

Four percent matters

Waël C. Hanna

Division of Thoracic Surgery, McMaster University, Hamilton, ON, Canada

Correspondence to: Waël C. Hanna, MDCM, MBA, FRCSC. St. Joseph's Healthcare Hamilton, 50 Charlton Ave. E, Juravinski Tower, suite T2105 F, Hamilton, ON L8N4A6, Canada. Email: hannaw@mcmaster.ca.

Provenance: This is an invited Editorial commissioned by Section Editor Dr. Jie Dai (Department of Thoracic Surgery, Shanghai Pulmonary Hospital, Tongji University, Shanghai, China).

Comment on: Flores RM, Nicastrì D, Bauer T, *et al.* Computed Tomography Screening for Lung Cancer: Mediastinal Lymph Node Resection in Stage IA Nonsmall Cell Lung Cancer Manifesting as Subsolid and Solid Nodules. *Ann Surg* 2017;265:1025-33.

Submitted Jul 02, 2017. Accepted for publication Jul 04, 2017.

doi: 10.21037/jtd.2017.07.44

View this article at: <http://dx.doi.org/10.21037/jtd.2017.07.44>

Studies like the International Early Lung Cancer Action Program (I-ELCAP) (1) have revolutionized our understanding of early-stage lung cancer and its management. In their recent article (2), Flores and colleagues challenge us with the notion that sublobar resection without mediastinal lymph node sampling may be an adequate treatment for clinical stage IA non-small cell lung cancer (NSCLC). Drawing on the database of the I-ELCAP project (1), they were able to stratify patients into two propensity matched cohorts who received mediastinal lymph node resection (MLNR) and those who did not. A solid statistical and survival analysis methodology failed to demonstrate any significant difference in overall survival between patients who received MLNR during their operation, and those who did not. The authors conclude that subsolid nodules less than 30 mm in diameter, and peripheral solid nodules less than 20 mm in diameter should be treated with sublobar resection without MLNR.

In support of their conclusion, the authors cite the results of multiple studies, including the American College of Surgeons Oncology Group (ACOSOG) Z0030 (3), which demonstrated that mediastinal sampling is equally effective for the treatment of T1 cancers, which are N0 or have non-hilar N1 disease, when compared to mediastinal lymph node dissection. However, a closer look at this paper prompts some caution in the interpretation of the results. Although imaging algorithms were strictly enforced in the I-ELCAP study, the clinical management and treatment decisions were left entirely to the discretion of the treating surgeon. Hence, surgeons got to select which patients they

operated on and which patients they sent for radiation. Among the patients who were operated, the surgeons got to choose whether the mediastinum was staged preoperatively, who received lobectomy or sublobar resection, and who received MLNR or not. Although the authors tried to adjust for this selection bias by propensity matching, it is not clear how the propensity score was calculated and which variables were used in this calculation (beyond the vague mention of imaging findings, baseline factors and type of surgery). Because one could only adjust for the confounders that are known in the dataset, it would be safe to assume that perhaps there still exists a significant selection bias in this sample.

The authors acknowledge another limitation of this study, namely the lack of standardization of the MLNR technique. They do point out, however, that the frequency of lymph node metastases in their sample (regardless of how highly selected it might be), is very low and equal to that which was found in the ACOSOG Z0030 trial (3), which used heavily standardized MLNR protocols that bordered on the non-applicable. The authors do not overstate their conclusion, but are bold enough to challenge the dogma that MLNR should be strictly performed in every lung cancer operation.

Should we start doing wedge resections without mediastinal node sampling for small subsolid or peripheral solid tumors? Those of us who argue “No”, will state the 20% upstaging to N1 disease (4), and that this will be missed if we do not perform anatomical resections that include the intralobar lymph node basins and the

mediastinal nodes. Recent work on sentinel node biopsies has shown that the prevalence of occult nodal disease is not trivial, and that this translates into poorer disease-free survival (4,5). Those of us who argue “Yes”, will state that the real prevalence of upstaging to N1 disease is 4% or less, and this doesn’t justify the risk of MLNR. While the debate rages on, I would urge us to consider this question from the point of view of the 4% of patients who will have missed nodal disease. Would they have wanted to know that they had lymph node metastases that were potentially curable with adjuvant chemotherapy?

Acknowledgements

None.

Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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Cite this article as: Hanna WC. Four Percent Matters. *J Thorac Dis* 2017;9(8):2286-2287. doi: 10.21037/jtd.2017.07.44