

Commentary: Minimally invasive versus open thymectomy for stage I to III thymoma—Big incision, small difference?



Andrew E. Giles, MD, MPH,^a Nicholas LeBlanc, MD,^a and Biniam Kidane, MD, MSc^{a,b,c}

From the ^aSection of Thoracic Surgery, Department of Surgery, Max Rady College of Medicine; and ^bDepartment of Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; and ^cResearch Institute in Oncology and Hematology, Cancer Care Manitoba, Winnipeg, Manitoba, Canada.

Disclosures: Authors have nothing to disclose with regard to commercial support.

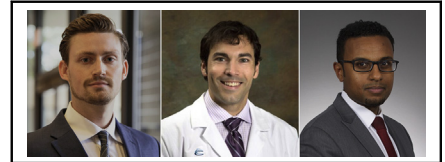
Drs Giles and LeBlanc are coequal first authors.

Received for publication Oct 4, 2019; revisions received Oct 4, 2019; accepted for publication Oct 7, 2019; available ahead of print Oct 16, 2019.

Address for reprints: Biniam Kidane, MD, MSc, GE-611, 820 Sherbrook St, Health Sciences Centre, Winnipeg, Manitoba R3A 1R9, Canada (E-mail: bkidane@hsc.mb.ca).

J Thorac Cardiovasc Surg 2020;160:568-9
0022-5223/\$36.00

Copyright © 2019 by The American Association for Thoracic Surgery
<https://doi.org/10.1016/j.jtcvs.2019.10.027>



Left to right: Andrew E. Giles, MD, MPH, Nicholas LeBlanc, MD, and Biniam Kidane, MD, MSc

Central Message

Minimally invasive thymectomy may be an acceptable alternative to open thymectomy, but longer follow-up is needed. Approach to stage III thymoma should be dictated by the pattern of invasion.

See Article page 555.

Thymoma is an uncommon mediastinal tumor.¹ Because of its rarity, heterogeneous presentation, and indolent recurrence pattern, study of this disease has required international collaboration and creative approaches to understand optimal management strategies and outcomes.

In the current issue of the *Journal*, Yang and colleagues² present data from the US National Cancer Data Base (NCDB). This database provides a unique perspective for researchers, allowing access to large numbers of patients and long-term outcomes reporting with low missing data rates. By means of propensity-score matching, Yang and colleagues² demonstrate that a minimally invasive surgical (MIS) approach to thymectomy in Masaoka stage I to II thymoma is safe and not associated with worse 5-year survival (MIS 89.4% vs open 81.6%). Multiple analyses are conducted in attempts to address pertinent issues, including the dogma that thymomas larger than 4 cm mandate an open approach.³ Yang and colleagues² conclude that in all cases patients in the MIS group are discharged from hospital 1 day earlier, with no appreciable differences in short- or long-term outcomes. They have done an excellent job of reporting their results in a transparent manner. Admirably, they have also framed their results in the context of a comprehensive and explicit list of limitations.

Considerable discussion is appropriately focused on margin status, noting lower R0 resection rates than in the comparable International Thymic Malignancy Interest Group study⁴ (72% vs 94% for MIS; 68% vs 86% for open, respectively). Given that 5-year survivals are similar to those in other studies, one major reason likely relates to how margin status is classified.⁵ In other studies, this is adjudicated by surgeons, who have the benefit of distinguishing whether a resection results in full removal (R0)—especially at sternal and pleural margins—even if

the specimen shows the tumor extending to the resection margin. In the NCDB, margin status is coded by pathologists, who are unable to make this assessment and would likely classify such a case as R1 resection, despite the lack of residual tumor noted at resection.

Deeper discussion is merited regarding Masaoka stage III tumors, in which invasion of other mediastinal structures is present. A thymoma invading pericardium is readily resectable (even by MIS), whereas a thymoma involving great vessels is challenging (even when performed open); yet both are equally categorized as stage III.⁶ This discrepancy has driven staging systems to make this distinction.⁷ This study shows stage III tumors are less likely to be treated by MIS approaches. Therefore, although the matched cohorts may have included 29 stage III thymomas in the open group and 26 in the MIS group, it is likely that the invasive pattern of these tumors differed dramatically.

These and other unmeasured confounders are the critical biases for which propensity-score matching cannot account. Although the subgroup analyses did compare approach for stage I to II tumors and size threshold of 4 cm, they cannot fully mitigate this shortcoming. Although one might conclude that randomized studies could better answer this question, that is entirely dependent on whether surgeons feel safe enough to randomly allocate patients who fall outside the traditional criteria for MIS resection. Although they cannot determine causation and cannot eliminate selection bias, nonrandomized studies such as this one

provide an important bridge to future randomized studies; they do this by demonstrating that surgeons can safely enroll patients in randomized studies, even those falling outside the traditional criteria for MIS resection.

In the end, is MIS an acceptable approach for all patients with stage I to III thymoma? Guidelines have concluded this cannot be determined due to a lack of long-term outcome data.⁸ This study, with a median follow-up of 36 months, suffers the same limitation (although a future repetition of the analysis would help). Certainly, the short-term outcomes appear promising; in fact, one could infer that MIS approaches may be better, on the basis of shorter median length of stay by about 1 day. Assuming this is a clinically important difference, one should remember that use of enhanced recovery after surgery protocols can result in equivalent length of stay in open and MIS groups, a finding replicated for various types of surgery.⁹ This is especially pertinent for this study, because sternotomy is a well-tolerated approach. On the basis of our experience and that of others, enhanced recovery after surgery practices can allow patients undergoing either open or MIS thymectomy to go home on postoperative day 1 to 2. Yang and colleagues² have appropriately highlighted the possibility that this “improvement” in length of stay may actually represent the c-intervention of enhanced recovery after surgery practices.⁹ In this light, this study supports the notion that either approach may be used, after first having considered

the characteristics of the tumor, the surgeon experience, and the choice of the appropriately informed patient.

References

1. Haniuda M, Kondo R, Numanami H, Makiuchi A, Machida E, Amano J. Recurrence of thymoma: Clinicopathological features, re-operation, and outcome. *J Surg Oncol*. 2001;78:183-8.
2. Yang C-FJ, Hurd J, Shah SA, Liou D, Wang H, Backhus LM, et al. A national analysis of open versus minimally invasive thymectomy for stage I to III thymoma. *J Thorac Cardiovasc Surg*. 2020;160:555-67.e15.
3. Girard N, Mormex F, Van Houtte P, Cordier JF, van Schil P. Thymoma: a focus on current therapeutic management. *J Thorac Oncol*. 2009;4:119-26.
4. Burt BM, Yao X, Shrager J, Antonicelli A, Padda S, Reiss J, et al. Determinants of complete resection of thymoma by minimally invasive and open thymectomy: analysis of an international registry. *J Thorac Oncol*. 2017;12:129-36.
5. Hess NR, Sarkaria IS, Pennathur A, Levy RM, Christie NA, Luketich JD. Minimally invasive versus open thymectomy: a systematic review of surgical techniques, patient demographics, and perioperative outcomes. *Ann Cardiothorac Surg*. 2016;5:1-9.
6. Dettterbeck FC, Nicholson AG, Kondo K, Van Schil P, Moran C. The Masaoka-Koga stage classification for thymic malignancies: clarification and definition of terms. *J Thorac Oncol*. 2011;6(7 Suppl 3):S1710-6.
7. In: Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, et al., eds. *AJCC cancer staging manual*. 8th ed. New York: Springer International Publishing; 2017.
8. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN guidelines): thymomas and thymic carcinomas v2. 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf. Accessed July 2, 2019.
9. Martin LW, Sarosiek BM, Harrison MA, Hedrick T, Isbell JM, Krupnick AS, et al. Implementing a thoracic enhanced recovery program: lessons learned in the first year. *Ann Thorac Surg*. 2018;105:1597-604.