Survival outcomes of lobectomy in comparison with segmentectomy in clinical stage I non-small-cell lung cancer: a meta-analysis

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Research article

Keywords: NSCLC; lobectomy; segmentectomy; meta-analysis

Posted Date: September 7th, 2019

DOI: <https://doi.org/10.21203/rs.2.14067/v1>

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Abstract

Background: The gold standard surgical therapy for patients with Clinical stage I non-small-cell lung cancer (NSCLC) is lobectomy with mediastinal lymph node dissection. While, segmentectomy has emerged as an alternative choice with the advantage of fewer postoperative complications. While the acceptance of this procedure still remains controversial, and conflicting results exist in the retrospective trials.

Objectives: The aim of this meta-analysis was to analysis the survival outcomes of Lobectomy in comparison with segmentectomy in treatment of Clinical stage I non-small-cell lung cancer. **Methods:** Computerized literature search was done on the published trials in Pubmed, Embase, Cochrane library databases to June, 2019 to identify clinical trials. Lung cancer-specific survival (LCSS) and overall survival (OS) were measured as outcomes. Statistical analysis was performed in the Meta-analysis Revman 5.3 software.

Results: A systematic literature search was conducted including 7 studies. In this meta-analysis, results indicate that lobectomy confers an equivalent survival outcome compared with segmentectomy.

Conclusion: No significant differences were found in survival outcomes between lobectomy and segmentectomy. Further prospective large-scale, prospective, randomized trials are needed to explore the reasonable surgical treatment for early resectable lung cancer.

Background

Wide-ranging use of low-dose spiral computed tomography (LDCT) and high-resolution computed tomography (HRCT) makes it possible to detect early non-small cell lung cancer (NSCLC) (1). Surgical resection has been accepted as the mainstay therapy for early-stage NSCLC (2).

A randomized controlled trial of the Lung Cancer Study Group showed that lobectomy is the preferred method for clinical stage I NSCLC (3). Although lobectomy along with mediastinal lymph node dissection remains the mainstay of care, some studies have reported the conflicting evidences regarding to the extent of parenchymal resection required for local control of the tumor and disease-free survival (4-5).

Recently, previous reports have shown similar survival with sublobar resection and lobectomy for early-stage NSCLC (6-9). Segmentectomy, as one of the limited resection surgical options, was first reported by Jensik et al (10). A large propensity-matched study demonstrated that compared with lobectomy, patients who underwent anatomic segmentectomy should be accepted as more reasonable and justifiable option than lobectomy in selected cases as the perioperative and oncologic results achieved with less lung tissue and better pre-served pulmonary function (2). Although anatomical segmentectomy have been introduced as an appropriate alternative to lobectomy, controversy still exists due to the lack of randomized trials and patient selection bias in available trials (11).

To deal with the biases inherent in any non-randomized comparison, we analyzed the propensity-matched analysis and randomized clinical trial. The aim of our meta-analysis was to evaluate the survival outcomes between lobectomy and segmentectomy in treatment outcomes of stage I NSCLC patients.

Methods

Search strategy

Two investigators conducted a systematic search of the Pubmed, Embase, Cochrane library up to June 2019 independently, using the MeSH terms and free key words 'lobectomy' or 'segmentectomy' or 'early-stage' or 'stage I' or

'non-small cell lung cancer' with 'propensity' or 'propensity score' or 'propensity match' or 'randomized clinical trial'. The reference lists of eligible studies were also hand-searched to check for additional studies.

Eligibility criteria

Inclusion criteria were articles relating to: (1) the studies are designed as randomized clinical trial or propensity score comparisons compare the lobectomy with segmentectomy; (2) articles that enrolled stage I NSCLC patients; (3) the outcomes of interest were lung cancer-specific survival (LCSS) and overall survival (OS); (4) the full-text literature were only included.

Risk-of-Bias Assessments

The risk of bias for each included study was systematically evaluated by Cochrane Collaboration based on the Cochrane Handbook version 5.1.0, independently assessed by two researchers.

Data extraction

The authors extracted the following information independently from each study and resolved the differences through discussion. A self-designed data extraction table is used to extract content independently: first author's last name, publication year, subject's demographic (subject number and age) and tumor size. The differences are based on consensus.

Statistical analysis

If the study does not provide data on HR or 95% CI, and all available data are in the form of Kaplan-Meier (K-M) curves. Survival data were extracted from amplified K-M curves, according to the methods described by Tierney JF (12).

Heterogeneity in all studies was measured by the I^2 statistic (13). If the heterogeneity assessment is not significant ($I^2 \leq 50\%$), a fixed effect model is used. If the source of heterogeneity is not significant ($I^2 > 50\%$) uncertain, we use a random effects model for further analysis (14). A P value of less than 0.05 was considered to be a statistically significant difference. Statistical analysis was performed in Review Manager version 5.3 software (Revman; The Cochrane collaboration Oxford, United Kingdom). The results of our meta-analysis are shown in forest plots.

Results

Study selection and Characteristics of study selection

A total of 357 studies were retrieved. Eleven publications were evaluated in more detail based on the criteria described in the method, but some publications did not provide sufficient detail on the results of the two methods. Finally, a total of seven trials (2, 4, 15-19) evaluated survival outcomes compared to lobectomy and segmentectomy. The search process is depicted in Figure 1. Table 1 shows the main features of the eligible studies in more detail.

Clinical and methodological heterogeneity

Pooled analysis of LCSS comparing lobectomy versus segmentectomy

The pooled LCSS data did not gain an advantage between the two groups (OR = 0.72, 95% CI = 0.41-1.26, P = 0.25). In other words, neither lobectomy nor segmentectomy has an LCSS advantage (Figure 2).

Pooled analysis of OS comparing lobectomy versus segmentectomy

The pooled results derived from the random-effects model are presented in figure 3. The data showed that there was no benefit comparing lobectomy versus segmentectomy for stage I NSCLC (OR=0.86,95%CI=0.60-1.23, P=0.40) (Fig. 3).

Discussion

Pneumonectomy has been the main treatment for resectable lung cancer in the past 20 years (20-21). Since the introduction of lobectomy in the late 1950s, it has become the surgical treatment of choice for patients with early NSCLC, with reduced morbidity and mortality, and the observed long-term survival after 5 years (22).

Surgery should not only be completely removed, but also have a good quality of life. Surgical treatment of patients may not be common, as evidence suggests that elderly patients with early NSCLC or patients who are intolerant to lobectomy due to poor cardiopulmonary reserve and multiple comorbidities may be beneficial for segmentectomy (19).

In addition, the JCOG team has conducted several promising RCTs to test the effectiveness of segmentectomy to determine if segmentectomy can be a suitable alternative to early stage lung cancer (23-24).

This meta-analysis failed to report a better segmentectomy than lobectomy, and the results were similar between the two groups in terms of OS and LCSS.

To the best of our knowledge, some trials have reported that an in vitro physician's decision and/or patient-related factors may influence the choice of surgery. Preoperative clinical factors may have an impact on the decision to perform accurate mediastinal LN resection, such as clinical stage, patient age, and limited resection.

A study by Smith et al. (25) showed that, based on surveillance, epidemiology and final outcome (SEER) - Medicare registration, segmental resection should be an alternative treatment for limited resection of patients with stage NS NSCLC.

In the Veluswamy study, the study reported differences in elderly patients with different histological subgroups (26). Conversely, for younger patients, resected lobectomy and lobectomy are preferred. Cao's meta-analysis suggests that "intentional selection" and "compromise" may influence the difference in prognosis between the two surgical approaches (27). Lungectomy can be chosen for young patients, and for older patients, resection should be more appropriate.

In addition, patients undergoing complete LN staging are considered to have a good clinical status, so lobectomy is planned. However, patients with poor medical conditions are more likely to be scheduled for a segmentectomy, which may result in laminectomy with comparable OS and LCSS and lobectomy in both.

Therefore, unbalanced baseline characteristics may result in false positive results. Since the number of LNs examined depends on the pathology report, further RCTs need to focus on the effect of the regional LN range on the difference in prognosis between the two surgical treatments (28).

In addition, due to the retrospective nature of all included studies, imbalances in baseline demographic and clinical characteristics, prejudice still exists, which may affect the comparison of outcomes of interest. Therefore, it shows that better design studies have stronger statistical power, which is essential for comparing the survival outcomes of segmentectomy and lobectomy.

Conclusions

In conclusion, our study showed that segmental resection and lobectomy resulted in similar local recurrence-free survival or overall survival in patients with clinical stage I NSCLC. From a survival perspective, further randomized controlled

trials will enter “personalized treatment,” which will benefit patients from subtypes, which can be instructive for driving treatment decisions while accepting acceptable adverse events.

Abbreviations

non-small-cell lung cancer	NSCLC
Lung cancer-specific survival	LCSS
overall survival	OS
low-dose helical computed tomography	LDCT
high- resolution computed tomography	HRCT
Kaplan-Meier	K–M
Surveillance, Epidemiology and End Results	SEER

Declarations

Conflict of Interest

The authors declare there is no conflict of interest existed in this study.

Declarations

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and material: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests: There is no competing interest.

Funding: No funding was received for this study.

Authors' contributions: Jian Feng and Yan-Yue Han have made substantial contributions to conception and design of the study, written the manuscript; Yue Wang and Xiu-Yu Wu earched literature, extracted data from the collected literature and analyzed the data; Jian Feng revised the manuscript; All authors approved the final version of the manuscript.

Acknowledgements: None.

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Tables

Table 1 Characteristics of the eligible studies

Study year	No. of patients		Age(Mean)		Sex(Male)		Tumor size(Mean)	
	Segmentectomy	Lobectomy	Segmentectomy	Lobectomy	Segmentectomy	Lobectomy	Segmentectomy	Lobectomy
Landreneau R-J 2014	312	312	68.5	68.4	139	144	2.2	2.2
Alfonso Fiorelli 2016	35	138	/	/	/	/	/	/
Whitson BA 2011	581	13892	/	/	320	6974	/	/
Ken Kodama 2015	69	69	/	/	33	32	/	/
M. Roman 2018	64	64	/	/	/	/	32.4	24.6
Moon M-H 2018	809	809	67.8	67.9	278	276	14.2	14.4
Xiao Qu 2017	1146	1146	/	/	452	449	/	/

Figures

Figure 1

PRISMA flow chart of selection process to identify studies eligible for pooling

Figure 2

Pooled analysis of LCSS comparing lobectomy versus segmentectomy

Figure 3

Pooled analysis of OS comparing lobectomy versus segmentectomy

Supplementary Files

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