



Sublobar resection for lung cancer: anatomic or non-anatomic?

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The article by Altorki and colleagues (1) published in *Journal of Thoracic oncology* reported the optimal method of sublobar resection (SR). SR includes anatomic segmentectomy (AS) and wedge resection (WR). Although AS has traditionally been considered superior to WR, there has been no comparative study so far. The objective of their study was to compare oncological outcomes following AS and WR in patients presenting with clinical stage I non-small cell lung cancer. They hypothesized that for cT1N0 non-small cell lung cancer (NSCLC), WR and AS are associated with comparable oncologic outcomes.

As for history of standard procedure for lung cancer, Cahan suggested that pneumonectomy with regional lymph node dissection should be a routine procedure in 1951 (2). Then in 1960, he reported the first 48 cases that successfully underwent lobectomy with regional lymph node dissection, which was called “radical lobectomy” (3). Since then, this procedure was universally accepted and has remained a standard surgery for lung cancer. Although Jensik reported their 15-year successful experience of segmentectomy for lung cancer patients in 1973 (4), the use of sublobar resection as definitive management of NSCLC has been a controversial issue. In 1995, Lung Cancer Study Group (LCSG) reported the results of the only randomized trial comparing sublobar resection with lobectomy for stage IA NSCLC patients (5). They observed a 75% increase in recurrence and a 50% increase in cancer death in the patients undergoing sublobar resection, compared to those in the patients undergoing lobectomy. This is the reason why lobectomy has remained a standard lung cancer surgery for more than a half century since Cahn’s successful report of “radical lobectomy” in 1960.

With the recent development of the CT scanner, however, the number of very early-stage lung cancer showing ground-glass opacity (GGO) on CT is rising as well, and a new therapeutic strategy for nodal dissection has been required. Proposals of sublobar resection for small-size lung cancer less than 2 cm have been undertaken in some previous reports. Many retrospective studies of sublobar resection have already been undertaken for stage IA NSCLC patients. Although these were non-randomized study, Okada (6) and Koike (7) conducted the comparative study between intentional sublobar resection and standard lobectomy in patients with tumors 20 mm or less in diameter. They showed no significant difference in survival between two groups and suggested that sublobar resection was acceptable operation for small-sized lung cancer. The significance and role of sublobar resection for subsolid tumor have become important so far, and then it will become more important to determine the optimal method of SR, that is, anatomic (AS) or non-anatomic resection (WR).

Altorki and colleagues (1) retrospectively reviewed prospective database of 289 patients underwent SR (129 AS and 160 WR) for cT1N0M0 NSCLC during 2000-2014 in New York Presbyterian Hospital - Weill Cornell Medical College. Poor performance status, and limited cardiopulmonary reserve were the primary indications for SR in 76% of WR patients and in 62% of AS patients ($P=0.011$). Patients undergoing AS were more likely to have nodal sampling/dissection [123 (95%) *vs.* 112 (70%), $P<0.001$], more stations sampled (3 *vs.* 2, $P<0.001$), and more total nodes resected (7 *vs.* 4, $P=0.001$). However, they found no difference in local recurrence [15 *vs.* 14, $P=0.68$]

or 5 year DFS (51% *vs.* 53%, $P=0.7$) between patients treated by either WR or AS, both in the multivariate model as well as in the propensity matched analysis. They concluded that WR and AS were comparable oncologic procedures for cT1N0M0 NSCLC patients. Although AS is associated with a more thorough lymph node dissection, this did not lead to a survival benefit in this population.

These findings are of interest since data from the LCSG randomized trial showed that locoregional recurrence after WR was two-fold higher than that after AS. The results that AS should be the preferred option for SR were supported by recent large population-based studies suggesting. Smith reported the results of evaluating a large population Surveillance, Epidemiology and End Result-Medicare registry (SEER) database (8). They found that WR were associated with inferior survival compared to AS. However, survival advantage of AS over WR in the SEER database is probably due to different patient selection criteria as well as inadequate wedge resections with sub-optimal resection margins and insufficient or no nodal assessment. Whether WR and AS were comparable oncologic procedures for cT1N0M0 NSCLC patients or not has been still controversial issue so far.

Japan Clinical Oncology Group (JCOG) has conducted a cohort study (JCOG0201) evaluating correlation between radiological and pathological findings in stage I adenocarcinomas. With pathologic non-invasive adenocarcinoma defined as those with no lymph node metastasis or vessel invasion, radiological non-invasive lung adenocarcinoma was defined as those with a consolidated maximum tumor diameter to tumor diameter ratio (C/T ratio) of less than 0.5 (9). Currently, a prospective, randomized, multi-institutional phase III trial for small-sized (≤ 2 cm) lung cancer patients is being conducted by Cancer and Leukemia Group B (CALGB140503) to determine the effectiveness of an intentional sublobar resection for small-sized peripheral tumors. Similar phase III study is also being conducted by Japan Clinical Oncology Group (JCOG0802), comparing lobectomy *vs.* segmentectomy for small-sized (≤ 2 cm) tumor with more than 0.5 C/T ratio. JCOG has already accumulated planned number of patients and now following the patients. JCOG is also conducting other two prospective multi-institutional phase II trials regarding the sublobar resection for GGO-dominant type tumors. One is JCOG0804, wide wedge resection for non-solid GGO lesion less than 2cm, and the other is JCOG1211, segmentectomy for part-solid GGO lesion with less than 0.5 C/T ratio and 2.1–3.0 cm in

tumor diameter. However, no large-scale randomized trial comparing AS with non-anatomic WR, which is technically much easier than AS, for small-sized NSCLC has been conducted so far.

Despite the fact that patients undergoing AS were more likely to have nodal sampling/dissection, and more LNs retrieved than patients undergoing WR in the present study, it did not lead to an improvement in survival. This is consistent with the results of the ACOSOG Z0030 trial comparing lymph node sampling with systematic nodal dissection in patients with T1-2 N0-1 NSCLC with no difference in survival between the two groups (10).

Since the clear evidence regarding the survival benefit of sublobar resection for lung cancer patient is lacking so far, lobectomy should be an appropriate therapy for medically operable lung cancer patient at the moment. Abovementioned randomized trials will clearly define the role of sublobar resection in patients with stage I patients. If these study showed that SR could be a standard procedure for selected stage IA patients, next step would be comparing AS and WR. As the number of early-stage peripheral lung cancers is increasing, and a certain number of patients are with multifocal small lesion, the choice of surgical procedure, that is, lobectomy, AS or WR, should be tailored to each case in the future.

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