

Anatomic segmentectomy for non-small cell lung cancer: can we believe the hype?

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Since first being intentionally used for treatment of small peripheral lung cancers by Jensik *et al.*, anatomic segmentectomy has garnered much attention when being considered as treatment for stage I non-small cell lung cancer (NSCLC) (1). Lobectomy has long been considered the standard of care. Support for this notion can be traced back to the findings of the Lung Cancer Study Group (LCSG) published in 1995 which revealed a 3-fold increase in local recurrence rates and decreased survival in patients who had undergone sublobar resection rather than lobectomy (2). However, controversy over these conclusions stemmed from the study's incorporation of wedge resections in the sublobar group leading many to question whether the same results would hold true when comparing lobectomy to true anatomic segmentectomy. The LCSG study results were further supported by analysis done with the Surveillance Epidemiology and End Results (SEER) database [1998-2007] by our group which showed statistically significant better survival outcomes in patients undergoing lobectomy compared to segmentectomy (3). Nonetheless, anatomic segmentectomy still has gained enthusiasm by many surgical groups. Many investigators have reported equivalent outcomes for anatomic segmentectomy and lobectomy with stage I NSCLC. It is clear that additional studies are needed to define the merits of anatomic segmentectomy for early stage NSCLC. Definitive answers in this area can't come fast enough when one considers the recent recommendations of CT screening from the National Lung Screening Trial where detection of more early stage peripheral tumors are on the horizon (4).

One such recent study aimed at improving our understanding of the potential merits of segmentectomy is

entitled "Recurrence and survival outcomes after anatomic segmentectomy versus lobectomy for clinical stage I non-small-cell lung cancer: a propensity-matched analysis" by the Pittsburgh group also compare segmentectomy to lobectomy for peripheral stage I NSCLC (5). In a highly selected group of small, peripheral, clinically node-negative NSCLC, Landreneau *et al.* reported the largest propensity score matched study of 312 pairs with a mean follow-up of 5.4 years, there was similar 5-year survival (54% *vs.* 60%; $P=0.258$) between the segmentectomy and lobectomy groups. Five-year freedom from recurrence showed no statistical significance as well between both groups (70% *vs.* 71%) (5). Lastly, multivariable analysis showed anatomic segmentectomy was not found to be an independent predictor of recurrence or overall survival (OS).

In a smaller, but important propensity matched retrospective review, Okada and colleagues evaluated 634 patients who had undergone lobectomy and segmentectomy for clinical T1N0M0 stage IA lung adenocarcinoma, Okada *et al.* was able to propensity score match 100 pairs with variables adjusted for age, gender, tumor size, maximum standard uptake value (SUV_{max}), and tumor location. They found that OS (94.8% *vs.* 93.3%) and 3-year recurrence free survival (RFS) (90.2% *vs.* 91.5%) were comparable after undergoing segmentectomy and lobectomy for stage IA lung adenocarcinoma (6).

Should these studies lead us to believe that segmentectomy should succeed lobectomy as the gold standard for treating peripheral stage I NSCLC? The safe answer is not yet. In a review of a large administrative database, we have demonstrated that lobectomy confers a significant survival advantage (3). Currently, two prospective

studies (CALGB-140503 in USA and JCOG0802/WJOG4607L in Japan) are underway to compare these two treatment modalities. With these important trials near completion, it may be premature to come up with a definitive conclusion favoring segmentectomy. The more complete answer is there are many factors to take into consideration regarding the utility of anatomic segmentectomy. Due to the variability of patients and their disease, the success of segmentectomy, like any treatment, begins with obtaining comprehensive insight into the clinical picture to identify whether it is the right procedure for them. Can the patient tolerate resection of an entire lobe? Is the lung nodule due to metastatic disease from another primary? Is the tumor confined to a single segment? Can one obtain an appropriate segmental margin to prevent a local recurrence? Landreneau *et al.* argues that lobectomy is not always the answer for peripheral stage I and actively points out that all of these questions are intimately bound to the decision-making of treating these patients and their peripheral stage I tumors. We need to keep in mind however, until the randomized studies are completed, lobectomy is the standard by which we compare outcomes in these patients.

Since the publication of the LCSG study, many of these favorable criteria have been identified to alleviate the fear of recurrence after anatomic segmentectomy. Clinical characteristics such as age >80, cardiopulmonary insufficiencies, and a metastatic lung lesion have been instances where anatomic segmentectomy was the more beneficial option (2,7). These identified circumstances favor segmentectomy due to the increased healthy lung parenchyma left behind after resection. With more lung functional lung parenchyma postoperatively, patients should in theory have improved pulmonary function and higher quality of life when comparing anatomic segmentectomy to lobectomy. However, these theories cannot be supported by this study as the main scope of Landreneau *et al.* was the OS and RFS. Much evidence also suggests that tumor size and location are amongst the most important variables when even considering anatomic segmentectomy. Many studies indicated tumors <2 cm in diameter confined in a discrete segmental boundary are amendable to complete resection with adequate margins after segmentectomy. Adequate margins were identified to be a pathologic margin >1 cm or a margin to tumor diameter ratio >1 (7). Landreneau *et al.*'s results show that under these circumstances, anatomic segmentectomy can produce results that are not statistically significantly different from that of lobectomy for their

highly selective population.

With all of this in mind, it is important to remember that lobectomy is not being replaced by anatomic segmentectomy. Landreneau and colleagues state that the results of their study are strictly geared towards small stage I peripheral tumors that are confined to a single segment. Ultimately, the most important intraoperative goal is to obtain clear, generous margins of resection with accurate intraoperative pathologic nodal staging. These are important points to stress especially with the emergence of enthusiasm for nonsurgical image-guided ablative and focused radiotherapeutic approaches. Though these new technologies offer reduced morbidity associated with lung resection surgery, they fail to accomplish a R0 resection or systematic nodal staging which may lead to an increase in recurrence. Moreover, though these treatment modalities are less invasive, they include their own risks of local lung injury that can lead to negative consequences such as progressive radiation pneumonitis, fibrosis, and ultimately a loss of pulmonary function.

Prospective analysis comparing segmentectomy and lobectomy will ultimately be needed to definitively identify the equivalence of both treatment modalities with one another. While the CALGB-140503 in the United States and JCOG0802/WJOG4607L in Japan is near completion, Landreneau *et al.* offers the best current insight into the potential merits of anatomic segmentectomy. We believe their study is not suggesting the replacement of lobectomy as the gold standard, but rather highlighting a possible alternative surgical viable surgical option that is patient-specific. The results indicate that when these clinical and oncologic circumstances are strictly adhered to, anatomic segmentectomy has the potential to be a viable option. We all eagerly await completion and analysis of the prospective trials to further define the current standard in the surgical treatment of early stage NSCLC.

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References

1. Jensik RJ, Faber LP, Milloy FJ, et al. Segmental resection for lung cancer. A fifteen-year experience. *J Thorac Cardiovasc Surg* 1973;66:563-72.
2. Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small

- cell lung cancer. Lung Cancer Study Group. *Ann Thorac Surg* 1995;60:615-22; discussion 622-3.
3. Whitson BA, Groth SS, Andrade RS, et al. Survival after lobectomy versus segmentectomy for stage I non-small cell lung cancer: a population-based analysis. *Ann Thorac Surg* 2011;92:1943-50.
 4. Whitson BA, D'Cunha J. The National Lung Cancer Screening Trial: the ripple effect begins? *Semin Thorac Cardiovasc Surg* 2010;22:274-5.
 5. Landreneau RJ, Normolle DP, Christie NA, et al. Recurrence and survival outcomes after anatomic segmentectomy versus lobectomy for clinical stage I non-small-cell lung cancer: a propensity-matched analysis. *J Clin Oncol* 2014;32:2449-55.
 6. Okada M, Mimae T, Tsutani Y, et al. Segmentectomy versus lobectomy for clinical stage IA lung adenocarcinoma. *Ann Cardiothorac Surg* 2014;3:153-9.
 7. Schuchert MJ, Pettiford BL, Keeley S, et al. Anatomic segmentectomy in the treatment of stage I non-small cell lung cancer. *Ann Thorac Surg* 2007;84:926-32; discussion 932-3.

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