

Recovery of lung function after segmentectomy versus lobectomy for early-stage lung cancer

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Surgery is the principal treatment for early stage lung cancer. Curative surgical resection of lung cancer not only needs to adequately remove all areas of malignant tissue without leaving any microscopic disease behind but also needs to provide adequate lymph node sampling for accurate staging to guide further adjuvant therapy. This primary goal of surgery, however, is sometimes in conflict with the patient's quality of life or technical operability. Removal of lung tissues invariably leads to a loss of lung function. Given the fact that lung cancer often occurs among smokers who may have chronic obstructive pulmonary disease, it is not always a simple task to determine if a given patient with lung cancer is an operable candidate and if so, to what extent the lung tissue should be removed. To aim for best possible oncologic outcome, some patients will be determined inoperable because not enough lung tissue can be removed to allow for free surgical margins. Given that surgery is the most well established curative therapy for lung cancer, it is desirable to maximize this opportunity. Over the years, several resection techniques have been developed and established for the treatment of lung cancer including lobectomy and segmentectomy.

Lobectomy, a removal of anatomical lobe of lung, has long been a standard treatment for lung cancer confining to a single pulmonary lobe. Lobectomy can achieve adequate oncologic clearance while leaving reasonable remaining lung function for most patients. Nevertheless, segmentectomy, a lesser resection, has increasingly gained acceptance. Recent retrospective studies have indicated that segmentectomy

can provide a comparable oncologic outcome to lobectomy, particularly for patients with peripheral tumors ≤ 2 cm in diameter (1,2) and one large prospective trial (CALGB 140503) of lobectomy versus lesser resection has just completed accrual of participants. Segmentectomy, despite its technical complexity, has become an attractive alternative to lobectomy due to the belief that it should help preserve lung tissue.

Since there are three to five pulmonary segments in each lobe, removing just one or a few segments will spare the remaining unaffected segments. Segmentectomy entails a deep dissection to the hilum for individual division and ligation of bronchial and vascular structure and is different from a wedge resection, in which lung parenchyma is minimally resected non-anatomically. To date, several early reports have lent support that segmentectomy can spare lung function better than lobectomy (3,4). However, other studies have found that segmentectomy, despite preserving lung tissue, did not really provide functional advantage over lobectomy at all (5,6). The degree of this controversy is reflected by the number of publications on this topic. One systematic review including 16 studies reaches a conclusion that segmentectomy spares lung function better than lobectomy, albeit by a small margin (7).

In a recent study by Nomori and colleagues, that conclusion is corroborated. In addition, the mechanism behind lung function preservation is further elucidated (8). The authors retrospectively compared a cohort of 103 patients who underwent segmentectomy with a matched

cohort of 103 patients who underwent lobectomy. Matching was performed by propensity score which was calculated from age, sex, smoking status, preoperative FEV₁, FEV₁/FVC, and %FEV₁. The aim was to characterize the lobe-specific lung function after surgery. All patients underwent perfusion single-photon emission computed tomography (SPECT)/computed tomography (CT) before surgery as well as 6 months after surgery to assess lung function, not only of the whole lung, but also of the contralateral lung and non-operated lobe. The results showed that, on average, FEV₁ is reduced from baseline by just 5% with segmentectomy compared with 13% with lobectomy. The authors found that, after segmentectomy, the operated lobe still retained about half of its original function. Assessment of contralateral lung revealed that there was a compensatory increase in the function observed, as expected, in both groups. However, assessment of the remaining ipsilateral non-operated lobe showed an unexpected finding. While there was a compensatory increase in lung function observed among patients who underwent segmentectomy, no such increase was observed with lobectomy.

This finding is interesting, providing mechanistic explanation in support of an assertion that lung function is better spared following segmentectomy than lobectomy. The study uses SPECT/CT to quantify lung function both before and after surgery, thus allowing for specific assessment in each pulmonary lobe. Nevertheless, a number of limitations will still need to be taken into consideration. Most importantly, the study was not a randomized controlled trial and, therefore, could still be confounded by any imbalance in the patient characteristics between the segmentectomy group and the lobectomy group. Even though the authors matched the groups using propensity score, there may still be other hidden confounders which might explain the observed finding. In fact, some experts have argued that propensity score technique offers minimal statistical advantage over simpler statistical techniques such as multi-variable regression adjustment (9). Furthermore, since this was a single-institutional study, the finding may not be generalizable to other centers. This is especially relevant as the authors uniformly used a specific segmentectomy technique, whereby the intersegmental plane was cut by electrocautery along the intersegmental vein in shallow lung tissue, then by a stapler in the deep tissue. They rightly suggest that use of surgical staplers for parenchymal dissection, a commonly employed technique, may limit re-expansion of the remaining lobe. As a result, those who employ different segmentectomy approaches

may not achieve a similar result. Finally, since the post-operative SPECT/CT was performed only at a 6-month time point, the findings may not be extrapolated to other time points especially the crucial perioperative period. In fact, some authors have reported that the recovery of lung function following segmentectomy does not occur fully at one month after surgery and the loss of lung function from segmentectomy is as severe as those of lobectomy when measured at that point in time (10). With these limitations in mind, what then could explain the preferential gain in lung function of the ipsilateral non-operated lobe occurring exclusively after segmentectomy but not after lobectomy?

The authors have provided two potential explanations. First, compensatory lung growth could have already occurred in the lobectomy group before the lung surgery, thus resulting in no further growth after surgery. This is possible because the median tumor size was larger in the lobectomy group than the segmentectomy group: 3.2 (range, 1.4 to 5.0) *vs.* 1.8 (range, 1.1 to 2.5) cm. Second, there may be a greater anatomic excursion of the ipsilateral non-operated lobe after lobectomy than after segmentectomy. Kinking of bronchial or arterial structure may occur more preferentially with lobectomy than segmentectomy and this can result in ventilation or perfusion impairment. Another alternative explanation, however, might be that the greater compensatory expansion of the contralateral lung in the lobectomy group (1.30+0.37l) reduced the opportunity for growth in the ipsilateral non-operated lobe compared to the segmentectomy group (1.23+0.33l). We also need to keep in mind that the FEV₁ calculations were based on SPECT imaging which delineates perfusion but not ventilation.

Regardless these observations have an important implication. Among patients who may be eligible to either segmentectomy or lobectomy, segmentectomy may be preferred when multifocal pathology is suspected. By this way, lung function can be preserved as much as possible for potential future necessary oncologic treatment which may include multiple resections or radiotherapy (11). It is important to address that most experts would agree that segmentectomy is safe and oncologically reasonable when tumor size is not greater than 2.0 cm and located in the peripheral lung because local recurrence is significantly increased with tumor size larger than 2 cm (12-14). In this regard, the results of the CALGB 140503 trial will be illuminating. The study by Nomori and colleagues was not statistically powered to detect any possible difference in oncologic outcomes such as survival and cancer recurrence.

Until then, segmentectomy is not for everyone who may otherwise be eligible for lobectomy. Furthermore, for those patients who have such impaired lung function that lobectomy cannot be carried out safely, it remains unclear if segmentectomy can be recommended because it takes time for lung function to recover fully following segmentectomy.

In conclusion, the study by Nomori and colleagues gave an insightful and useful look into the mechanism of lung recovery following segmentectomy versus lobectomy. It becomes clearer now why segmentectomy preserves lung function better than lobectomy.

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Footnote

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

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