



Surgical Supremacy in Stage III Thymic Tumors with Vascular Invasion: Re-evaluating the Induction Paradigm

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Abstract

Stage III Thymic Epithelial Tumors (TETs) with vascular invasion represent one of the most complex scenarios in thoracic oncology. While multimodality therapy remains the standard approach, the optimal sequencing-particularly the role of Induction Therapy (IT)-is still debated when great vessels are involved. Recent analyses from the European Society of Thoracic Surgeons (ESTS) database have demonstrated that the completeness of Resection (R0) is the strongest prognostic factor, whereas IT provides no proven survival advantage. Even in cases of microscopic Residual Disease (R+), long-term survival remains satisfactory when radical surgery is attempted by experienced vascular thoracic teams. These findings challenge the traditional induction paradigm, suggesting that in technically resectable cases, upfront surgery followed by adjuvant therapy should be prioritized. The emphasis should shift from treatment sequence to patient selection and surgical expertise. For locally advanced TETs with vascular invasion, radical resection is not only justified but represents an oncologic imperative.

Keywords: Induction Therapy; Multimodality Treatment; Surgical Resection; Thymic Epithelial Tumors; Thoracic Oncology; Vascular Invasion; Vascular Reconstruction

In Stage III thymic epithelial tumors with vascular invasion, surgical radicality remains the principal determinant of long-term survival. Evidence from recent multi-institutional studies demonstrates that Induction Therapy (IT) does not improve outcomes, while complete resection-even with vascular reconstruction-offers excellent results. When performed by specialized teams, upfront surgery should be considered the standard approach for technically resectable disease. Stage III Thymic Epithelial Tumors (TETs) are characterized by direct invasion into adjacent structures (such as the pericardium, chest wall, or great vessels) and represent a significant challenge for thoracic surgeons as well as oncologists.

[1] Given that the completeness of resection (R0 status) remains the single most critical determinant of long-term survival, multimodality therapy is the standard of care [2]. However, the optimal sequencing of treatment-specifically the role of IT before surgery-becomes highly nuanced when dealing with vascular involvement, pushing the technical limits of surgical radicality [3]. Local invasion of great vessels, most commonly the Superior Vena Cava (SVC) system, necessitates highly specialized surgical expertise. These complex resections are required in a significant minority of locally advanced cases, accounting for 20% to 40% of all Stage III TETs in major multicenter series [4,5]. In this context, vascular resection (VR) requiring complex reconstructions (using materials such as Polytetrafluoroethylene or bovine pericardium) [6,7] often translates into greater perioperative morbidity

compared to standard resections [6]. Furthermore, in addition to the perceived technical complexity and associated risks, some authors have suggested that VR might be linked to a worse overall prognosis compared to Stage III tumors without vascular involvement [1]. Modern retrospective analyses, however, have helped to delineate the true prognostic landscape of this super-selective group. The prognostic hierarchy in patients undergoing VR is driven by several independent factors: a negative influence is exerted by R+ status, the presence of Thymic Carcinoma (TC), and administration of IT [5], while the strongest positive driver remains the ultimate achievement of an R0 resection [4,5] and the subsequent administration of Adjuvant Therapy (AT) [3]. The multi-institutional ESTS database, recently reported by Mendogni et al. [5], specifically analyzed outcomes after VR in this subset of patients. This analysis confirmed that among patients achieving an R0 resection, the presence of thymic carcinoma acts as a strong negative prognostic factor. Crucially, this study also provided robust justification for an aggressive surgical strategy: despite the technical challenge, patients with incomplete resection demonstrated a satisfactory 5-year and 10-year overall survival (OS) of 47.0% and 38.0%, respectively, and a median progression time of 72 months [5]. This powerful observation strongly suggests that the pursuit of surgical resection-even if R0 status is not definitively secured-is warranted in most cases of locally advanced TETs with vascular invasion. In this scenario, the established rationale for IT in Stage III TETs is to downstage the tumor and increase the probability of R0 resection.

Yet, in the super-selective group requiring VR, the utility of IT remains highly debatable. Data from the ESTS show that IT was administered to 27-52% of patients with vascular invasion [3,5], indicating substantial practice variability across high-volume European centers. The central question is whether this pre-operative systemic treatment offers a survival advantage over upfront radical surgery followed by AT. Comparison studies in this context show that IT fails to provide a statistically significant OS benefit [6,8]. On the other hand, ESTS analysis for Disease-Free Survival (DFS) in R0 patients showed an increased hazard of recurrence for the IT group, revealing the “Double-Edged Sword of IT”: even when IT helps in achieving an R0 resection, it often masks a more aggressive TETs biology that is prone to early recurrence, rather than IT itself causing recurrence. These findings solidify the principle that once the tumor is pathologically contained and removed-whether the R0 margin is achieved via IT facilitation or upfront surgical skill-the long-term prognosis is excellent and driven primarily by the R0 status. The omission of IT for resectable disease avoids treatment-related toxicities, potential delays to curative surgery, and the risk of tumor progression while on systemic treatment. In the complex environment of vascular invasion, where R0 is

the goal but R+ is still associated with an acceptable long-term survival [5], the experienced surgeon’s judgment on resectability holds the most significant value. As a result, these data suggest that for a patient whose tumor is technically resectable by a dedicated vascular thoracic team, proceeding directly to surgery does not compromise survival. The current body of evidence suggests that the benefit of IT in Stage III TETs with vascular invasion is primarily technical-a tool to aid resectability-rather than a definitive survival mechanism. For tumors deemed radically resectable, the priority lies in complete, timely removal of the mass. The high and satisfactory survival rates achieved even in R+ patients compel and justify an aggressive surgical approach in all viable candidates. The debate must move beyond the sequence of treatment, focusing on proper patient selection: in the absence of clear radiologic signs of unresectability, radical surgery for Stage III thymic tumors with great vessel involvement is not merely justifiable, but an oncological imperative!

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References

1. Marulli G, Lucchi M, Margaritora S, Cardillo G, Mussi A, et al. (2011) Surgical treatment of stage III thymic tumors: a multi-institutional review from four Italian centers. *Eur J Cardiothorac Surg* 39: e1-7.
2. Cardillo G, Lucchi M, Marulli G, Infante M, Leuzzi G, et al. (2016) Induction therapy followed by surgical resection in Stage-III thymic epithelial tumors: Long-term results from a multicentre analysis of 108 cases. *Lung Cancer* 93: 88-94.
3. Leuzzi G, Rocco G, Ruffini E, Sperduti I, Detterbeck F, et al. (2016) ESTS Thymic Working Group. Multimodality therapy for locally advanced thymomas: A propensity score-matched cohort study from the European Society of Thoracic Surgeons Database. *J Thorac Cardiovasc Surg* 151: 47-57.e1.
4. Liu L, Zhang J, Wang G, Guo C, Chen Y, et al. (2020) Extended thymectomy with blood vessel resection and reconstruction improves therapeutic outcome for clinical stage III thymic carcinoma patients: a real-world research. *J Cardiothorac Surg* 15: 267.
5. Mendogni P, Toker A, Moser B, Trancho FH, Aigner C, et al. (2022) European Association of Thoracic Surgeons (ESTS) Thymic Working Group. Surgical resection of Masaoka stage III thymic epithelial tumours with great vessels involvement: a retrospective multicentric analysis from the European Society of Thoracic Surgeons thymic database. *Eur J Cardiothorac Surg* 62: ezac021.

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6. Leo F, Bellini R, Conti B, Delledonne V, Tavecchio L, et al. (2010) Superior vena cava resection in thoracic malignancies: does prosthetic replacement pose a higher risk? Eur J Cardiothorac Surg 37: 764-769.
7. Gao HJ, Shi GD, Pan MJ, Liu XT, Wei YC (2021) Autogenous pericardial angioplasty for thymic malignancies: a narrative review. Mediastinum 5: 6.
8. Maurizi G, Poggi C, D'Andrilli A, Vanni C, Ciccone AM, et al. (2019) Superior Vena Cava Replacement for Thymic Malignancies. Ann Thorac Surg 107: 386-392.