

# Competing risks analysis in the prognostic assessment of patients undergoing lung resection

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*Provenance:* This is an invited article commissioned by the Section Editor Ming-Hui Zhang (Department of Medical Oncology, Harbin Medical University Cancer Hospital, Harbin, China).

*Response to:* Taylor LJ, Maloney JD. Moving beyond disease-focused decision making: understanding competing risks to personalize lung cancer treatment for older adults. *J Thorac Dis* 2017;9:8-12.

Submitted Mar 01, 2017. Accepted for publication Mar 03, 2017.

doi: 10.21037/jtd.2017.03.144

**View this article at:** <http://dx.doi.org/10.21037/jtd.2017.03.144>

## Invited response

Based on a competing risk analysis of cause-specific mortality, we recently (1) demonstrated that noncancer-specific mortality is a significant competing event against lung cancer-specific mortality in patients who have undergone curative intent lung resection for stage I non-small cell lung cancer (NSCLC). We have demonstrated that elderly patients  $\geq 65$  years of age had a higher noncancer-specific cumulative incidence of death (CID) compared with lung cancer-specific CID for as long as 2.5 years after resection. This early-phase mortality was relatively higher in patients  $\geq 75$  years of age compared with patients 65 to 74 years of age. We also demonstrated that, in contrast with lobectomy, sublobar resection is associated with a lower incidence of severe postoperative morbidity and, in particular respiratory events, is perhaps influenced by the selection bias of choosing sublobar resection for patients with diminished pulmonary function and higher comorbidities. Taylor and Maloney highlighted the potential contribution of our study results in personalizing treatment decisions for elderly patients through consideration of competing risks in those patients (2). Our published results are derived from an analysis of patients treated at a single institution in the United States. In order to broadly apply our approach of using competing risks analysis in the prognostic assessment of patients who will undergo surgical resection

for early-stage NSCLC we will compare our study cohort with publications that were focused on cohorts of NSCLC patients from developing nations and Asian countries. We also emphasized the need to consider cardiopulmonary and functional status rather than only age when deciding between sublobar resection and lobectomy for elderly patients.

A recent analysis of global cancer incidence and mortality demonstrated that lung cancer ranked highest in the elderly patient population compared with other cancers; this is based on data from 32 cancer groups in 195 countries between 1990 and 2015 (3). Our study demonstrated the importance of competing risks, cause-specific mortality analysis that is based on individual patient preoperative variables such as smoking status, comorbidity, and pulmonary function. While applying this analysis to patient cohorts from developing nations and Asian countries, differences in smoking status, air pollution, and incidence of chronic lung comorbidities, such as chronic obstructive lung disease (COPD) and tuberculosis, should be taken into account (4). Clinicians should also consider the potential differences in “aging” including the physical and social disparities between elderly patients in developed and developing countries. In our study, COPD and smoking history were independent risk factors for severe postoperative morbidity and lung cancer-specific mortality,

respectively. Previous studies have suggested the importance of smoking cessation for reducing morbidity following lung resection and reducing the incidence of recurrence. The potential prognostic impact of these factors should be taken into consideration during analysis of outcomes for patients from developing nations and Asian countries. Despite the possible influence of these specific variables, the overall utility of competing risks analysis for these populations was demonstrated in the *Journal of Thoracic Diseases* by George *et al.* who evaluated mortality as a competing event to readmission in patients who were treated for COPD (5).

There is a growing number of elderly patients who are undergoing sublobar resection (6) despite concerns regarding its higher risk of recurrence when compared with lobectomy (7). There are currently two ongoing, large, multi-institutional, prospective randomized trials (CALGB140503 and JCOG0802) assessing outcomes of sublobar resection versus lobectomy of small ( $\leq 2$  cm) tumors. To address the role of sublobar resection, particularly in elderly patients, a multi-institutional prospective randomized trial in China is currently recruiting patients to examine intentional use of sublobar resection versus lobectomy in patient  $\geq 70$  years of age (8). We are eagerly awaiting the results of these ongoing trials and we believe they can add to the knowledgebase for personalizing surgical resection for individual lung cancer patients based on cancer-specific and noncancer-specific risk assessments.

In our study we focused on patients with stage I NSCLC who have not undergone induction therapy. To date, the majority of stage I NSCLC patients have been treated with surgery alone. To identify the prognostic factors that are influenced solely by surgical resection it is important to avoid the confounding effects of chemotherapy or radiotherapy, which can affect patient perioperative outcomes, especially in elderly patients. One limitation of our study was that we grouped different histologic types and subtypes within a single uniform stage I NSCLC cohort. Increasing evidence points to the fact that histologic subtypes influence outcomes (9) and can determine the type of surgical resection (10). Although histologic information during our study period was available post-resection, with increasing use of image-guided core biopsies the utility of preoperative biopsies may extend beyond diagnosis and can influence outcomes.

In summary, age alone should not deter use of lung resection for patients with stage I NSCLC. A cause-specific risk assessment that focuses on competing risks based on individual patient medical histories can help identify the

appropriate surgical candidates and help clinicians make proper treatment decisions, particularly for elderly patients.

### Acknowledgements

We thank Alex Torres of the Memorial Sloan Kettering Thoracic Surgery Service for his editorial assistance.

### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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**Cite this article as:** Eguchi T, Adusumilli PS. Competing risks analysis in the prognostic assessment of patients undergoing lung resection. *J Thorac Dis* 2017;9(4):E395-E397. doi: 10.21037/jtd.2017.03.144