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

References

1. Zhang J, Gold KA, Lin HY, Swisher SG, Xing Y, Lee JJ, et al. Relationship between tumor size and survival in non-small-cell lung cancer (NSCLC): an analysis of the surveillance, epidemiology, and end results (SEER) registry. *J Thorac Oncol*. 2015;10:682-90.
2. Foulkes WD. Size surprise? Tumour size, nodal status, and outcome after breast cancer. *Curr Oncol*. 2012;19:241-3.
3. Yun JK, Kim HR, Kim DK, Kim YT, Chung KY. Tumor size as a prognostic factor in limited-stage thymic epithelial tumors: a multicenter analysis. *J Thorac Cardiovasc Surg*. 2021;162:309-17.e9.
4. Bian D, Zhou F, Yang W, Zhang K, Chen L, Jiang G, et al. Thymoma size significantly affects the survival, metastasis and effectiveness of adjuvant therapies: a population based study. *Oncotarget*. 2018;9:12273-83.
5. Nicholson AG, Detterbeck FC, Marino M, Kim J, Stratton K, Giroux D, et al. Staging and Prognostic Factors Committee; Members of the Advisory Boards; Participating Institutions of the Thymic Domain. The IASLC/ITMIG thymic epithelial tumors staging project: proposals for the T component for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2014;9(9 suppl 2):S73-80.

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Commentary: Size may matter after all

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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

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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

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Disclosures: The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Drs Raman and Jawitz were supported by National Institutes of Health T-32 grants 5T32CA093245 and 5T32HL069749, respectively.

Received for publication May 19, 2020; revisions received May 19, 2020; accepted for publication May 20, 2020; available ahead of print May 27, 2020.

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J Thorac Cardiovasc Surg 2021;162:319-20
0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2020.05.030>

surgery offered to patients in their cohort, interobserver variation in measurement of tumor size, limited subsets of patients undergoing adjuvant therapies, and the problem of multiple comparisons in use of concordance to evaluate a potential cutoff.

This study raises some important questions about the significance of tumor size in patients with limited TETs: (1) should tumor size be reconsidered in prognostication (ie, staging) in this patient population?; (2) should patients with larger tumors undergo more frequent surveillance or adjuvant therapies? A 2014 study by the International Association for the Study of Lung Cancer/International Thymic Malignancy Interest Group (ITMIG) evaluated the prognostic significance of tumor size in TETs using log-rank test statistics and found that the putative size threshold of 10 cm was not “statistically significant,” with a recursive partitioning analysis demonstrating that tumor size had a minor prognostic role compared with other variables; ultimately, tumor size was not included in staging.² It is unclear whether that study used multivariable regression and adjustment for interactions, and in light of this current study,

future efforts by the ITMIG may seek to analyze this question further to gauge the external validity of the findings. Unfortunately, the current study was also not primarily designed to examine whether tumor size had a relationship with survival associated with receipt of adjuvant therapies. Further studies, perhaps by this same group, may consider investigating this question in greater detail to study the practical implications of their findings.

Yun and colleagues are to be congratulated on this methodologically accomplished study, which generates important hypotheses about the role of tumor size in survival for patients with completely resected TETs.

References

1. Yun JK, Kim HR, Kim DK, Kim YT, Chung KY. Tumor size as a prognostic factor in limited-stage thymic epithelial tumors: a multicenter analysis. *J Thorac Cardiovasc Surg*. 2021;162:309-17.e9.
2. Nicholson AG, Detterbeck FC, Marino M, Kim J, Stratton K, Giroux D, et al. The IASLC/ITMIG thymic epithelial tumors staging project: proposals for the T component for the forthcoming (8th) edition of the TNM classification of malignant tumors. *J Thorac Oncol*. 2014;9(Suppl 2):S73-80.