Lobar or Sublobar Resection, That is the Question

The clinical question

Is there a difference in disease free survival between patients undergoing lobar versus sublobar resection for peripheral stage 1A non-small cell lung cancer (NSCLC)?

AABIP take home message

Sublobar resection is non inferior to lobectomy with regard to disease free survival for peripheral stage T1aN0 NSCLC in patients in whom the absence of metastasis to hilar and mediastinal lymph nodes is pathologically confirmed.

Background

Study Conclusion

In patients with peripheral stage 1A NSCLC, sublobar resection was not inferior to lobectomy with respect to disease free survival. Both groups had similar overall survival

Study Background

In 1995, the lung cancer study group reported increased lung cancer mortality and recurrence in patients undergoing sublobar resection for T1N0 NSCLC as compared to lobectomy in a randomized trial. More recently, a randomized trial in Japan (JCOG0802) showed that anatomical segmentectomy was superior to lobectomy for overall survival over a 7-year period. Segmentectomy was also non inferior to lobectomy for relapse free survival. Given increased detection of small peripheral NSCLC, there is renewed interest in determining the difference in survival and disease recurrence in patients undergoing sublobar resection in lieu of lobectomy.

Current practice / Guidelines

Lobectomy is generally accepted as optimal procedure for early stage NSCLC who are ideal surgical candidates. Sublobar resection has been reserved for patients with small tumors (<2cm) in the periphery of the lung (outer third) or for patients who cannot tolerate a full lobectomy due to compromised lung function, comorbidities or advanced age.

Study Design

Study Design

- **Type of trial:** Multicenter, International, Randomized, non inferiority trial
- **Randomization, blinding, controls:** once intraoperative eligibility was confirmed, patients underwent randomization in a 1:1 ratio to either sublobar or lobar resection on the basis of a permuted block randomization scheme. Further stratification was done

based off tumor size, histology and smoking status. Trial group assignments were not concealed to patients, surgeons, nurses, data managers or statisticians. The choice of type of sublobar resection (segementectomy vs wedge) was at the surgeon's discretion.

- **N:** 697
- **Study groups:** Lobar resection (n=357), sublobar resection (n=340)
- **Settings:** 83 academic and community hospitals in the United States, Canada and Australia
- **Enrollment:** 125 surgeons at 83 institutions enrolled
- **Treatment period:** June 2007 to March 2017
- **Follow up:** 7 years (median)
- **Primary outcome:** Disease free survival (time between randomization and disease recurrence or death from any cause)

Population

Inclusion criteria
Age > 18, presence of solid peripheral nodule <2 cm, presumed or confirmed NSCLC, center of nodule in outer third of lung, tumor location suitable for sublobar or lobar resection, ECOG: 0-2, no malignancy in past three years (except non-melanoma skin cancer, superficial bladder cancer or cervical carcinoma in situ), no prior chemotherapy or radiation for lung cancer, confirmation of N0 status intraoperatively.

Exclusion criteria
Pure ground glass nodule, pathologically confirmed N1 or N2 disease.

Baseline Characteristics
1080 patients were enrolled, of those 697 were randomized after meeting intraoperative criteria. Participants in the lobectomy and sublobar resection group had similar baseline characteristics (age, race, sex, ecog status, smoking status, tumor size and histology)

Interventions

Patients were randomized to either sublobar resection or lobectomy after intraoperative findings confirmed absence of metastatic disease. For patients who underwent sublobar resection, the type of lobar resection and surgical approach was at the discretion of the surgeon.

Outcomes

Primary outcomes:
Sublobar resection was non-inferior to lobectomy (HR-1.01, 90% CI 0.83-1.24) for disease free survival (time between randomization and disease recurrence or death from any cause)

- Sublobar resection (5 year disease free survival was 63.6%, 95% CI 57.9 to 68.6)
- Lobar resection (5 year disease free survival was 64.1%, 95% CI 58.5 to 69.0)

Secondary outcomes:
Overall Survival was similar in sublobar and lobar resection group (HR-0.95, 95% CI 0.72 to 1.26)

- Sublobar resection (5y- 80.3%, 95% CI 75.5 to 84.3)
- Lobar resection (5y-78.9%, CI 74.1 to 82.9)

Locoregional or systemic recurrence: Recurrence free survival was similar in the sublobar resection group and the lobar resection group (HR-1.05, 95% CI 0.80 to 1.39)

- Sublobar resection (5y recurrence free survival 70.2%, 95% CI 64.6 to 75.1)
- Lobar resection (5y recurrence free survival 71.2%, 95% CI 65.8 to 75.9)

Pulmonary function tests: The magnitude of reduction from baseline FEV1 (-6.0 vs -4.0, respectively) and FVC (-5.0 vs -3.0 respectively) was greater for the lobectomy group than the sublobar resection group 6 months after the operation.

Adverse events: None reported.

Article critique

Study Strengths

- This randomized trial was international and included 83 different institutions across three countries.
- The trial allowed for wedge resection and segmentectomy to be included as forms of sublobar resection unlike the recent Japanese trial (JCOG0802) which only compared lobar resection to segmentectomy. This is important as wedge resection is the most commonly practiced form of sublobar resection in North America and Europe.
- This trial also excluded ground glass nodules unlike the Japanese trial which included partial ground glass nodules and had a higher proportion of patients with adenocarcinoma. These part solid nodules tend to be less aggressive than solid nodules which were represented in this study, adding further support to the efficacy of sublobar resection for peripheral stage IA NSCLC.

Study Limitations and Potential for Bias

- The randomization of patients to sublobar or lobar resection could not be concealed from patients, surgeons, nurses, data managers or statisticians introducing the potential for bias.

- The study was not powered to analyze differences in outcomes between wedge resection vs segmentectomy.

Research Question
Is there a difference in outcomes between wedge resection vs anatomic segmentectomy in patients with peripheral stage T1a N0 NSCLC

Funding

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Suggested Reading

1.Ginsberg RJ, Rubinstein LV; Lung Cancer Study Group, Randomized Trial of lobectomy versus limited resection for T1N0 non-small cell lung cancer. Ann Thorac Surg 1995; 60: 615-23
2. 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 2014l 147: 7540764
3. Saji H, Okada M, Tsuboi M et al. Segmentectomy versus lobectomy in small sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomized controlled, non-inferiority trial. Lancet 2022; 399: 1607-17

Article citation

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