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REVIEW ARTICLE – THORACIC ONCOLOGY

Comparison Between Wedge Resection and Lobectomy/ Segmentectomy for Early-Stage Non-small Cell Lung Cancer: A Bayesian Meta-analysis and Systematic Review

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ABSTRACT

Background. Surgery has become an accepted method for the treatment of early-stage non-small cell lung cancer (NSCLC). The purpose of this Bayesian meta-analysis was to compare the overall survival (OS), disease-free survival (DFS), and relapse-free survival (RFS) between wedge resection and lobectomy/segmentectomy for treatment of early-stage NSCLC.

Methods. Eligible studies were retrieved from Web of Science, PubMed, MEDLINE, Cochrane Library, EMBASE, CNKI, and WanFang up to July 2021 and screened based on established selection criteria. The Bayesian meta-analysis was performed with the combination of the reported survival outcomes of the individual studies using a random-effect model. The OS, DFS, and RFS of the wedge resection group was compared with the lobectomy/segmentectomy group. The hazard ratio (HR) and standard error were extracted or calculated for each study using the Kaplan-Meier method.

Results. This study was registered with PROSPERO (INPLASY202080090).The pooled OS hazard ratio between segmentectomy and lobectomy was 1.1 [95% confidence interval (CI) 0.92–1.4], the pooled HR between lobectomy and wedge resection was 0.71 [95% CI 0.52–0.96], and the pooled HR between segmentectomy and wedge was 0.80 [95% CI 0.56–1.10]. The pooled HR of DFS or RFS was not statistically significant among the three surgical approaches.

Conclusions. Patients with early-stage NSCLC received lobectomy had the lowest hazard ratio of OS than patients received wedge resection, indicating that the overall survival of patients received lobectomy was higher than patients received wedge resection. However, regarding DFS and RFS, the three surgical approaches showed no significant difference.

Keywords Non-small cell lung cancer · Meta analysis · Surgery method

Lung cancer is the most common cancer in both males and females. It accounted for 11.6% of the total cases and 18.4% of deaths in 2018.[1] Surgery is the preferred treatment for lung cancer, and lobectomy has been the standard of care for stage I NSCLC since the 1960s.[2,3] Modern technologies, such as computerized tomography (CT) screening, and other latest imaging techniques can detect a small range of lesions, which makes surgery in such an early stage the first choice.[4] Other alternative surgical techniques are currently being considered in patients with severe comorbidities, such as segmentectomy and sublobar.[5]

Lobectomy with mediastinal lymph node dissection has a high 5-year survival rate of approximately 60%.[3,6] However, these statistics could include various contraindications for lobectomy, especially for patients with poor pulmonary status.[4] NSCLC is a malignancy of the elderly, the median age of patients diagnosed with this

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disease is 67.7–70 years.[7,8] Resection of excess healthy tissue can have severe implications for the patient's quality of life.[9] To preserve the patient's lung function as much as possible, the investigation of sublobar resection (segmentectomy or wedge resection) has started to gain attention. Although the surgical approach was based on tumor location and surgeon's choice. For NSCLC, sublobar resections could preserve lung function.[4,10–12] Compared with lobectomy, wedge and segmentectomy take advantage of the anatomical parenchyma-sparing effect. Older people benefit most from less invasive surgical approach also with the saving of lung parenchyma.[13] However, regardless of the age and general status of the patients, it is questionable whether major resection is still justified in early-stage NSCLC.[14–16] Sublobar resections, especially wedge resection, are still controversial.[4,17–19] There are some concerns about sublobar resections, considering that sublobar resections has a higher recurrence rate than lobectomy resection.

We applied network analysis of the largest studies of these three resections of early-stage NSCLC. The goal of the present Bayesian meta-analysis was to compare the overall survival (OS) for HR of early-stage NSCLC patients who underwent lobectomy, segmentectomy or wedge resection with or without chemoradiotherapy.

MATERIAL AND METHODS

Search Strategy

A systematic online search of the published literature was conducted. The language of the strategy was limited to Chinese or English. There were no restrictions on publication year or publication status. The dates of the search were from the inception of online databases until July 2021. Chinese language databases included CNKI Database (www.cnki.net) and WanFang Database (https://www.wanfangdata.com.cn). English language databases included Web of Science, PubMed, MEDLINE, Cochrane Library, and EMBASE. Manual searches also were used to collect papers. The keywords included the following: "lung cancer," "segmentectomy," "segmental resection," "lobectomy," "wedge resection," and "wedge." The search strategy of PubMed is described in the supplementary. Similar search terms were adopted for the other databases. Details of the protocol for this systematic review has been registered on INPLASY with the registration number INPLASY202080090 (https://doi.org/10.37766/inplasy2020.8.0090). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement was used to improve the report of the systematic review (PRISMA-Checklist).

Data Inclusion Standards

Studies were included based on the following criteria: (1) a study population comprising stage I NSCLC patients, with all histologic types and pathologic confirmation; (2) any two or three of the following three surgical procedures: segmental, lobectomy, and wedge resection; (3) study outcomes including OS; (4) any of the following study designs: randomized controlled trial, cohort, or case-control (retrospective or prospective) and the group has been matched; (5) the study must have a sample size of more than 20 patients; and (6) the study must allow full access to its content, with languages limited to Chinese and English.

Data Exclusion Standards

The exclusion criteria were as follows: (1) studies not written in English; (2) studies with only abstracts provided in the database; (3) the subjects of the study were not patients with early non-small cell lung cancer who did not undergo any two or three of the three surgical methods of lobectomy, segmental resection of the lung, or results showed no OS rates for which data could be extracted; and (4) studies that had low readability or trustworthiness.

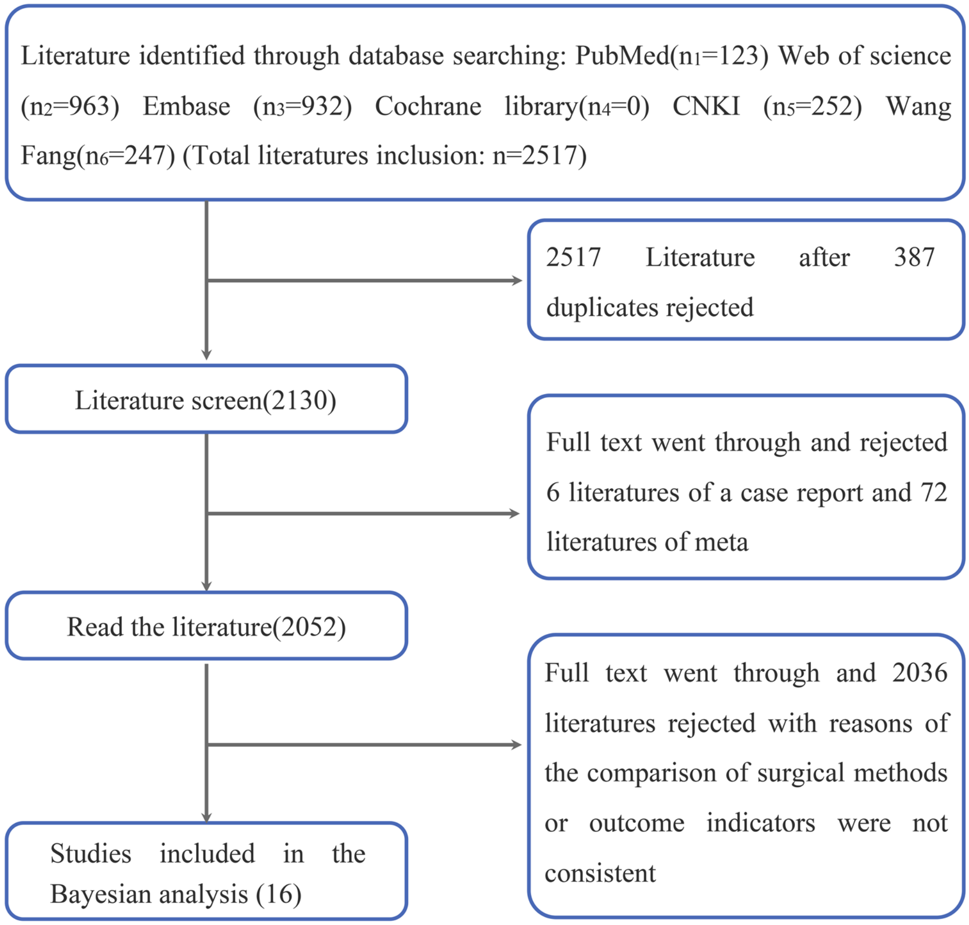
Literature Screening and Data Extraction

The first step in the screening of studies was to use Endnote X9 to exclude duplicates. Abstracts and full text were screened independently by two investigators (Y.C.S. and S.Z.W.) to establish whether the studies were likely to provide relevant data based on the inclusion/exclusion criteria. When there was a disagreement, it was resolved by introducing a third investigators (Y.C.S.) to discuss either the inclusion or exclusion of data. Finally, information extracted from each study included study topic, number of research cases, patients' ages and gender intervention measures, sample size for each group, tumor size and stages, and OS. In addition, we screened the studies for post-match survival analysis and for the included studies conducted statistical analysis of the base-line differences before surgical comparison ($p > 0.05$), including pathology, sex, tumour size, the total number of excised lymph nodes, tumour and grade, tumour location, and so on. At the same time, mean standardized difference (MSD) evaluation was performed, and the standard MSD < 0.10 matching was required to effectively control the imbalance of covariables.

Study Quality Evaluation Process and Risk of Bias

Two of the authors (Y.C.S. and S.Z.W.) independently assessed the studies according to the criteria in the

FIG. 1 Selection of studies for systematic review



Cochrane Handbook for Systematic Reviews of Interventions. Bias analysis and sensitivity analysis were used to assess the methodological quality of each study. Six domains were assessed: performance bias, detection bias, selection bias, reporting bias, attrition bias, and other bias. The risk of bias was analyzed using Review Man 5.3 software. The last four of the MINORS items also are used to evaluate the quality.

Statistical Analysis

A random-effects model within a Bayesian meta-analysis framework was performed by using Markov chain Monte Carlo methods in Win/OpenBUGS (MRC Biostatistics Unit, Cambridge, UK)[20] and R software 3.4.4. The operation codes are described in the supplementary information. The binary outcomes in every treatment group of every study were modeled and the relations among the hazard ratios (HRs) across studies was specified, by making different comparisons. Hazard ratio and associated 95% confidence interval (CI) were obtained from each study to perform meta-analysis of OS/DFS/RFS. When HR and its variance were not reported directly, other published data and survival curves from original papers were extracted to provide an estimation using Engauge Digitizer (Version 4.1) and Microsoft Excel (Version 16.49), which are Parmar and Tierney's techniques.[21,22] This method combines direct and indirect evidence for any given pair of surgical methods. We selected p values < 0.05 and 95% CIs (according to whether the CI included the null value) to analyze significance and looked at a plausible range for the magnitude of the population difference.[23] Then, 95% CIs were calculated, and $p < 0.05$ was regarded as significant. The inconsistency test was evaluated according to Bayesian meta-analysis p values ($p < 0.05$ indicates significant inconsistency). The I^2 test was analyzed ($I^2 > 50\%$ indicates significant heterogeneity) to verify homogeneity; 95% CIs were calculated, and $p < 0.05$ was regarded as significant. A key assumption behind multiple-treatments meta-*analysis* was that the analyzed network was coherent—i.e., direct and indirect evidence on the same comparisons did not disagree beyond chance. To estimate incoherence, we calculated the ratio of HR for indirect versus direct evidence whenever indirect estimates could be constructed with a single common comparator. In the

TABLE 1 Baseline characteristics of studies included in the Bayesian meta-analysis

Study	Age (mean, years)			Total number of female (proportion of female, %)			Tumor size (mean, cm)		
	S	L	WR	S	L	WR	S	L	WR
Nasser (2016)	73 (67–79)		72 (67–80)	42 (55)		40 (53)	2 (2–2.7)		2 (2–2)
Cheng (2012)	74 (70–81)	72 (70–78)		27 (32)	26 (32)		≤ 3	≤ 3	
Deng (2014)									
Rodney (2014)	68.5 ± 9.2	68.4 ± 9.2		173 (55.4)	168 (53.8)		2.2 ± 1.0	2.2 ± 1.1	
Morihito (2001)							< 2	< 2	
Morihito (2014)	66 (32–89)	63 (33–82)		50 (50)	54 (54)		1.6 (0.6,3.0)	1.6 (0.7,3.0)	
Yasuhiro (2019)	74.5 (68–80)		75				(70.3–80.3)	11 (28.2)	
18(30.0)	1.6 (1.3–2.6)		1.5 (1.1–1.9)						
Ken (2016)	62.6 ± 7.81	62.1 ± 9.52		46 (57.5)	109 (47.0)		≥ 1.6, 34 (49.3)	< 1.6, 35 (50.7)	
Terumoto (2016)	68 (42–83)	68 (37–81)		36 (41)	39 (45)		1.6 (0.6,2.0)	1.6 (0.8,2.0)	
Hyoung (2018)	67.8 ± 10.0	67.9 ± 9.5		531	533		1.42 ± 0.41	1.44 ± 0.42	
Shin-ichi (2011)	72 (34–82)	68 (42–83)		16 (42)	27 (38)		1.5 (0.7–4.0)	2.5 (0.9–1.7)	
Moon (2019)		63.6 ± 10.5	69.4 ± 8.8		132 (56.2)	9 (31)		2.0 (±0.6)	1.6 (±0.3)
Yamashita (2012)		69 (31–87)	68 (50–90)		49 (55)	51(41)	1.5 (0.7–3.0)	2.0 (0.9–3.0)	
Zhang (2016)	76.7 ± 4.8	75.8 ± 4.3		480 (58.6)	6263 (54.4)		1.94 ± 0.63	2.09 ± 0.62	
Smith (2013)	70 ± 10		70 ± 9	216 (57)		869 (55)	1.95 ± 0.06		1.82 ± 0.06
Khullar (2015)									

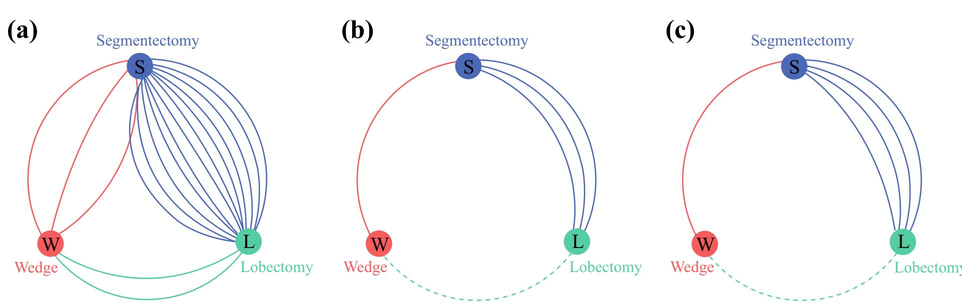


FIG. 2 Network meta-analysis of eligible comparisons for **a** OS, **b** DFS, and **c** RFS. Solid lines connect treatments that are directly compared in at least one study. Interrupted lines show the indirect comparisons for the treatments that have not been previously compared head-to-head and is formulated through the network model. Studies contributing with only one arm are not presented. Distances are for plot clarity alone. *OS* overall survival, *DFS* disease-free survival, *RFS* relapse-free survival

TABLE 2 Baseline characteristics of studies included in the Bayesian meta-analysis

Tumor stage	No. included cases			OS	DFS	RFS
	S	L	WR			
cT1N0	76		76		0.95 (0.49, 1.86)	
I	32	32		0.81 (0.46,1.43)		
IA	31	93		1.50 (0.38,5.94)	1.34 (0.48, 3.73)	
IA/IB	312	312		1.17 (0.89,1.52)		1.11 (0.87, 1.40)
cT1N0M0	68	104		0.89 (0.22,3.63)		
	100	100		0.83 (0.21,3.33)		0.83 (0.24, 2.85)
I	39		60	1.21 (0.57, 2.59)		1.07 (0.54, 2.15)
T1a N0 M0	69	69		0.89 (0.22, 3.56)		1.10 (0.29, 4.25)
cT1a N0 M0	87	87		0.99 (0.57, 1.75)	1.14 (0.46–2.82)	
	809	809		0.84 (0.69, 1.01)		
I	38	71		2.16 (0.35, 13.3)		1.13 (0.26, 4.86)
IA2		235	29	0.31 (0.10, 0.93)		
	90	124		1.22 (0.29, 5.15)	1.27 (0.59, 2.75)	
	11503	821		1.28 (1.10, 1.49)		
IA	378		1568	0.77 (0.66–0.91)		
		209	209	0.59 (0.44, 0.78)		
	209	209		1.45 (1.10, 1.91)		

end, survival rate among the three surgical methods were compared.

RESULTS

Screening Results of the Literature

A total of 16 literature searches were retrieved from the databases. The time span was from the inception of each of the databases to July 2021, which included 123 literature searches in databases of PubMed, 963 in Web of Science, 932 in Embase, 0 in Cochrane Library, 252 in CNKI, and 247 in WanFang. After data rejection, 6 literature searches of case reports were rejected, and 72 literature searches of meta-analyses were rejected. A total of 2,114 literature searches were not consistent with the comparison of surgical methods or outcome indicators. In the end, 16 studies were included in the Bayesian meta-analysis after the filtering process. We used the latest publication of each trial for the network meta-analysis, as cited in the main publication (Fig. 1).

Basic Information to be Included in the Study

The 16 studies were retrospective, which included 16 studies that reported OS. Baseline characteristics of patients were well balanced in each study. Study characteristics are presented in Table 1. The methodological quality of trials included was high overall (Supplementary Table S1). Random sequence generation was not adequate in all trials. None of the trials was blinded. However, for the endpoint of overall survival, we think that bias is unlikely, because death is an endpoint not susceptible to patient, physician, or outcome assessor bias. Figure 2 shows all the comparisons analysed within the network (Table 2).

Bayesian Meta-analysis of OS

A total of 15 studies reported OS (Fig. 3a–e).[24–38] The convergence diagnostic plot drawn according to the Gelman Rubin-Brooks diagnostic method suggested that the median value of the reduction factor and 97.5% tended to be stable after 25,000 iterations. The Bayesian meta-analysis was as follows: type = “consistency”; factor = 2.5; n.chain = 4; linearModel = “random” model sampler = NA; n.adapt = 5000; n.iter = 20000, thin = 10. Consistency analysis was performed using a node analysis model. The p values of all the comparison groups after the split were >0.05, indicating that the direct results were consistent with the indirect results.

The combined hazard ratio for segmentectomy vs lobectomy was 1.1, with a 95% confidence interval of 0.92–1.4. Heterogeneity was negligible, as the I^2 statistic was lower than 50% and the p value was >0.05 (Fig. 3b). Comparing the OS hazard ratio of segmentectomy with wedge resection, the pooled HR was 0.80 [95% CI 0.56–1.10, $p > 0.05$] (Fig. 3c). Comparing the OS hazard ratio of lobectomy with wedge resection, the pooled HR was 0.71 [95% CI 0.52–0.96, $p < 0.05$] (Fig. 3c).

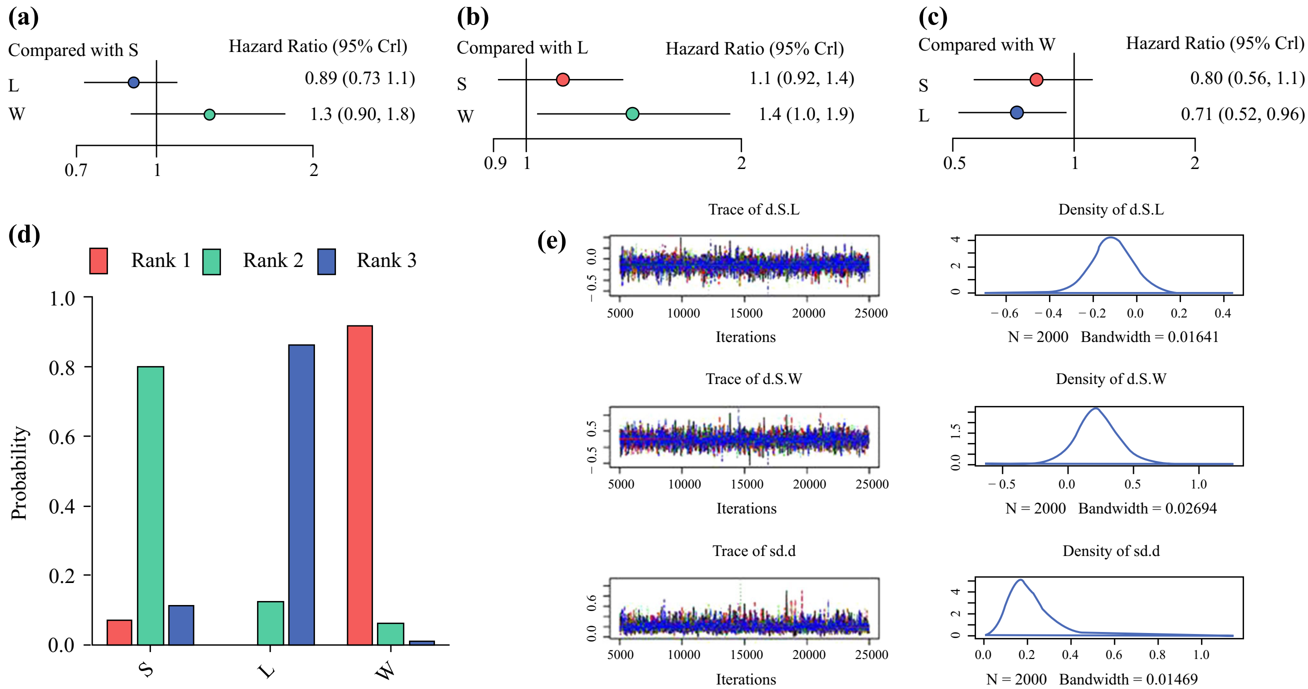


FIG. 3 Bayesian meta-analysis of hazard ratio (HR) for OS. **a** Forest plot compared with segmentectomy. **b** Forest plot compared with lobectomy. **c** Forest plot compared with wedge resection. **d** Rankogram bar chart representing the ranking probability of each intervention. The *X*-axis is the intervention measure, and the *Y*-axis is the ranking probability. It represents the probability that the intervention is ranked in the NTH place. **e** Trajectories of different iterations and density map of different iterations. The pre-iteration times and the iteration times were set to 5000 and 20,000. Each Markov Chain Monte Carlo (MCMC) chain has reached stable fusion from the initial part. The overlapping area accounts for most of the fluctuation range of the chain in the subsequent calculation. The fluctuation of a single chain cannot be recognized by the naked eye. The convergence degree is satisfactory. Density graph showing the distribution of a posteriori value of a parameter. Its function is the same as that of a trajectory graph, which is used to diagnose the degree of a model. The value N represents the number of iterations. The value of Bandwidth represents the difference between the posterior distribution and the prior distribution. The smaller the value is, the smaller the difference between the distribution range of the parameter posterior value and the preset distribution range is. The curve distribution is normal distribution, and the convergence degree of the model is satisfactory. *CI* confidence interval, *S* segmentectomy, *L* lobectomy, *W* wedge resection, *RFS* relapse-free survival

Bayesian Meta-analysis of DFS

A total of four studies reported DFS (Fig. 4a–e).[25,29,33,39] The combined hazard ratio for segmentectomy versus lobectomy was 1.20, with a 95% confidence interval of 0.71–2.10 (Fig. 4b). Comparing the DFS hazard ratio of segmentectomy with wedge resection, the pooled HR was 0.96 [95% CI 0.46–2.00] (Fig. 4c). Comparing the DFS hazard ratio of lobectomy with wedge resection, the pooled HR was 0.77 [95% CI 0.31–1.90] (Fig. 4c).

Bayesian Meta-analysis of RFS

Five studies reported RFS (Fig. 5a–e).[26,28,33,37,38] The combined hazard ratio for segmentectomy vs lobectomy was 1.10 [95% CI 0.82–1.50] (Fig. 5b). Comparing the RFS hazard ratio of segmentectomy with wedge resection, the pooled HR was 1.10 [95% CI 0.53–2.20] (Fig. 5c). Comparing the RFS hazard ratio of lobectomy with wedge resection, the pooled HR was 0.99 [95% CI 0.46–2.10] (Fig. 5c).

Sensitivity Analysis and Publication Bias

Biased data indicates that if random studies in the selection database are excluded, the final results have little effect. Therefore, the sensitivity test was good, and the results were problematic and credible. All 16 studies were retrospective. Detailed results are shown in Figs. 6 and 7. The results that followed the quality evaluation of the MINORS item showed that all of them were two marks for reporting and providing sufficient information. It indicates that the quality standards of the included studies have been strictly controlled.

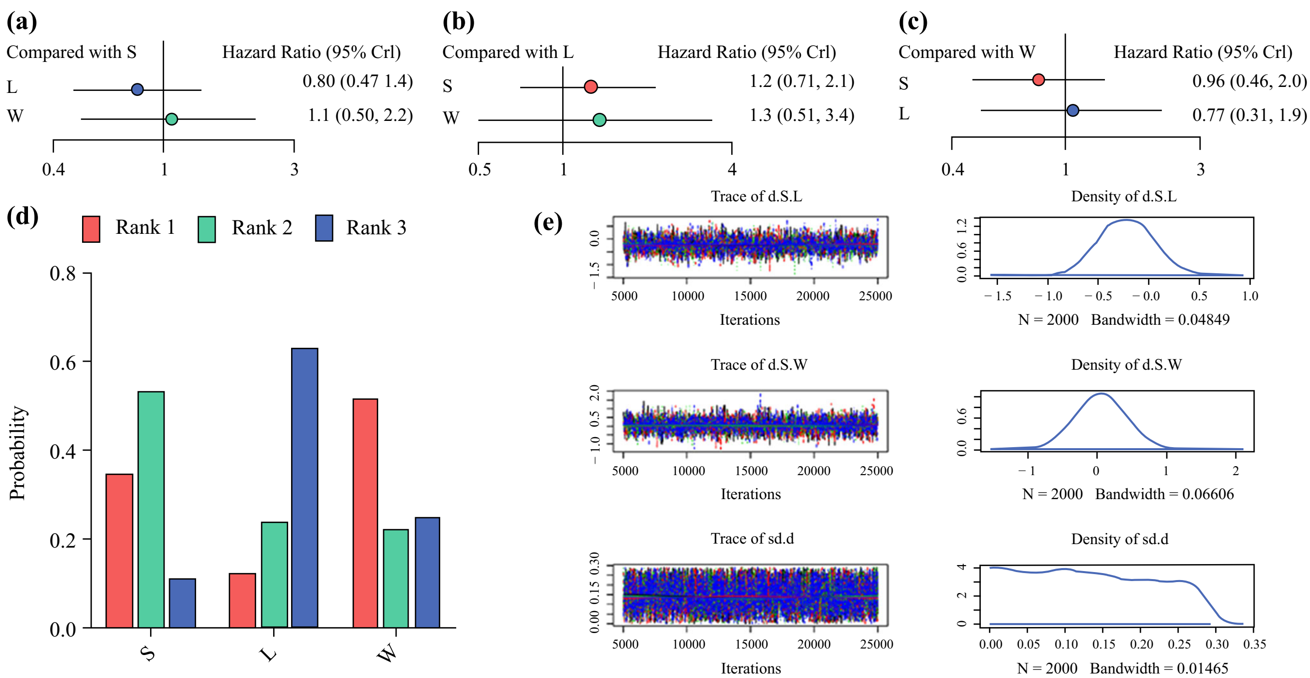


FIG. 4 Bayesian meta-analysis of hazard ratio (HR) for DFS. **a** Forest plot compared with segmentectomy. **b** Forest plot compared with lobectomy. **c** Forest plot compared with wedge resection. **d** Rankogram is a bar chart representing the ranking probability of each intervention. The *X*-axis is the intervention measure, and the *Y*-axis is the ranking probability. It represents the probability that the intervention is ranked in the NTH place. **e** Trajectories of different iterations and density map of different iterations. The convergence degree is satisfactory. The curve distribution is normal distribution. *CI* confidence interval, *S* segmentectomy, *L* lobectomy, *W* wedge resection, *RFS* relapse-free survival

DISCUSSION

Early diagnosis, therapy and surgery, and long-term tracing are three essential steps for cancer treatment.[40] During the past two decades, substantial progress has been made in the early detection, diagnosis, and treatment of NSCLC.[41] Low-dose computed tomography (LDCT) is effective for the early detection of lung cancer in high-risk populations; it identifies early-stage lung cancers with high sensitivity and reduces lung cancer mortality.[42,43] Cancer-specific biomarkers, such as DNA, RNA, or proteins, exist in a bodily fluid, and these can be valuable in the early diagnosis and treatment of cancer.[44] Modern improved diagnosis technology helped more patients with early-stage NSCLC have the option of surgical procedures.

All surgical resections were indicated by principles and practice of oncological therapy. Regardless of surgical approach, the overriding issue is strict adherence to contemporary oncologic principles and techniques. It is very important to know the function of operation in the therapeutic process completely. The following three principles should be dealt with well: the radical resection of tumors; the safety procedure for reducing operational risks; and the importance of preserving organic function of the patients. Surgical resection remains the standard treatment for early-stage NSCLC management.

For some types of tumors, the recurrence rate depends mainly on the adequacy of the initial surgical resection.[45] There is a view that patients undergoing limited resections (i.e., wedge or segmentectomy) had a significantly increased risk of intrathoracic recurrence.[46,47] A different opinion holds that there is no significant difference in survival between patients with stage I NSCLC who underwent sublobectomy resection (wedge resection and segmentectomy) and standard lobectomy, especially for early stage NSCLC.[48–51] NSCLC is a malignancy of the elderly, the median age of patients diagnosed with this disease is 67.7–70 years.[7,8] Resection of excess healthy tissue can have severe implications for the patient's quality of life.[9] This Bayesian meta-analysis is not intended to select the best surgical resection method in wedge resection and lobectomy/segmentectomy, because there is never a uniform standard for the best surgical resection method. The purpose of this study was to clarify whether wedge resection that preserves more normal tissue has the same survival rate and recurrence rate as lobectomy/segmentectomy. When the three resection methods are suitable for an individual, wedge resection that can preserve more normal tissue may not be given priority.

A wedge resection is a non-anatomical procedure in which the tumor and some surrounding lung tissues are directly removed. The differences between lobectomy and

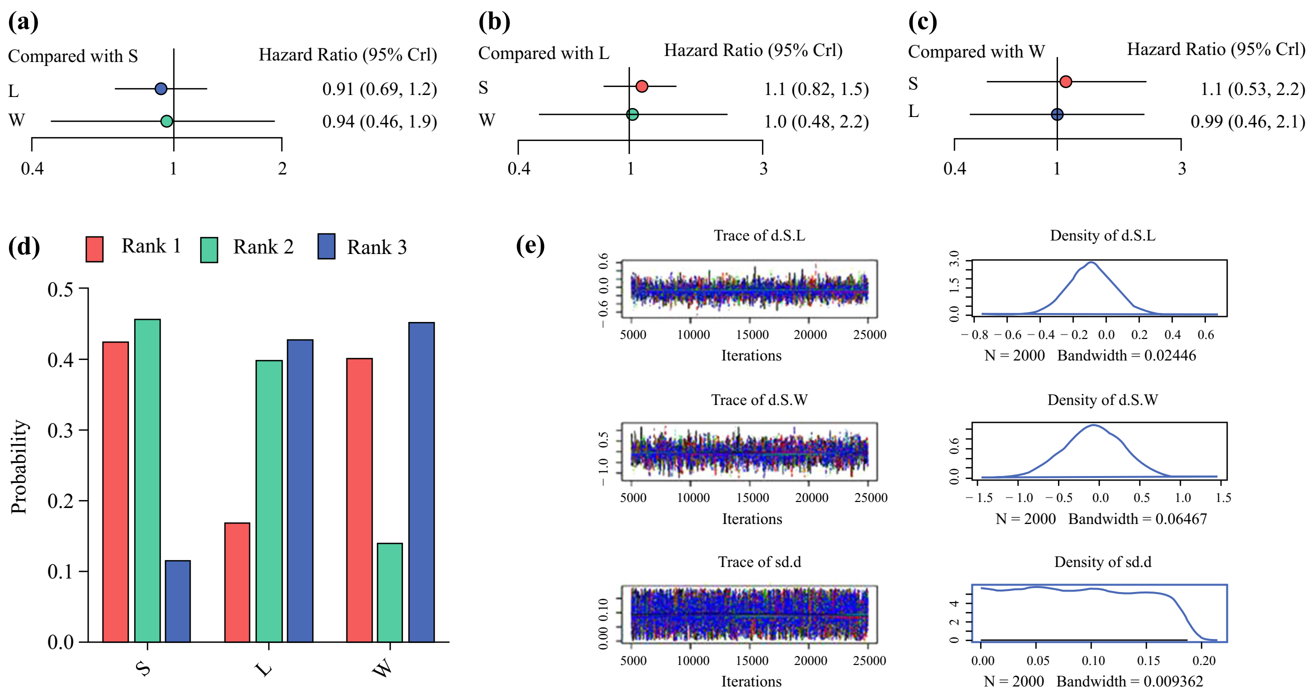
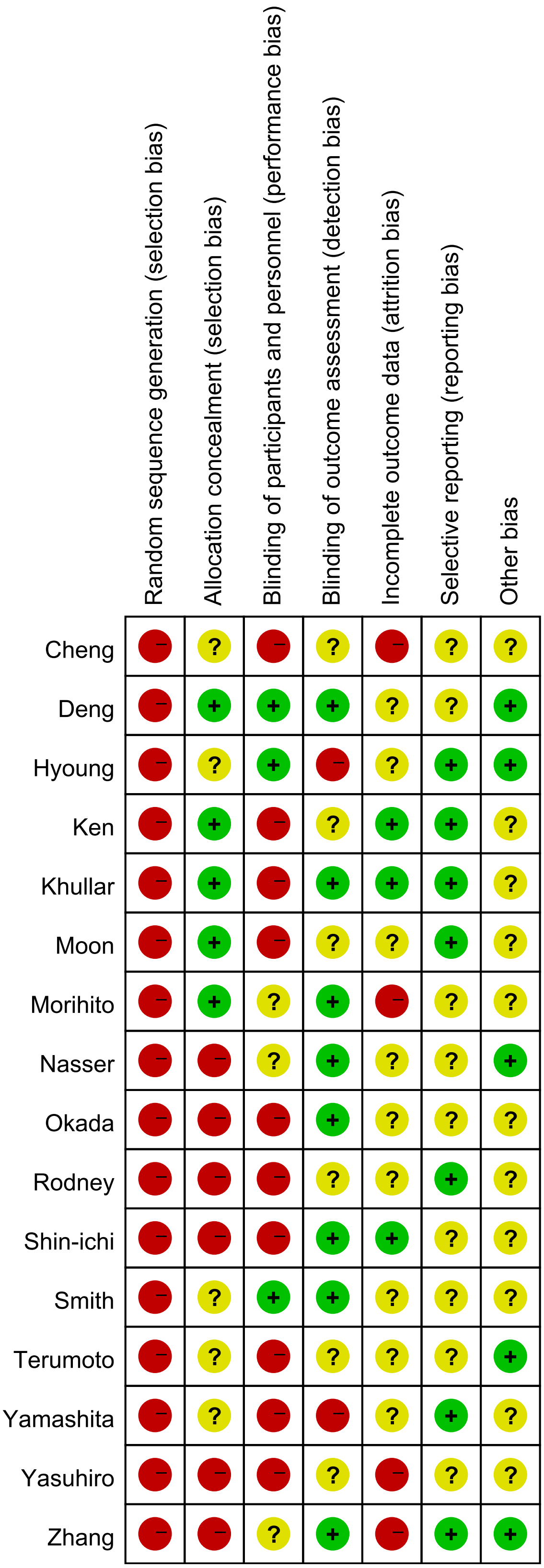


FIG. 5 Bayesian meta-analysis of hazard ratio (HR) for RFS. **a** Forest plot compared with segmentectomy. **b** Forest plot compared with lobectomy; **c** Forest plot compared with wedge resection. **d** Rankogram is a bar chart representing the ranking probability of each intervention. The *X*-axis is the intervention measure, and the *Y*-axis is the ranking probability. It represents the probability that the intervention is ranked in the NTH place. **e** Trajectories of different iterations and density map of different iterations. The convergence degree is satisfactory. The curve distribution is normal distribution. *CI* confidence interval; *S* segmentectomy; *L* lobectomy; *W* wedge resection; *RFS* relapse-free survival

segmentectomy in the preservation of postoperative lung function are widely debated, and segmentectomy differs in the difficulty of surgery. The only randomized, controlled trial comparing lobectomy with sublobectomy for stage Ia NSCLC, conducted in 1995, showed that sublobectomy had a shorter overall survival and three times the local recurrence rate compared with lobectomy. Since then, lobectomy has been recommended as the standard procedure for stage I NSCLC.[52] Subsequent studies concluded that there was little difference in survival between the two procedures.[53–57] Does segmental pulmonary resection, which preserves more lung tissue based on the same postoperative survival, provide an advantage in preserving lung function after surgery? Several studies have compared the differences in postoperative lung function between lobectomy and segmentectomy, and some studies have concluded that there is little difference in postoperative lung function preservation between the two surgical procedures.[58–60] However, other studies have found significant differences.[61,62] The differences in postoperative lung function preservation between the two surgical methods are quite controversial. Segmental pulmonary resection can be divided into typical segmental pulmonary resection and segmental pulmonary resection for SARS according to the site of resection. There are differences between the two surgical methods in terms of difficulty of operation, intraoperative bleeding, length of operation, and postoperative risk.[63–66] Lobectomy for all of these patients has now been questioned, leading to an increase in the frequency of intentional sublobectomy.[67] It has been shown that sublobectomy for Ground Glass Opacity(GGO) in early-stage NSCLC has a good prognosis.[68,69] In addition, pulmonary segmentectomy is receiving increasing attention, because it can preserve more lung tissue and better improve short-term outcomes. Some retrospective reports have shown that segmental pulmonary resection for small ($\leq$ 2.0 cm in diameter) stage Ia NSCLC is comparable to lobectomy in terms of prognosis and local recurrence.[70–72] At this point, the extent of surgical resection of early NSCLC remains controversial.

There is currently no literature comparing the survival rate and recurrence rate of lobectomy, segmentectomy, and wedge resection. For segmentectomy and lobectomy resection, Zheng et al. stated that patients who received segmentectomy to treat early-stage NSCLC had shorter OS compared with patients who underwent lobectomy, but there was no significant difference in recurrence-free survival between the two surgical strategies.[73,74] This may be related to the selection of case inclusion at the time of implementation of the clinical randomized controlled trial;



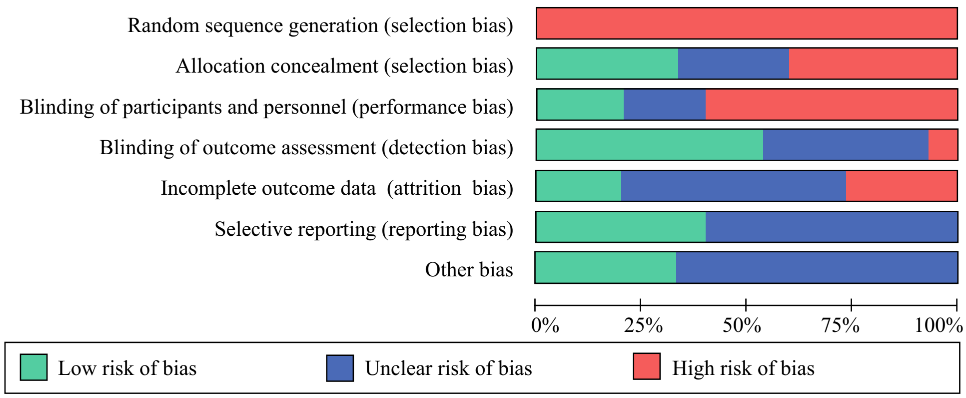
◀**FIG. 6** Risk of bias in each included study. Review authors' judgements about each risk of bias item for each included study. Analyze from the following aspects: random sequence generation (selection bias), Allocation concealment (selection bias), Blinding of participants and personnel (performance bias), Blinding of outcome assessment (detection bias), Incomplete outcome data (attrition bias), Selective reporting (reporting bias), and other bias. +, low risk; −, high risk; ?, unclear risk)

that is, patients who were compromised may have chosen segmentectomies for cardiopulmonary limitations or medical comorbidities.[75] However, patients who underwent wedge resection showed lower complication rates than those who underwent lobectomy, and the OS of segmentectomy was superior to that of wedge resection.[76–78] Segmentectomy and wedge resection for patients with stage I NSCLC was compared with another meta-analysis study published in 2016.[78] The results showed that for patients with stage I NSCLC, segmentectomy results in higher survival rates than wedge resection, whereas the outcomes of wedge resection are comparable to those of segmentectomy for patients with stage Ia NSCLC with tumor size $\leq$ 2 cm. This is consistent with our results. In our study, the pooling HR of OS between three main surgical approaches at present, including segmentectomy resection, lobectomy resection, and wedge resection, was compared in pairs, and our study was updated to include the results of recent studies, so the results may be more persuasive.

According to our findings, patients with early-stage NSCLC received lobectomy had the lowest hazard ratio of OS than patients received wedge resection, indicating that the overall survival of patients received lobectomy was higher than patients received wedge resection. Patients who underwent segmentectomy did not demonstrate some significant OS differences compared with patients who underwent lobectomy or wedge resection. Overall, a significant benefit of segmentectomy over wedge resection and lobectomy on OS and DFS in patients with early-stage NSCLC could not be confirmed. Similarly, it was uncertain that wedge resection and segmentectomy were better alternatives to lobectomy. Previous meta-analyses found that segmentectomy produced similar oncologic outcomes compared with lobectomy, which is consistent with our findings.[5,76,79–81] In particular, patients who were "intentionally" selected to go through a sublobar.[18,75]

This Bayesian meta-analysis presents some limitations. The large number of retrospective data in the study would raise uncertainties and questions as to the final conclusion, which should be resolved by more prospective, randomized, and controlled trials. Selection bias in retrospective studies could be extremely high unless employing the propensity score matching method.[79] The major problem of this study is

FIG. 7 Summary of risk of bias



a selection bias to determine the surgical procedure. When determining surgical procedure for NSCLC, whole tumor size, solid tumor size, location, and the preoperative general condition, including cardiopulmonary function. For example, the passive selection of lobectomy, wedge resection, or segmentectomy should be separately investigated from intensive selection. In addition, only summarized data, not individual patient data, was included in the main part of this study; dealing with summarized data is a well-accepted standard for this type of analysis. More randomized, controlled studies are needed in which all three surgical procedures can be selected at the same time under the premise that other factors are not affected.

CONCLUSIONS

The hazard ratio of OS was not significantly different in patients with early-stage NSCLC who received segmentectomy resection and lobectomy resection. Patients with early-stage NSCLC received lobectomy resection had the lowest hazard ratio of OS compared with patients who had wedge resection, indicating that the overall survival of patients who had lobectomy resection was higher than patients who had wedge resection. However, regarding DFS and RFS, the three surgical approaches showed no significant difference.

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