

Survival Outcomes of Lobectomy in Comparison With Segmentectomy in Clinical Stage I Non-small-cell Lung Cancer: a Meta-analysis

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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. However, 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 using 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.

Introduction

The widespread use of low-dose helical computed tomography (LDCT) and high-resolution computed tomography (HRCT) have made it possible to detect early stage non-small cell lung cancer (NSCLC) (1). Surgical resection has been accepted as the mainstay therapy for these patients (2).

The randomized controlled trial by the Lung Cancer Study Group stated that lobectomy was the approach of choice for clinical stage I NSCLC (3). Although lobectomy along with mediastinal lymph node dissection remains the mainstay of care, previous studies have reported the conflicting evidences regarding to the extent of parenchymal resection, which is required for local control of the tumor and disease-free survival (4–5).

Recently, previous studies have shown similar survival with sub-lobar 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 in each included study were evaluated based on Cochrane handbook version 5.1.0 for Systematic Reviews by Cochrane Collaboration by two investigators independently

Data extraction

Two authors independently extracted the following information from each study—differences were settled through discussion. A self-designed data extraction form was used to independently extract contents: first author's family name, year of publication, demography of subjects (number of subjects and age) and tumor size. Disagreement was resolved by consensus.

Statistical analysis

If the study provided no the data of HRs or 95% CIs, and all the available data were 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). Fixed-effect model was used if the assessment of heterogeneity was insignificant ($I^2 \leq 50\%$). If the source of heterogeneity was not insignificant ($I^2 > 50\%$) uncertain, we used the random-effect model for further analysis (14). A P value less than 0.05 was considered statistically significant difference. The statistical analyses were performed in the Review Manager version 5.3 software (Revman; The Cochrane collaboration Oxford, United Kingdom). Findings of our meta-analysis were shown in forest plots.

Results

Study selection and Characteristics of study selection

A total of 357 studies were retrieved. Based on the criteria described in the methods, 11 publications were assessed for more detail, but some did not provide enough detail of outcomes of two approaches. Finally, a total of 7 trials (2, 4, 15–19) evaluate the survival outcome of comparing lobectomy with segmentectomy. The search process is described in Fig. 1. Table 1 shows the primary characteristics of the eligible studies in more detail.

Table 1
Characteristics of the eligible studies

Study year	No. of patients		Age(Mean)		Sex(Male)		Tumor size(Mean)(mm)	
	Segmentectomy	Lobectomy	Segmentectomy	Lobectomy	Segmentectomy	Lobectomy	Segmentectomy	Lobectomy
Landreneau R-J 2014	312	312	68.5	68.4	139	144	22	22
Alfonso Fiorelli2016	35	138	/	/	/	/	/	/
Whitson BA 2011	581	13892	/	/	320	6974	/	/
Ken Kodama 2015	69	69	/	/	33	32	/	/
Roman M 2018	64	64	/	/	/	/	32.4	24.6
Moon M-H 2018	809	809	67.8	67.9	278	276	14.2	14.4
Qu X 2017	1146	1146	/	/	452	449	/	/

Clinical and methodological heterogeneity

Pooled analysis of LCSS comparing lobectomy versus segmentectomy

The pooling LCSS data did not achieve advantage between two groups (OR = 0.72,95%CI = 0.41–1.26, P = 0.25). In other words, neither lobectomy nor segmentectomy leads a LCSS advantage (Fig. 2).

Pooled analysis of OS comparing lobectomy versus segmentectomy

The pooled results derived from the random-effects model are presented in Fig. 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 was the mainstay therapy for resectable lung cancer for nearly two decades (20–21). Since the introduction of lobectomy by the late 1950s, it has become the preferred surgical treatment for early stage NSCLC patients with a reduction in operative morbidity and mortality, as well as a result of observed benefits in long-term survival at 5 years (22).

Surgery should not only perform with complete resection, but also achieve a good quality of life. The surgical therapy for patients may not be universal, as evidence suggests that elderly patients with early-stage NSCLC or patients with intolerance to lobectomy due to poor cardio-pulmonary reserve and multiple comorbidities may favor segmentectomy (19).

Moreover, there have been several promising ongoing RCTs by the JCOG group testing the efficacy of segmentectomy to determine whether segmentectomy could be an appropriate alternative treatment for early lung cancer (23–24).

This meta-analysis failed to report the superiority of segmentectomy over lobectomy. In terms of OS and the LCSS, similar results were shown between two groups.

To the best of our knowledge, some trials have reported that individual surgeon's decision and/or patient-related factors that may influence the surgical's choice. Preoperative clinical factors may have effect on the decision to perform accurate mediastinal LN resection, such as clinical stage, patients' age, differences in limited resections.

The study by Smith et al (25) demonstrated that segmentectomy should be the optional treatment for limited resection of patients with stage IA NSCLC according to the Surveillance, Epidemiology and End Results (SEER)- Medicare registry.

In Veluswamy's study, which reported that differences arise in elderly patients with the different histology subgroups (26). Conversely, both segmentectomy and lobectomy could be preferred for younger patients. Cao's meta-analysis demonstrated that "intentionally selected" and "compromised" might have effect on the prognostic difference between two surgical options (27). Lobectomy might be selected for younger patients, whereas segmentectomy should be more adequate for elderly patients.

In addition, patients undergoing complete LN staging were thought to be with a good quality of clinical status and thus scheduled for lobectomy. However, patients with a poor medical condition were more likely to be scheduled for segmentectomy, which may result in that segmentectomy confers a comparable OS and LCSS with lobectomy in both.

Thus, unbalanced baseline characteristics may lead to false-positive results. Since the number of LN examined depends on pathologic reports, further RCTs need to focus on the effect of regional LN scope on the prognostic difference between two surgical treatments (28).

Furthermore, due to all included studies' retrospective nature, imbalance in baseline demographics and clinical characteristics, bias still exist, and this may impact the comparison of interested outcomes. Thus, it indicated that more well-designed studies with greater statistical power would be imperative to compare the survival outcomes of segmentectomy and lobectomy.

Conclusion

In summary, our study shown that segmentectomy and lobectomy have similar lung cancer-specific survival or overall survival rates among patients with clinical stage I NSCLC. From a survival standpoint, as far as we know, large prospective randomized trials on standard lobectomy versus anatomical segmentectomy are on its way, while so far only results on perioperative outcome and quality of life of the European SevLoT1a trial have been published (29). Further RCTs into "personalized therapy" that will benefit patients by subtype, which can be instructive in driving treatment decisions, while conferring with acceptable adverse events.

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:

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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 searched 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.

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Figures

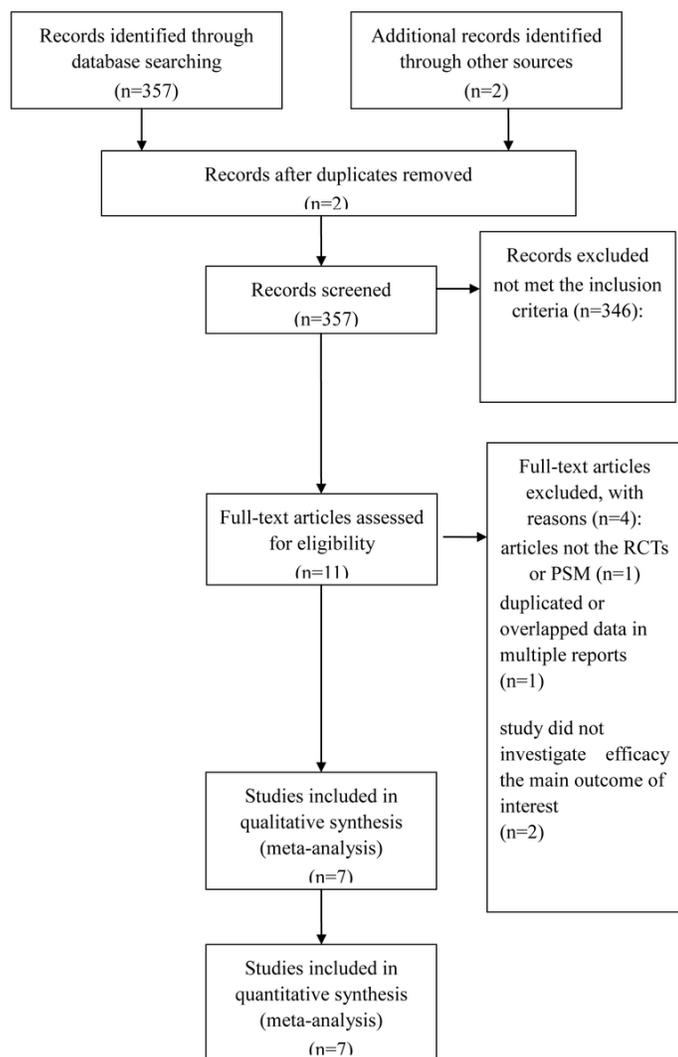


Figure 1

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

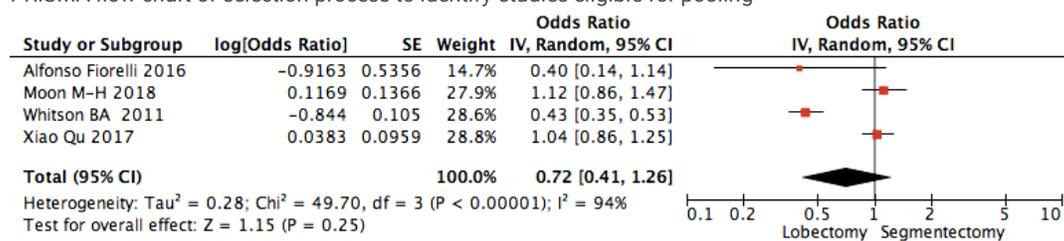


Figure 2

Pooled analysis of LCSS comparing lobectomy versus segmentectomy

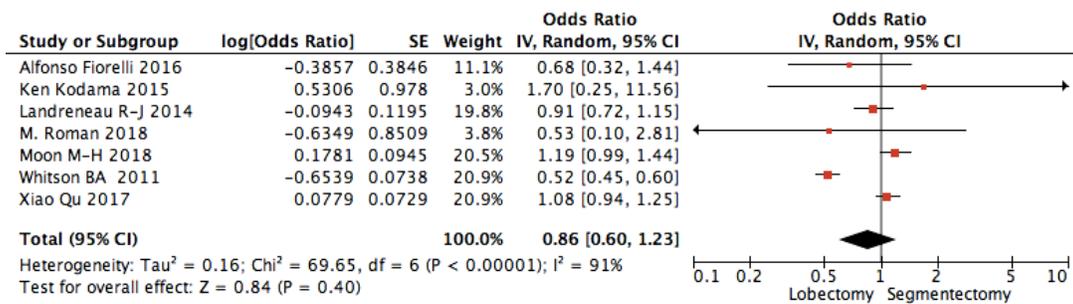


Figure 3

Pooled analysis of OS comparing lobectomy versus segmentectomy