ORIGINAL ARTICLE

Stereotactic ablative radiotherapy versus lobectomy for stage I non-small cell lung cancer: A systematic review

Siwei Wang[1,2*], Xiaoxiao Wang[3*], Qing Zhou[4*], Youtao Xu[1], Wenjia Xia[1], Weizhang Xu[1,2], ZhiFei Ma[1,2], Mantang Qiu[5], Ran You[6], Lin Xu[1] & Rong Yin[1]

1 Department of Thoracic Surgery, Jiangsu Key Laboratory of Molecular and Translational Cancer Research, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research and Nanjing Medical University Affiliated Cancer Hospital, Nanjing, China
2 The Fourth Clinical College of Nanjing Medical University, Nanjing, China
3 GCP Research Center, Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, China
4 Department of Medical Oncology, Jiangsu Cancer Hospital, Jiangsu Institute of Cancer Research and Nanjing Medical University Affiliated Cancer Hospital, Nanjing, China
5 Department of Thoracic Surgery, Peking University People's Hospital, Beijing, China
6 Department of Interventional Radiology, Medical School of Nantong University, Nantong University Affiliated Hospital, Nantong, China

Abstract

Background: There is debate regarding the use of stereotactic ablative radiotherapy (SABR) or surgery for patients with early stage non-small cell lung cancer (NSCLC). This meta-analysis compared the clinical efficacy of SABR and lobectomy in stage I NSCLC patients.

Methods: An online search identified eight eligible articles (including 2 trials and 7 cohort studies) for inclusion. The odds ratio (OR) was used as a summary statistic. Overall survival (OS), cause-specific survival (CSS), and recurrence-free survival (RFS) were selected to calculate ORs with 95% confidence intervals (CI). Fixed-effects or random-effects models were conducted according to study heterogeneity.

Results: There were no significant differences between SABR and lobectomy in terms of one-year OS or CSS. Significant benefits of surgery were observed in three-year OS (OR 2.11, 95% CI 1.55–2.86), three-year CSS (OR 1.94, 95% CI 1.05–3.57), three-year RFS (OR 1.63, 95% CI 1.12–2.36), and five-year OS (OR 2.40, 95% CI 1.71–3.36). In addition, lobectomy demonstrated a beneficial trend in one-year RFS, five-year RFS, and CSS.

Conclusion: Meta-analyses of current evidence suggested that lobectomy provides better long-term survival outcomes for stage I NSCLC patients.

Introduction

Lung cancer remains the most common cause of cancer death globally. Non-small cell lung cancer (NSCLC) accounts for 80–85% of lung cancers.[1] Surgery has been the most promising treatment option for patients diagnosed with early stage non-small cell lung cancer (NSCLC).[2] Presently, the standard treatment for operable stage I NSCLC is lobectomy with mediastinal lymph node dissection or sampling. However, many patients with stage I NSCLC do not undergo surgery because of comorbidities or patient preference. Surgical approaches carry risks, and findings from research of video-assisted thoracoscopic surgery (VATS) and open thoracotomy lobectomy suggests that complications occur in 16.4% and 31.2% of patients, respectively.[3] Even with minimally invasive surgical techniques, operative mortality rates within 30–90 days after surgery are still 2–5.4%.[4,5]

Stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiotherapy (SBRT), is a non-invasive

radiation therapy that is considered to be a favorable option for inoperable early stage patients.[6] Two retrospective studies and one phase II prospective study demonstrated that SABR is associated with similar overall survival as surgery for potentially operable NSCLC patients.[7–9] When SABR is performed with the planning volume receiving a biologically equivalent dose of > 100 Gy, local control is achieved in > 90% of tumors with little acute or chronic severe toxicity. However, other comparative retrospective studies have yielded conflicting results, revealing benefits of SABR[10,11] or a lack thereof.[12,13] Debate over the efficacy of surgery compared to SABR has been ongoing for several years.

To compare the therapeutic effects between lobectomy and SABR, we conducted a meta-analysis including seven retrospective cohort studies and two randomized trials. The patients in each cohort study were matched by propensity score. Propensity score matching (PSM) can reduce bias from confounding variables when estimating treatment effects and generates two similar groups, as in a randomized controlled trial (RCT).[14] Because no relevant RCTs have been conducted, two terminated RCTs (STARS NCT00840749 and ROSEL NCT00687986) were also included in the meta-analysis. These two RCTs were closed early as a result of slow enrollment; however, Chang *et al.* combined and analyzed the existing data.[15] Therefore, confounding factors, such as age, performance score, and comorbidity score were minimized in this meta-analysis. In addition, we removed potential duplicated data by investigating research from the same community during the process of identification.

Methods

Search strategy

A comprehensive search of online databases, including PubMed, Embase, and Google Scholar, was conducted. The disease term "lung cancer" and the therapy terms "SABR," "SBRT," "Stereotactic Body Radiotherapy," "Surgery," and "Surgical Method" were used to locate studies for comparison. The search was limited to articles published prior to September 2016. Two reviewers independently evaluated the titles and abstracts of the identified papers. Only studies published in English language with full-text articles were included in the meta-analysis.

Criteria for inclusion and exclusion

Studies were included in our meta-analysis and systematic review if they met the following criteria: (i) retrospective cohort studies (RCS) or RCTs; (ii) the differences between patients who underwent SABR or surgery were minimized,

and RCS was balanced or adjusted by PSM; (iii) the study focused on lobectomy, regardless of the use of VATS or thoracotomy; (iv) patients included were diagnosed with stage I NSCLC; and (v) the study outcomes included at least overall survival (OS).

When patient samples overlapped in two or more studies, only the article that best satisfied the criteria was selected. During screening, we found that the patient sample in a study by Puri *et al.* overlapped that of a study by Crabtree *et al.* published in 2010, therefore the results of survival analyses in these two studies were pooled.[12,16]

Data extraction and quality assessment

Data extraction was carefully performed on all of the eligible studies. Two reviewers independently extracted the following items from each included study: general information (first author, publication year, type of study, and patient source); sample size (number of patients who underwent surgery or SABR); details of NSCLC stage distribution; treatment details (surgical method, total radiation dose, and dose per fraction); and propensity score matched clinical characteristics (age, gender, World Health Organization [WHO] performance score [PS], comorbidity score, and details of pulmonary function testing). All data was tabulated to facilitate quantitative data synthesis. To extract survival outcomes from the identified articles, we surveyed associated survival curves at one, three, and five-years using Engauge Digitizer version 10.0 (https://markummitchell.github.io/engauge-digitizer/). The number of events and survival rates were applied to calculate odds ratios (ORs).[11,12,15,17–21]

The quality of identified studies was assessed using the validated Newcastle–Ottawa Scale (NOS) for cohort studies. The NOS awards a maximum of eight points to each cohort study (4 for quality of selection, 1 for comparability, and 3 for quality of outcome). We considered studies with scores of > 7 as high quality, and those with scores of ≤ 7 as low-quality studies. All cohort studies included in this systematic review were estimated at > 7, and therefore could be considered high quality.

Statistical analysis

Overall survival, cause-specific survival (CSS), and recurrence-free survival (RFS) were calculated separately. ORs with 95% confidence intervals (CIs) were used as a summary statistic. Subgroup meta-analyses of one, three, and five-year survival rates were then conducted.

During meta-analyses of OS, we found that a study by Crabtree *et al.* published in 2014 contained a possible overlap with part of the patient sample of a study by Robinson *et al.* published in 2013.[18,19] Because the study by Crabtree

et al. demonstrated fewer differences in characteristics between patients who underwent SABR and surgery, the one and three-year OS rates were extracted from this study. However, the study by Crabtree *et al.* did not include five-year follow-up rates, therefore these rates were extracted from the study by Robinson *et al.* Additionally, during meta-analyses of RFS, locoregional and distant control rates in a study by Mokhles *et al.* were pooled to calculate cumulative one, three, and five-year RFS.[21]

Statistical heterogeneity between studies was assessed using the Q statistic, while the I^2 statistic was used to estimate the percentage of total variation across studies. Heterogeneity was considered as $P < 0.05$. The measure effect OR with 95% CI was calculated using a fixed-effect (using the Mantel–Haenszel method) or random-effect (using the inverse variance method) model according to the heterogeneity.[22,23] Begg's funnel plot and Egger linear regression were used to assess potential publication bias.[24] $P > 0.05$ was considered to indicate the absence of potential publication bias.

All *P* values were two sided. All analyses were conducted using Stata version 11.0 (Stata Corporation, College Station, TX, USA).

Results

Search results and study characteristics

Our predefined search strategy yielded a total of 103 articles. After screening the titles and abstracts, 18 studies were selected for further review. Finally, eight unique studies were selected as potentially appropriate for inclusion, including five single-center RCSs, two two-center RCS, and two RCTs. Our search strategy is presented in Figure 1 and the details of the eligible studies are summarized in Table 1.

Propensity score matching adjustment was performed in each of the seven retrospective cohort studies between SABR and surgery patients to reduce their physical differences. Adjusted factors included patient age, gender, WHO PS, Adult Comorbidity Evaluation/Charlson Comorbidity Index score, and forced expiratory volume in 1 second/diffusing capacity of the lung for carbon monoxide percentage (FEV1/DLCO%). A total of 870 patients (SABR $n = 435$, surgery $n = 435$) were included in this systematic review. In addition, data of 27 operative patients and 31 SABR patients were obtained from two incomplete trials (NCT00940749 and NCT00687986). Patient characteristics are summarized in Table 2.

Assessment of overall survival

All studies reported OS results of patients who underwent SABR or surgery, which produced a total sample size of 928 patients for evaluation. Among these, 462 were treated with surgery, and 466 with SABR. Seven studies included one and three-year OS results. Only five studies included five-year OS outcomes. The pooled ORs and 95% CIs of the one, three, and five-year OS meta-analyses were 0.98 (0.53–1.82), 2.11 (1.55–2.86), and 2.40 (1.71–3.36), respectively (Fig 2). Significant benefits were observed for lobectomy in the three and five-year OS meta-analyses.

Notably, after sensitivity analysis, significant heterogeneities were observed in the three and five-year OS rates primarily relating to data from studies by Chang *et al.* and Varlotto *et al.*, respectively.[15,17] Meta-analyses of RCS rates were also conducted, and a significant three-year OS rate was observed for lobectomy (Fig S1).

Assessment of cause-specific survival

Three identified studies were included in CSS meta-analyses, and all articles reported one, three, and five-year CSS. The pooled ORs and 95% CIs of the one, three, and five-year CSS were 1.20 (0.33–4.36), 1.94 (1.05–3.57), and 1.32 (0.81–2.14), respectively (Fig 3). A significant benefit was observed for three-year CSS after surgery. No significant heterogeneity was detected between the studies.

Assessment of recurrence-free survival

Five studies were included in the meta-analyses of RFS. All articles demonstrated one and three-year RFS, but only three reported five-year RFS. The pooled ORs and 95% CIs of the one, three, and five-year RFS were 1.48 (0.85–2.54), 1.63 (1.12–2.36), and 1.42 (0.94–2.15), respectively (Fig 4). Additional meta-analyses on RCS were also conducted and the results of one and three-year RFS were 1.47 (0.84–2.55) and 1.74 (1.18–2.57), respectively (Fig S2). Significant three-year RFS benefits were observed after lobectomy. Lobectomy also demonstrated a beneficial trend in the one and five-year RFS meta-analyses. Significant heterogeneities were observed in the three and five-year RFS meta-analyses.

Publication bias

We found no evidence of publication bias in any analyses using Begg's or Egger tests (all $P > 0.05$).

Discussion

The choice between SABR and surgery for early stage NSCLC has been debated for years. At present, standard therapy for operable clinical stage I NSCLC is lobectomy with sampling or dissection of mediastinal lymph nodes.[2] Although the risks of performing surgery are considered
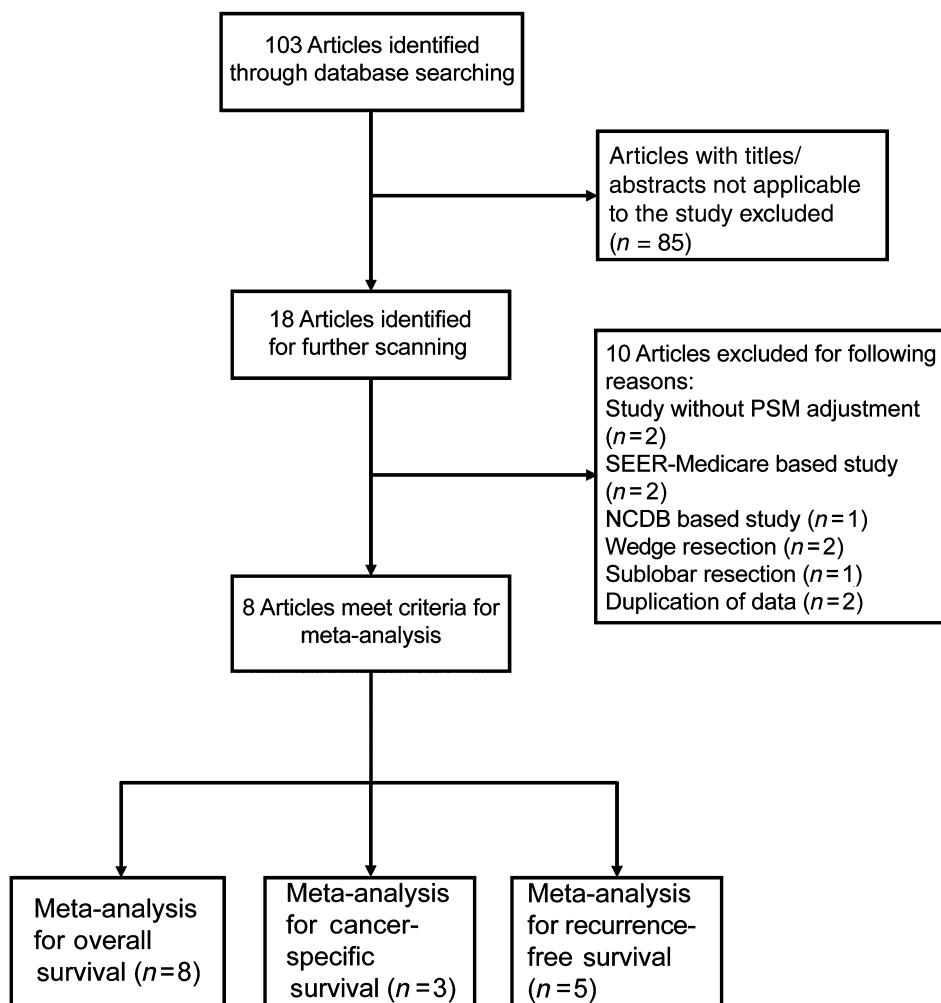
Figure 1 Flow diagram of articles screened and selected for this meta-analysis. NCBD, National Cancer Database; PSM, propensity score matching; SEER, Surveillance Epidemiology and End Results.

acceptable, use of this procedure has only gradually increased over the past decade. SABR has emerged as a non-invasive standard treatment alternative to surgery for inoperable patients, such as elderly patients and those with clinically significant comorbidities. Findings from our meta-analysis demonstrated that surgery (lobectomy) remains a better alternative for stage I NSCLC patients.

Five single-center RCSs, two two-center RCS, and two RCTs were included in this systematic review. Seven RCSs contained relevant patient data from six medical centers located in Japan, the Netherlands and the US; the STARS trial enrolled patients from 28 locations in China, France and the US, while the ROSEL trial enrolled patients from four centers in the Netherlands. VATS or thoracotomy lobectomy procedures accounted for > 80% of the surgery group of each study. In regard to radiotherapy, the total SABR dose ranged from 48 Gy to 60 Gy, and the delivered fractions from 3 to 5. All RCSs matched SABR and surgery patients with propensity scores, which dramatically reduced the differences in physical characteristics between

the groups. All RCSs matched age and gender between SABR and surgery groups separately; one RCS matched WHO PS; seven RCSs matched comorbidity score; and five RCSs matched pulmonary function test results. The study by Chang *et al.* that pooled data from these two trials revealed no differences between age, gender, or WHO PS.[15] In summary, the differences in physical characteristics between SABR and surgery patients were minimized.

In this systematic review, the evidence was robust for determining the efficacy of SABR and lobectomy for patients with stage I NSCLC. The results (three and five-year OS, three-year CSS, and three-year RFS) indicated better efficacy of lobectomy compared to SABR. In addition, lobectomy demonstrated a beneficial trend in one and five-year RFS. Notably, heterogeneities were found in three and five-year OS and RFS rates, primarily resulting from the data used by Chang *et al.* and Varlotto *et al.*[15,17] Two of the RCTs included in the pooled analysis by Chang *et al.* were terminated because of slow enrollment; therefore, the small patient sample size may induce potential selection bias.

Table 1 Study characteristics

| Study | Year | Design | Data Source | No. of patients | | | NSCLC stage | | Treatment | | |
				SABR Surgery	SABR Total	SABR Operable (%)	Surgery	SABR	Surgery Total	Lobectomy (%)	SABR Dose/fractions (median)
Crabtree et al.[12]	2010	OC	WUSTL	57	57	0 (0%)	C IA + B	C IA + B	46 lobectomy; 11 sublobar resection	80.70%	54 Gy/3F
Palma et al.[11]	2011	OC	ACR	60	60	11 (18.3%)	C IA + B	C IA + B	49 lobectomy; 2 pneumonectomy; 9 sublobar	81.70%	60 Gy/5F
Robinson et al.[18]	2013	OC	WUSTL	76	76	0 (0%)	C IA + B	C IA + B	72 lobectomy; 2 biolobectomy; 2 pneumonectomy	94.70%	54 Gy/3F
Varlotto et al.[17]	2013	OC	PSH	72	72	0 (0%)	C IA + B	C IA + B	72 lobectomy	100%	60 Gy/3F
Crabtree et al.[19]	2014	OC	WUSTL	56	56	0 (0%)	C IA + B	C IA + B	1 bilobectomy; 44 lobectomy; 6 segmentectomy; 5 wedge	80.40%	54 Gy/3F
Mokhles et al.[21]	2015	OC	VUMC & EMC	73	73	Abbr50%†	C IA + B	C IA + B	32 VATS lobectomy; 41 thoracotomy lobectomy	100%	60 Gy/5F
Chang et al.[15]	2015	RCT	STARS & ROSEL	27	31	100%	P IA + B	P IA + B	19 lobectomy; 5 VATS lobectomy; 1 VATS biopsy; 1 open wedge resection; 1 aborted resection	88.90%	54 Gy/3F
Hamaji et al.[20]	2015	OC	Kyoto-U	41	41	100%	C IA + B	C IA + B	VATS lobectomy	100%	48 Gy/4F

†Data source Verstegen et al.[25] ACR, Amsterdam Cancer Registry; C IA + B, clinical stage IA + B; EMC, Erasmus Medical Center; Kyoto-U, Kyoto University Hospital; NSCLC, non-small cell lung cancer; OC, cohort study; P IA + B, pathological stage IA + B; PSH, Penn State Hershey; RCT, randomized controlled trial; ROSEL, Trial of Either Surgery or Stereotactic Radiotherapy for Early Stage (IA) Lung Cancer (NCT00687986); SABR, stereotactic ablative radiotherapy; STARS, Randomized Study to Compare CyberKnife to Surgical Resection in Stage I Non-small Cell Lung Cancer (NCT00840749); VUMC, VU-University Medical Center; WUSTL, Washington University School of Medicine, St Louis.

Table 2 Patient characteristics

Study	Year	Age (year)			Male			WHO PS			Comorbidity Score			Pulmonary function test		
		Surgery	SABR	P	Surgery	SABR	P	Surgery	SABR	P	Surgery	SABR	P	Surgery	SABR	P
Crabtree et al.[12]	2010	73 (mean)	71 (mean)	NS	59.6%	40 &	0.039	—	—	—	ACE 2 (mean)	ACE 2 (mean)	NS	FEV1% (mean) 77%; DLCO% (mean) 81%	FEV1% (mean) 50%; DLCO% (mean) 50%	< 0.01/0.01
Palma et al.[11]	2011	79 (mean)	79 (mean)	NS	67%	67%	NS	—	—	—	—	—	—	—	—	—
Robinson et al.[18]	2013	65 (median)	76 (median)	< 0.01	48.7%	55.4%	NS	—	—	—	ACE 1 (median); CCI 3 (median)	ACE 2 (median); CCI 4 (median)	< 0.01	FEV1% (median) 51%; DLCO% (median) 62%	FEV1% (median) 79%; DLCO% (median) 79%	< 0.01/< 0.01
Varlotto et al.[17]	2013	ND	ND	NS	ND	ND	NS	—	—	—	ND	ND	NS	—	—	—
Crabtree et al.[19]	2014	70 (mean)	70.7 (mean)	NS	57.1%	51.8%	NS	—	—	—	ACE 2 (median)	ACE 2 (median)	NS	FEV1% (mean) 62%; DLCO% (mean) 73%	FEV1% (mean) 64%; DLCO% (mean) 55%	NS/< 0.01
Mokhles et al.[21]	2015	67 (mean)	67 (mean)	NS	60.3%	57.5%	NS	1 (median)	1 (median)	NS	CCI 1 (median)	CCI 1 (median)	NS	FEV1% (mean) 80.37%	FEV1% (mean) 81.38%	NS
Chang et al.[15]	2015	67.3 (mean)	67.3 (mean)	NS	41%	45%	NS	0 (median)	0 (median)	NS	—	—	—	—	—	—
Hamaji et al.[20]	2015	74 (median)	73 (median)	NS	78.0%	75.6%	NS	—	—	—	CCI 1 (median)	CCI 1 (median)	NS	FEV1% (mean) 76.5%	FEV1% (mean) 70.1%	NS

ACE, Adult Comorbidity Evaluation; CCI, Charlson Comorbidity Index; DLCO, diffusing capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; ND, no detail; NS, not significant; SABR, stereotactic ablative radiotherapy.

Figure 2 Meta-analysis of overall survival (OS) following stereotactic ablative radiotherapy (SABR) versus lobectomy for stage I non-small cell lung cancer. Comparison of (**a**) one-year, (**b**) three-year, and (**c**) five-year OS rates of SABR and lobectomy. CI, confidence interval; OR, odds ratio.
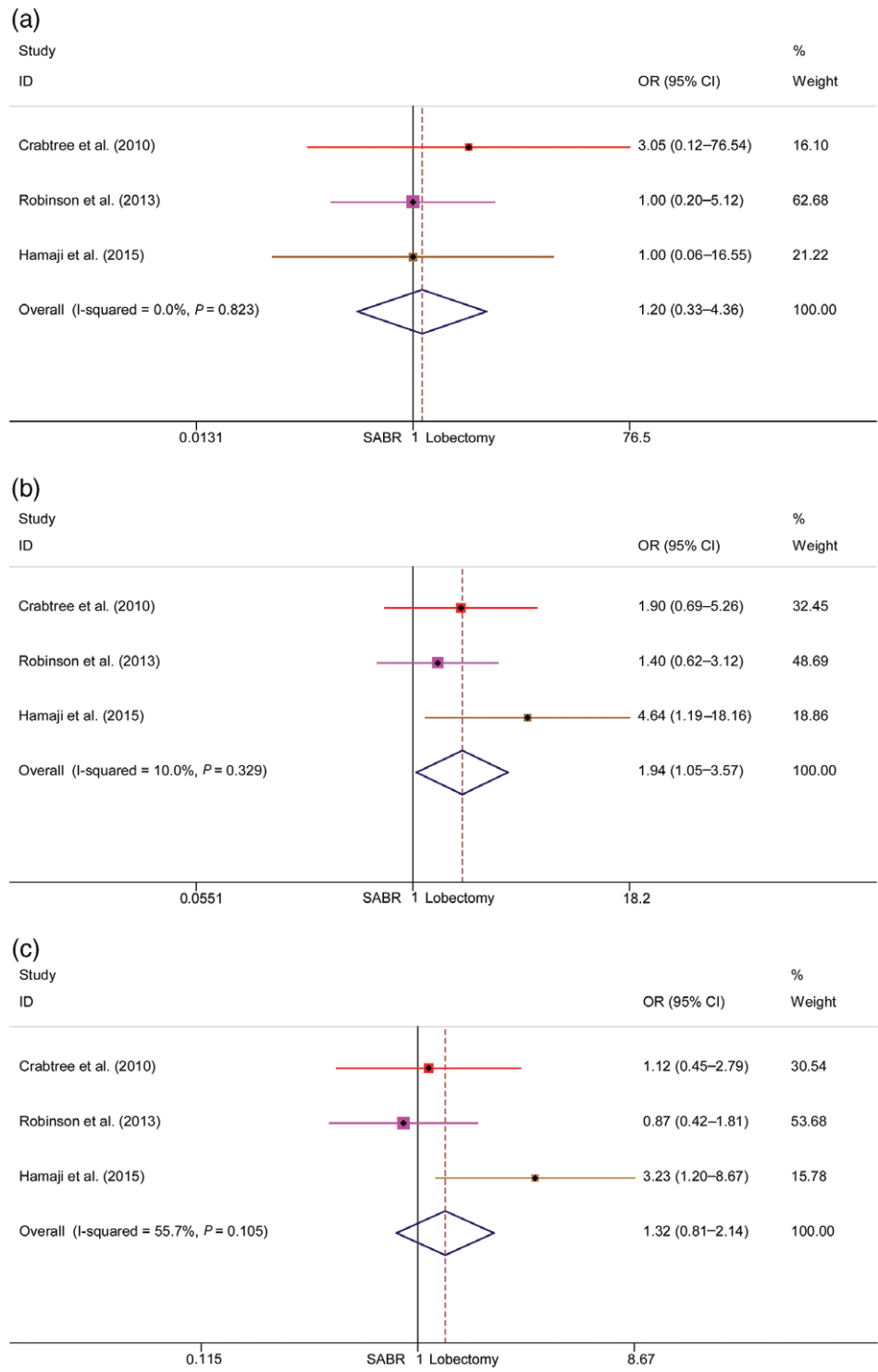
(a)

(b)

(c)
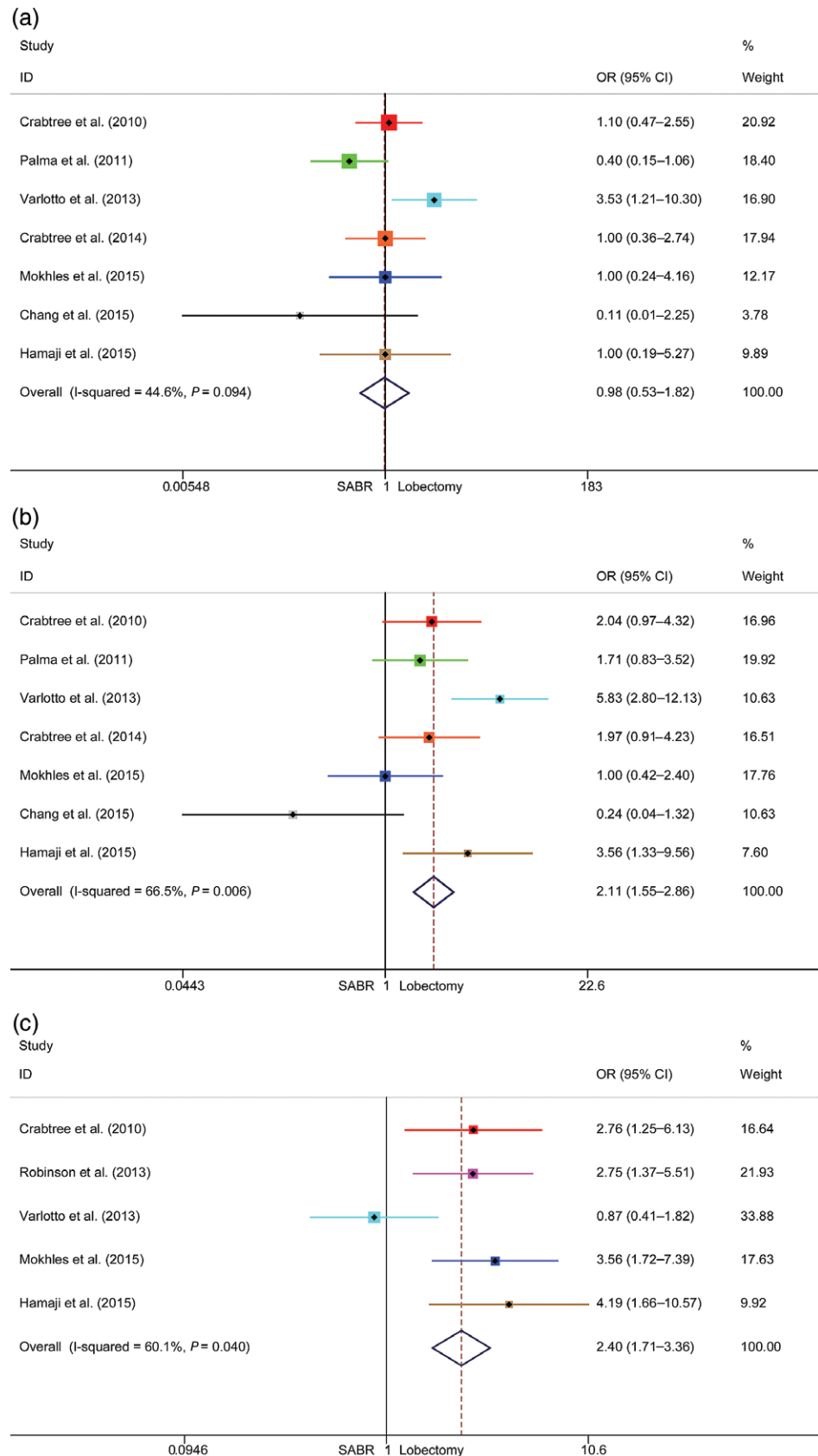
Figure 3 Meta-analysis of cause-specific survival (CSS) following stereotactic ablative radiotherapy (SABR) versus lobectomy for stage I non-small cell lung cancer. Comparison of (a) one-year, (b) three-year, and (c) five-year CSS rates of SABR and lobectomy. CI, confidence interval; OR, odds ratio.

Most of the data on deaths occurring after surgery ($n = 5$) up to the three-year follow-up were derived from STARS, which significantly increased overall surgery mortality rates. We observed that data in a study by Mokhles *et al.* may have overlapped SABR data in a study by Verstegen *et al.*

published in 2013, thus we excluded research by Verstegen *et al.* because of their shorter follow-up period.[21,25] However, the two studies came to opposite survival conclusions, including OS, control, and progression-free survival rates. The patients' physical characteristics were similar between

Figure 4 Meta-analysis of recurrence-free survival (RFS) following stereotactic ablative radiotherapy (SABR) versus lobectomy for stage I non-small cell lung cancer. Comparison of (**a**) one-year, (**b**) three-year, and (**c**) five-year RFS rates of SABR and lobectomy. CI, confidence interval; OR, odds ratio.
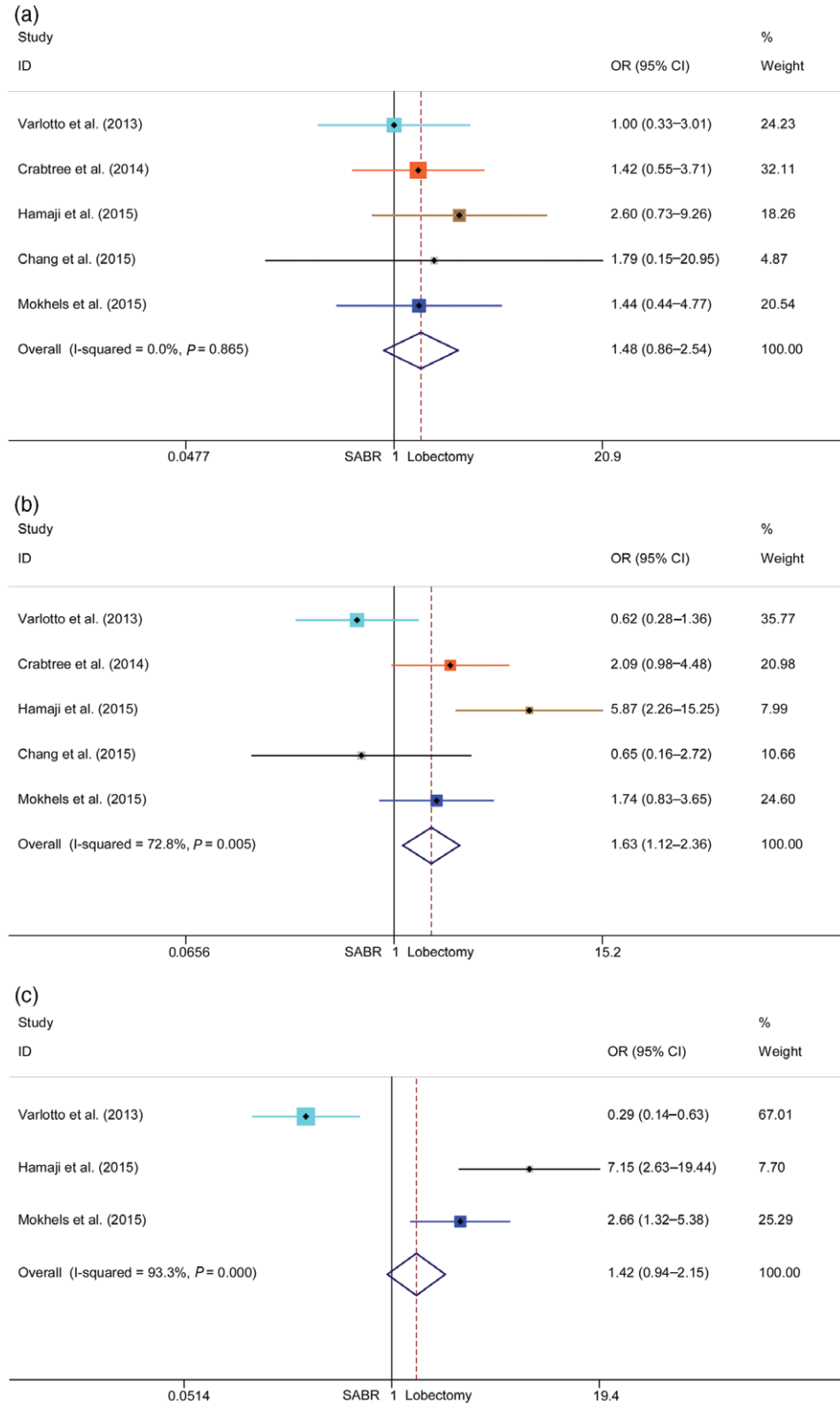
these studies as a result of PSM; however, surgical data in the study by Mokhles *et al.* was obtained from the Erasmus Medical Center, while surgical data for the study by Verstegen *et al.* was obtained from the VU University Medical Center. Notably, a recently published meta-analysis by Deng *et al.* focusing on three-year survival rates between SABR and surgery also included a large number of studies and reached similar conclusions.[26] Another earlier systematic review focusing on matched-pair comparisons between SABR and surgery in early stage NSCLC was published in 2014 by Zhang *et al.*[27] The original data from this systematic review were extracted from six studies with propensity score matched analyses. Their findings indicated that surgery was associated with better long-term survival in patients with early stage NSCLC (OR 1.31; 95% CI 0.81–2.12; $P = 0.27$); however, there were no significant differences between local or distant control. The major deficiencies of the systematical review by Zhang *et al.* were overlapping data between studies by Robinson *et al.* and Crabtree *et al.*, and the lack of comparison of five-year ORs.

In conclusion, our meta-analysis demonstrated that lobectomy is a better treatment strategy for stage I NSCLC patients. The OS results in this study were promising and the CSS and RFS rates both suggested that lobectomy is associated with better long-term efficacy. However, we did also observe some heterogeneity, including ratios between VATS and lobectomy, SABR treatment parameters, and proportions of operable SABR patients. Additionally, no tissue diagnosis was made in many of the patients who underwent SABR, and data on whether invasive mediastinal upstaging had been conducted was not available. These confounding factors could impact survival results. Although each retrospective study included in this article matched cases with PSM, some heterogeneities still existed between physical characteristics, thus our results may be impacted by incomparability across studies regarding variables that were not included when matching. Our results can be used as a reference to determine the best treatment strategy for patients with stage I NSCLC.

Acknowledgments

Disclosure

No authors report any conflict of interest.

References

1 Spira A, Ettinger DS. Multidisciplinary management of lung cancer. (Published erratum appears in *N Engl J Med* 2009; **360**: 1917.) *N Engl J Med* 2004; **350**: 379–92.

2 Scott WJ, Howington J, Feigenberg S, Movsas B, Pisters K, American Colleage of Chest Physicians. Treatment of non-small cell lung cancer stage I and stage II: ACCP evidence-based clinical practice guidelines. *Chest* 2007; **132** (3 Suppl): 234S–42S.

3 Whitson BA, Groth SS, Duval SJ, Swanson SJ, Maddaus MA. Surgery for early-stage non-small cell lung cancer: A systematic review of the video-assisted thoracoscopic surgery versus thoracotomy approaches to lobectomy. *Ann Thorac Surg* 2008; **86**: 2008–16.

4 Boffa DJ, Allen MS, Grab JD, Gaissert HA, Harpole DH, Wright CD. Data from the Society of Thoracic Surgeons General Thoracic Surgery Database: The surgical management of primary lung tumors. *J Thorac Cardiovasc Surg* 2008; **135**: 247–54.

5 Pezzi CM, Mallin K, Mendez AS, Greer Gay E, Putnam JBJ. Ninety-day mortality after resection for lung cancer is nearly double 30-day mortality. *J Thorac Cardiovasc Surg* 2014; **148**: 2269–77.

6 Timmerman R, Paulus R, Galvin J *et al.* Stereotactic body radiation therapy for inoperable early stage lung cancer. *JAMA* 2010; **303**: 1070–6.

7 Lagerwaard FJ, Verstegen NE, Haasbeek CJ *et al.* Outcomes of stereotactic ablative radiotherapy in patients with potentially operable stage I non-small cell lung cancer. *Int J Radiat Oncol Biol Phys* 2012; **83**: 348–53.

8 Onishi H, Shirato H, Nagata Y *et al.* Stereotactic body radiotherapy (SBRT) for operable stage I non–small-cell lung cancer: Can SBRT be comparable to surgery? *Int J Radiat Oncol Biol Phys* 2011; **81**: 1352–8.

9 Nagata Y, Hiraoka M, Shibata T *et al.* A phase II trial of stereotactic body radiation therapy for operable T1N0M0 non-small cell lung cancer: Japan Clinical Oncology Group (JCOG0403). *Int J Radiat Oncol Biol Phys* 2010; **78** (3 Suppl): S27–8.

10 Grills IS, Mangona VS, Welsh R *et al.* Outcomes after stereotactic lung radiotherapy or wedge resection for stage I non-small-cell lung cancer. *J Clin Oncol* 2010; **28**: 928–35.

11 Palma D, Visser O, Lagerwaard FJ, Belderbos J, Slotman B, Senan S. Treatment of stage I NSCLC in elderly patients: A population-based matched-pair comparison of stereotactic radiotherapy versus surgery. *Radiother Oncol* 2011; **101**: 240–4.

12 Crabtree TD, Denlinger CE, Meyers BF *et al.* Stereotactic body radiation therapy versus surgical resection for stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2010; **140**: 377–86.

13 Shirvani SM, Jiang J, Chang JY *et al.* Comparative effectiveness of 5 treatment strategies for early-stage non-

small cell lung cancer in the elderly. *Int J Radiat Oncol Biol Phys* 2012; **84**: 1060–70.

14 Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983; **70**: 41–55.

15 Chang JY, Senan S, Paul MA *et al.* Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: A pooled analysis of two randomised trials. *Lancet Oncol* 2015; **16**: 630–7.

16 Puri V, Crabtree TD, Kymes S *et al.* A comparison of surgical intervention and stereotactic body radiation therapy for stage I lung cancer in high-risk patients: A decision analysis. *J Thorac Cardiovasc Surg* 2012; **143**: 428–36.

17 Varlotto J, Fakiris A, Flickinger J *et al.* Matched-pair and propensity score comparisons of outcomes of patients with clinical stage I non-small cell lung cancer treated with resection or stereotactic radiosurgery. *Cancer* 2013; **119**: 2683–91.

18 Robinson CG, DeWees TA, El Naqa IM *et al.* Patterns of failure after stereotactic body radiation therapy or lobar resection for clinical stage I non-small-cell lung cancer. *J Thorac Oncol* 2013; **8**: 192–201.

19 Crabtree TD, Puri V, Robinson C *et al.* Analysis of first recurrence and survival in patients with stage I non-small cell lung cancer treated with surgical resection or stereotactic radiation therapy. *J Thorac Cardiovasc Surg* 2014; **147**: 1183–91.

20 Hamaji M, Chen F, Matsuo Y *et al.* Video-assisted thoracoscopic lobectomy versus stereotactic radiotherapy for stage I lung cancer. *Ann Thorac Surg* 2015; **99**: 1122–9.

21 Mokhles S, Verstegen N, Maat AP *et al.* Comparison of clinical outcome of stage I non-small cell lung cancer treated surgically or with stereotactic radiotherapy: Results from propensity score analysis. *Lung Cancer* 2015; **87**: 283–9.

22 DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177–88.

23 Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies. *J Natl Cancer Inst* 1959; **22**: 719–48.

24 Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315**: 629–34.

25 Verstegen NE, Oosterhuis JW, Palma DA *et al.* Stage I–II non-small-cell lung cancer treated using either stereotactic ablative radiotherapy (SABR) or lobectomy by video-assisted thoracoscopic surgery (VATS): Outcomes of a propensity score-matched analysis. *Ann Oncol* 2013; **24**: 1543–8.

26 Deng HY, Wang YC, Ni PZ *et al.* Radiotherapy, lobectomy or sublobar resection? A meta-analysis of the choices for treating stage I non-small-cell lung cancer. *Eur J Cardiothorac Surg* 2017; **51**: 203–10.

27 Zhang B, Zhu F, Ma X *et al.* Matched-pair comparisons of stereotactic body radiotherapy (SBRT) versus surgery for the treatment of early stage non-small cell lung cancer: A systematic review and meta-analysis. *Radiother Oncol* 2014; **112**: 250–5.

Supporting Information

Additional Supporting Informationmay be found in the online version of this article at the publisher's website:

Figure S1 Meta-analysis of overall survival (OS) following stereotactic ablative radiotherapy (SABR) versus lobectomy of retrospective cohort studies (RCSs). Comparison of (**a**) one-year and (**b**) three-year OS rates of SABR and lobectomy.

Figure S2 Meta-analysis of recurrence-free survival (RFS) following stereotactic ablative radiotherapy (SABR) versus lobectomy of retrospective cohort studies (RCSs). Comparison of (**a**) one-year and (**b**) three-year OS rates of SABR and lobectomy.