohistochemical profiles with areas of gradual transition, suggesting type A thymoma and MNTLS share a common histogenesis.

Keywords: Mixed type A thymoma and micronodular thymoma with lymphoid stroma; thymoma; case report

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AB048. Thymoma in children, a rare mediastinal tumour: pathological case series of 6 cases and review of the literature

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Background: Mediastinal tumours in children are rare. Around 25% of them can be malignant. The thymoma is an uncommon neoplasm, and during adulthood it corresponds to 30% of anterior mediastinum tumours. The peak incidence is between 55–65 years. The aim of this study was to describe clinicopathological characteristics of this entity with literature review.

Case Description: Between 2004 and 2024, six children with thymomas were diagnosed at our department of pathology. Hospital files were reviewed for presenting complaints, clinical, radiologic, and pathological characteristics. There were 2 male and 4 female patients, aged between 12 and 19 years, with a mean of 15.5 years. Most common initial complaints were dyspnea, cough, chest pain, and fever. Chest X-rays and/or thoracic computed tomography displayed masses in anterior mediastinum accompanied by pulmonary metastases (n=1), and cervical lymph node metastasis (n=1). Five cases underwent initial tumor resection; one case experienced Trucut biopsies. On gross examination, tumors size ranged between 7 and 15 cm with mean of 9,87 cm. Histological examination identified type B1 thymomas in 4 cases, type B2 in one case and type AB thymoma in one case. Immunohistochemically, epithelial cells expressed epithelial membrane antigen (EMA) and cytokeratin, while immature T lymphocytes expressed CD1a, Terminal deoxynucleotidyl transferase (TdT), and CD99 markers. The outcome was satisfactory in all cases.

Conclusions: Thymoma in children are rare tumours but should be considered in the differential diagnoses for mediastinal anterior lesion. It poses a significant challenge due to its unclear histogenesis and its atypical clinical presentation. Early diagnosis and complete resection are the basis for management and prognosis.

Keywords: Thymoma; children; pathology; case series

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AB049. Continuing challenges of primary neuroendocrine neoplasms of the thymus: clinicopathological characteristics of an uncommon tumor in a case series

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Background: Primary neuroendocrine neoplasms (PNEs) of the thymus are highly aggressive tumors that rarely occur. They account for 2–5% of all thymic neoplasms, and only 0.4% of all PNEs. Relatively few previously published studies have focused on neuro-endocrine tumors (TNEs). The aim of this study was to describe clinicopathological characteristics of this aggressive entity with literature review.

Case Description: We report a retrospective study of 8 cases of PNEs of the thymus, diagnosed at our department of pathology and treated at our institution, with a hindsight of 20 years, from 2004 to 2024. The review of these 8 cases showed that there was no sex preponderance, with 4 male and 4 female patients, aged between 32 and 64 years, with a mean age of 49 years. The diagnosis was made on surgical resection (n=5) and transparietal biopsy (n=3). Intraoperative frozen sections were performed (n=7), showing a malignant tumor process (n=4), a non-small cell carcinoma (n=2) and malignancy that may be consistent with non-Hodgkin's lymphoma or thymic carcinoma (n=1). The histological examination revealed tumors of only two

subtypes and grades: intermediate grade carcinoid tumors (n=6) and high grade neuroendocrine carcinomas (n=2). The tumor cells shared similar immunohistochemical patterns, as all of the 8 cases were positive for synaptophysin and chromogranin, negative for muscle actin, PS100, CD5 and thyroid transcription factor-1 (TTF1). However, they are positive for CD56 (n=6), epithelial membrane antigen (EMA) (n=3) and pancytokeratin (n=1).

Conclusions: Primary NEs of the thymus were observed to be an extremely aggressive but very rare malignant lesion. Their main differential diagnoses are extension or metastases of their bronchopulmonary counterparts. Early diagnosis and surgical resection are the most important methods to improve prognosis. In the future, multi-center, large-sample database and clinical studies are urgently needed to explore better treatment modality.

Keywords: Neuroendocrine neoplasms (PNEs); thymus; case series

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AB050. The thymic epithelial tumors according to the new 2021 WHO classification: Tunisian experience

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Background: Although thymic epithelial tumors (TETs) are rare, they account for approximately 50% of anterior mediastinal tumors. These tumors, including thymomas and thymic carcinomas, are distinguished by specific histological and immunohistochemical characteristics, necessitating the development of precise classifications. The revised World Health Organization (WHO) classification in 2021 has refined diagnostic criteria, identified new entities and variants, and integrated advances in immunohistochemistry and molecular biology. The main objective of our work is to describe the histopathological aspects of thymic epithelial tumors and reclassify them according to the new 2021 WHO classification, as well as to compare the histopathological findings with clinical and radiological data.

Methods: This is a single-center, descriptive, retrospective study involving 100 patients diagnosed with and operated on for thymic epithelial tumors. The cases were collected from the Department of Pathology and Cytology at Abderrahman Mami Hospital in Ariana, spanning from January 2010 to December 2022.

Results: The study included 54 women and 46 men (sex ratio: 0.85). The average age was 50 years, with extremes ranging from 12 to 81 years. The primary reason for consultation was myasthenia (44%, n=44), which was preferentially associated with type B2 thymomas (52.3%). Thoracic X-rays, performed as a first-line examination, revealed a mediastinal opacity in 48% of cases. However, chest Computed Tomography scans were the reference

examination, allowing better characterization of mediastinal masses and detecting signs of locoregional invasion in 11% of cases. Surgical resection was performed in all cases, preceded by a transpleural biopsy in 15% of cases. Histological examination revealed 95 cases of thymomas and 5 cases of thymic carcinomas. Type B2 thymomas were the most frequent (41.1% of cases), followed by type AB thymomas (23.1%) and type B1 thymomas (18.9%). Immunohistochemically, the epithelial cells expressed epithelial membrane antigen (EMA) and cytokeratin (CK). The lymphoid component in thymomas showed a B-cell phenotype, with CD20 expression in 5 cases, and a T-cell phenotype, expressing CD3 in 52 cases. Immature T lymphocytes expressed CD1a, Terminal deoxynucleotidyl transferase (TdT), and CD99 markers in all cases. Regarding thymic carcinomas, each subtype had specific immunohistochemical markers. The Masaoka-Koga classification revealed that stage IIb was the most common for thymomas, with a frequency of 52.6%.

Conclusions: Though rare, TETs have distinct characteristics that require a multidisciplinary approach, incorporating advances in pathology, radiology, and molecular biology. A better understanding of these tumors allows for optimized treatment, particularly through precise surgery and rigorous evaluation of clinical and radiological data. This study highlights the importance of the updated classification of thymic epithelial tumors in refining diagnosis and improving patient management.

Keywords: Thymic epithelial tumors (TETs); mediastinum; histology; immunohistochemistry

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AB051. Immunopathological profile of patients with thymic epithelial tumour and Good syndrome in advanced stage

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Background: Thymic epithelial tumours (TETs) are frequently accompanied by Good syndrome (GS), a rare immunodeficiency characterized by hypogammaglobulinemia and B lymphopenia and other autoimmune diseases (ADs). Altered immunological mechanisms make necessary the monitoring of the immunophenotype in TET patients. The objective of this study is to evaluate differences in immunoglobulins, immunophenotype, and cytokine profiles in TET patients with or without GS (GS+/GS-) and in the presence/absence of other AD (AD+/AD-), and to assess whether these alterations differ according to disease stage (IVA/IVB) and in patients with no evidence of disease (NED).

Methods: Seventy TET patients were enrolled from 2019 to 2023 at Rare Tumors Coordinating Center of Campania Region. Immunoglobulin A (IgA), immunoglobulin M (IgM) and immunoglobulin G (IgG) were measured and the immunophenotype was analysed by 8-color immunophenotyping kit and Treg detection kit (CD4/CD25/CD127). Cytokines in serum samples were quantified by Enzyme-Linked Immunosorbent Assay (ELISA) multiplex assay.

Results: We observed reduction of IgM (0.8 ± 0.1) and IgG (9.0 ± 0.6) in GS+ patients; however, considering the stages and other AD presence, the decrease was maintained

only for IgM in GS+AD- NED patients (0.2 ± 0.1). B lymphopenia was detected in GS- patients in IVA/B (1.5 ± 0.2) *vs.* NED, and in GS+ patients in both IVA/B (0.3 ± 0.1) and NED (0.4 ± 0.1) stages and independent of other AD presence. No difference was observed in other immune cells with the exclusion of Treg that increased in IVA/B (6.7 ± 0.8) stage *vs.* NED in GS- patients, particularly in the presence of AD. Increase of Treg was detected in GS+AD+ NED (6.4 ± 1.1) patients *vs.* both GS-AD+ and GS+AD- NED patients. A trend like that observed for Treg was reported for a panel of proinflammatory cytokines, namely interleukin-1 beta (IL-1 β), interleukin-8 (IL-8), tumor necrosis factor alpha (TNF α), Regulated on Activation, Normal T Cell Expressed and Secreted (RANTES), and others.

Conclusions: Our results suggest that B lymphopenia is more specific than hypogammaglobulinemia to detect GS at different stages of the disease and independent of the presence of other AD. Unlike B cells, Treg increase in disease progression in GS- patients and particularly in AD+ patients. The increase of Treg in NED patients is associated with both GS+ and AD+. In addition, changes in Treg might parallel proinflammatory cytokine modulation. Overall, we suggest that immune modulation represents a key factor in TET diagnostic profile.

Keywords: Thymic epithelial tumours (TETs); Good syndrome (GS); autoimmune diseases (ADs); immunophenotype; cytokines

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AB052. Indications for postoperative radiation therapy for thymic tumors based on the new ninth TNM stage classification: a protocol of a multicenter, retrospective study

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Background: The indication for radiation therapy in thymic tumors requires more precise definition, particularly in light of the recently established 9th edition tumor-node-metastasis (TNM) classification. While surgical treatment is already aligned with the TNM system, radiation oncologists still primarily rely on the Masaoka-Koga classification due to the absence of TNM-based data on postoperative radiation therapy (PORT). Here we present our study protocol and project plan for an international, multi-center, retrospective study to evaluate the outcomes after surgical resection and PORT in thymic tumors using both the Masaoka-Koga and TNM classifications. We aim to define the role of PORT in the context of the new TNM staging system.

Methods: This study focuses on patients with completely resected (R0) Masaoka-Koga stages I–III thymomas, thymic carcinomas, and neuroendocrine thymic tumors (NETTs), with and without PORT. Recruitment of international partner institutions is ongoing to establish a large and

diverse patient cohort. In addition to tumor stage, the study collects variables related to surgical outcomes, radiation therapy doses, target volumes, and oncologic outcomes.

Discussion: Preliminary data from the Freiburg University Hospital identified 52 patients for the study. The observation period for our study spans from January 1, 2010, to June 1, 2024. The cohort included 45 thymomas, 2 NETTs, and 5 thymic carcinomas. The median follow-up period was 46.1 months. According to the TNM classification, 49 patients were classified as stage I, 2 as stage II, and 1 as stage III. The median age was 60.5 years; 23 patients were male and 29 were female. Paraneoplastic syndromes were observed in 18 of the 52 patients, including 17 cases of myasthenia. 10 patients received PORT, with a median dose of 50 Gy. We have received verbal commitments from 55 centers worldwide to participate in this project. The geographic distribution of these centers includes 32 from Europe, 13 from North America, and 10 from Asia. Contracting for data exchange with these centers is ongoing, and we are actively seeking additional institutions to support the development of a new indication for PORT in thymic tumors. We expect to collect the data until the end of 2025.

Trial Registration: None.

Keywords: Postoperative radiation therapy (PORT); Masaoka-Koga classification; 9th TNM stage classification

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AB053. The role of local therapy in oligo-recurrent metastatic thymic epithelial tumors: a monocentric retrospective analysis

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Background: Thymic epithelial tumors (TETs) are rare cancers, and limited data are available in the literature regarding the management of metastatic disease. In particular, for patients with metastatic oligo-recurrent disease, the use of local treatments instead of systemic therapy is sometimes considered by clinicians, although the supporting evidence is weak. We aim to retrospectively evaluate a series of patients with metastatic oligo-recurrent TETs treated with local therapy.

Methods: A monocentric retrospective trial was conducted selecting patients with TETs who were treated with local therapy (surgery or radiotherapy) for metastatic oligo-recurrent disease following radical surgery of the primary tumor. Data were collected on clinical characteristics, date and localization of recurrences, type of local treatments, date of disease progression after local therapy, and follow-up. The data were analyzed using Statistical Analysis System (SAS) version 9.4.

Results: A total of 38 patients with TETs (30 thymomas; 8 thymic carcinomas) were included. Disease recurrence was detected in a single site in 18 patients (47.4%), in two

sites in 14 patients (36.8%), and in three or more sites in 6 patients (15.8%). The most frequent sites of recurrence were pleura alone in 14 patients (36.8%), chest wall in 14 patients (36.8%), and lung in 10 (26.3%). Oligo-recurrent disease was confined to a single organ in 25 patients (65.8%) and to multiple organs in 13 patients (34.2%). Local therapy for oligo recurrence consisted of surgery alone in 15 patients (39.5%), radiotherapy alone in 7 (18.4%), radiotherapy plus surgery in 6 (15.8%), surgery plus chemotherapy in 6 (15.7%), radiotherapy plus chemotherapy in 2 (5.3%), and surgery combined with both radiotherapy and chemotherapy in 2 (5.3%). Following local therapy, 26 patients (68.4%) experienced progression of disease. Among them, 16 patients (61.5%) received an additional local therapy, while 10 (38.5%) received systemic treatment. The median progression-free survival (PFS) was 26.5 months [95% confidence interval (CI): 16–41]. The 6- and 12-month PFS rates were 85.9% and 79.7%, respectively. The median overall survival (OS) was 100.3 months (95% CI: 84–not reached) with the 1- and 5-year OS rates of 100% and 89%, respectively.

Conclusions: Local treatment of metastatic oligo-recurrent TETs seems to be associated with prolonged survival. An enlargement of the case study and a prospective evaluation could provide stronger evidence to support this therapeutic approach.

Keywords: Oligo-recurrent; metastatic disease; local therapy.

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aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the regional ethics board (Comitato etico territoriale Lombardia 5) (No. 4370) and individual consent for this retrospective analysis was waived.

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AB054. Survival outcomes in thymic carcinoma: a single-center experience

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Background: Thymic carcinomas (TCs) are rare neoplasms of the anterior mediastinum, accounting for 14% to 22% of thymic epithelial tumors. They are distinguished by aggressive biological behavior, frequent metastatic spread, and a poorer prognosis than thymomas. Despite therapeutic advances, prognostic determinants remain unexplored, particularly in real-world settings. We aimed to describe overall survival (OS) in a monocentric cohort of patients with TC and explore its association with key clinical and pathological variables.

Methods: We conducted a retrospective analysis of 30 patients with a diagnosis of TC referred to the University of Naples Federico II from January 2007 to December 2022. Data collected included age at diagnosis, sex, surgery, disease stage, and presence of autoimmune conditions. OS was defined as the time from histological diagnosis to death from any cause or last follow-up (data cut-off: April 29, 2025). Survival analyses were performed using the Kaplan-Meier method and compared with the log-rank test.

Results: The median age at diagnosis was 55 years (range, 32–77 years), with 12 (40%) females and 18 (60%) males. According to the Masaoka-Koga system, disease stage was III in 5 patients (17%), IVA in 6 (20%), and IVB in 19 (63%). Only 5 patients underwent thymectomy (16.6%). Autoimmune conditions were present in 13 patients, including 9 with Good's syndrome, 3 with myasthenia gravis (MG), and 1 with rheumatoid arthritis. Among these patients, three were found to have a concurrent B3 thymoma component, and two of these presented with MG.

The median OS for the study cohort was 41.8 months. No association between OS and sex was observed ($P=0.64$). In contrast, any autoimmune condition was significantly associated with prolonged survival (median OS: 137.5 *vs.* 46.8 months; $P=0.02$).

Conclusions: In this single-center cohort of patients with TC, autoimmune conditions were associated with significantly prolonged OS. It may be linked to an underlying B3 thymoma component or the lack of systematic screening for autoimmunity in TC. These findings suggest that autoimmunity may identify a clinically distinct subset of patients with more favorable outcomes and warrant further investigation in larger, prospective cohorts.

Keywords: Thymic carcinomas (TCs); survival outcomes; autoimmune disorders

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AB055. FGFR1 amplification in thymic epithelial tumors (TETs): a study from 48 cases

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Background: Thymic epithelial tumors (TETs) are rare tumors with variable aggressiveness. More than 30% of the patients develop metastases requiring systemic treatment. Previously, a few clinical trials evaluated different FGFR kinase inhibitors showing diverse promising results. FGFR1 amplification is found in around 20% of lung squamous cell

carcinomas (LSCC) representing a potential therapeutic target of these tumors. In this context, squamous cell thymic carcinomas (TCs) showing an FGFR1 amplification could be eligible to target therapy. The purpose of this article is to analyse the presence of FGFR1 amplification in TET with clinical, pathological and prognosis factors correlation.

Methods: Forty-eight specimens from surgically resected patients with diagnosis of TET validated by RYTHMIC national tumor board from January 2009 to May 2015 were included. Specimens were centrally reviewed by a panel of expert pathologists with diagnoses made according to the 2021 World Health Organization (WHO) histological classification. FGFR1 amplification was performed by fluorescence in situ hybridization (FISH) (ZytoLight-Clinisciences). The slides were scanned and analysed by two independent observers.

Results: Among 48 specimens (31 squamous TC and 17 B3 thymoma), 6/48 (12.5%) tumors were FGFR1 amplified [5/31 TC (16%) and 1/17 B3 thymoma (6%)]. All these cases demonstrated low-level amplification, with polysomy (≥ 2 CEN8 signals on average). FGFR1/CEN8 ratios ranged from 1.01 to 1.5 (≤ 2). No significant differences were observed between the two groups (amplified or not) according to age, gender, autoimmune disease, histology, and stage. The median follow-up was 97 months (range, 73–186 months). Median progression-free survival (PFS) was similar between the two groups (43.2 *vs.* 42.7 months, amplified *vs.* non-amplified, respectively) and median overall survival was not significantly different (132 months in the amplification-positive group *vs.* 79.2 months; $P=0.72$) these results should be interpreted however with caution due to the small sample size of the series and FGFR1 amplified cases.

Conclusions: In our series, FGFR1 amplification detected by FISH was found in 16% of TC and 6% of thymoma. TETs level amplification is much lower than in LSCC and is associated with a polysomy in all cases. This molecular alteration is potentially targetable similar to the FGFR3 and should be therefore potentially evaluated in refractory TC or thymoma.

Keywords: Thymic epithelial tumors (TETs); FGFR1 amplification; thymic carcinoma (TC); fluorescence in situ hybridization (FISH)

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. This study was approved by a national ethics committee for observational studies (Comité d'Evaluation des Protocoles de Recherche Observationnelle, CEPRO) on 18/12/2014, by the French Advisory Committee on Information Processing in Material Research in the Field of Health (Comité Consultatif sur le Traitement de l'Information en Matière de Recherche dans le Domaine de la Santé, CCTIRS) on 17/03/2016 and by the National Commission of Informatics and Liberty

(CNIL) on 24/05/2016, according to French laws. The patients included in this study received information from their referring clinician, as recommended by competent authorities, that specified that, according to French laws, they were allowed to ask for complete access to/removal of their own collected data. Individual consent for this retrospective analysis was waived.

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AB056. Surgical outcomes and prognostic impact of complete resection in thymic epithelial tumors: a 15-year experience from the National Cancer Institute of Mexico

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Background: Thymic epithelial tumors are rare, with thymoma being the most frequent histological subtype. The most important prognostic factors include tumor stage and completeness of surgical resection. We aim to describe retrospectively the demographic, clinical characteristics, surgical approach, histopathological results, postoperative complications, and oncological outcomes in patients undergoing thymectomy between 2009 and 2024 at the National Cancer Institute of Mexico.

Methods: This is a retrospective observational cohort study of patients who underwent thymectomy for thymic epithelial tumors at the National Cancer Institute of Mexico between January 2010 and December 2024. Primary endpoints were overall survival (OS) and disease-free survival (DFS).

Results: A total of 47 patients were included. Median follow-up was 50 months (range, 1–171 months). Mean age was 59 years, and 59% were female. Median tumor size was 8.4 cm (range, 3.0–18.0 cm). Paraneoplastic syndromes were present in 36%, with myasthenia gravis being the most common (25%). Neoadjuvant chemotherapy was administered in 13% of cases. A transsternal approach was used in 60% of cases; 8 patients underwent minimally invasive surgery [video-assisted thoracoscopic surgery (VATS) or robotic-assisted thoracic surgery (RATS)]. Extended thymectomy was required in 80% to achieve negative margins. Complete (R0) resection was achieved in 83% of patients. Most patients were Masaoka-Koga stage I (36.2%) and II (38.2%). Most frequent histology was World Health Organization (WHO) AB (40.4%). Only 38.3% of patients received adjuvant treatment, with radiotherapy being the most common strategy (77.8%). The 90-day morbidity rate was 27.7%, mostly Clavien-Dindo grade I–II. Mortality was 6.4%. Median OS was 156 months (range, 22–289 months). Complete resection was the only factor significantly associated with improved OS: 155.0 months (range, 1.0–334.8 months) for R0 *vs.* 15.0 months (range, 1.0–93.4 months) for incomplete resections ($P=0.14$). DFS was also higher in patients with complete resection: 135.9 months (range, 111.0–160.8 months) *vs.* 69.3 months (range, 37.3–101.3 months) ($P=0.07$).

Conclusions: Our experience in the National Cancer Institute of Mexico demonstrate that Complete surgical resection is the cornerstone of curative treatment for thymic epithelial tumors. In our cohort, R0 resection was consistently associated with significantly improved overall and disease-free survival, regardless of tumor size or approach. These findings underscore the critical importance of achieving negative margins through tailored surgical strategies, including extended thymectomy when necessary.

Keywords: Thymoma; thymic carcinoma; surgery; survival

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The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki and its subsequent amendments. The study was approved by the institutional ethics committee of the National Cancer Institute of Mexico (No. INCAN/CI/837/17) and individual consent for this retrospective analysis was waived.

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AB057. Two decades of robotic thymectomy: trends and insights from a retrospective study

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Background: Over the past decades, there has been a shift towards robotic resection for thymic tumors. The objective of our study was to characterize the transition to robotic-assisted thymectomy (RATS) in a historical cohort of patients undergoing thymectomy for thymic tumors.

Methods: We conducted a retrospective, single-center review of all robotic thymectomies for thymic epithelial tumors (TETs) between 2002 and 2022. Additionally, we analyzed data from patients who underwent resection of TETs using other approaches during the same period.

Results: During the study period, 348 patients were treated

for TETs. The RATS group included 123 patients, 27% of whom were female, with a median [interquartile range (IQR)] age of 57 [48–66] years. Sixty-three (51%) patients had associated myasthenia gravis. In 16 (13%) cases, resection of structures other than the thymus was necessary. The conversion rate was 10%, with no intraoperative mortality. Pathological analysis revealed that most patients had a thymoma (97.6%), while there were only 2 cases of thymic carcinoma (1.6%) and 1 case of thymic carcinoid (0.8%). Tumor-node-metastasis (TNM) staging showed that the majority of patients had early-stage disease (stages I–II: 96%), with a median tumor size of 4.5 cm (range, 3–6 cm). The median duration of follow-up was 48 months (range, 24–72 months). There were 3 recurrences, and the 5-year disease-free survival (DFS) rate was 97%. While in the first half of our experience, RATS accounted for only 14% of thymectomies, in the latter half, this proportion increased to 45% ($P<0.001$), particularly for stage I–II cases (58%) ($P<0.001$). Additionally, we observed an increase in the dimension of lesions removed using the robotic approach (Figure 1), particularly the proportion of large tumors (≥ 5 cm) increased from 3% to 32% ($P<0.001$).

Conclusions: Over the past 20 years, there has been a significant shift towards robotic thymectomy, particularly for early-stage disease. With increasing experience, more advanced-stage tumors and larger lesions are being considered for a robotic approach.

Keywords: Thymoma; robot; recurrence; trends

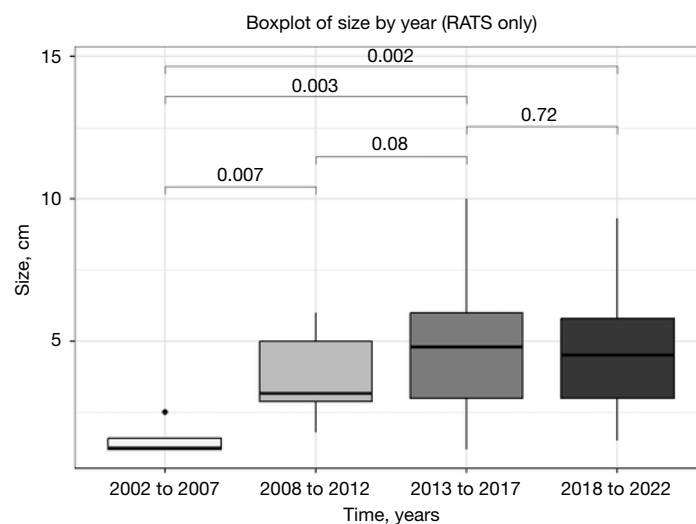


Figure 1 Distribution of the resected tumors' dimension stratified by year-range. RATS, robotic-assisted thymectomy.

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AB058. Surgical management of TNM stage IVA thymoma and thymic carcinoma: the network TYME experience (4TYMEs)

Riccardo Orlandi¹, Paolo Mendogni², Mario Nosotti^{1,2}, Annalisa Trama³, Monica Ganzinelli⁴, Giovanni Comacchio⁵, Giovanni Leuzzi⁶, Emanuele Voulaz⁷, Paolo Andrea Zucali^{8,9}, Giulia Pasello¹⁰, Irene De Simone¹¹, Francesca Galli¹¹, Giovannella Palmieri¹², Erica Pietroluongo¹³, Marcello Carlo Ambrogi¹⁴, Vittorio Aprile¹⁴, Lorenzo Rosso^{1,2};
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Background: Tumor-node-metastasis (TNM) stage IVA thymic epithelial tumors (TETs) are rare and pose

significant challenges due to limited and heterogeneous data. A major difficulty in managing stage IVA disease is the lack of clarity on the optimal treatment approach, particularly concerning the role of surgery, which remains controversial. This study aimed to evaluate clinical characteristics, pathological findings, and oncological outcomes in a consecutive cohort of surgically treated patients from the referring centers of the ThYmic MalignanciEs (TYME) Italian Network.

Methods: Patients with pathologically confirmed stage IVA TETs undergoing surgery were retrospectively reviewed from the TYME Network database. Demographic, clinical, and histopathological variables were analyzed, including prior cancer, autoimmune disease, Eastern Cooperative Oncology Group (ECOG) and American Society of Anesthesiologists (ASA) scores, histologic subtype, resection status, and use of perioperative treatments. Survival outcomes were estimated using Kaplan-Meier analysis, and predictors of recurrence-free survival (RFS) and overall survival (OS) were explored through univariable and multivariable methods.

Results: Fifty patients were enrolled. The median age was 51 years; 64% were male. All patients underwent surgery with curative intent; R0 resection was achieved in 73.3%. The most common histotypes were B2 (22%), B1 (20%), B3 (16%), and squamous thymic carcinoma (16%). Preoperative chemotherapy was administered to 45% of patients, postoperative radiotherapy to 42% of patients. Median OS was 122.9 months (*Figure 1*). There was no significant survival difference by resection margin ($P=0.68$) or preoperative chemotherapy ($P=0.74$). Median disease-free interval from the first surgery was 18 months (range, 1–181 months). R0 patients showed longer mean RFS (28.3 months) than R1–R2 (19.0 months), but the difference was not statistically significant. Histologic subtype was strongly associated with RFS ($P=0.03$). B1 thymoma had the longest RFS (61 months), significantly longer than thymic carcinoma (6.6 months, $P=0.03$). In multivariable analysis, histologic type and tumor volume were independent predictors of RFS ($P<0.001$ and $P=0.03$, respectively).

Conclusions: Surgical resection in TNM stage IVA TETs is feasible and can achieve long-term survival in selected patients within a multimodal treatment strategy. Histologic subtype is a key determinant of both recurrence risk and survival. These findings support surgery as a critical component of multimodal therapy, with histopathology and tumor volume guiding postoperative management and follow-up strategies.

Keywords: Thymoma; thymic carcinoma; stage IVA; surgery; multimodal treatment

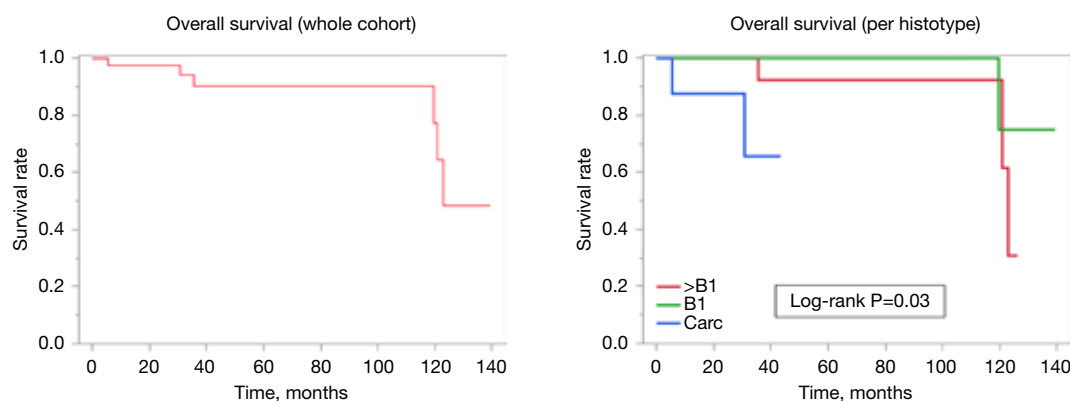


Figure 1 Overall survival for the whole cohort and per histotype.

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AB059. Enrollment in clinical trials among Italian patients with metastatic thymic epithelial tumors: a retrospective TYME network analysis

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Background: Thymic epithelial tumors (TETs) are rare malignancies with a limited therapeutic armamentarium. Enrollment in prospective clinical trials involving novel agents or new treatment combinations represents a therapeutic opportunity for patients with TETs. However, the availability to such trials is often limited due to poor engagement by pharmaceutical companies in rare cancer research. This study retrospectively investigated the proportion of Italian patients with metastatic TETs

treated with experimental systemic therapy (any lines) in prospective clinical trials.

Methods: Clinicoradiological, histopathological, and oncological data were retrospectively collected for 135 patients with unresectable metastatic TETs who received systemic therapy between January 2000 and December 2020. Data were sourced from the large multicenter database of the Italian collaborative group for ThYmic MalignanciEs (TYME). Survival analyses were performed using the Kaplan-Meier method and stratified by histology.

Results: A total of 135 patients were included: 73 (54%) treated within clinical trials (any lines of therapy) and 62 (46%) treated outside of trials. Among the trial group, 59 patients (80.8%) had thymoma B3 or thymic carcinoma (TC), and 14 (19.2%) had other thymoma subtypes. In the non-trial group, 35 patients (56.4%) had thymoma B3 or TC, and 27 (43.5%) had other thymoma subtypes. Overall, 46 out of 63 patients (73%) treated in a protocol study received experimental drugs in the second or third-line setting. At 36 months, the overall survival (OS) rate was 75.8% in the trial group and 83.5% in the non-trial group. Stratifying by histology, patients with TC or thymoma B3 had a 36-month OS rate of 71.5% in the trial group and 73.7% in the non-trial group. Among patients with other thymoma subtypes, the 36-month OS was 92.8% in the trial group and 95.8% in the non-trial group.

Conclusions: Our analysis showed that, within the Italian TYME network, the majority of patients with metastatic TETs were treated with systemic therapy in the context of a clinical trial. Moreover, these patients presented a higher proportion of histologies associated with a poor prognosis compared to those not treated with experimental drugs. Further data collection is needed to explore whether meaningful differences exist between patients treated within and outside.

Keywords: Thymic epithelial tumors (TETs); clinical trials; rare cancers; ThYmic MalignanciEs collaborative group (TYME collaborative group)

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AB060. A predictive model for surgical resectability in thymic epithelial tumors using clinical data: a step towards integrating radiomics and histopathology

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Background: Thymic epithelial tumors (TETs) are rare, heterogeneous malignancies. Surgery is the primary treatment for early-stage TETs, while induction strategies aim to reduce tumor mass and improve R0 resection likelihood. However, treating borderline resectable TETs remains a challenge. Machine learning (ML) can offer insights beyond traditional methods and the field of RaPtomics applies ML to radiologic and pathological images. The purpose of this article is to establish a baseline model that will allow future evaluation of implicit features like texture and homogeneity against current clinical standards. To start, we hypothesize that a clinical model can accurately predict surgical resectability in TET patients.

Methods: From a REDCap database of 1,089 TET patients at Indiana University's thoracic oncology clinic, 202 patients met the following criteria: confirmed clinical stage I–III TET, confirmed resection status, and surgery with curative intent. Clinical and demographic data points, including tumor size, World Health Organization (WHO) staging, age, and concurrent autoimmune diagnoses, were used to encode 52 features. Patients were divided into cohorts based on resection: R0 resection (135 patients) and R1/R2 resection (67 patients). Five ML models were assessed via stratified cross-validation, evaluating accuracy and area

under the curve (AUC).

Results: An ensemble model combining Random Forest, AdaBoost, and XGBoost classifiers achieved 66% accuracy and an AUC of 0.73, indicating moderate discriminatory power in distinguishing R0 from R1/R2 resection cases. A sensitivity of 0.78 for R1/R2 suggests that the model effectively identifies unresectable cases, while a precision-recall AUC of 0.876 supports its utility for ranking patients by resectability risk. Top contributing features included WHO and Masaoka staging, highlighting the predictive power of current oncologic staging systems. Notably, sex assigned at birth and race/ethnicity also emerged as meaningful contributors, suggesting possible demographic associations with resectability.

Conclusions: This study establishes a foundational ML model for predicting surgical resectability in TETs. Future work will address current model limitations by incorporating RaPtomics features and expanding the cohort to differentiate between direct-to-surgery and neoadjuvant chemotherapy patients. This may enhance decision-making for neoadjuvant therapy and improve R0 resection likelihood.

Keywords: Thymic epithelial tumor (TET); machine learning (ML); RaPtomics; clinical modeling

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