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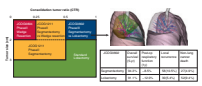

POTENTIAL BENEFITED POPULATION FOR SUBLOBAR RESECTION

To the Editor:

In 1995, a study conducted by North American Lung Cancer Study Group compared sublobar resection and lobectomy for patients with T1N0 non–small cell lung cancer (NSCLC), and its results consolidated the status of standard lobectomy.[1] In recent years, sublobar resection for the treatment of early-stage NSCLC has aroused widespread and ongoing controversy and discussion. In the JCOG0201 study, tumor size $\leq$3 cm and consolidation tumor ratio (CTR) $\leq$0.5 showed an excellent prognosis and potentially suitable for sublobar resection.[2] Based on this result, several clinical trials, including JCOG0802, JCOG0804, and JCOG1211, were designed to explore the potential benefited population for sublobar resection.[3] At the 101st American Association for Thoracic Surgery annual meeting in 2021, Nakagawa and colleagues[3] reported the incredible result of JCOG0802. This phase 3 trial enrolled the patients with invasive peripheral NSCLC (maximum tumor diameter $\leq$2 cm and CTR >0.5) who were randomly assigned to lobectomy or segmentectomy. The 5-year overall survival was 94.3% for segmentectomy and 91.1% for lobectomy. However, several issues remain unclear.

First of all, why did the segmentectomy group have greater local recurrence proportion (10.5% vs 5.4%) but better prognosis? It must be noted that 52 (63%) of 83 patients in the lobectomy group died of other cancer including second lung cancer, or non-neoplastic diseases compared with 27 (47%) of 58 patients in segmentectomy arm. Therefore, does the advantage of prognosis in segmentectomy come from the benefit of other cancer or nontumor factors? The lung cancer–specific survival should be considered as one of the evaluation indicators. Under the premise of similar baseline clinicopathologic characteristics, the segmentectomy arm had better protection of respiratory function than lobectomy (decreased forced expiratory volume in 1 second, 6 months: 10.4% vs 13.1%, 1 year: 8.5% vs 12.0%, $P < .001$, respectively), which may be reflected in reduced death from non-neoplastic diseases. In particular, the study included 38% (422) of patients $\geq$70 years, and the protection of lung function was probably particularly important. Further analysis of the prognostic differences between the 2 groups at different ages is necessary. Is lobectomy more suitable for younger patients whereas segmentectomy more suitable for older patients? Can we speculate that in early lung cancer, the benefit of lobectomy is mainly reflected in tumor recurrence, whereas the benefit of segmentectomy is manifested in nontumor diseases? What's more, considering some of patients received adjuvant therapy, it should be disclosed that the genetic mutations situations of patients with or without local recurrence and whether they received other treatments, for example, second surgery, targeted therapy, radiotherapy, etc. Second, 553 (50%) patients had the nodules with CTR = 1.0. It was generally believed that solid components were a factor of poor prognosis[4] and lobectomy was the optimal option for the solid nodules. In the JCOG 0201 study, patients with tumor size $\leq$2 cm and CTR >0.5 undergone lobectomy showed 84.1% 10-year overall survival.[2] The median follow-up was 7.3 years in JCOG 0802. It is not clear whether the survival advantage of segmentectomy will persist if follow-up time is extended to 10 years or longer. Last but not least, JCOG0802 does not demonstrate the specific pathologic types and subtypes of 2 arms. Considering that 88% (968) of them were lung adenocarcinoma, it remains unknown whether segmentectomy can be applied to nonadenocarcinoma NSCLC, or whether segmentectomy can maintain a survival advantage for solid, papillary, or micropapillary-subtyped lung adenocarcinoma. Besides, since visceral pleural invasion, vascular invasion,[5] tumor spread through air space,[6] and margin are the high-risk factors for recurrence of stage I lung adenocarcinoma, people need the information in JCOG0802 about pathologic features, resection margins, and margin/tumor size rate. The survival analysis of specific lung segments, the numbers and stations of lymph nodes, and proportion of metastasized lymph nodes also should be disclosed.

Before we change the long-term standard treatment strategy for T1N0 NSCLC, further analysis is necessary to identify the best potential benefited population for segmentectomy.

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