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Commentary: Thymic epithelial tumors—time to move beyond traditional staging?

Sandeep Sachidananda, MD,^a and
Chadrick E. Denlinger, MD^b

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CENTRAL MESSAGE

Thymomas represent a group of heterogeneous tumors with different staging systems that exclude tumor size. Given their heterogeneity, a predictive risk model may be more appropriate than traditional staging systems.

Thymomas comprise a diverse spectrum of rare diseases with the singular common feature of arising from residual thymic tissues in the anterior mediastinum. Most thymic tumors progress slowly, and patients experience prolonged disease-free survival periods of 70% to 90% at 15 years, depending on their specific histologic type and initial tumor involvement. The heterogeneous nature of thymic tumors contributed to the development of numerous staging systems related to degree of local tumor invasion or histologic type. Historically, the most frequently used staging systems were the Masaoka–Koga, for tumor invasion, and the World Health Organization system, based on histology. More recently, the American Joint Commission on Cancer included a tumor–node–metastasis staging system for thymic malignancies in the eighth edition of their staging manual. Interestingly, the most frequently used staging systems have not recognized tumor size as a prognostic factor.

Tumor size is a well-established prognostic indicator in many cancers such as lung and breast.^{1,2} Yun and colleagues³ analyzed the influence of size on overall survival and recurrence-free survival in thymic epithelial tumors. Size was an independent prognostic factor in completely resected, limited-stage (confined within the surrounding fatty tissues without invasion) tumors but not in more

advanced-stage tumors. Similarly, a Surveillance, Epidemiology, and End Results database review demonstrated stepwise decrements in survival with increasing tumor size.⁴ In contrast, Nicholson and colleagues⁵ analyzed multiple international databases and demonstrated that size was only predictive among Masaoka–Koga stage III–IV tumors with incomplete resections. Other staging characteristics were more predictive of outcomes, with size playing only a minor role, and the tumor size did not correlate with the ability to perform a complete resection. As a result, the only clinical value of tumor size related to prognosis among advanced-stage patients with R_{1/2} resection, and tumor size did not impact any clinical decisions.⁵

The current study and other retrospective studies have challenged this notion and suggested that size could be used to predict overall and recurrence-free survival. There is, however, no agreement on size cutoffs that convey the greatest differences in prognostication. Conflicting results from retrospective studies with comparable patient numbers imply that additional factors contribute to long-term outcomes. With thymic malignancies, we have already recognized tumor histology, outlined by the World Health Organization staging system, as a prominent contributing factor. Given the heterogeneity of thymic malignancies and discrepant results correlating tumor size and prognosis,

From the ^aDivision of Cardiothoracic Surgery, Indiana University, Indianapolis, Ind; and ^bDivision of Cardiothoracic Surgery, Medical University of South Carolina, Charleston, SC.

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Address for reprints: Chadrick E. Denlinger, MD, Department of Surgery, Division of Cardiothoracic Surgery, Medical University of South Carolina, 114 Doughty St, Charleston, SC 29425 (E-mail: denlinge@musc.edu).

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perhaps a risk model rather than traditional staging is more appropriate.

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Commentary: Size may matter after all

Vignesh Raman, MD, MHS, and
Oliver K. Jawitz, MD, MHS

Yun and colleagues report a multicenter retrospective cohort study examining tumor size in patients with completely resected thymic epithelial tumors (TETs).¹ They found that tumor size was independently associated with survival in patients with limited-stage tumors, and that tumor size >5.5 cm was associated with worse survival.

This study is a valuable addition to the cornucopia of existing literature about tumor size in TETs, primarily because it represents a methodically rigorous analysis of a complicated question in a heterogeneous patient population. In particular, unlike the vast majority of other studies, the authors considered tumor size as a continuous variable, focusing their main analyses on both identification of a potential threshold tumor size above which survival was worse and on the use of interaction terms to characterize the relationship between tumor size and other prognostic and

Vignesh Raman, MD, MHS, and Oliver K. Jawitz, MD, MHS

CENTRAL MESSAGE

In this retrospective cohort study, tumor size >5.5 cm was associated with worse survival in patients with completely resected limited-stage thymic epithelial tumors.

treatment factors. Using a combination of maximally selected rank statistics and concordance, they demonstrate that in their cohort, tumor size >5.5 cm was associated with worse adjusted survival in patients with limited-stage tumors. They also found that tumor size was not associated with survival in patients with more advanced tumors. Using interaction terms in multivariable regression, they did not find a meaningful relationship between tumor size and survival associated with receipt of adjuvant radiation.

The authors also candidly acknowledge the numerous limitations of their study, ranging from likely selection bias and unmeasured confounding to heterogeneity of

From the Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, NC.

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Address for reprints: Vignesh Raman, MD, MHS, Duke University Medical Center, 2301 Erwin Rd, Box 3443, Durham, NC 27710 (E-mail: vignesh.raman@duke.edu).

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