Original Article

Sleeve lobectomy compared with pneumonectomy for operable centrally located non-small cell lung cancer: a meta-analysis

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Background: The purpose of this meta-analysis was to evaluate evidence comparing sleeve lobectomy (SL) and pneumonectomy (PN) in the treatment of non-small cell lung cancer (NSCLC).

Methods: The English literature search was undertaken in January 2018 and included studies dating back to 1996. Comparative studies were identified, evaluating survival, local recurrence, and distant recurrence rates, operative mortality, 30-day mortality, as well as complications. A pooled odds ratio (OR) and 95% confidence intervals (95% CI) were calculated with either the random or fixed-effect model.

Results: A total of 27 studies were identified, with publication dates between 1996 and 2018. These 27 studies included a total of 14,194 patients: 4,145 treated with SL and 10,049 treated with PN. The overall survival was significantly higher in the SL group compared to the PN one at 1, 3, 5 years. In patients with N0 and N1 disease, 5-year survival rates following SL exceeded those following PN. There was no statistically significant difference in the 3-, 5-year overall survival of N2 patients, according to the extent of surgery. The PN group had a higher rate of operative mortality, 30-day mortality and distant recurrence incidence. However, no statistical difference in complications and local recurrence between SL and PN were observed.

Conclusions: SL is an effective treatment option for hilar NSCLC with improved long-term survival compared to PN, with no increase of recurrence rate or postoperative complications. Furthermore, N2 disease is an important factor related to survival, and lymph node downstaging is a favorable prognostic factor.

Keywords: Sleeve lobectomy (SL); pneumonectomy (PN); lung cancer; meta-analysis

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Introduction

Lung cancer is the most common cancer in the world. Surgery remains the standard of care for localized disease, even when the location or extent of the disease needs pneumonectomy (PN) to be radically treated. The treatment of centrally located tumors has always been controversial. Bronchial sleeve resection was introduced in 1947 (1) by Thomas as a means to preserve functional lung parenchyma in patients with compromised pulmonary function; the first sleeve lobectomy (SL) report dates 1954 (1,2) by Allison and Coll. SL was considered as an alternative to PN since then several institutions worldwide (2-7) proposed SL in alternative to PN. Recent studies (8,9) have shown that SL compared to PN can improve lung cancer patients' quality of life also prolonging long-term survival. Most surgeons agree that SL has to be performed with technical precision in order to accomplish surgery complete tumor resection without increasing complications. Some recent studies suggested that sleeve resection should be used routinely in the management of patients with anatomically appropriate hilar tumors, regardless of preoperative lung function (10-13). One criticism to SL over PN is their potential risk for local recurrence. These reports suggest that local recurrence following SL was comparable, and long-term survival was similar to or better than after PN. Unfortunately, most of the reports show that tumor' TNM stage distribution is very different between the two surgical approaches, and comparisons of the survival and local recurrence rates of comparison for the 2 different approaches over an appropriate stage stratification is not easy to perform.

The primary purpose of our research was to compare SL and PN's outcome, focusing on (I) survival rates, (II) local and distant recurrence rates, (III) operative mortality, (IV) 30-day mortality, and (V) type and rate of complications of these procedures, as well as to evaluate whether SL can be accepted as a favorable alternative procedure to PN for patients with non-small cell lung cancer (NSCLC).

Methods

Study selection

Electronic searches were performed of the MEDLINE, EMBASE databases and Cochrane Controlled Trial Register (CENTRAL) until January 2018. We use the following Mesh search headings to search: (sleeve lobectomy), (pneumonectomy), (centrally located lung cancer or lung carcinoma), (comparative study) and [randomized controlled trials (RCTs)] in English literature (*Figure 1*).

Data extraction and quality assessment

Three independent researchers followed the standard procedures for data extraction. The recorded data included: (I) the number of patients, (II) the 1-, 3-, 5-year overall survival, (III) the local and distant recurrence rates, (IV) the operative mortality, (V) the 30-day mortality, and (VI) the complications rates. The quality of all selected documents was ranked following the score of the non-randomized controlled clinical trial quality evaluation standard.

Study selection criteria

Inclusion criteria for this study were as follows: (I) absence of extrapulmonary metastasis; (II) lung function was appropriate for PN; (III) no prior or concurrent other neoplasms; (IV) the patients should be suitable for treatment with either SL or PN, and (V) they should have similar baseline demographics.

Exclusion criteria

The following publication criteria were excluded: abstracts, letters, editorials and expert opinions, reviews without original data, case reports and studies lacking control groups. Studies evaluating unresectable lung cancer or recurrence after lobectomy and those without reported outcomes of interest were excluded.

Surgical technique

The sleeve resection includes the resection of one lobe and the end-to-end bronchial anastomosis. The procedure for SL is the same as for standard lobectomy until the bronchus is isolated. The bronchus needs a single sharp incision divides, and the incision should avoid ragged edges. It should be noted that beyond the proposed line of the transaction, it is taken not to revascularize the bronchus. Several anastomosis techniques are described, mainly depending on the surgeon's expertise and preference; even if any of them have to respect the basic surgical and oncological principles: (I) achieve tumor-free bronchial margins at the frozen section; (II) perform a tension-free anastomosis; (III) try to avoid bronchial mismatch and (IV) proceed with an *en-bloc* resection.

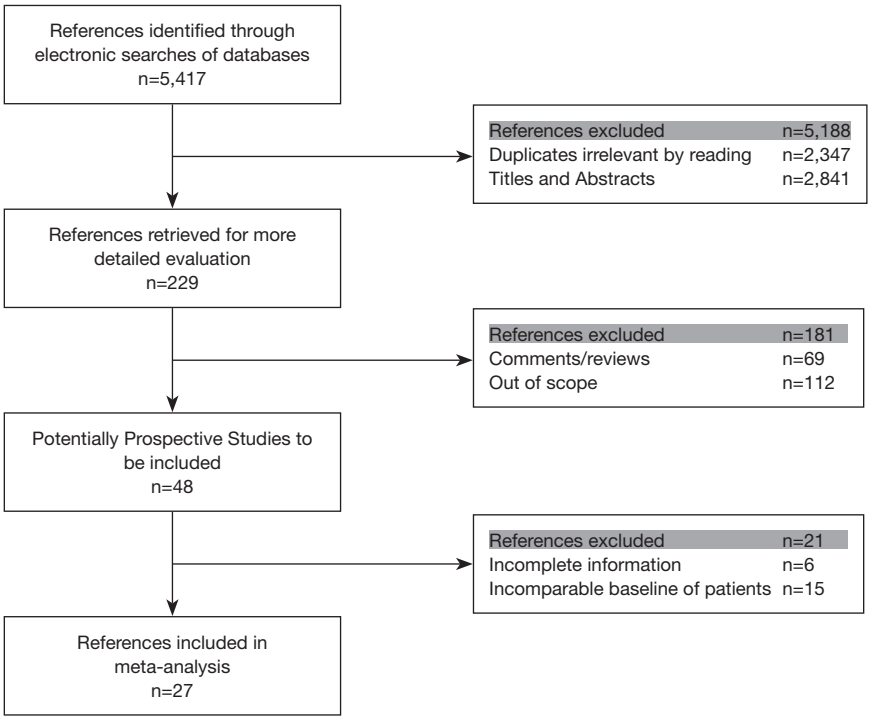

Figure 1 Identification of studies for inclusion.

The anastomosis could be done mainly in four different ways: (I) a running suture for the membranous part and single stitches for the cartilage (knots are tied outwards); (II) double continuous suture; (III) a single continuous suture for the whole anastomosis; (IV) fully interrupted sutures.

No difference in definitive outcome is observed by the different suture techniques.

Before proceeding to the bronchial anastomosis, a pathological frozen section confirmation of neoplastic cells absence in the proximal margin is required. At the end of the suture, the air leakage check is performed by submerging the lung in saline solution and re-ventilating it. If necessary, intra-operative fiberoptic bronchoscopy could be performed to examine the anastomosis directly. Usually, the bronchial anastomosis and the vascular structures are separated by vital pedicled pleura and pericardial fat, to prevent possible fistula. Additionally, a sleeve resection of more than 1 lobe with atypical bronchial resection and reconstruction was terminated as an extended SL by Okada *et al.* The extended procedure could be more complicated than the standard SL, and was classified as Okada type A–D based on the extent of resection and location of anastomose. Generally, lymph-node resection, according to the international guidelines (14) is performed before completing the bronchial anastomosis.

Statistical analysis

Statistical analysis was performed using the software package RevMan 5.1.0. Odds ratio (OR) or mean difference with 95% confidence intervals (95% CI) were calculated for dichotomous outcomes and continuous outcomes respectively. A random-effects and fixed-effect models were done using 'intention-to-treat' analysis. If the results were not different between the two models, the random-effects model was reported, as this model was used for indirect comparisons. If results differed between the two models, both results were reported. Heterogeneity was explored by χ^2 and I^2. I^2<25% and I^2>50% reflect small and large inconsistency, respectively. If P>0.10, these studies were deemed to exhibit homogeneity and a fixed-effect analysis model was used. When P<0.10 and I^2<50%, these studies were considered to exhibit heterogeneity, but the heterogeneity could be accepted, and a fixed-effect analysis model was used too. When P<0.10 and I^2>50%, the heterogeneity was too high to be accepted, and a random-effect analysis model was used. A P value of <0.05 was considered significant.

Subgroup analysis

A subgroup analysis was performed by including patients with pathological N0, N1 and N2 diseases.

Publication bias

We used funnel plots model to check for bias. Asymmetry in the funnel plot of trial size against treatment effect was used to assess the risk of bias.

Results

Description of studies

After screening (*Figure 1*), 27 studies were included. Of 14,194 patients in these 27 studies, 4,145 were allocated to the SL group, whereas 10,049 to the PN group. Patient characteristics and evaluation index are shown in *Table 1*. Selected articles were ranked 7–8 on a quality-indicator scale by Newcastle-Ottawa scale (NOS). Results of the meta-analysis are summarized in *Table 2*.

Operative mortality (operating room and the perioperative period after surgery)

The meta-analysis {13 trials reported this data include 22 [839] and 130 [2,064] patients in SL and PN} showed operative mortality in the PN group was significantly higher than in the SL group (6.30% *vs.* 2.62%) (OR: 0.40; 95% CI: 0.25–0.63; P<0.0001), with no evidence of significant heterogeneity.

30-day mortality

Twelve trials reported data {include 89 [3,195] and 463 [7,890] patients in SL and PN} on 30-day mortality and showed that there was statistical difference between SL and PN relative to 30-day mortality (2.78% *vs.* 5.86%) (OR: 0.55; 95% CI: 0.32–0.96; P=0.04), with specific heterogeneity.

Complications

Concerning to perioperative complications, the meta-analysis (15 trials reported this data) showed that there was no statistically significant difference between the SL and the PN groups (OR: 1.07; 95% CI: 0.87–1.31; P=0.55), with specific heterogeneity.

Local recurrence rates

Fifteen trials reported data on local recurrence. There was no statistically significant difference between the SL and the PN groups (OR: 1.09; 95% CI: 0.72–1.64; P=0.69), with specific heterogeneity.

Distant recurrence rates

Nine trials reported data on distant recurrence rates and demonstrated a higher risk of distant recurrence with PN compared to SL (OR: 0.61; 95% CI: 0.45–0.82; P=0.001), with no evidence of significant heterogeneity (*Figure 2*).

Overall survival rates

One-year survival rates: the meta-analysis (8 trials reported this data) showed that the group of SL experienced a significantly higher survival rate compared to PN (OR: 1.53; 95% CI: 1.31–1.80; P<0.00001), with no evidence of significant heterogeneity.

Three-year survival rates: the meta-analysis (11 trials reported this data) showed that survival in PN group was significantly lower compared to SL (OR: 1.78; 95% CI: 1.47–2.17; P<0.00001), with specific heterogeneity (*Figure 3*).

Five-year survival rates: the meta-analysis (20 trials reported this data) showed that survival in PN group as significantly lower compared to SL one (OR: 1.96; 95% CI: 1.70–2.27; P<0.00001), with specific heterogeneity (*Figure 4*).

Comparison of overall survival rates between the two groups in N0 and N1, N2 (pathological) patients

When survival was evaluated according to the lymph node involvement and the type of resection, the results of 5 trials demonstrated improved 5-year overall survival rates for patients with N0–N1 disease who underwent SL as compared to PN (OR: 2.14; 95% CI: 1.66–2.78; P<0.00001), with specific heterogeneity (*Figure 5*). In patients with N2 disease, there was no statistically significant difference in 3- or 5-year overall survival concerning the type of resection (OR: 1.12; 95% CI: 0.47–2.68; P=0.79; OR: 1.27; 95% CI: 0.65–2.45; P=0.48), with specific heterogeneity.

Publication bias and sensitivity analysis

When no significant findings remain unpublished, the publication bias may exist, thus artificially inflating the

Table 1 Characteristics of included trials

Author, years	Country	Type of study	Treatment	No. of patients	Gender (M/F)	Mean age, years	Stage			
							I	II	III	IV
Gaissert (15), 1996	USA	Cohort	SL	72	56/16	–	29	31	12	0
			PN	56	42/14	–	9	25	21	1
Yoshino (10), 1997	Japan	Retrospective case-control	SL	29	26/3	60.6±8.7†	9	12	8	0
			PN	29	23/6	58.2±9.5†	9	12	8	0
Suen (11), 1999	USA	Cohort	SL	58	41/17	63.7‡	18	28	12	0
			PN	142	81/61	66.5‡	37	46	58	1
Okada (13), 2000	Japan	Retrospective case-control	SL	60	52/8	60.9±9.5†	–	–	–	–
			PN	60	53/7	60.6±9.0†	–	–	–	–
Martin-Ucar (16), 2002	UK	Cohort	SL	38	27/11	65‡	10	16	12	0
			PN	81	62/18	63‡	10	32	36	3
Ghiribelli (17), 2002	Italy	Cohort	SL	38	36/2	65‡	16	10	12	0
			PN	127	102/25	62.4‡	29	43	55	0
Deslauriers (8), 2004	Canada	Cohort	SL	184	152/32	60.0±10.0†	82	72	30	0
			PN	1,046	827/219	60.7±9.4†	164	361	466	55
Kim (18), 2005	Korea	Retrospective case-control	SL	49	44/5	58.7±7.6†	14	20	15	0
			PN	49	46/3	58.1±8.2†	24	13	11	1
Ludwig (19), 2005	Germany	Cohort	SL	116	–	62‡	31	41	44	0
			PN	194	–	59‡	32	52	110	0
Bagan (20), 2005	France	Cohort	SL	66	58/8	60.7±8.2†	40	14	12	0
			PN	151	138/13	58.2±9.6†	35	35	81	0
Lausberg (12), 2000	Germany	Cohort	SL	104	88/16	62.1±11.4†	22	50	30	2
			PN	63	56/7	60.9±11.8†	7	32	21	3
Takeda (21), 2006	Japan	Cohort	SL	62	46/16	61.1±10.2†	26	19	17	0
			PN	110	92/18	59.3±9.6†	24	14	70	2
Jiménez (22), 2006	Spain	Cohort	SL	35	34/1	62‡	–	–	–	–
			PN	220	205/5	62‡	–	–	–	–
Balduyck (23), 2008	Belgium	Cohort	SL	10	–	65.3‡	2	1	7	0
			PN	20	–	63.3‡	3	9	8	0
Melloul (24), 2008	Switzerland	Cohort	SL	69	–	–	–	–	–	–
			PN	78	–	–	–	–	–	–
Parissis (25), 2009	Ireland	Cohort	SL	79	54/25	60.4‡	–	–	–	–
			PN	129	91/38	62.5‡	–	–	–	–
Hanagiri (26), 2010	Japan	Cohort	SL	24	18/6	65.1‡	5	8	10	1
			PN	72	61/11	64.7‡	5	13	50	4

Table 1 (*continued*)

Table 1 (*continued*)

Author, years	Country	Type of study	Treatment	No. of patients	Gender (M/F)	Mean age, years	Stage			
							I	II	III	IV
Park (27), 2010	Korea	Retrospective case-control	SL	105	99/6	61.25±8.89†	44	32	26	3
			PN	105	98/7	62.24±8.42†	43	36	24	2
Bölükbas (28), 2011	Germany	Cohort	SL	31	25/6	73.6‡	5	17	8	1
			PN	29	25/4	74.2‡	2	10	15	2
Gómez-Caro (29), 2011	Spain	Cohort	SL	55	51/4	63.5±10.2†	19	27	9	0
			PN	21	18/3	62.4±8.2†	3	14	4	0
Lee (30), 2011	Korea	Cohort	SL	19	15/4	62.1±8.9†	5	8	6	0
			PN	20	16/4	64.3±8.8†	8	5	7	0
Maurizi (14), 2013	Italy	Retrospective case-control	SL	39	28/11	62.1±8.9†	0	6	33	0
			PN	39	30/9	64.3±8.8†	0	1	38	0
Cusumano (31), 2014	Italy	Cohort	SL	51	40/11	63.0±8.2†	0	7	44	0
			PN	68	54/14	59.7±10.7†	0	3	65	0
Andersson (32), 2015	Finland	Cohort	SL	40	29/11	61.5	8	19	13	0
			PN	67	49/18	60	16	26	25	0
Ma (33), 2016	China	Cohort	SL	58	50/8	58.5±10.3†	0	30	28	0
			PN	42	40/2	57.8±7.9†	0	18	40	0
Pagès (34), 2016	France	Cohort	SL	941	716/225	60.9±12.6†	190	408	169	32
			PN	5,318	4,216/1,102	61.9±10.2†	347	1,813	1,482	690
Abdelsattar (35), 2017	USA	Retrospective case-control	SL	1,713	959	57.8±15.0†	315	388	118	68
			PN	1,713	981	55.4±14.9†	273	419	124	78

†, mean ± standard deviation; ‡, mean. SL, sleeve lobectomy; PN, pneumonectomy; M, male; F, female.

apparent magnitude of an effect. Survival and local recurrence rates following SL or PN for the treatment of NSCLC were calculated by the fixed-effect model and random-effect model, respectively. The two results are similar, and the combination of the two results makes them more reliable.

Funnel plots of the study results are shown in *Figure 6*. The funnel plots on 5-year overall survival rates following SL or PN for the treatment of NSCLC showed symmetry, which suggested there was no publication bias.

Discussion

Sleeve resection for lung cancer can prevent more lung parenchyma sacrifice, limiting the physiologic effects of PN. Many studies published over the past 20 years show similar or better results for parenchymal sparing resections compared to PN. Both Deslauriers (8) and Okada (13) reported a better prognosis after SL in patients with stages I and II NSCLC. Takeda (21) did not show any difference in 5-year survival for stage I and II patients after SL or PN, but the overall 5-year survival in the SL group was better than in the PN group (54% *vs.* 33%). In this meta-analysis 1-, 3-, 5-year survival rates were 18.26%, 10.95%, 7.34% in the PN group and 38.00%, 27.80%, 25.77% in the SL group respectively, which is in line with the data of the literature.

From the oncological point of view, each patient must have an *en-bloc* complete resection of the tumor to ensure that the margin of resection is negative. Induction therapy has shown to improve local and systemic control in locally-advanced NSCLC (36-38). However, induction therapy may cause fibrosis and treatment-related changes, which make dissection of lobar bronchus or artery and

Table 2 Summary of the results between SL and PN in the management of NSCLC

Variables	No. of studies furnishing data	Results, %		OR (95% CI)	P value	I^2, %
		SL	PN			
Operative mortality	13 (8,10,11,17-19,23-28,30)	2.62	6.30	0.40 (0.25–0.63)	<0.0001	0
30-day mortality	12 (14-16,20-22,29,32-36)	2.78	5.86	0.55 (0.32–0.96)	0.04	55
Local recurrence	15 (8,10,13,16,17,19,21,25,27,28,30-34)	15.65	22.81	1.09 (0.72–1.64)	0.69	50
Distant recurrence	9 (10,21,27,28,30-34)	19.81	30.64	0.61 (0.45–0.82)	0.001	0
Complication	15 (10,13,14,16-21,24,28,29,31-33)	29.39	30.58	1.07 (0.87–1.31)	0.55	27
Overall survival						
1-year	8 (11,14,15,20,21,28,29,35)	38.00	18.26	1.53 (1.31–1.80)	<0.00001	4
3-year	11 (11,13,17,20,21,27-30,32,35)	27.80	10.95	1.78 (1.47–2.17)	<0.00001	30
5-year	20 (8,11,13,14,16-22,25-29,32-35)	25.77	7.34	1.96 (1.70–2.27)	<0.00001	43
Subgroup overall survival (N0, N1 and N2 patients)						
3-year (N2 patients)	3 (13,17,22)	29.78	19.51	1.12 (0.47–2.68)	0.79	35
5-year (N2 patients)	3 (8,13,18)	19.77	18.69	1.27 (0.65–2.45)	0.48	44
5-year (N0 and N1 patients)	5 (8,13,17,18,22)	57.77	37.29	2.14 (1.66–2.78)	<0.00001	13

SL, sleeve lobectomy; PN, pneumonectomy; NSCLC, non-small cell lung cancer; OR, odds ratio; 95% CI, 95% confidence interval.

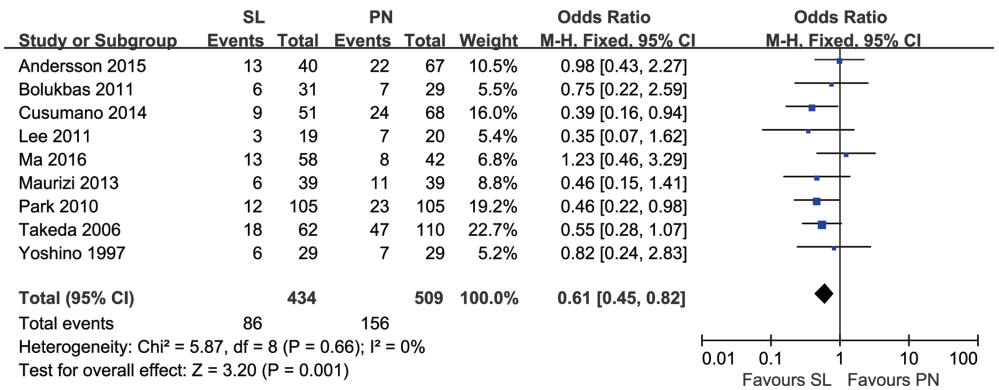

Figure 2 Distant recurrence rates of SL *vs.* PN. SL, sleeve lobectomy; PN, pneumonectomy; OR, odds ratio; 95% CI, 95% confidence interval.

reconstructive procedures more complex. Okada (13) described that there was a significant difference among patient classification of nodal disease N0 or N1 in favor of SL. Moreover, Deslauriers (8) reported that among patients with N0 disease there was a significant difference in favor SL. Mehran and colleagues (39) demonstrated a significant difference in survival between N1 and N2 disease irrespectively to the type of surgical resection performed, but they found no difference between N0 and N1. Van Schil and colleagues (40) showed there was a highly significant difference in survival between patients with N0 and N1/N2 disease, even if a similar difference in survival was not observed between N1 and N2. Finally, both Okada (13) and Deslauriers (8) showed that there was no significant difference in survival in N2 disease when the type of surgery was taken into account. Mehran and

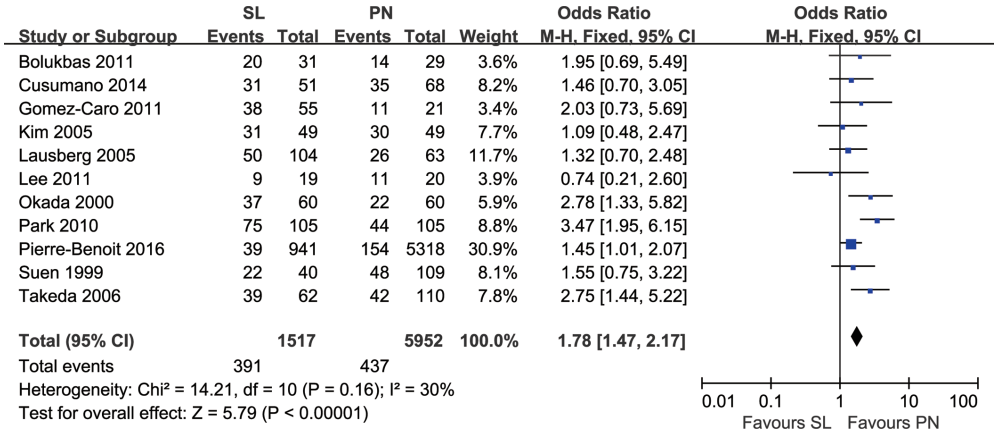

Figure 3 Three-years overall survival rates for SL *vs.* PN. SL, sleeve lobectomy; PN, pneumonectomy; OR, odds ratio; 95% CI, 95% confidence interval.

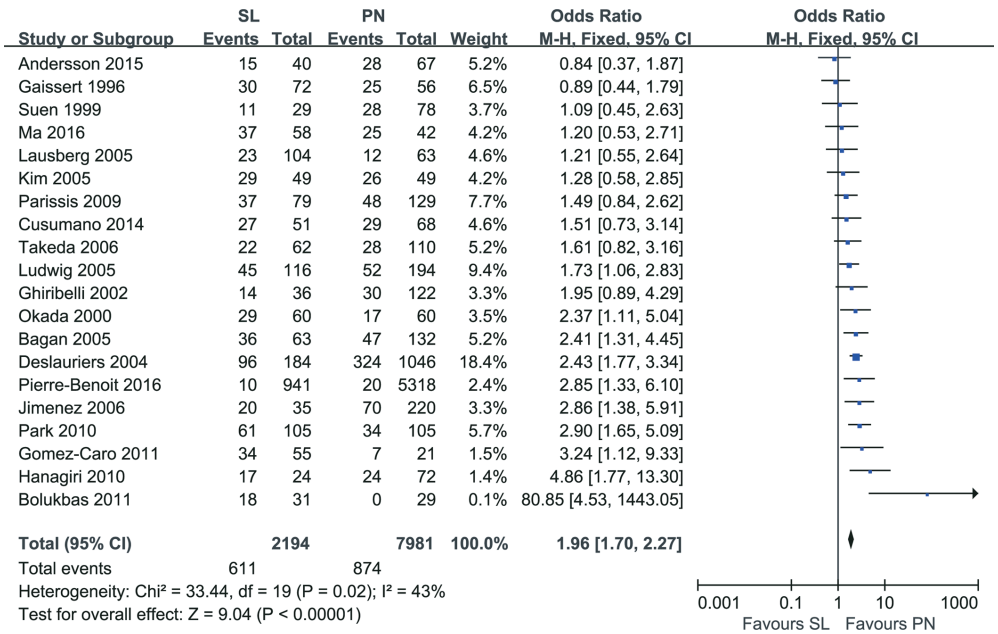

Figure 4 Five-years overall survival rates for SL *vs.* PN. SL, sleeve lobectomy; PN, pneumonectomy; OR, odds ratio; 95% CI, 95% confidence interval.

colleagues (39) reported that no patients with N2 disease survived longer than 5 years after sleeve resection, and Okada and colleagues (13) reported a 21% 5-year survival rate after sleeve resection in the same subgroup of patients. In this meta-analysis, a better 5-year OS was observed after SL in case of N0 and N1 patients, but no difference in 3- and 5-year OS was observed in case of N2 disease.

Recent reports have shown that an SL can be performed with a much lower rate of operative mortality (1.2–7.5%) as compared with PN (4.9–12.0%) (8,9,12,19,41). SL was a safe procedure with few operative morbidities (10,15,42,43). In a meta-analysis, Ferguson and Lehman (9) reported that the weighted mean operative mortality was 4.1% after SL and 6.0% after PN (P=0.3). Deslauriers and colleagues (8) described four times greater operative mortality after PN compared to SL (5.3% *vs.* 1.6%, P=0.036). Recently, SL mortality has been reported ranging between 2% (37) and 5% (44). Also, our results confirm this trend and are in line

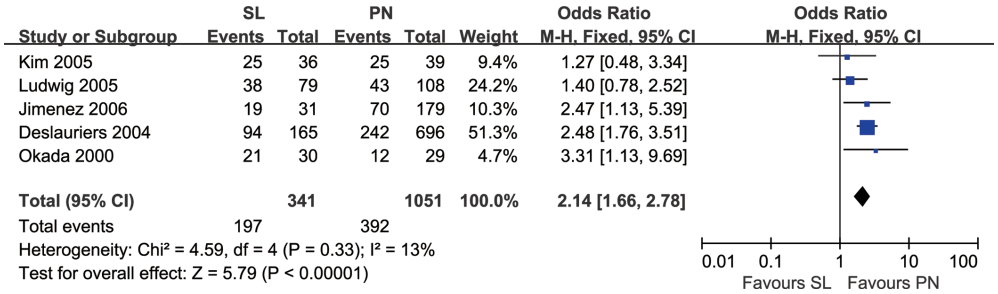

Figure 5 Five-year overall survival-N0 and N1 patients. SL, sleeve lobectomy; PN, pneumonectomy; OR, odds ratio; 95% CI, 95% confidence interval.

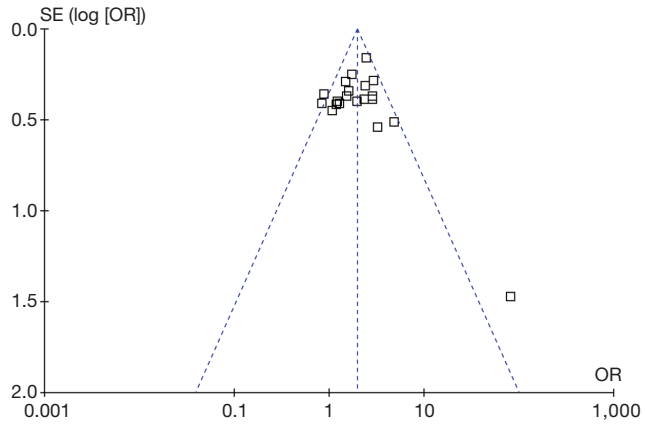

Figure 6 Funnel plot 5-year overall survival rates. SE, standard error; OR, odds ratio.

with those of the international literature.

Our study showed that there was no statistically significant difference in 30-day mortality. Deslauriers is often quoted as saying that "pneumonectomy is a disease". The main causes of death after PN were: circulation complications [heart failure (45)], acute respiratory failure, acute respiratory distress syndrome (ARDS) (46), arrhythmia and renal disease. Compared with SL, PN can cause sudden and significant hemodynamic changes, hypoxemia, and mediastinal displacement. PN can also predispose to arrhythmia. Right ventricular overload and dysfunction can occur as a result of pulmonary hypertension and subtle fluid overload is often poorly tolerated. Postoperative quality of life has been advocated as one of the most reliable indicators that should influence the decision to perform an SL rather than a PN. Several studies indicate that lung parenchyma sparing improves postoperative quality of life because of a greater pulmonary reserve. Gómez-Caro (29) and Melloul (24) reported there was a statistically significant difference favoring SL in terms of postoperative loss of forced expiratory volume in 1 second (FEV1).

On the other hand, SL may have a unique set of complications in its own right. Anastomotic dehiscence may be life-threatening, and often completion PN is needed. Anastomotic stenosis and consequent obstructive atelectasis are also major complications after SL, while postpneumonectomy empyema and respiratory failure are the most common complications after PN. Our study reports that the rate of postoperative complications was 29.39% and 30.58% in the SL and PN group, respectively, without statistically significant difference.

We may be concerned that bronchoplasty for malignant tumors may increase the potential for local recurrence. According to Tedder and colleagues (44), the local recurrence rate was 13% after SL. Other series reported an estimated 20% to 23% rate of local recurrence (39). In this study, the weighted 15.6% mean local recurrence rate after SL and 22.8% after PN (P=0.69). The significant lower recurrence rate after SL (19.81% *vs.* 30.64% after PN, P=0.001) might also explain why the SL group experienced a better overall survival. The lower distant recurrence rate is an essential explanation in the survival advantage of SL, and the survival also may be influenced by the lesser physiological insult of SL. Alterations in immune response following the physiologic changes with PN have been suggested to play a role in distant recurrence (47).

Limitations of the study

The conclusions of our study may be limited by several factors. First, the studies analyzed have a very long period. This can lead to false positive or false negative results (risk of random errors). Second, not all data comes from RCTs. Therefore, the overall level of clinical evidence was

relatively low.

There was a concern for publication bias in the studies included. Those surgeons with less than optimal experiences or outcomes inferior to a thoracotomy would likely be less than enthusiastic about publishing their data if they were accepted for publication at all. Moreover, there are many subtle differences in technique between surgeons. Also, funnel plots can show the cause of asymmetry rather than publication bias. As a result, our merger may overestimate the real effect. Due to these data limitations, our meta-analysis was unable to analyze the quality of life score and stratified analysis of other possible confounding factors. If the method is to be more effective, then larger samples and randomized controlled studies with longer follow-up are required.

Finally, we failed to perform a separated analysis according to the tumor's histology because of the very limited data available. Darling's IIIA NSCLC study and Deslauriers excellent results indicated that if the surgery is performed the surgery it has some clinical impact.

Conclusions

Our study demonstrates improved survival following SL *vs.* PN in patients with NSCLC. This effect was irrespective of lymph node involvement when the disease was N0–N1. The presence of mediastinal lymph node metastases (N2) portended worse survival, that was irrespective of the type of surgery. SL is a useful alternative to PN for operable cases of lung cancers and should be taken into account. Further RCTs are warranted to clarify the exact value of SL and PN for NSCLC to get a higher level of evidence.

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Footnote

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

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was approved by institutional ethics committee board of Shenyang Chest Hospital and Cancer Hospital of China Medical University/Liaoning Cancer Hospital (ethical number KYXM-2018-001-01 and 20171125).

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