



# Thymic epithelial tumors: still enigmatic neoplasms!

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Thymic epithelial tumors comprising thymomas and thymic carcinomas, are quite fascinating tumors due to their specific location in the mediastinum, their association with several paraneoplastic syndromes, and different clinical behavior (1). In contrast to lung cancer and pleural mesothelioma, thymic epithelial tumors usually have a good prognosis when a complete resection is obtained. Operative morbidity and mortality are low unless extended resections are necessary and recurrences occur at a lower frequency compared to the other thoracic tumors. Specific tumor characteristics related to recurrent disease have not been firmly established.

In the present study 235 cases originating from the National Yang Ming University in Taipei, Taiwan were analyzed (2). Long-term survival and recurrence rate were studied. All patients underwent surgical resection with a complete resection rate of 97.02% as mentioned in table 1 of the manuscript (and not 93.44% as mentioned in the text). Surgical procedures included extended thymectomy (removal of the entire thymic gland including thymoma) by median sternotomy, or thymectomy (removal of the thymoma only) by thoracotomy or video-assisted thoracic surgery (VATS). Overall mortality was 5.6% (13 patients). Median follow-up time was 105 months (8.8 years). During follow-up recurrences were detected in 25 patients (10.7%). These were subdivided into local recurrence (6 patients), regional recurrence (12 patients) and distant recurrence (10 patients). Distant metastatic disease included bone metastasis (3 patients), liver metastasis (1 patient) and intraparenchymal pulmonary nodules (6 patients). Overall survival rate was 94.4%. In univariate analysis Masaoka stage, histological type, tumor size, adjuvant therapy and margin status were related to tumor recurrence (2). The authors conclude that due to the indolent behavior

of thymoma, tumor recurrence appears to be the best parameter to study oncological outcome.

This retrospective study includes a large series of patients with thymic epithelial tumors. However, it expands over an almost 16-year time period during which diagnostic and therapeutic algorithm most probably have changed substantially. Patients who had neoadjuvant chemoradiation were excluded which is unfortunate as they represent a challenging group of patients with more advanced disease. Overall, a detailed survival analysis is presented and recurrence studied according to specific clinical factors for which the authors are to be commended. Although the title mentions outcome of thymic carcinoma, no such patients are enlisted in the first table where all 235 patients were categorized as having thymoma. This means that the recurrence rate which is higher in thymic carcinoma compared to thymoma, was in fact not studied (3). Regarding staging itself in the first table, only Masaoka stage (or was it Masaoka-Koga?) and World Health Organization (WHO) histological type are listed although the authors state in the Materials and Methods section that they used the new, 8th edition of the Tumor-Node-Metastasis (TNM) staging system (4-6). In the figures overall and disease-free survival were not depicted according to this new edition of the TNM-classification, although for recurrence rate (the third table) this TNM stage was included, which is rather confusing. In total, 43.4% of patients had adjuvant radiotherapy or chemoradiation which is surprising as 97.0% had a complete R0 resection. Indications for adjuvant therapy are not clearly mentioned by the authors.

Factors related to recurrence of thymoma which is the main objective of this study, are as can be expected. Patients with more advanced stage, larger tumors, unfavorable

histology, adjuvant therapy and doubtful margins presented a high risk of recurrence. Regarding the type of resection, the authors performed as well a thymomectomy as an extended thymothymectomy. This is still a controversial issue in literature, but as also mentioned by the authors, in case of myasthenia gravis extended resection is necessary, not only to remove the tumor but also all possible sources of antibody production (7,8).

Although the authors provide details on risk of recurrence, they do not detail specific therapy and outcome in these patients with recurrent thymoma. In literature there are no clear recommendations but repeat resection of recurrent disease, whether it be purely local or locoregional, seems to provide the best long-term results (9-11).

The present study highlights the specific problems and possible bias encountered with retrospective studies associated with a low number of events. As also mentioned by the authors, they were only able to perform a univariate analysis. A detailed multivariate analysis was not possible due to the limited number of patients with recurrent disease. Single-institution experiences are not able to resolve completely the specific question of which factors significantly determine long-term survival and recurrence rate. Only joint efforts with creation of large prospective databases as initiated by the International Thymic Malignancies Interest Group (ITMIG) are able to collect enough data to provide more definite answers (12). All thoracic surgeons and thoracic oncologists are encouraged to participate in this worldwide effort and include as many patients as possible. In this way, thymic epithelial tumors will become less enigmatic in the near future.

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## References

1. Girard N, Mornex F, Van Houtte P, et al. Thymoma: a focus on current therapeutic management. *J Thorac Oncol* 2009;4:119-26.
2. Tseng YC, Tseng YH, Kao HL, et al. Long term oncological outcome of thymoma and thymic carcinoma - an analysis of 235 cases from a single institution. *PLoS One* 2017;12:e0179527.
3. Cardillo G, Carleo F, Giunti R, et al. Predictors of survival in patients with locally advanced thymoma and thymic carcinoma (Masaoka stages III and IVa). *Eur J Cardiothorac Surg* 2010;37:819-23.
4. Detterbeck FC, Stratton K, Giroux D, et al. The IASLC/ITMIG Thymic Epithelial Tumors Staging Project: proposal for an evidence-based stage classification system for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol* 2014;9:S65-72.
5. Marx A, Ströbel P, Badve SS, et al. ITMIG consensus statement on the use of the WHO histological classification of thymoma and thymic carcinoma: refined definitions, histological criteria, and reporting. *J Thorac Oncol* 2014;9:596-611.
6. Detterbeck FC, Nicholson AG, Kondo K, et al. The Masaoka-Koga stage classification for thymic malignancies: clarification and definition of terms. *J Thorac Oncol* 2011;6:S1710-6.
7. Narm KS, Lee CY, Do YW, et al. Limited thymectomy as a potential alternative treatment option for early-stage thymoma: A multi-institutional propensity-matched study. *Lung Cancer* 2016;101:22-7.
8. Keijzers M, Maessen JG. Thymomectomy in early stage thymomas-case closed? *J Thorac Dis* 2016;8:1440-2.

9. Heyman S, Van Schil P. Surgery for isolated pleural recurrence from thymoma. *Eur J Cardiothorac Surg* 2008;34:707-8.
10. Marulli G, Margaritora S, Lucchi M, et al. Surgical treatment of recurrent thymoma: is it worthwhile? *Eur J Cardiothorac Surg* 2016;49:327-32.
11. Sandri A, Cusumano G, Lococo F, et al. Long-term results after treatment for recurrent thymoma: a multicenter analysis. *J Thorac Oncol* 2014;9:1796-804.
12. Huang J, Ahmad U, Antonicelli A, et al. Development of the international thymic malignancy interest group international database: an unprecedented resource for the study of a rare group of tumors. *J Thorac Oncol* 2014;9:1573-8.

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