CORRESPONDENCE

Lung Transplantation for Lung Cancer
To the Editor:

We read with interest the article by Ahmad and associates [1] regarding the utility of lung transplantation for lung cancer, which concluded that lung transplantation was a reasonable option for patients who did not benefit from medical or surgical therapies to control their cancers. However, we would like to raise some questions that require further clarifications.

Lung cancer was earlier considered an absolute contraindication for lung transplantation, but study has begun to focus on the benefits for long-term survival after lung transplantation for bronchoalveolar carcinoma (BAC) [2, 3]. However, lung transplantation is not supported for patients with other types of bronchogenic carcinoma owing to high risk of cancer recurrence [2]. Ahmad and colleagues [1] comment that “lymph node metastases did not preclude survival.” Despite this, does N1 or N2 disease as a marker of tumor metastasis actually not predict the outcome of transplanted patients? Perrot and coworkers [3] have demonstrated that patients with stage II or III bronchogenic carcinoma had worse prognosis than patients with stage I, and usually succumb to cancers due to extensive tumor recurrence. Thus, lymph node invasion in these patients causes a clinical dilemma of recipient selection and greatly affects actual survival.

Patients with suspicious N2 nodes should be investigated by mediastinoscopy as discussed by Ahmad and colleagues [1]; N2-positive lung cancer is generally considered a contraindication to surgical therapy, even though surprisingly reasonable survival was achieved in this study. Endobronchial ultrasound–fine-needle aspiration in addition to mediastinoscopy can facilitate the detection of N1 disease; N1 disease rather than N2 disease as the cutoff for exclusion of lung transplantation may turn to optimal selection of patients. Thus, N2 disease as the cutoff is not convincing.

Whether patients with bronchogenic carcinoma benefit from lung transplant should be confirmed by a large prospective trial. However, several ethical issues related to lung transplant should be resolved. Patients with bronchogenic carcinoma receiving lung transplants only accounted for 0.1% of the total number, and waiting-list mortality is commonly ascribed to donor scarcity; therefore, how to allocate the limited donors will be discussed before the trial is launched. Should patients not amenable to surgical resection (no N2 disease) receive lung transplant or chemotherapy-based treatment? Transplant is inadequate for some patients who can benefit largely from chemotherapy. Furthermore, whether chemotherapy should be performed after lung transplant remains undecided. In addition, it is still unknown whether postoperative immunosuppressive regimens can increase the risk of cancer relapse, and that requires the proof of further research.

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References


Reply
To the Editor:

We read with interest the letter by Mao and colleagues [1]. Our study of the small number of lung transplants for lung cancer is an exploratory analysis of a rare practice; it demonstrates what is possible, not what is probable [2]. Our study demonstrated that: (1) several centers were able to select patients with lung cancer for transplantation that survived longer than would have been expected for advanced lung cancer, (2) invasive lung cancer and lymph node metastases did not preclude patients from surviving longer than expected for advanced lung cancer, and (3) the average life expectancy of patients transplanted for lung cancer was on par with lung transplantation for other indications. The first and last observations support earlier findings by other research teams. The fact that invasive cancer was not a “deal breaker” for posttransplant survival, as many clinicians in the field currently suspect, is a novel concept, and a critical one as pathologists may become increasingly reluctant to call tumors completely free of invasion. We recognize the limited availability of lungs for transplant, but the ethics surrounding this topic are complex. Fair and just organ utilization is most likely to be achieved by a comprehensive understanding of all patients that could benefit, rather than closing a resource to a particular cohort, which would be similar to not telling a particular group of passengers on a sinking boat where to find the lifeboats because the lifeboats are getting full. In conclusion, this work was not meant to serve as the leading argument in favor of the practice of lung transplantation for lung cancer, rather the beginning of the conversation to consider this practice fully.

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References


Management of T2N0 Esophageal Cancer
To the Editor:

We read with interest the recent paper by Martin and colleagues [1] on the role of radiotherapy for T2N0 esophageal cancer, suggesting that surgery alone might be adequate for this subset of patients. There is reasonable evidence-based consensus [2] on the need for neoadjuvant therapy in localized esophageal cancer but most trials addressing this issue have very few
patients with T2N0 disease. Nonavailability of individual patient data metaanalysis makes a subgroup analysis of these patients impossible. The management of patients with T2N0 esophageal cancer is controversial [8], and the data from the Multinativity study (almost equal proportion of patients received multimodality treatment and surgery alone) demonstrate this ambivalence in clinicians’ minds. The current National Comprehensive Cancer Network guidelines [4] recommend neoadjuvant chemoradiation followed by surgery as the “preferred option” for these patients. Considering that the overall benefit of neoadjuvant chemoradiation over surgery alone is modest [2], it seems likely that the benefit, if any, for early node-negative disease is likely to be marginal. The lack of accurate preoperative staging, infrequent and inconsistent use of endoscopic ultrasonography and positron emission tomography–computed tomography scan in the neoadjuvant randomized trials makes subgroup analysis of these trials unreliable for T2N0 disease. With this background, the study by Martin and colleagues [1] describing the real-life data drawn from the Surveillance Epidemiology and End Results (SEER) database gains added importance.

While we could continue to argue about the inherent drawbacks of a nonrandomized comparison and the differential stage determination (clinical in patients getting neoadjuvant treatment versus pathologic in patients operated on upfront) of the SEER database, it appears clear that the surgery-alone group had at least equivalent overall and cancer-specific survival as the group that received (chemo)radiation in spite of several factors (younger age, more lower-third cancers) favoring the radiation group. We recognize the challenges in conducting randomized trials on multimodality treatment in this subgroup alone; however, we urge a prospective data collection of endoscopic ultrasonography–staged T2N0 patients treated either with multimodality treatment or surgery alone to get more definitive answers. Presently, with strong evidence that endoscopic ultrasonography in experienced hands has high accuracy with T and N stage [5], it appears reasonable to offer surgery alone for patients with endoscopic ultrasonography–staged T1,2N0 disease. This strategy would help avoid the toxicity of neoadjuvant chemoradiation for the vast majority of patients with early node-negative esophageal cancer.

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Reply
To the Editor:

We appreciate the comments of Dr Pramesh and colleagues [1] regarding our recent publication examining the role of radiation for patients with T2N0 esophageal cancer [2]. They have succinctly summarized some of the controversies and clinical difficulties regarding the management of this subset of patients with esophageal cancer. We believe that our article has added strength to the argument that upfront surgery does not compromise long-term outcomes, although it is still important to acknowledge characteristics of the Surveillance, Epidemiology and End Results cancer registry database that limit the ability to draw definitive conclusions regarding patient care. As Dr Pramesh has suggested, prospective data are required to guide treatment better. Considering both the relative uncommon nature of this stage of disease and the difficulties inherent in enrolling patients in multi-institution randomized surgical trials, creating a registry to examine treatment of these patients is probably the optimal method for studying this topic. We encourage all esophageal surgeons to participate in order to obtain the best patient outcomes while potentially avoiding the morbidity and cost of treatment that does not provide benefit.

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