Received: 11 August 2024 | Accepted: 24 September 2024

DOI: 10.1111/1759-7714.15463

ORIGINAL ARTICLE

WILEY

Prophylactic cranial irradiation in patients with resected small-cell lung cancer: A systematic review and meta-analysis

Haoning Peng | **Jianqi Hao** | **Bo Dong** | **Minqi Chen** | **Zongyuan Li** | **Cong Chen** | **Lunxu Liu**

Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu, China

Correspondence
Lunxu Liu, Department of Thoracic Surgery, West China Hospital, Sichuan University, No. 37, Guoxue Alley, Chengdu 610041, China.
Email: lunxu_liu@aliyun.com

Funding information
1.3.5 Project for Disciplines of Excellence, West China Hospital, Sichuan University, Grant/Award Number: ZYJC21002

Abstract

Prophylactic cranial irradiation (PCI) was recommended for limited-stage small-cell lung cancer (SCLC) patients with complete or partial response to primary chemoradiotherapy. But it is still controversial regarding its role in SCLC patients who have had radical resection. This meta-analysis aims to evaluate the efficacy of PCI in resected SCLC patients. We searched PubMed, EMBASE, Web of Science, CENTRAl, and ClinicalTrials for controlled trials and cohort studies regarding PCI in postoperative SCLC patients. The correlation between PCI and post-operative outcomes in SCLC patients, including survival and brain metastasis rate (BMR), was examined using hazard ratios (HRs) and risk ratios with corresponding 95% confidence intervals. Quality of studies was assessed by the Newcastle–Ottawa Scale (NOS), and publication bias was assessed by Begg's test. Meta-analysis of eight studies with 2688 patients in total showed PCI was associated with improved overall survival (OS) for resected SCLC (HR: 0.65, 95% CI: 0.57–0.75, $p < 0.01$). In addition, subgroup analysis on three studies including 923 patients confirmed the protective role of postoperative PCI in N0 SCLC patients (HR: 0.79, 95% CI: 0.61–0.97, $p < 0.05$). There was also a significant reduction in BMR in the PCI group pooled from six studies (HR: 0.58, 95% CI: 0.40–0.85, $p < 0.01$). The use of PCI delayed brain recurrence and improved OS in patients with resected, stage I-III SCLC. Importantly, patients with N0 SCLC can also benefit from postoperative PCI. In future studies, PCI's role in patients with resected N0 SCLC at different T stage may need to be explored.

KEYWORDS
cranial irradiation, small-cell lung carcinoma, thoracic surgery

INTRODUCTION

The latest global cancer burden statistics indicate that small-cell lung cancer (SCLC) accounts for 9% of new lung cancer cases in men and 11% in women.[1] At the time of diagnosis, two-thirds of SCLC patients have distant metastasis and about 50% patients develop brain metastases in the course of the disease.[2,3] Prophylactic cranial irradiation (PCI) was found to reduce the incidence of brain metastasis and improved overall survival (OS) for both limited and extensive stage SCLC in the previous research[4–7] However, it is still controversial whether patients with early-stage SCLC should undergo PCI since brain metastases are relatively uncommon in these patients[8–10] and the adverse effect of PCI cannot be ignored.[11,12]

The results of multiple retrospective studies indicated surgery followed by adjuvant chemotherapy is superior to chemoradiotherapy for limited, especially early-stage SCLC.[13–17] A growing number of SCLC patients are undergoing surgery in a real-world setting, but the role of PCI in

Haoning Peng and Jianqi Hao contributed equally to this work.

surgically resected SCLC patients is still unclear.[18] Considering the limited patient population, it is difficult to conduct randomized controlled trials to determine the effectiveness of PCI in postoperative SCLC. A meta-analysis carried out by Y Yang et al. in 2018 demonstrated that resected SCLC patients may benefit from PCI except for p-stage I patients.[19] However, the illustration of these conclusions should be cautious due to the limited number of studies enrolled and small sample sizes in subgroup analyses. Herein, we performed a comprehensive meta-analysis assessing survival outcomes and brain metastasis rate (BMR) of SCLC patients with or without postoperative PCI based on more recent studies. In addition, subgroup analysis for N0 patients was conducted to facilitate clinical decision making.

METHOD

Study design

This systematic review and meta-analysis was preregistered in INPALSY, with registration number INPLASY202480054. The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, and no individual patient data were used.

Search strategy

The literature search was performed in PubMed, EMBASE, Cochrane library (CENTRAL), Web of Science, and ClinicalTrials by two independent reviewers. A combination of Medical Subject Headings (MeSH) terms and keywords in title and abstract were used to search for "small cell lung cancer," "cranial irradiation," and "surgery." No special restrictions were applied to any of the available studies published up to July 2024. The complete search strategy is demonstrated in the supplementary materials S1. Saturation of potentially eligible studies were ensured by scanning the reference lists of identified review articles.

Selection criteria

Literatures were firstly screened for duplication based on title and abstract by two researchers. Case reports, conference abstracts, letters, editorials, commentaries, meta-analysis, and review articles were excluded. The remaining articles were selected through the following criteria: population: small-cell lung cancer patients with radical resection; intervention: postoperative PCI; comparison: patients without PCI; outcomes: OS, BMR; study design: randomized controlled trials (RCT) or cohort studies. Literatures written in languages other than English were excluded. Disagreement over included studies were solved through discussion.

Data extraction and quality assessment

Two authors (H. Peng and J. Hao) extracted data independently using a predetermined extract table including author, year of publication, nationality, accrual years, TNM stage of patients, PCI regime, sample size in both PCI and non-PCI group, median follow-up time, proportion of patients received adjuvant chemotherapy and thoracic radiotherapy (TRT), hazard ratio (HR) and 95% confidence interval (CI) for OS, and BMR. Any conflict was resolved by discussion or consensus with a third reviewer.

Studies included in the review were assessed using the Newcastle–Ottawa Scale (NOS). A study that receives a score of >6 was considered high quality based on the NOS rating scale.

Statistical analysis

The impact of PCI on survival of postoperative SCLC patients were pooled with HR. A subgroup analysis for N0 patients was conducted for OS. Statistical heterogeneity across studies were assessed by Q statistics and I^2 test. Random effect model was adopted for data analysis when the I^2 value exceeded 50%, indicating significant heterogeneity. Otherwise, fixed effect model was used. Sensitivity analysis was performed for identifying possible origin of heterogeneity. The publication bias was assessed using Egger's tests and funnel plots, and trim-and-fill method was performed for evaluating pooled HR after adjusting potential bias. All statistical analyses were conducted in STATA 15.0.

RESULTS

Search results

The process of literature screening and studies selection are depicted in Figure 1. Database retrieval initially yielded 800 records. After removal of 292 duplicated studies, 508 records were screened based on title and abstract and 452 among them were excluded due to irrelevant topics or incorrect article types. A total of 56 studies underwent full-text review, and 11 articles were finally enrolled for meta-analysis.

Basic characteristics of included studies

The basic characteristics of all eligible studies were showed in Table 1. All literatures included in meta-analysis were retrospective cohort studies. Though not reported in few studies, most patients enrolled in this study received adjuvant chemotherapy, while proportion of patients received adjuvant TRT was various between PCI and non-PCI group among different studies. An independent review by two authors showed good consistency in evaluating the quality of the included studies. All studies in this review received a

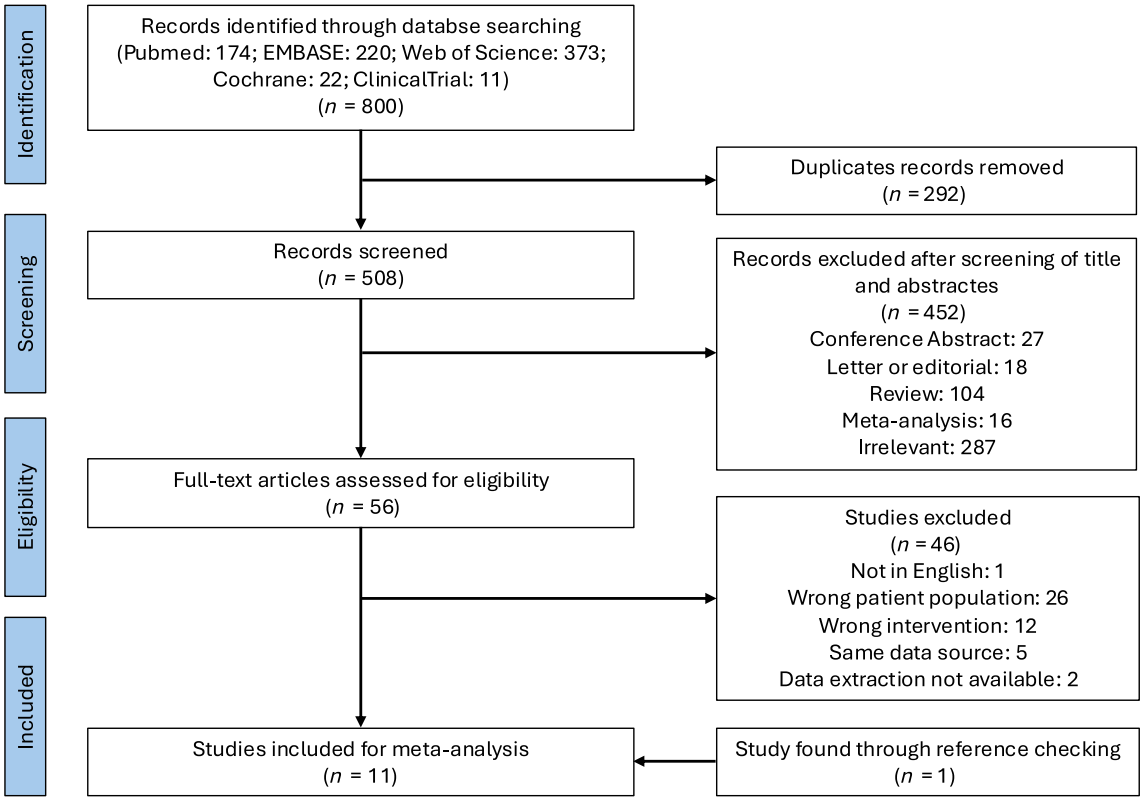


FIGURE 1 The flowchart of study selection.

score of 7 or more according to NOS quality assessment, indicating that they were of high quality (Table 2).

Survival outcomes

Eight studies with 2688 patients in total, 642 in the PCI group, and 2046 in the non-PCI group were included in the meta-analysis of OS for resected SCLC staged I to III (one study including few stage IV patients). SCLC patients with postoperative PCI had longer OS compared to those who did not undergo PCI (HR: 0.65, 95% CI: 0.57–0.75, $p < 0.01$; Figure 2). There was little heterogeneity between studies ($I^2 = 29.2\%$, $H = 1.19$).

Three studies reported OS data for N0 patients. Totally, 923 patients with 263 in PCI group and 660 in non-PCI group were enrolled in N0 subgroup meta-analysis. Similarly, PCI was associated with improved OS in the N0 subgroup of resected SCLC (HR: 0.79, 95% CI: 0.61–0.97, $p < 0.05$; Figure 3). There was a high degree of homogeneity among studies ($I^2 = 0.00\%$, $H = 1.00$).

BMR

A meta-analysis of BMR was conducted on six studies with 953 patients, 278 in the PCI group, and 675 in the non-PCI group. With little heterogeneity ($I^2 = 0.00\%$, $H = 1.06$), BMR was found to be significantly lower in the PCI group (HR: 0.58, 95% CI: 0.40–0.85, $p < 0.01$; Figure 4).

For patients with N0 SCLC, Lou et al. reported 10.9% (5/46) of patients in the PCI cohort and 10.0% (10/100) of those in the non-PCI cohort had brain metastases 2 years after surgery.[20] But in Chen et al.'s research, the incidence of brain metastasis in patients with p-stage I disease was 0% (0/5) and 16.6% (2/12) in the PCI and non-PCI groups, respectively.[21]

Sensitivity analysis and publication bias

We performed sensitivity analysis for eight included studies for meta-analysis of OS (Figure 5). A single study removed from the analysis did not significantly affect the pooled HR, indicating the robustness of pooled results.

As can be seen in the funnel plot of the Begg's test, the result was asymmetric, and Egger's test showed a significant publication bias ($p < 0.05$). We then evaluated the reliability of integrated HRs for OS using the trim-and-fill method (Figure 6). Although two studies were filled to the funnel plot, the pooled HR showed limited changes, suggesting that publication bias did not significantly affect reliability of HR in OS (Figure 7).

Due to the small number of eligible studies reporting BMR and OS for N0 patients, sensitivity analysis, Egger's test, and funnel plots were not performed.

TABLE 1 The characteristics of included studies.

Study	Year of publication	Country	Accrual years	Total number of patients	PCI	Non-PCI	PCI regime	TNM stage	Median follow-up (months)	Adjuvant chemotherapy (PCI/non-PCI or overall proportion)	Adjuvant TRT (PCI/non-PCI or overall proportion)	Outcomes
Yang* et al.[26]	2021	China	2006–2014	664	124	540	NR	I-III	NR	89.5%/68.9%	73.4%/39.3%	OS
Zhou et al.[29]	2021	USA	1986–2019	164	43	121	25 Gy/10 fr	I-III	NR	86%/62%	26%	OS and BMR
Guo et al.[30]	2020	China	2005–2016	251	59	192	NR	I-III	46.8	87.30%	31.50%	OS
Resio et al.[25]	2019	USA	2004–2015	859	202	657	NR	I-III	NR	NR	0%	OS
Chen et al.[21]	2018	China	2003–2015	52	19	33	25 Gy/10 fr	I-III	NR	100%/75.8%	42.1%/18.2%	OS and BMR
Xu et al.[9]	2016	China	2006–2014	349	115	234	NR	I-III	NR	93.0%/91.5%	70.4%/63.2%	OS and BMR
Yokouchi et al.[31]	2015	Japan	2003–2013	156	13	143	25 Gy/10 fr or 30 Gy/15 fr	I-IV	25.5	64.10%	NR	OS and BMR
Zhu et al.[23]	2014	China	2003–2009	193	67	126	25 Gy/10 fr	I-III	39.4	100%	58.2%/43.7%	OS and BMR
Yang* et al.[26]	2021	China	2006–2014	111	37	74	NR	T1-4N0M0	NR	75.70%	73.90%	OS for N0 subgroup
Lou et al.[20]	2020	China	2006–2017	146	46	100	NR	T1-4N0M0	27.5	89.1%/89%	NR	OS for N0 subgroup
Uprety et al.[18]	2019	USA	2004–2013	666	180	486	NR	T1-2N0M0	31.8	100%	0%	OS for N0 subgroup
Bischof et al.[32]	2007	German	1995–2006	39	21	18	30 Gy/15 fr	T1-2N0-1M0	29	90%	41%	BMR

Note: *This study was included in the meta-analysis of OS for patients with resected stage I-III SCLC as well as for the No subgroup. The characteristics of the different patients group are presented seperately.
Abbreviations: BMR, brain metastasis rate; NR, not reported; OS, overall survival; PCI, prophylactic cranial irradiation; TRT, thoracic radiotherapy.

TABLE 2 The Newcastle–Ottawa Scale (NOS) assessment of the eligible studies.

	Selection				Comparability	Outcome			
Study	Representativeness of the exposed cohort	Selection of the nonexposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	Total
Bischof (2007)	*	*		*	*	*	*	*	7
Chen (2018)	*	*		*	*	*	*	*	7
Guo (2020)	*	*	*	*	*		*	*	7
Lou (2020)	*	*	*	*	*	*		*	7
Resio (2019)	*	*	*		*	*	*	*	7
Uprety (2019)	*	*		*	*	*	*	*	7
Xu (2016)	*	*	*	*	*	*	*	*	8
Yang (2021)	*	*	*	*	*	*		*	7
Yokouchi (2015)		*	*	*	*	*	*	*	7
Zhou (2021)	*	*	*	*	*	*	*	*	8
Zhu (2014)		*	*	*	*	*	*	*	7

Note: *The study meets assessment criteria.

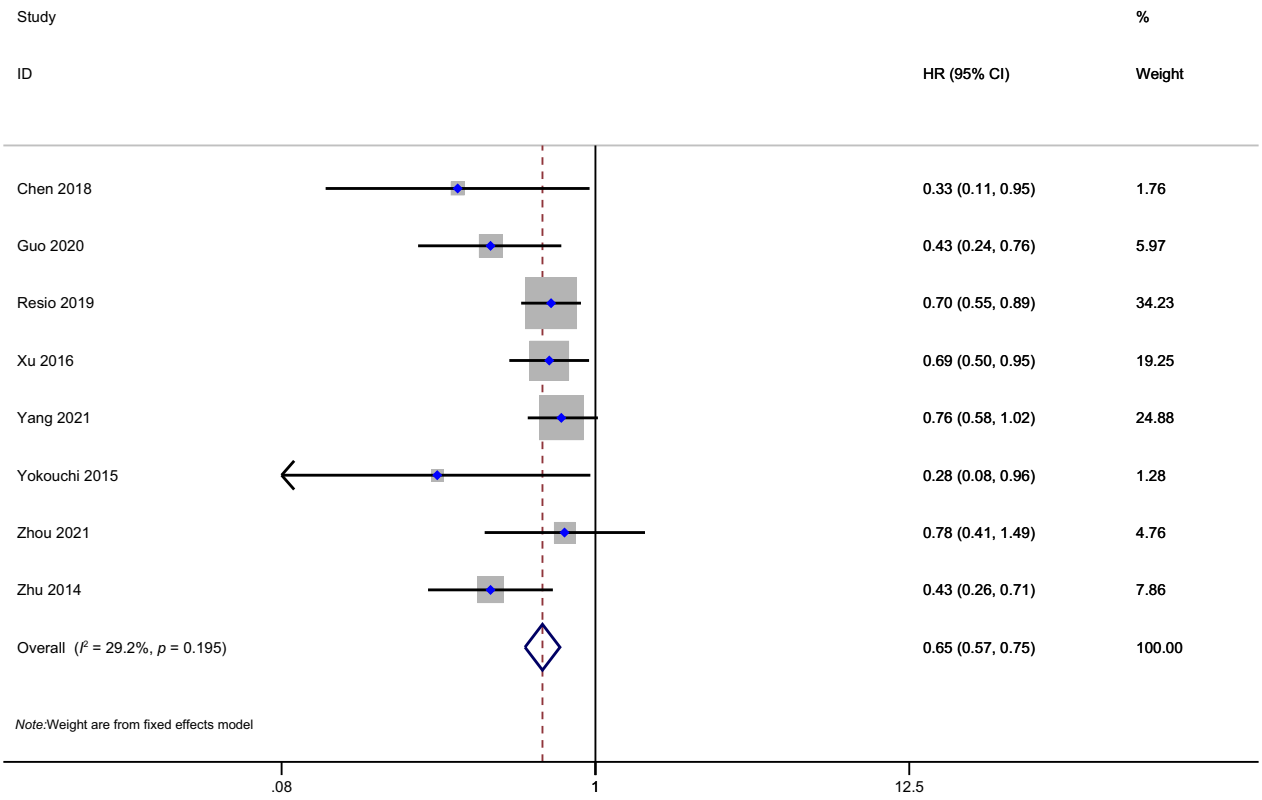


FIGURE 2 Forest plot of HR for overall survival between PCI and non-PCI group. CI, confidence interval; HR, hazard ratio; PCI, prophylactic cranial irradiation.

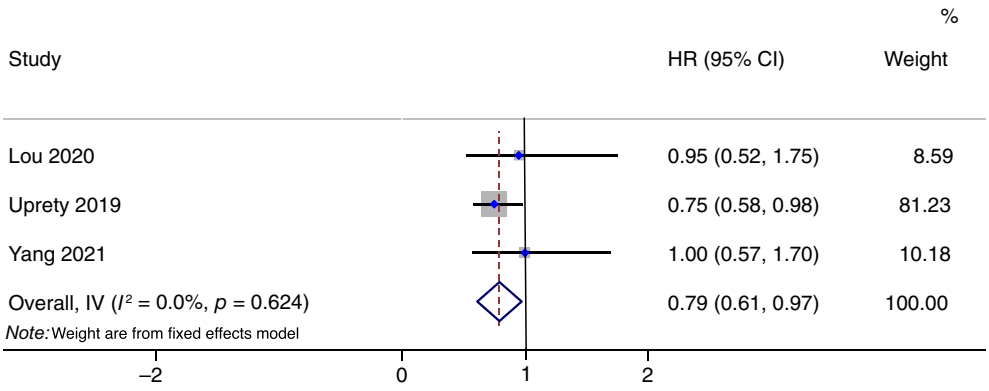


FIGURE 3 Forest plot of HR for overall survival between PCI and non-PCI group in N0 SCLC. CI, confidence interval; HR, hazard ratio; PCI, prophylactic cranial irradiation; SCLC, small-cell lung cancer.

DISCUSSION

This study found PCI can significantly improve OS and reduce BMR for patients with resected SCLC. The results of this study are consistent with previous systematic reviews and retrospective studies comparing the PCI group and non-PCI group among limited-stage SCLC patients receiving either surgery or chemoradiation as their primary treatment.[5,6,19,22]

The current NCCN guidelines for small-cell lung cancer recommend surgery should be considered for patients with T1-T2N0M0. But due to the relatively low incidence of brain metastasis for stage I SCLC patients, it is still unclear whether PCI is beneficial for patients with resected SCLC at an early stage.[10] In order to investigate the role of PCI in early-stage SCLC, we performed subgroup analysis of OS for N0 patients with radical resection. To our knowledge, this is the first meta-analysis indicating postoperative PCI was associated with survival benefit for N0 SCLC patients. A previous meta-analysis showed that patients with stage I, resected SCLC were not benefit from PCI.[19] However, several limitations of meta-analysis for pooled HR of OS in resected, stage I SCLC patients in their study should be noticed. First, HR was calculated from Kaplan–Meier curve instead of cox proportional hazard regression from study of Zhu et al.[23] Second, the control group in study of Yang

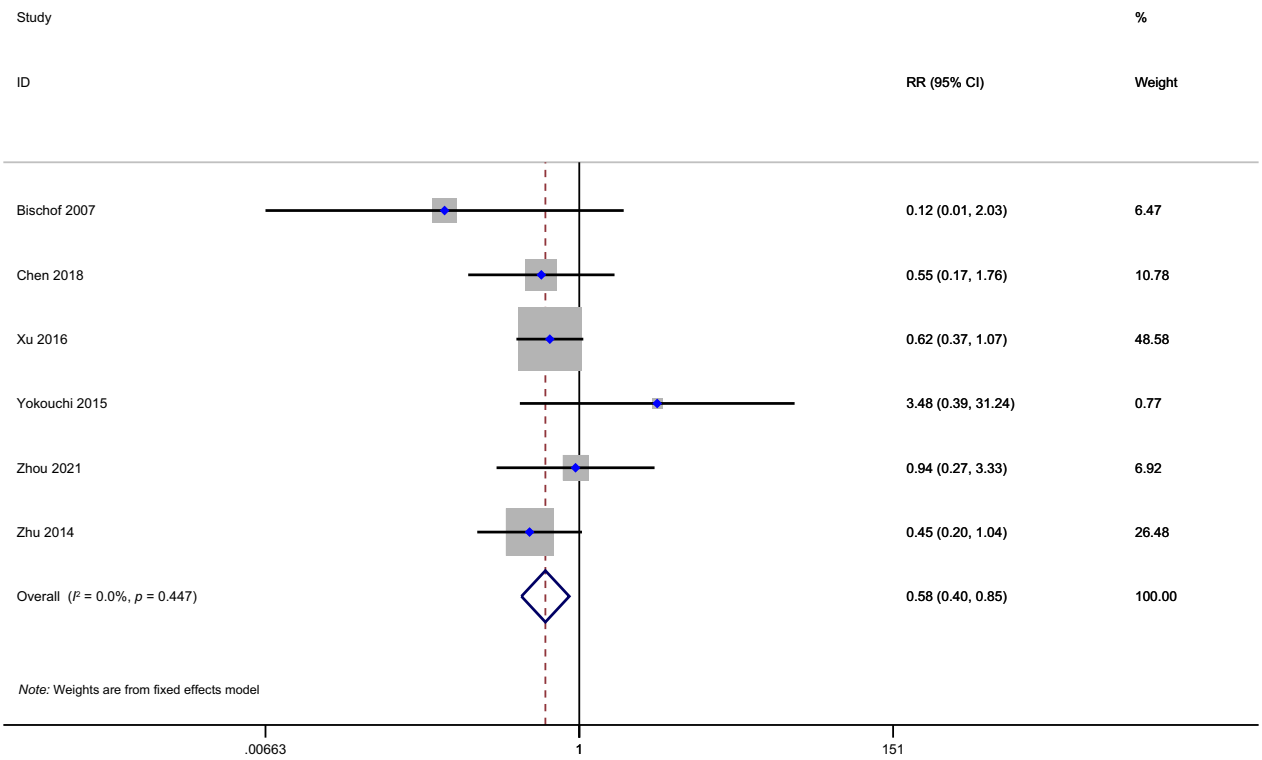
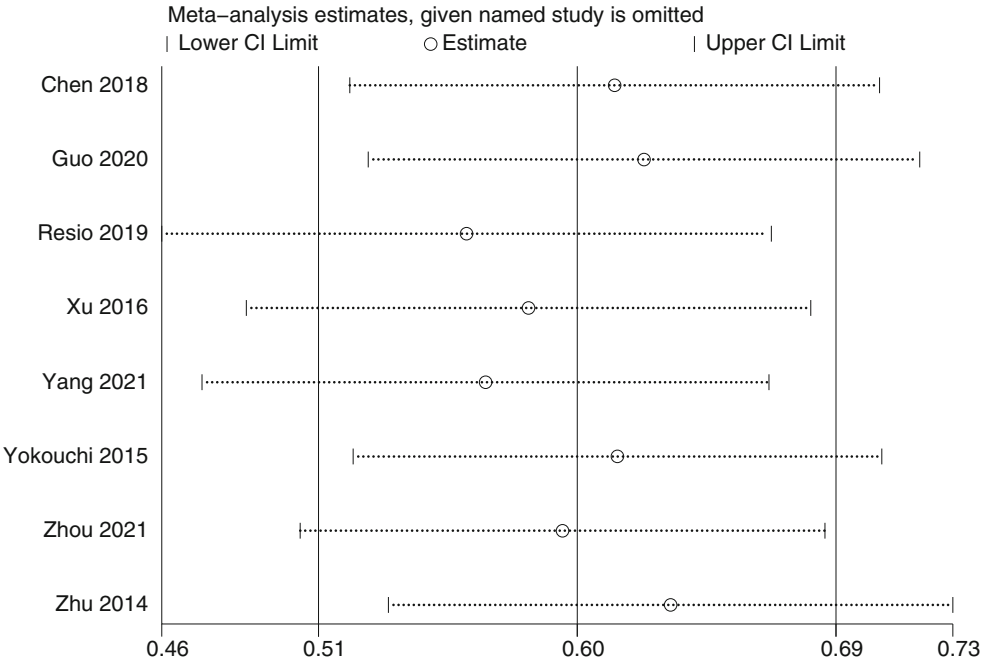


FIGURE 4 Forest plot of HR for brain metastasis rate between PCI and non-PCI group. CI, confidence interval; PCI, prophylactic cranial irradiation; RR, risk ratio.

FIGURE 5 Sensitivity analysis assessing the stability of pooled HR. CI, confidence interval; HR, hazard ratio.



et al.[24] did not receive chemotherapy, while the PCI group did. Since the different definition of T stage between the 6th or 7th AJCC and the 8th or 9th AJCC staging system, few studies were eligible for stage I subgroup analysis according to the latest edition of TNM classification. Therefore, we performed meta-analysis on N0 subgroup instead. Resio et al.[25] reported that patients with N0 SCLC numerically benefited from PCI, but the lack of information about chemotherapy made this study ineligible for the meta-analysis. Instead, we included data from Uprety et al.[18] with more detailed clinical information based on the same database. Data from Yang et al.[26] covered data from Xu et al.,[9] so only

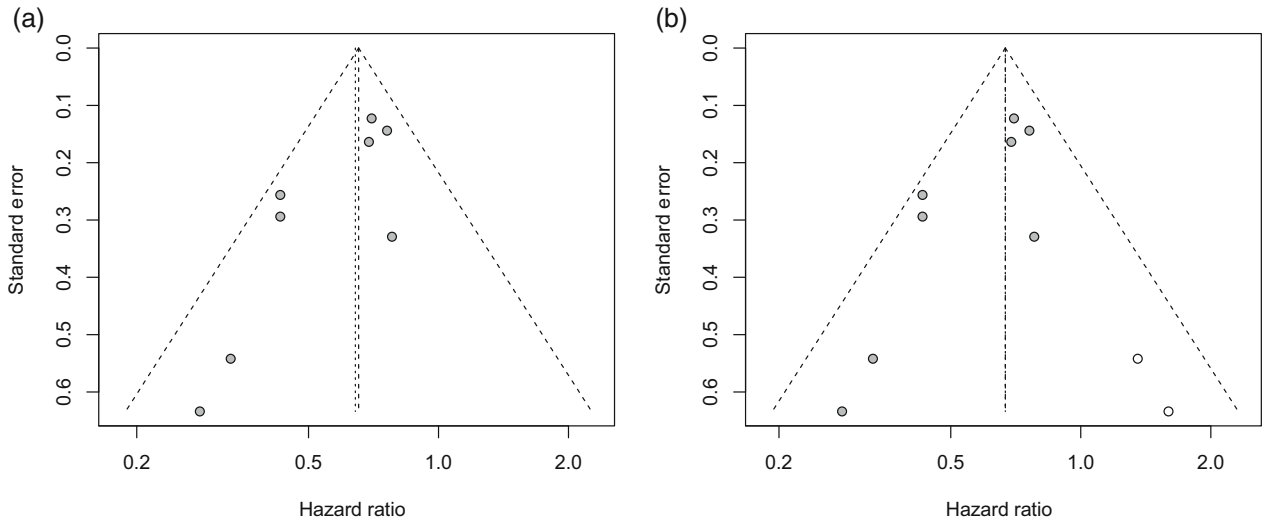


FIGURE 6 (a) Bugg's funnel plots showing publication bias for overall survival. (b) Adjusted funnel plots with two missing studies added after trim-and-fill analysis.

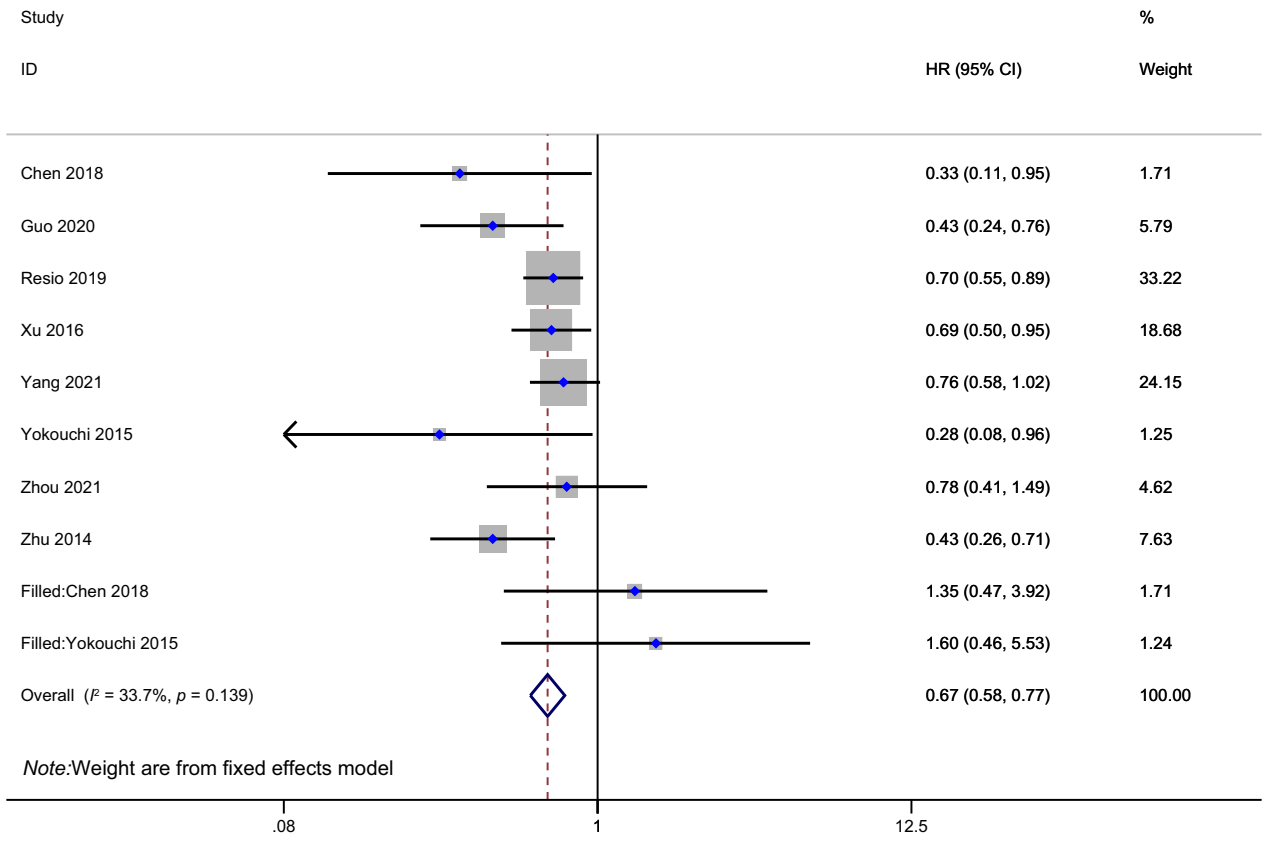


FIGURE 7 Adjusted forest plot of HR for overall survival in resected SCLC patients after trim-and-fill analysis. CI, confidence interval; HR, hazard ratio; PCI, prophylactic cranial irradiation.

the former study was considered for N0 subgroup analysis. Of noticed, studies conducted by Yang et al.[26] included patients with T1-4N0M0, while study of Uprety et al.[18] and Lou et al.[20] contained patients with T1-3N0M0 when converting to the 9th edition of AJCC. Although we found that postoperative PCI may benefit patients with N0 SCLC, whether N0 patients with different T stage according to the latest AJCC classification would benefit from PCI remains to be studied. Uprety et al.[18] reported survival benefits with postoperative PCI in clinical T1 patients (HR, 0.72; 95% CI,

0.53–0.98; $P = 0.03$). Controversially, Xu et al.[9] found PCI failed to significantly extend OS for patients with p-stage I disease (HR 1.61, 95% CI: 0.68–3.83; $P = 0.282$). Future perspective studies are needed to solve this issue.

In the context of general low incidence of brain metastasis and possible risk of neurotoxicity, PCI's role in early-stage SCLC was controversial. Due to small sample sizes, BMRs of N0 patients undergoing radical resection in both PCI and non-PCI group were various among studies. In addition, data about PCI related acute adverse effect and neurocognitive side effect in patients with resected SCLC were not available in most studies. A multicenter randomized clinical trial showed that fatigue, headache, vomiting, or nausea were most common acute toxic events of PCI in patients with limited-stage SCLC in complete remission after chemoradiotherapy.[12] Another phase III randomized controlled trial including patients with extensive-disease SCLC after chemotherapy treatment found PCI had very limited impact on role functioning, cognitive functioning, etc.[27] Moreover, several randomized clinical trials found the neurotoxicity and acute side effects were milder for patients assigned to standard 25 Gy compared to higher 36 Gy PCI total dose.[12,28] The neurologic side effects of postoperative PCI could be controlled to a low level as long as PCI was not given concurrently with adjuvant chemotherapy and given at a low dose (25 Gy in 10 daily fraction).

Several limitations need to be identified in this study. First, covariables including adjuvant chemotherapy and TRT were hard to be unified among different studies. Though multivariable cox was used for HR calculation, these covariates may still confound differences between PCI and non-PCI group. In addition, few studies use propensity score matching to reduce the impact of selection bias and potential confounders. And there is not enough data for us to do the subgroup analysis based on histology type, adjuvant therapy, tumor size, etc. Of noticed, few patients who received neoadjuvant chemotherapy were included in this study. As neoadjuvant are increasingly used in SCLC, survival benefits of PCI may need further validation in these subgroups. Second, many studies did not report exact PCI regime, which may cause various treatment effect among different studies. Third, more than half of studies enrolled for OS and BMR meta-analysis were from east Asia, leading to a selection bias which cannot be ignored. Forth, all 11 studies include in this meta-analysis were retrospective. Perspective cohort studies or randomized controlled trials may need to confirm the effectiveness of PCI in resected SCLC patients in a real-world setting. Fifth, few studies compared postoperative PCI with non-PCI in resected, N0 SCLC patients, and there are even fewer studies comparing these two groups in T1-2N0M0 patients. Though more than 10 studies reported PCI's role in resected SCLC, many of them used patients' data from the same database, such as national cancer database from USA and Shanghai Chest hospital Database from China. To reduce duplicate counting and ensure the authenticity of the research, we only selected one representative study from each database for pooled analysis. Therefore, limited number of studies were included for the N0 subgroup analysis, and our findings needs more external validation.

CONCLUSION

Our findings suggest PCI can significantly reduce BMR and improve OS for SCLC patients after radical resection. Postoperative PCI also showed survival benefits for N0 patients. More retrospective or prospective studies are needed to investigate whether postoperative PCI is effective in improving long-term survival for patients with N0 SCLC at different T stages.

AUTHOR CONTRIBUTIONS

(I) Conception and design: H. Peng, J. Hao, L. Liu; (II) literature screening and selection: H. Peng, Z. Li, C. Chen; (III) data extraction: H. Peng, J. Hao, M. Chen; (IV) statistical analyses: J. Hao, Z. Li, B. Dong; (V) manuscript writing: H. Peng, J. Hao, L. Liu; (VI) final approval of manuscript: all authors.

ACKNOWLEDGMENTS

This research was supported by the 1.3.5 Project for Disciplines of Excellence, West China Hospital, Sichuan University (No. ZYJC21002 to Lunxu Liu).

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data underlying this article are available in the article and in its supplementary material. Further inquiries can be directed to the corresponding author.

ORCID

Haoning Peng https://orcid.org/0000-0003-1388-3255
Lunxu Liu https://orcid.org/0000-0003-3964-5378

REFERENCES

1. Zhang Y, Vaccarella S, Morgan E, Li M, Etxeberria J, Chokunonga E, et al. Global variations in lung cancer incidence by histological subtype in 2020: a population-based study. Lancet Oncol. 2023;24(11):1206–18.
2. Rudin CM, Brambilla E, Faivre-Finn C, Sage J. Small-cell lung cancer. Nat Rev Dis Primers. 2021;7(1):3.
3. Hirsch FR, Paulson OB, Hansen HH, Larsen SO. Intracranial metastases in small cell carcinoma of the lung. Prognostic Aspects Cancer. 1983;51(3):529–33.
4. Sharma S, McMillan MT, Doucette A, Cohen RB, Berman A, Levin W, et al. Effect of prophylactic cranial irradiation on overall survival in metastatic small-cell lung cancer: a propensity score-matched analysis. Clin Lung Cancer. 2018;19(3):260–9.
5. Patel S, Macdonald OK, Suntharalingam M. Evaluation of the use of prophylactic cranial irradiation in small cell lung cancer. Cancer. 2009;115(4):842–50.
6. Aupérin A, Arriagada R, Pignon JP, Le Péchoux C, Gregor A, Stephens RJ, et al. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic Cranial

Irradiation Overview Collaborative Group. N Engl J Med. 1999; 341(7):476–84.
7. Bang A, Kendal WS, Laurie SA, Cook G, MacRae RM. Prophylactic cranial irradiation in extensive stage small cell lung cancer: outcomes at a comprehensive cancer centre. Int J Radiat Oncol Biol Phys. 2018; 101(5):1133–40.
8. Verma V, Simone CB, Allen PK, Lin SH. Outcomes of stereotactic body radiotherapy for T1-T2N0 small cell carcinoma according to addition of chemotherapy and prophylactic cranial irradiation: a multicenter analysis. Clin Lung Cancer. 2017;18(6):675–81.
9. Xu J, Yang H, Fu X, Jin B, Lou Y, Zhang Y, et al. Prophylactic cranial irradiation for patients with surgically resected small cell lung cancer. J Thorac Oncol. 2017;12(2):347–53.
10. Gong L, Wang QI, Zhao L, Yuan Z, Li R, Wang P. Factors affecting the risk of brain metastasis in small cell lung cancer with surgery: is prophylactic cranial irradiation necessary for stage I-III disease? Int J Radiat Oncol Biol Phys. 2013;85(1):196–200.
11. Sun A, Bae K, Gore EM, Movsas B, Wong SJ, Meyers CA, et al. Phase III trial of prophylactic cranial irradiation compared with observation in patients with locally advanced non-small-cell lung cancer: neurocognitive and quality-of-life analysis. J Clin Oncol. 2011;29(3):279–86.
12. Le Péchoux C, Dunant A, Senan S, Wolfson A, Quoix E, Faivre-Finn C, et al. Standard-dose versus higher-dose prophylactic cranial irradiation (PCI) in patients with limited-stage small-cell lung cancer in complete remission after chemotherapy and thoracic radiotherapy (PCI 99-01, EORTC 22003-08004, RTOG 0212, and IFCT 99-01): a randomised clinical trial. Lancet Oncol. 2009;10(5):467–74.
13. Yang CFJ, Chan DY, Shah SA, Yerokun BA, Wang XF, D'Amico TA, et al. Long-term survival after surgery compared with concurrent chemoradiation for node-negative small cell lung cancer. Ann Surg. 2018; 268(6):1105–12.
14. Wakeam E, Acuna SA, Leighl NB, Giuliani ME, Finlayson SRG, Varghese TK, et al. Surgery versus chemotherapy and radiotherapy for early and locally advanced small cell lung cancer: a propensity-matched analysis of survival. Lung Cancer. 2017;109:78–88.
15. Weksler B, Nason KS, Shende M, Landreneau RJ, Pennathur A. Surgical resection should be considered for stage I and II small cell carcinoma of the lung. Ann Thorac Surg. 2012;94(3):889–93.
16. Yang CFJ, Chan DY, Speicher PJ, Gulack BC, Tong BC, Hartwig MG, et al. Surgery versus optimal medical management for N1 small cell lung cancer. Ann Thorac Surg. 2017;103(6):1767–72.
17. Gao L, Shen L, Wang K, Lu S. Propensity score matched analysis for the role of surgery in stage III small cell lung cancer based on the eighth edition of the TNM classification: a population study of the US SEER database and a Chinese hospital. Lung Cancer. 2021;162:54–60.
18. Uprety D, Arjyal L, Vallatharasu Y, Bista A, Borgert A, Fitzsimmons AJ, et al. Utilization of surgery and its impact on survival in patients with early stage small-cell lung cancer in the United States. Clin Lung Cancer. 2020;21(2):186–93.
19. Yang Y, Zhang D, Zhou X, Bao W, Ji Y, Sheng L, et al. Prophylactic cranial irradiation in resected small cell lung cancer: a systematic review with meta-analysis. J Cancer. 2018;9(2):433–9.
20. Lou Y, Zhong R, Xu J, Qiao R, Teng J, Zhang Y, et al. Does surgically resected small-cell lung cancer without lymph node involvement benefit from prophylactic cranial irradiation? Thorac Cancer. 2020;11(5): 1239–44.
21. Chen M, Hu X, Xu Y, Chen M. The impact of prophylactic cranial irradiation for post-operative patients with limited stage small cell lung cancer. Medicine. 2018;97(44):e13029.
22. Maroufi SF, Fallahi MS, Kankam SB, Sheehan JP. Prophylactic cranial irradiation effect on survival in patients with small cell lung cancer: a comprehensive systematic review and meta-analysis. Neurosurg Focus. 2023;55(2):E4.
23. Zhu H, Guo H, Shi F, Zhu K, Luo J, Liu X, et al. Prophylactic cranial irradiation improved the overall survival of patients with surgically resected small cell lung cancer, but not for stage I disease. Lung Cancer. 2014;86(3):334–8.
24. Yang CFJ, Chan DY, Speicher PJ, Gulack BC, Wang X, Hartwig MG, et al. Role of adjuvant therapy in a population-based cohort of patients with early-stage small-cell lung cancer. J Clin Oncol. 2016; 34(10):1057–64.
25. Resio BJ, Hoag J, Chiu A, Monsalve A, Dhanasopon AP, Boffa DJ, et al. Prophylactic cranial irradiation is associated with improved survival following resection for limited stage small cell lung cancer. J Thorac Dis. 2019;11(3):811–8.
26. Yang H, Al-Hurani MF, Xu J, Fan L, Schmid RA, Zhao H, et al. pN1 but not pN0/N2 predicts survival benefits of prophylactic cranial irradiation in small-cell lung cancer patients after surgery. Ann Transl Med. 2021;9(7):562.
27. Slotman BJ, Mauer ME, Bottomley A, Faivre-Finn C, Kramer GWPM, Rankin EM, et al. Prophylactic cranial irradiation in extensive disease small-cell lung cancer: short-term health-related quality of life and patient reported symptoms: results of an international phase III randomized controlled trial by the EORTC Radiation Oncology and Lung Cancer Groups. J Clin Oncol. 2009;27(1):78–84.
28. Wolfson AH, Bae K, Komaki R, Meyers C, Movsas B, Le Pechoux C, et al. Primary analysis of a phase II randomized trial Radiation Therapy Oncology Group (RTOG) 0212: impact of different total doses and schedules of prophylactic cranial irradiation on chronic neurotoxicity and quality of life for patients with limited-disease small-cell lung cancer. Int J Radiat Oncol Biol Phys. 2011;81(1):77–84.
29. Zhou N, Bott M, Park BJ, Vallières E, Wilshire CL, Yasufuku K, et al. Predictors of survival following surgical resection of limited-stage small cell lung cancer. J Thorac Cardiovasc Surg. 2021;161(3):760–71.
30. Guo Y, Yang L, Liu L, Wei J, Teng F, Zhang J, et al. Comparative study of clinicopathological characteristics and prognosis between combined and pure small cell lung cancer (SCLC) after surgical resection. Thorac Cancer. 2020;11(10):2782–92.
31. Yokouchi H, Ishida T, Yamazaki S, Kikuchi H, Oizumi S, Uramoto H, et al. Prognostic impact of clinical variables on surgically resected small-cell lung cancer: results of a retrospective multicenter analysis (FIGHT002A and HOT1301A). Lung Cancer. 2015; 90(3):548–53.
32. Bischof M, Debus J, Herfarth K, Muley T, Kappes J, Storz K, et al. Surgery and chemotherapy for small cell lung cancer in stages I-II with or without radiotherapy. Strahlenther Onkol. 2007;183(12):679–84.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Peng H, Hao J, Dong B, Chen M, Li Z, Chen C, et al. Prophylactic cranial irradiation in patients with resected small-cell lung cancer: A systematic review and meta-analysis. Thorac Cancer. 2024;15(32):2309–18. https://doi.org/10.1111/1759-7714.15463