Lobar or sublobar resections are safe procedures for management of early lung cancer

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Despite the advancement in chemotherapy, radiotherapy, and biological therapy, surgery still remains the best treatment with curative intent for early stage non-small cell lung cancer (NSCLC). Among the different type of resections, lobectomy with radical lymph node resections is the strategy of choice, when anatomically and clinically feasible, based on the results of the randomized controlled trial (RCT) from the Lung Cancer Study Group (LCSG) (1). This study was published more than 30 years ago, but over the years no other RCT studies compared sublobar versus lobar resection for early stage NSCLC. However, in the last decades the growing number of screening programs using low-dose high resolution computed tomography (CT) scan have increased the detection of small NSCLC, and the 8th TNM edition proposed by the International Association for the Study of Lung Cancer (IASLC) group reclassified the T1 factor in three sub-categories as T1a (≤1 cm), T1b between (>1 to ≤2 cm), and T1c (>3 cm) (2). Thus, there is the growing perception among thoracic surgeons that lobectomy could be an extended resection for management of small NSCLC (≤2 cm), and that intentional sublobar resection could be indicated as treatment of choice for these tumors (3-10). In theory, a lung sparing resection (i.e., segmentectomy or wedge resection) compared to lobectomy could reduce the perioperative morbidity and mortality, but preserving the same oncological validity considering the small diameter of the tumor (≤2 cm) and the lack of lymph nodes involvement (N0 stage).

To evaluate this issue, Altorki *et al.* performed a post-hoc analysis of an international, randomised, phase III trial (CALGB/Alliance 140503) (11). This trial prospectively enrolled patients with T1aN0M0 NSCLC (staged according to the 7th edition of TNM staging system) who were randomized to undergo sublobar resections (segmentectomy or wedge resection) or lobectomy. The authors compared the 30- and 90-day mortality, and perioperative morbidity between two study groups, supposing that sublobar resection could be associated with lower mortality and complications rates than lobectomy. A total of 697 patients were included in the analysis, of which 347 undergoing lobectomy, and 340 receiving sublobar resections including segmentectomy and wedge resection. The overall rate of 30- and of 90-day mortality was 0.9% (n=6/697) and 1.4% (10/697), respectively. Comparison of sublobar *vs.* lobar resection regarding 30-day (0.6% *vs.* 1.1%) and 90-day mortality (1.2% *vs.* 1.7%) showed no significant difference. Complications of any grade occurred in 193/337 (54%) patients after lobectomy, and in 172/337 (51%) after sublobar resections. However, overall major complications (Grade 3 or Grade 4) occurred only in 15% of patients. No significant difference was found between two study groups, also when the complications were stratified according to the 5 Grades of the Common Terminology Criteria for Adverse Events version 4.0.

First, this study clearly confirmed that lobectomy and sublobar resections were associated with a low rate of perioperative mortality in line with more recent studies. Furthermore, no significant difference was found between 30- and 90-day mortality in two study groups. Operative mortality after lobectomy has been decreasing over the past 50 years. Before 1970 the mortality rate after lung cancer resection was 10% and it reduced to 3% in the 1980s (12,13). Several papers in the last 10 years have reported a mortality of ≤2% after lobectomy, while the National Lung Cancer Screening Trial (NLST) showed that mortality after lobectomy was 1% in patients participating in low-dose CT scan screening programs (14). Similar results were obtained by the study from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) that reported a mortality rate of 3.13% for open lobectomy, and of 1.19% for video-assisted thoracoscopic surgery (VATS) lobectomy (15).

Second, sublobar group compared to lobectomy presented higher rate of adverse events of grade 3 or worse (15% *vs.* 14%), despite not significant. These results could be surprising, and in contrast with the hypothesis of the same authors who supposed lower rate of complications after sublobar resection than after lobectomy, and with previous evidences that recommended sublobar resection as alternative to lobectomy in high risk NSCLC patients due to lower morbidity and mortality rates (16-21). However, in the Altorki's study all patients presented normal cardio-respiratory conditions, and the choice of performing sublobar resection instead of lobectomy or viceversa was dictated by randomization and not by patient's clinical conditions. Thus, since all patients were fit to receive both type of resections, it could explain the low perioperative mortality, and morbidity not only in sublobar group but also in lobectomy group. Conversely, previous studies (16-23) included elderly and patients with severe preoperative comorbidities and it could explain a higher post-operative morbidity and 90-day mortality especially when a more extended resection as lobectomy was performed.

Third, one of criticisms moved against the LCSG study (1) was that the authors did not differentiate in their analysis segmentectomy from wedge resection, but considered in the same group these different types of resection. Despite segmentectomy is an anatomical resection with a different oncological validity than wedge resection, also in the Altorki's study these two types of resection were considered together. Thus, future studies that differently evaluate wedge resection from segmentectomy are needed.

In conclusion, the present paper shows that lobar and sublobar resections are associated with a low peri-operative morbidity, and mortality without significant difference among different type of resections in physically and functionally fit patients with early stage NSCLC. However, it does not provide any information on the survival that remains crucial to define the oncological validity of sublobar resection *vs.* lobectomy. Thus, we need to wait the publication of the primary (comparison of disease free survival between two subgroups) and of the secondary endpoints (comparison of overall survival, recurrence, and expiratory flow rates 6 months postoperatively between two subgroups) of CALGB/Alliance 140503 study and of the other ongoing RCT study from Japan Clinical Oncology Group (JCOG 0802) (24) to establish whether intentional sublobar resection could be a valuable alternative to lobectomy for management of early stage lung cancer.

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Footnote

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

References

1. Ginsberg RJ, Rubinstein LV; Lung Cancer Study Group. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Ann Thorac Surg 1995;60:615-22.
2. Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2016;11:39-51.
3. Martin-Ucar AE, Nakas A, Pilling JE, et al. A case-matched study of anatomical segmentectomy versus lobectomy for stage I lung cancer in high-risk patients. Eur J Cardiothorac Surg 2005;27:675-9.
4. Okada M, Koike T, Higashiyama M, et al. Radical sublobar resection for small-sized non-small cell lung cancer: a multicenter study. J Thorac Cardiovasc Surg 2006;132:769-75.
5. Kodama K, Higashiyama M, Okami J, et al. Oncologic

Outcomes of Segmentectomy Versus Lobectomy for Clinical T1a N0 M0 Non-Small Cell Lung Cancer. Ann Thorac Surg 2016;101:504-11.
6. Altorki NK, Yip R, Hanaoka T, et al. Sublobar resection is equivalent to lobectomy for clinical stage 1A lung cancer in solid nodules. J Thorac Cardiovasc Surg 2014;147:754-62; Discussion 762-4.
7. Nakamura H, Kawasaki N, Taguchi M, et al. Survival following lobectomy vs limited resection for stage I lung cancer: a meta-analysis. Br J Cancer 2005;92:1033-7.
8. Fan J, Wang L, Jiang GN, et al. Sublobectomy versus lobectomy for stage I non-small-cell lung cancer, a meta-analysis of published studies. Ann Surg Oncol 2012;19:661-8.
9. Bao F, Ye P, Yang Y, et al. Segmentectomy or lobectomy for early stage lung cancer: a meta-analysis. Eur J Cardiothorac Surg 2014;46:1-7.
10. Cao C, Chandrakumar D, Gupta S, et al. Could less be more?-A systematic review and meta-analysis of sublobar resections versus lobectomy for non-small cell lung cancer according to patient selection. Lung Cancer 2015;89:121-32.
11. Altorki NK, Wang X, Wigle D, et al. Perioperative mortality and morbidity after sublobar versus lobar resection for early-stage non-small-cell lung cancer: post-hoc analysis of an international, randomised, phase 3 trial (CALGB/Alliance 140503). Lancet Respir Med 2018;6:915-24.
12. Weiss W. Operative mortality and five-year survival rates in men with bronchogenic carcinoma. Chest 1974;66:483-7.
13. Ginsberg RJ, Hill LD, Eagan RT, et al. Modern thirty-day operative mortality for surgical resections in lung cancer. J Thorac Cardiovasc Surg 1983;86:654-8.
14. Chudgar NP, Bucciarelli PR, Jeffries EM, et al. Results of the national lung cancer screening trial: where are we now? Thorac Surg Clin 2015;25:145-53.
15. Bravo Iñiguez CE, Armstrong KW, Cooper Z, et al. Thirty-Day Mortality After Lobectomy in Elderly Patients Eligible for Lung Cancer Screening. Ann Thorac Surg 2016;101:541-6.
16. Fiorelli A, Sagan D, Mackiewicz L, et al. Incidence, Risk Factors, and Analysis of Survival of Unexpected N2 Disease in Stage I Non-Small Cell Lung Cancer. Thorac Cardiovasc Surg 2015;63:558-67.
17. Okami J, Ito Y, Higashiyama M, et al. Sublobar resection provides an equivalent survival after lobectomy in elderly patients with early lung cancer. Ann Thorac Surg 2010;90:1651-6.
18. Mery CM, Pappas AN, Bueno R, et al. Similar long-term survival of elderly patients with non-small cell lung cancer treated with lobectomy or wedge resection within the surveillance, epidemiology, and end results database. Chest 2005;128:237-45.
19. Fiorelli A, Caronia FP, Daddi N, et al. Sublobar resection versus lobectomy for stage I non-small cell lung cancer: an appropriate choice in elderly patients?. Surg Today 2016;46:1370-82.
20. Okami J, Higashiyama M, Asamura H, et al. Pulmonary resection in patients aged 80 years or over with clinical stage I non-small cell lung cancer: prognostic factors for overall survival and risk factors for postoperative complications. J Thorac Oncol 2009;4:1247-53.
21. 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.
22. Caronia FP, Fiorelli A, Ruffini E, et al. A comparative analysis of Pancoast tumour resection performed via video-assisted thoracic surgery versus standard open approaches. Interact Cardiovasc Thorac Surg 2014;19:426-35.
23. Pezzi CM, Mallin K, Mendez AS, et al. Ninety-day mortality after resection for lung cancer is nearly double 30-day mortality. J Thorac Cardiovasc Surg 2014;148:2269-77.
24. Nakamura K, Saji H, Nakajima R, et al. A phase III randomized trial of lobectomy versus limited resection for small-sized peripheral non-small cell lung cancer (JCOG0802/WJOG4607L). Jpn J Clin Oncol 2010;40:271-4.

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