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Percutaneous local tumor ablation *vs.* stereotactic body radiotherapy for early-stage non-small cell lung cancer: a systematic review and meta-analysis

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Abstract

Background: Percutaneous local tumor ablation (LTA) and stereotactic body radiotherapy (SBRT) have been regarded as viable treatments for early-stage lung cancer patients. The purpose of this study was to compare the efficacy and safety of LTA with SBRT for early-stage non-small cell lung cancer (NSCLC).

Methods: PubMed, Embase, Cochrane library, Ovid, Google scholar, CNKI, and CBMdisc were searched to identify potential eligible studies comparing the efficacy and safety of LTA with SBRT for early-stage NSCLC published between January 1, 1991, and May 31, 2021. Hazard ratios (HRs) or odds ratios (ORs) with 95% confidence intervals (CIs) were applied to estimate the effect size for overall survival (OS), progression-free survival (PFS), locoregional progression (LP), and adverse events.

Results: Five studies with 22,231 patients were enrolled, including 1443 patients in the LTA group and 20,788 patients in the SBRT group. The results showed that SBRT was not superior to LTA for OS (HR = 1.03, 95% CI: 0.87–1.22, $P = 0.71$). Similar results were observed for PFS (HR = 1.09, 95% CI: 0.71–1.67, $P = 0.71$) and LP (HR = 0.66, 95% CI: 0.25–1.77, $P = 0.70$). Subgroup analysis showed that the pooled HR for OS favored SBRT in patients with tumors sized >2 cm (HR = 1.32, 95% CI: 1.14–1.53, $P = 0.0003$), whereas there was no significant difference in patients with tumors sized ≤2 cm (HR = 0.93, 95% CI: 0.64–1.35, $P = 0.70$). Moreover, no significant differences were observed for the incidence of severe adverse events (≥grade 3) (OR = 1.95, 95% CI: 0.63–6.07, $P = 0.25$) between the LTA group and SBRT group.

Conclusions: Compared with SBRT, LTA appears to have similar OS, PFS, and LP. However, for tumors >2 cm, SBRT is superior to LTA in OS. Prospective randomized controlled trials are required to determine such findings.

INPLASY Registration Number: INPLASY202160099

Keywords: Stereotactic body radiotherapy; Percutaneous local tumor ablation; Lung cancer

Introduction

Lung cancer, of which there were an estimated 2.2 million new cases and 1.8 million deaths in 2020, is the second most common cancer and the leading cause of cancer mortality globally. The 5-year survival rate of patients diagnosed with lung cancer is poor, ranging from only 10% to 20% in most countries.[1] Surgical resection is traditionally identified as the standard treatment for early-stage non-small cell lung cancer (NSCLC).[2] However, 20% of early-stage NSCLCs have been regarded as medically inoperable because of patient age, cardiopulmonary reserve, presence and extent of medical comorbidities, and overall performance status.[3] Most unresectable lung cancer patients only derive limited benefits from chemotherapy and conventional radiotherapy; therefore, many novel local treatment modalities have emerged.

Percutaneous local tumor ablation (LTA), including radiofrequency, laser, and microwave cryoablation or hypothermal ablation, is a safe and feasible modality for the treatment of lung neoplasms.[4,5] LTA has been used to treat lung cancer for 20 years since the first clinical use of LTA to treat lung tumors in 2000.[6]

Stereotactic body radiotherapy (SBRT) was developed on the basis of cranial radiotherapy,[7] whose principles and

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practices were transferred to the extracranial site. In the mid-1990s, groundbreaking work was carried out at the Karolinska Hospital, and the concept of SBRT was adopted soon and further developed in Germany and Japan.[8-10] With the local control rates ranging from 85% to 95%,[11-14] SBRT has been considered an effective and safe treatment for NSCLC, and has become the standard care for patients with medically inoperable early-stage NSCLC.[15]

LTA is an invasive therapy that is constrained by tumor location and tumor size. Considering SBRT can sufficiently overcome the limitations of LTA, it appears to be a more optimal modality.[16] However, to our knowledge, there are limited phase III clinical studies comparing the efficacy and safety of LTA and SBRT in early-stage NSCLC. Recently, a pooled analysis suggested that SBRT has an advantage in local control rate and has a similar survival rate to LTA.[17] A study from National Cancer Database reported similar results, however, two recent retrospective studies declared minimal advantages of SBRT for local control and overall survival.[18-20] Therefore, a systematic review and meta-analysis was performed to identify the more favorable modality between LTA and SBRT.

Methods

A comprehensive search was conducted in PubMed, Embase, Cochrane library, Ovid, Google scholar, CNKI, and CBMdisc to identify published literature that compared the efficacy of LTA and SBRT between January 1, 1991, and May 31, 2021. Keywords used in this search included: (pulmonary carcinoma or NSCLC or lung tumor or lung cancer or lung neoplasm) AND (SBRT or stereotactic body radiation therapy [SBRT] or stereotactic ablative radiotherapy or stereotactic radiotherapy or stereotactic radiosurgery or hyperfraction radiotherapy or cyberknife or gammaknife or tomotherapy [TOMO]) AND (radiofrequency ablation or microwave ablation or hypothermal ablation or LTA). Relevant literature was screened manually for potential articles written in English or Chinese.

Eligibility criteria

Two researchers reviewed all studies captured from the search. When confronted with discrepancies, a third reviewer rechecked the articles. Early-stage NSCLC in the current analysis included patients with T1N0M0 and T2N0M0 classifications. The eligibility criteria were as follows: (1) studies including patients with clinically confirmed or pathologically confirmed early-stage primary NSCLC; (2) studies including LTA and SBRT treatment groups; (3) hazard ratio (HR) and corresponding 95% confidence intervals (CIs) could be obtained directly or indirectly by calculation. The following studies were excluded: (1) studies that included patients receiving simultaneous treatments, such as chemotherapy; (2) studies in which survival data were unavailable; (3) studies derived from the same data sources; (4) case reports, comments, letters, conference abstracts, and reviews.

Endpoints

Endpoints included overall survival (OS) (from the beginning of treatment to death or the last follow-up) progression-free survival (PFS), locoregional progression (LP), and adverse effects.

Quality assessment

The modified Newcastle-Ottawa Scale (NOS) was applied to evaluate the quality of the included studies.[21] Studies with <4 stars were considered low quality; studies with ≥7 stars were considered high quality; and studies with 4 to 6 stars were considered medium quality.

Statistical analysis

The meta-analysis was performed using RevMan Version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Cochrane Q test and I^2 statistics were used to assess heterogeneity; a $P > 0.10$ and $I^2 < 25\%$ indicated no heterogeneity. The random-effects model was utilized to assess the effect size and to determine if the hypothesis of homogeneity was rejected. Correspondingly, the fixed-effects model was used to assess studies without significant heterogeneity. Publication bias was not assessed for studies that included <10 studies.

Results

Baseline characteristics of the included studies

In the initial search, 162 studies were obtained, and 152 studies were excluded following screening of the titles and abstracts. Five retrospective cohort studies[18-20,22,23] remained after the elimination of three studies[24-26] from one database and two studies in which the survival data were not available[27,28] [Figure 1].

In total, 22,231 patients were included in our analysis, including 1443 patients in the LTA group and 20,788 patients in the SBRT group. The characteristics of the included studies are summarized in Table 1. The NOS scores of each study are listed in Table 2. Two studies scored eight points[19,23] and three scored seven points.[18,20]

Overall survival

OS data for LTA and SBRT were available from five studies,[18-20,22,23] including 1143 patients in the LTA group and 20,788 patients in the SBRT group. No significant differences were observed in the pooled HR for OS between the LTA and SBRT groups (HR= 1.03, 95% CI: 0.87–1.22, $P = 0.71$) using a random-effects model ($I^2 = 28\%$, $P = 0.24$, Figure 2). The efficacy of LTA and SBRT for NSCLC was estimated based on tumor size, pathology, age, and sex in two studies.[18,22] In the SBRT group, 10,122 patients were included in the subgroup of patients with tumors ≤2 cm in size, and 829 patients were included in the RFA group. The pooled HR suggested that the difference for OS between the two groups was not significant (HR = 0.93, 95% CI: 0.64–1.35, $P = 0.70$, random-effects model, Figure 3). The number of patients

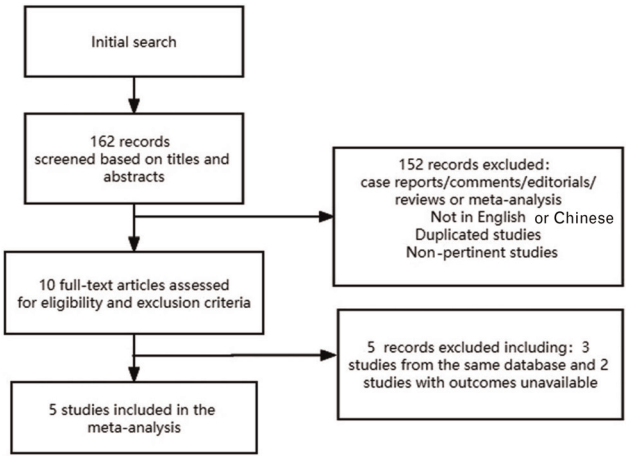

Figure 1: Flowchart of literature search and review of studies comparing percutaneous local tumor ablation *vs.* stereotactic body radiotherapy for early-stage non-small cell lung cancer.

with tumors >2 cm in size was 10,522 in the SBRT group and 501 in the LTA group. The pooled HR for OS was in favor of SBRT (HR = 1.32, 95% CI: 1.14–1.53, $P = 0.0003$, fixed-effects model, Figure 4). Moreover, 2-year OS rate [Supplementary Figure 1, http://links.lww.com/CM9/B30], 4-year OS rate [Supplementary Figure 2, http://links.lww.com/CM9/B30], and subgroup analyses of pathology [Supplementary Figures 3, http://links.lww.com/CM9/B30 and 4, http://links.lww.com/CM9/B30], age [Supplementary Figures 5, http://links.lww.com/CM9/B30 and 6, http://links.lww.com/CM9/B30], and sex [Supplementary Figures 7, http://links.lww.com/CM9/B30 and 8, http://links.lww.com/CM9/B30] showed no significant differences between the groups.

Progression-free survival

We compared the PFS of the LTA and SBRT groups from two of the included studies,[20,23] which included 63 patients and 86 patients, respectively. Using a fixed-effects model ($I^2 = 0\%$, $P = 0.94$, Figure 5), the pooled HR analysis for PFS showed no significant difference (HR = 1.09, 95% CI: 0.71–1.67, $P = 0.71$, Figure 5).

Locoregional progression

LP from two studies[19,20] was available for analysis, which included 73 patients in the LTA group and 74 patients in the SBRT group. The pooled HR for LP showed no significant difference (HR = 0.66, 95% CI: 0.25–1.77, $P = 0.70$, Figure 6).

Adverse events

Adverse events from three studies[19,20,23] were analyzed. Severe adverse events for LTA included pneumothorax, pleural effusion, and hemothorax. In the SBRT arm, severe adverse events included pneumonia/fibrosis, dyspnea, and brachial plexopathy. The incidence of severe adverse events (grade ≥3) ranged from 0 to 16% in the LTA arm and from 0 to 10.4% in the SBRT arm [Table 3].

Table 1: Characteristics of the included studies comparing LTA *vs.* SBRT for early-stage non-small cell lung cancer.

Studies	Design	Treatment	Power/Doses and fractions	Population	Patients before PSM	Patients after PSM	Age (years)	Gender (male/female)	Histology (A/S)	Tumor size	OS (1 year/3 years)	*P* value	PFS (1 year/3 years)	*P* value	Follow-up (months)
Ochiai et al 2014[19]	Retrospective Single center	LTA	NA	Single tumor ≤ 5 cm	48	NA	75.0 ± 7.5	30/18	22/17	>/≤2 cm: 28/20	93.4%/86.4%	0.738	NA/NA	NA	NA
		SBRT	40–60 Gy/4–10 f	Single tumor ≤ 5 cm	47	NA	77.0 ± 9.2	21/26	12/4	>/≤2 cm: 24/23	97.6%/79.6%		NA/NA		NA
Safi et al 2015[20]	Retrospective Single center	LTA	NA	T1-2N0M0	25	NA	71.2 ± 6.4	18/7	17/6	21.9 ± 7.3 mm	86%/74%	0.67	50%/NA	0.77	13
		SBRT	45 Gy/3 f	T1-2N0M0	28	NA	73.5 ± 7.2	NA	NA	28.4 ± 9.8 mm	93%/69%		65%/NA		10
Ager et al 2019[18]	Retrospective NCDB	LTA	NA	T1-2N0M0	1141	NA	75 (32–90)	515/626	675/466	1.8 (0.1–5.0 cm)	87.5%/52.2%	<0.001	NA/NA	NA	28.0 (3.0–144.4)
		SBRT	34–55 Gy/1–5 f	T1-2N0M0	146,51	NA	75 (26–90)	6758/7893	8327/6324	2.1 (0.1–5.0 cm)	83.5%/45.9%		NA/NA		26.1 (3.0–148.7)
Iguchi et al 2020[23]	Retrospective Single center	LTA	NA	IA/IB	38	38	75.03 ± 7.76	22/16	28/9	20.95 ± 6.68 mm	93.0%/70.8%	0.701	80.4%/37.1%	0.091	49.2 (1.9–129.4)
		SBRT	48 Gy/4 f; 60 Gy/8 f	IA/IB	58	58	77.83 ± 6.67	46/12	34/23	19.20 ± 7.13 mm	94.3%/73.3%		89.0%/63.1%		31.8 (8.0–80.0)
Li et al 2021[22]	Retrospective SEER	LTA	NA	T1N0M0	191	172	74.37 ± 9.03	80/111	101/47	<2/2–3 cm: 134/55	83.3%/48.5%	0.97	NA/NA	NA	NA
		SBRT	NA	T1N0M0	6004	516	74.48 ± 8.89	2617/3387	2897/2017	<2/2–3 cm: 3198/2795	83.8%/48.3%		NA/NA		NA

A/S: Adenocarcinoma/squamous carcinoma; LTA: Percutaneous local tumor ablation; M: Metastasis; N: Node; NA: Not available; NCDB: National Cancer Database; OS; Overall survival; PFS: Progression-free survival; PSM: Propensity score matching; SBRT: Stereotactic body radiotherapy; SEER: Surveillance, Epidemiology, and End Results; T: Tumor.

Table 2: Newcastle-Ottawa Scale for assessing the quality of studies comparing LTA *vs.* SBRT for early-stage non-small cell lung cancer.

Studies	Selection				Comparability	Outcome			Scores
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome of interest was not presented at start of study		Assessment of outcome	Follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
Ochiai et al 2014[19]	*	*	*	*	*	*	*	*	8
Safi et al 2015[20]	*	*	*	*	*	*		*	7
Ager et al 2019[18]	*	*	*	*	*		*	*	7
Iguchi et al 2020[23]	*	*	*	*	*	*	*	*	8
Li et al 2021[22]	*	*	*	*	*		*	*	7

*Represents one score. LTA: Percutaneous local tumor ablation; SBRT: Stereotactic body radiotherapy.

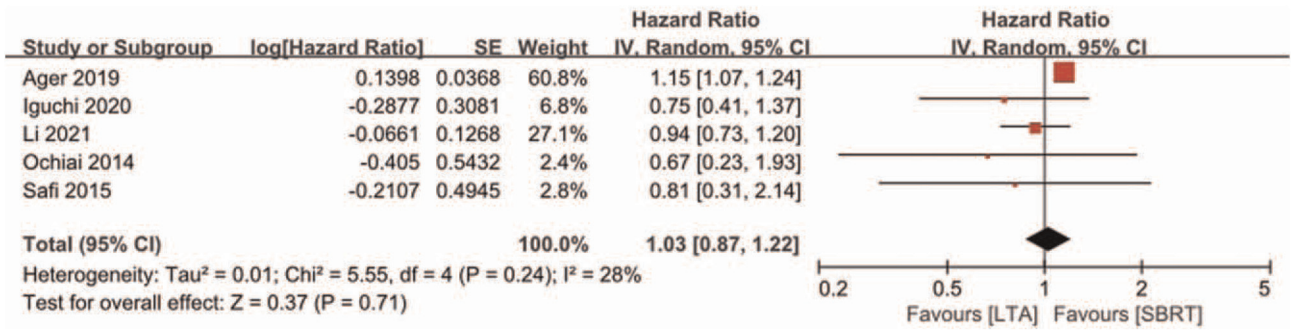

Figure 2: Forest plot of OS for groups of LTA and SBRT. CI: Confidence interval; LTA: Percutaneous local tumor ablation; OS: Overall survival; SBRT: Stereotactic body radiotherapy; SE: Standard error.

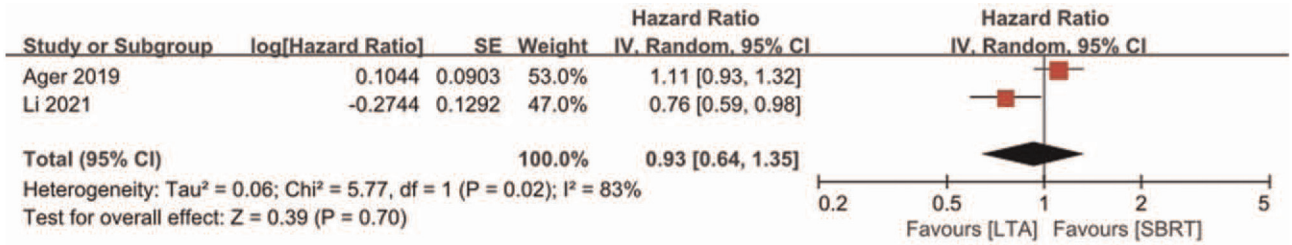

Figure 3: Subgroup analysis of OS for groups of LTA and SBRT for tumor sized ≤2 cm. CI: Confidence interval; LTA: Percutaneous local tumor ablation; OS: Overall survival; SBRT: Stereotactic body radiotherapy; SE: Standard error.

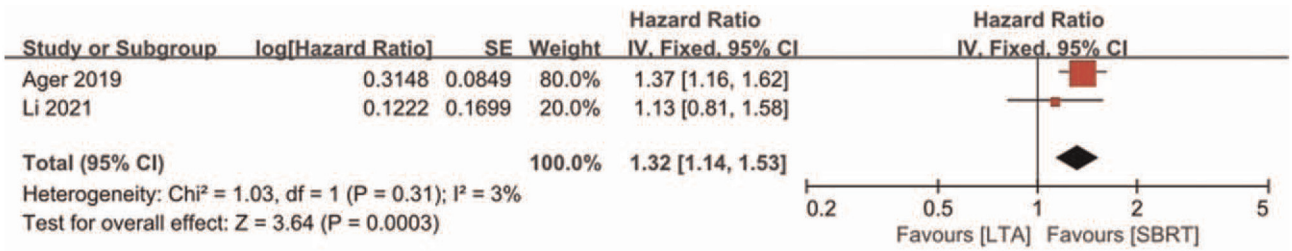

Figure 4: Subgroup analysis of OS for groups of LTA and SBRT for tumor sized >2 cm. CI: Confidence interval; LTA: Percutaneous local tumor ablation; OS: Overall survival; SBRT: Stereotactic body radiotherapy; SE: Standard error.

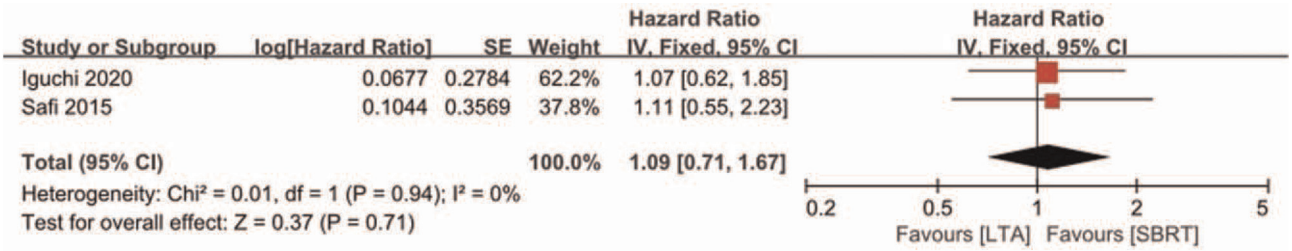

Figure 5: Forest plot of progress-free survival for groups of LTA and SBRT. CI: Confidence interval; LTA: Percutaneous local tumor ablation; SBRT: Stereotactic body radiotherapy; SE: Standard error.

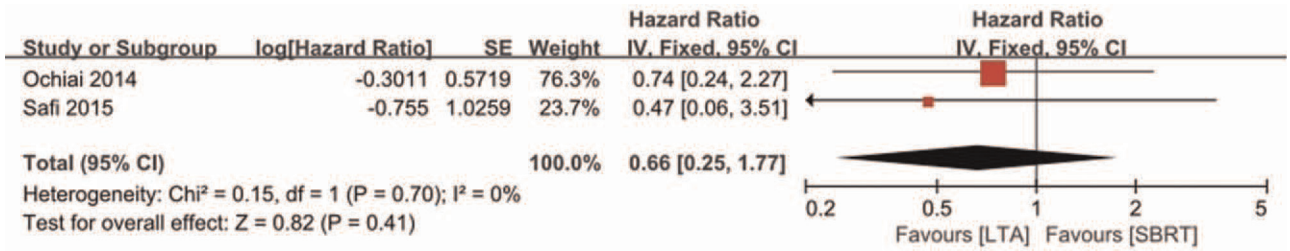

Figure 6: Forest plot of LP for groups of LTA and SBRT. CI: Confidence interval; LP: Locoregional progression; LTA: Percutaneous local tumor ablation; SBRT: Stereotactic body radiotherapy; SE: Standard error.

Table 3: Adverse events in studies comparing LTA *vs.* SBRT for early-stage non-small cell lung cancer.

Studies	Treatment	Number of Patients	Related adverse events ≥Grade 3	*P* values
Ochiai et al 2014[19]	LTA	48	2 pneumothorax, 2 pleural effusion, 1 hemorrhage	$P > 0.999$
	SBRT	47	1 pneumonia/fibrosis, 2 dyspnea, 1 brachial plexopathy	
Safi et al 2015[20]	LTA	25	1 hemothorax, 3 contralateral pleural effusion and ipsilateral pneumothorax	NA
	SBRT	28	1 acute exacerbation of pain	
Ager et al 2019[18]	LTA	1141	NA	NA
	SBRT	14,651	NA	
Iguchi et al 2020[23]	LTA	38	No complications ≥Grade 3	NA
	SBRT	58	No complications ≥Grade 3	
Li et al 2021[22]	LTA	191	NA	NA
	SBRT	6004	NA	

LTA: Percutaneous local tumor ablation; NA: Not available; SBRT: Stereotactic body radiotherapy.

The pooled odds ratio (OR) for the incidence of adverse events in the LTA group was 1.95 (95% CI: 0.63–6.07, $P = 0.25$, fixed-effects mode, Figure 7) compared with that in the SBRT group.

Discussion

Surgical resection remains the standard modality for early-stage NSCLC patients.[29] However, for patients that are unsuitable for surgery or refuse surgery, SBRT and LTA can be viable alternatives.[15] LTA, a minimally invasive curative treatment, is an effective and more economic treatment strategy than surgery.[30-33] However, the inherent defects mentioned previously for LTA have restricted its clinical practice. SBRT, a less invasive but effective treatment, is another option that can substitute resection surgery.[34-37] Although some studies have demonstrated the efficacy of LTA[38,39] and SBRT,[40,41] to our knowledge, there have been no prospective randomized controlled trials to compare LTA and SBRT. In this meta-analysis, five studies with a total of 22,231 patients were analyzed to assess the clinical efficacy of LTA *vs.* SBRT. To our knowledge, this is the first meta-analysis that included control studies to compare the efficacy and safety of LTA and SBRT.

Renaud *et al*[42] performed a literature review of English language articles that compared LTA with SBRT for radically treatable primary lung cancer unfit for surgery. The 23 studies analyzed in their review clearly supported the use of stereotactic ablation rather than RFA in patients with primary NSCLC who were ineligible for surgery. Over an 18-month follow-up period, SBRT provided 5-year local control rates ranging from 83% to 89.5%,

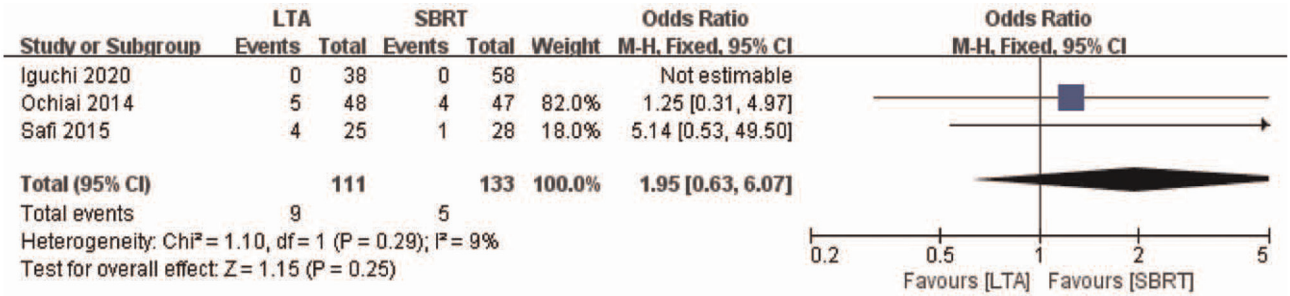

Figure 7: Forest plot of adverse events for groups of LTA and SBRT. CI: Confidence interval; LTA: Percutaneous local tumor ablation; SBRT: Stereotactic body radiotherapy.

compared with 58% to 68% for LTA. They also declared that stereotactic ablation had better OS and tumor-specific survival, with a 3-year OS of 38% to 84.7% and a 3-year tumor-specific survival of 64% to 88%. However, more recent studies were not included in these analyses and no statistical methods were used to analyze the data in the review, which may account for the differences from our results. A pooled analysis by Bi *et al*[17] compared LTA with SBRT in patients diagnosed with early-stage inoperable NSCLC. Thirty-one studies on SBRT (2767 patients) and 13 studies on LTA (328 patients) were analyzed. The authors found that the local control rates at 1, 2, 3, and 5 years were 77% (70–85%), 48% (37–58%), 55% (47–62%), and 42% (30–54%) for LTA, respectively, and 97% (96–98%), 92% (91–94%), 88% (86–90%), and 86% (85–88%) for SBRT, respectively ($P < 0.001$). Conversely, the efficacy of LTA was the same as SBRT for OS (1-, 2-, 3-, and 5-year OS: 85% [80–89%], 67% [61–74%], 53% [45–61%], and 32% [22–43%] for LTA *vs*. 85% [84–87%], 68% [66–70%], 56% [53–59%], and 40% [36–45%] for SBRT, $P > 0.05$). These OS results were consistent with the present study, whereas the results for the local control rate were different. However, the analysis in the study by Bi *et al*[17] was limited to studies prior to 2012, and all of the studies were single-arm studies. The present analysis included five controlled studies for OS analysis and two controlled studies for the analysis of local control rate; none of these studies were included in the analysis by Bi *et al*.

In this meta-analysis, SBRT did not confer OS benefits, LP benefits, or PFS benefits. However, subgroup analysis found that SBRT was superior to LTA for tumors >2 cm in size compared with tumors ⩽2 cm in size. A strong correlation between the size of the targeted tumor and the LTA treatment has been previously reported. RFA treatment results from the American College of Surgeons Oncology Group Z4033 (Alliance) Trial[38] revealed a lower 2-year OS rate (83% *vs*. 78%) and lower local tumor recurrence-free rate for patients with tumors ≥2 cm in size. A study by Lanuti *et al*[43] found that the average tumor size in local failure patients was 2.3 ± 1.0 cm and tumors <2 cm in size had the lowest local recurrence rate (50%), whereas tumors >3.0 cm in size had the highest recurrence rate in patients receiving LTA. Huang *et al*[44] also discovered that patients with tumors <2.0 cm in size had a significantly improved 3-year survival rate of 78.9%. Altogether, this evidence suggests that SBRT is superior to LTA for OS in patients with tumors >2 cm in size.

In the current analysis, SBRT and LTA showed a limited risk of severe complications. Pneumothorax, pleural effusion, and hemothorax were observed in the LTA group. According to previous studies, pneumothorax is the most common complication for LTA treatment, accounting for 31% to 34.3% of complications,[17,45] and about 11% to 12.3% of patients require interventional therapy (chest tube placement). Pleural effusion occurred in 5.2% to 9.6% of patients (95% CI: 1.5–22.4%) and only 0.3% to 0.6% of patients had severe pleural effusion requiring intervention in previous studies.[45] Pseudoaneurysm from vascular injury was rare, occurring in 0.2% of patients.[46] As a consequence of the associated complications, LTA is not recommended for centrally located lesions or lesions located near to major vessels, the diaphragm, or trachea. In our analysis, the SBRT group presented with pneumonia/fibrosis, dyspnea, and brachial plexus disease. The most common Grade 3 or greater toxicity of SBRT was radiation pneumonia.[17] The incidence of pneumonitis of greater than Grade 3 was extremely low compared with that of conventional radiotherapy, which occurred in 2% of patients.[17,42,47] Deadly pneumonia is uncommon—only 0.5% to 1.2% of patients had deadly pneumonia in the survey reported by Nagata *et al*.[48] Other complications included pleural effusion, brachial plexopathy, and liver dysfunction. The rate of complications in the JCOG 0403 trial[49] was very low, in the instance that dose constraints were maintained. LTA had an overall incidence of adverse events of 33% to 100%, whereas SBRT had a lower incidence of adverse events ranging from 3% to 38%.[42] Based on the studies described above, SBRT appeared to have a lower rate of complications compared with LTA, which was inconsistent with our analysis. This discrepancy may be due to the lack of available data on complications in the literature. Thus, the appropriate treatment modality for patients at risk for certain complications should be decided based on the spectrum of complications for each treatment.

Treatment of lung cancer poses a severe financial burden on patients and healthcare systems; the cost of medical expenses for lung cancer is £33,143 per patient in the Netherlands.[50] Cost-effectiveness is of growing importance in medical decisions.[51] Wang *et al*[30] reported that microwave ablation and surgical resection for stage I NSCLC showed similar OS and disease-free survival; however, microwave ablation had a lower cost. A medico-economic study by Paix *et al*[52] that evaluated SBRT and surgical resection in early-stage NSCLC demonstrated that SBRT was a more favorable modality

compared with surgical resection. To compare the cost-effectiveness of conventional radiotherapy, SBRT, and LTA, Sher *et al*[25] developed a Markov model to describe the health conditions of patients with medically inoperable NSCLC after receiving 3-dimensional conformal radiation therapy, SBRT, and LTA. Their results showed that the incremental cost-effectiveness ratio for SBRT over LTA was 14,100 United States dollars/quality-adjusted life-year, which suggests that SBRT is a more cost-effective treatment for medically inoperable stage I NSCLC. However, the results on surgical resection, SBRT, and LTA were based on hypotheses or retrospective studies; therefore, decision makers should consider additional factors, such as accessibility of equipment and technology, and financial capacity.

The present meta-analysis has several limitations. First, there was unavoidable selection bias and retrospective bias because the enrolled studies were retrospective. Second, the differences in characteristics between the different studies that were analyzed resulted in significant heterogeneity, despite the fact that a random-effects model analysis was applied and subgroup analyses were conducted. Third, doses and fractions of SBRT were not standardized, and four of the five studies compared SBRT with RFA without any other LTA methods; together, these factors may have generated treatment bias. Lastly, conference abstracts and unpublished studies were not included in this meta-analysis because of the inability to assess literature quality; therefore, this may have increased the presence of publication bias. Thus, a large-scale, phase III controlled clinical study is needed.

In conclusion, this review and meta-analysis showed no significant differences for OS, PFS, or LP between LTA and SBRT treatment for early-stage NSCLC patients. Both modalities were comparable regarding adverse events. For tumors larger than 2 cm, SBRT is preferred over LTA, whereas LTA appears to be an alternative to SBRT for tumors $\leq$2 cm in size.

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Conflicts of interest

None.

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