

Original Article

Meta-analysis for curative effect of lobectomy and segmentectomy on non-small cell lung cancer

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Abstract: Objective: To systematically evaluate 5-year survival, local recurrence rate, long-term recurrence rate and complications for lobectomy and segmentectomy in the treatment of NSCLC. Methods: Articles on randomized and non-randomized clinical studies of 5-year survival, local recurrence, long-term recurrence and complications after lobectomy and segmentectomy for treatment of NSCLC. Results: Among the included patients, no difference was found between the two groups in local recurrence. However, the incidence of complication in the segmentectomy group was found to be significantly higher than in the lobectomy group. Conclusion: For treatment of NSCLC, as compared with segmentectomy, suggesting that lobectomy is the preferable method.

Keywords: Lung cancer, segmentectomy, lobectomy

Introduction

With increasing environmental pollution, the incidence of lung cancer has been rising rapidly. Lung cancer is now the most lethal of malignant tumors in the world [1]. The number of new cases of lung cancer diagnosed each year is rising, of which NSCLC accounts for 80% of the total [2].

Surgery has been used to treat lung cancer for over 70 years. During this time, the standard procedure has evolved from pneumonectomy to lobectomy. Currently, many combined therapies and individualized treatment options are available for lung cancer. However, surgery still plays a leading role in the treatment of NSCLC and also in combined therapy for lung cancer, with significant implications for prognosis. The International Association for the Study of Lung Cancer recommends that surgery be used as a major component in combined therapy.

In 1933, Graham [3] performed the first successful left whole lung resection for lung cancer. This was followed by resection of less lung tissue to reduce post-operative mortality and complications, and by segmentectomy. In 1973, Jensik, et al. [4] reported their experience using segmentectomy for the treatment of

early peripheral lung cancer. They found that post-operative rates of survival were 56% and 27% at five and ten years, respectively.

Amid growing controversy over the treatment of stage I NSCLC, the North American Lung Cancer Study Group [5] reported that in a randomized clinical study of stage I NSCLC, local recurrence in patients who underwent limited resection (including segmentectomy and wedge resection) was 3 times that of those who underwent lobectomy; And while total mortality for limited resection increased by 30%, lung cancer-specific mortality increased by 50%. Therefore, lobectomy has become the ideal treatment option for lung cancer and is the major surgical procedure for early-stage disease. Campione, et al. [6] performed segmentectomy and lobectomy for 121 patients with stage IA lung cancer. They found that the median overall survival was 98 months for lobectomy and 104 months for segmentectomy, a statistically insignificant difference. Although lobectomy has many advantages, some healthy tissue is lost during tumor resection [7]. Therefore, it is of great importance to explore more limited surgeries such as wedge resection and segmentectomy for small peripheral lung cancer to minimize the removal of healthy lung tissue.

In this study, we performed a meta-analysis of the differences in curative effects between lobectomy and segmentectomy for NSCLC to assist clinical planning.

Materials and methods

Study selection

Articles reporting studies on lobectomy and segmentectomy for NSCLC published before October 2013 were searched in different databases using keywords described below. For the China Biology Medicine (CBM) database, searches were made in default fields, including titles, abstracts, authors, subject terms, feature words, key words and journal names, using the key phrases NSCLC and lobectomy segmentectomy. For PubMed, articles were retrieved using the search conditions (Randomized Controlled Trial [ptyp] OR Clinical Trial [ptyp]) AND (“non-small cell lung cancer” [All Fields] AND “Lobectomy” [All Fields]) AND (“Segmentectomy” [All Fields]) AND (English [lang] OR Chinese [lang])). For CNKI-China Journal Net, articles were searched with the key phrase NSCLC and lobectomy and segmentectomy.

Literature screening

Articles were selected based on the inclusion criteria: (1) published in or outside China without duplication; (2) experimental design was a randomized controlled trial; (3) the year of study or publication was indicated; (4) sample size clearly described; (5) there were clear standards of diagnosis; (6) study subjects were patients with Alzheimer disease; (7) Study results were reported as comparisons of indicators such as recurrence rate, survival rate, complications, and so on; (8) data were collected scientifically and (9) analyzed scientifically. Articles with the following conditions were excluded: (1) clinical trials that did not provide sources of patients and controls, or were not therapeutic clinical trials, or were not original reports, or did not clearly report patient numbers in study groups; (2) diagnostic criteria for diseases were not clear; (3) involved lung cancers other than NSCLC; (4) animal experiments; (5) data were not collected scientifically; (6) data analysis methods were incorrect or not provided; (7) duplicated article; (8) retrospective analysis; or (9) review articles.

Article review, data extraction and analysis

A double parallel evaluation method was used. Articles were analyzed by two researchers separately and independently to collect information on the following: (1) general information such as names of the first author and date of publication; (2) study design; (3) number of patients enrolled, patient characteristics and treatment outcomes; (4) study findings.

Statistical analysis

The software RevMan 5.0 was used for meta-analysis. Binary data were expressed as RR with 95% confidence interval (CI). Differences were considered statistically significant for $P < 0.05$. Continuous data were expressed as SMD with 95% CI.

Results

Articles included

After initial screening, a total of 184 relevant articles were obtained. 24 review articles, 80 non-clinical studies, 7 retrospective analyses, and 67 articles that were not relevant were excluded after review. Six articles met all the qualifications and were included in our study [8-13].

General information

Table 1 lists general information about the articles we analyzed, including names of authors, date of publication, journal names, study periods, and number of patients included in each study. A total of 2307 patients were included in the six studies, with the number of patients in each study ranging from 83 to 899. Of these, 1511 were in the lobectomy group (Group A) and 796 in the segmentectomy group (Group B). The articles were published between 2012 and 2013, and report on studies that began between 1955 and 2011.

Clinical information

Clinical information in the selected articles is listed in **Table 2**, such as operation time, amount of blood lost, and day of hospitalization, FEV1, DLCO and tumor size. There were four articles [8-10, 12], that reported operation time and amount of blood lost, and four [8, 10,

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Table 1. General information of the included articles

Author	Publication date	Journal	Numbers		Average age		Study period
			Total	Group A/Group B	Total	Group A/Group B	
Hamatake [8]	2012	Interact Cardiovasc Thorac Surg	109	77/32	64 (43-82)		1995-2011
Zuin [13]	2013	Eur J Cardiothorac	83	61/22	68 (50-83)		1995-2010
Soukiasian [11]	2012	J Thorac Cardiovasc Surg	339	266/73		NA	1998-2010
Zhong [12]	2012	Ann Thorac Surg	120	81/39		64.9/63.6	2006-2011
Schuchert [9]	2012	Ann Thorac Surg	757	432/325	67.0	66.2/68.3	2002-2010
Schuchert [10]	2012	Ann Thorac Surg	899	594/305	69.2	68.4/70.0	1999-2010

Note: Group A: Lobectomy; Group B: Segmentectomy.

Table 2. Clinical information in the included articles

Author	Operation time (min)	Estimated blood loss (ml)	Morbidity n (%)		Mortality %		Hospital stay (d)		FEV ₁ (%)	D _{LCO} (%)	Tumor size (cm)
			Total	Group A/Group B	30-d	90-d	Total	A/B	A/B	A/B	
Hamatake [8]	185.7	113.9	15 (10.5)		0						
Zuin [13]			14 (16.9)	8 (12.8)/6 (27.7)							
Soukiasian [11]							5.5/3.3				
Zhong [12]	144/156	190/145	10 (12.3)/5 (12.8)				6.3/6.1	75.1/73.6	77.4/76.1	1.5/1.1	
Schuchert [9]	134	100			1.1	3.0		73.0	65.6		
Schuchert [10]	216/147	291/185	381 (42.4)	272 (45.7)/109 (35.7)	2.2/1.3	4.4/3.6	6/6	88.4/70.8	73.8/62.9	2.5/2.0	

Note: Group A: Lobectomy; Group B: Segmentectomy.

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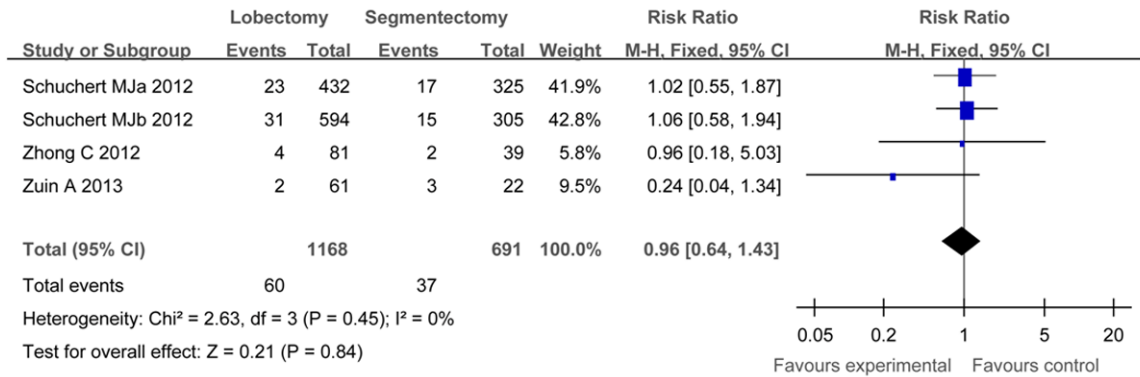


Figure 1. Forest plots for local recurrence of the lobectomy and segmentectomy groups in the studies analyzed.

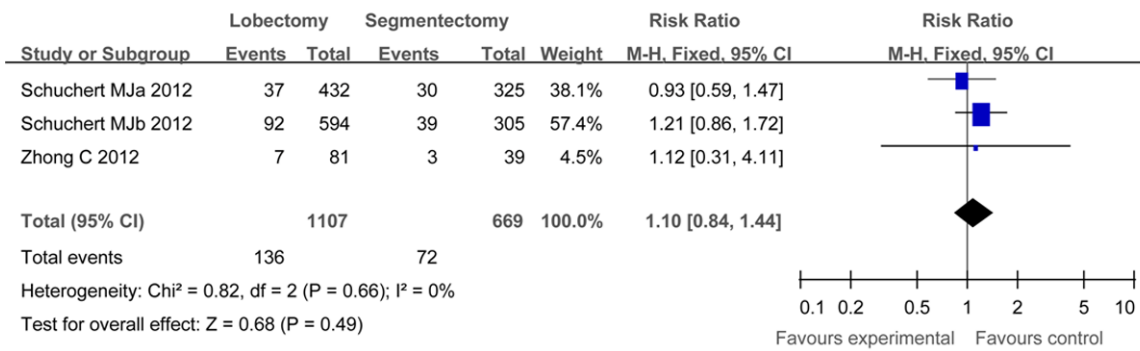


Figure 2. Forest plots for distant recurrence of the lobectomy and segmentectomy groups in the studies analyzed.

12, 13] that reported mortality, of which 2 [10, 13] reported mortalities in Group A and Group B. The mortalities at 30 days and 90 days were reported in two articles [9, 10] and the days of hospitalization in three articles. FEV1 and DLCO were presented in three papers [9, 10, 12] and tumor sizes were described in two reports [10, 12].

Comparison of post-operative indicators between the lobectomy and segmentectomy groups

Local recurrence

The outcomes of local recurrence in the lobectomy and segmentectomy groups were reported in four studies [9-12]. Testing showed that there was no heterogeneity (P = 0.45, I² = 0%) among the studies, so a fixed effects model was used for meta-analysis. The results showed that the combined RR for local recurrence was 0.96 with a 95% CI between 0.64 and 1.43, not

statistically different (Z = 0.21, P = 0.84) between the two groups (**Figure 1**).

Distant recurrence

Distant recurrence in the lobectomy and segmentectomy groups was reported in three (two) articles [9, 10]. Since no heterogeneity (P = 0.66, I² = 0%) was detected, the studies were analyzed using a fixed effects model. The combined RR for distant recurrence was 1.10 with a 95% CI between 0.84 and 1.44. The rate of distant recurrence was not statistically different (Z = 0.68, P = 0.49), between the two groups (**Figure 2**).

5-year survival

5-year survival rates were calculated in three studies [9, 10, 12] for the two groups. We found no heterogeneity (P = 0.53, I² = 0%) among the studies. Analysis using a fixed effects model showed that the combined RR for 5-year survival was 1.03 with a 95% CI of 0.98-1.09, and

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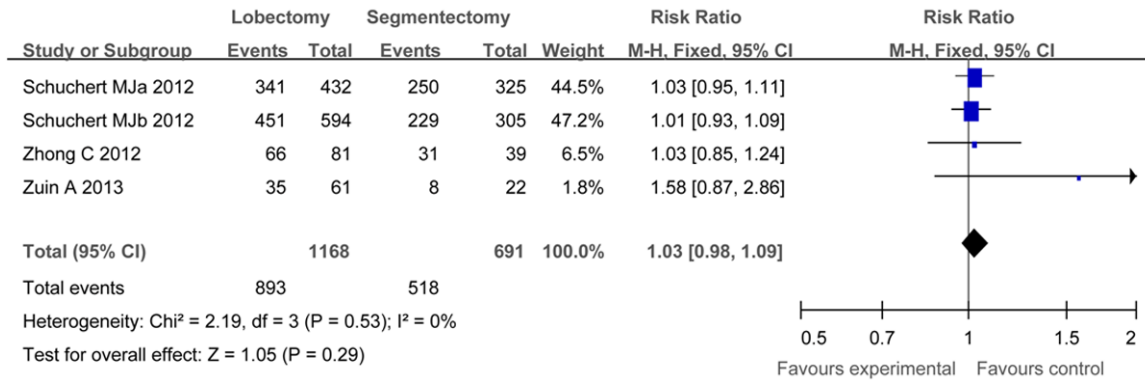


Figure 3. Forest plots for 5-year survival of the lobectomy and segmentectomy groups in the studies analyzed.

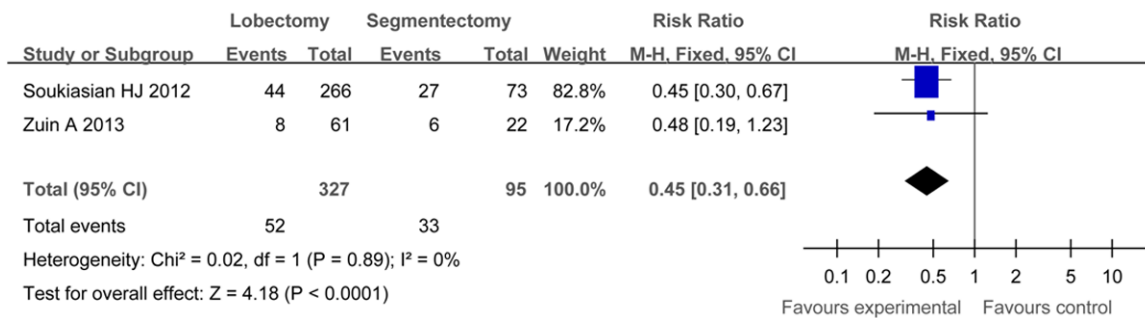


Figure 4. Forest plots showing the incidence of complication in the lobectomy group is significantly higher than that in the segmentectomy group in the studies analyzed.

was not statistically different ($Z = 1.05$, $P = 0.29$) between the two groups (Figure 3).

Complications

In three articles [9, 10, 12], complications in the lobectomy and segmentectomy groups were reported. Testing showed there was no heterogeneity ($P = 0.89$, $I^2 = 0\%$) among the studies. Using a fixed effects model, the combined RR for complications was 0.45 with a 95% CI between 0.31 and 0.66, significantly different ($Z = 4.18$, $P < 0.0001$) between the two groups (Figure 4).

Discussion

Surgery is the main treatment option for NSCLC with a relatively good post-operative prognosis. It is recommended mainly for stage I and II patients with limited lesions and without significant invasion into intrathoracic organs or distant metastasis, as well as for stage III patients who are considered able to tolerate lobectomy. Prevention of micro-metastasis in NSCLC is key to the success of surgical intervention. Early

diagnosis, surgical removal and lymphadenectomy can prolong life in NSCLC patients. Lobectomy is the first line option for patients with perioperative low-risk and tolerance to the procedure. With the improvement of imaging technology, tumors can increasingly be detected at an early stage [14]. In this study, meta-analysis was applied to a number of indicators such as local recurrence, distant recurrence and 5-year survival after lobectomy and segmentectomy, in order to better understand the applicability and efficacy of the two methods.

The results showed that there was no significant difference in local recurrence, distant recurrence or 5-year survival between the two surgeries. However, the incidence of complications was higher in the segmentectomy group than in the lobectomy group.

There were several limitations in our study: (1) differences in gender ratio, tumor size and pathological type distribution between the lobectomy and segmentectomy groups might be sources of heterogeneity and would affect the accuracy of the meta-analysis; (2) in the

included studies, no information was provided on subsequent therapies, such as chemotherapy, which might have affected our results; (3) the included articles were written in English, reporting high quality research in major scientific journals. However, these journals do not publish research written in other languages, thus creating language and publication bias, and limiting the literature included in the present analysis.

In summary, our analysis indicated that local recurrence, distant recurrence, and 5-year survival are similar between lobectomy and segmentectomy for NSCLC. This will be useful in determining treatment of clinically diagnosed NSCLC patients. However, caution should be taken when interpreting our results. More randomized clinical trials are needed to confirm that segmentectomy that keeps more lung tissue can provide patients with better quality of life without compromising mortality, as compared with lobectomy. In the future, limited resection has to be performed on the basis of surgical oncology treatment principles for early-stage patients with sufficient excision margin, after rational assessment of the lung hilum and mediastinal lymph nodes.

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Disclosure of conflict of interest

None.

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