Comparative effectiveness and toxicity of radiotherapy regimens in limited stage small cell lung cancer: A network meta-analysis

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Abstract

Purpose: The aim of this Network Meta-analysis was to compare the current radiotherapy regimens of limited-stage small cell lung cancer (LS-SCLC), in terms of overall survival (OS), progression-free survival (PFS), and the incidence of acute radioactive esophagitis and radioactive pneumonia.

Methods: PubMed, Embase, Web of Science, and the Cochrane Library were comprehensively searched until January 2022. The studies were included, comparing radiotherapy regimens in LS-SCLC patients. We compared hypofractionated radiotherapy (HypoTRT), hyperfractionated radiotherapy (HyperTRT), and conventionally fractionated radiotherapy (ConvTRT1(<60 Gy), ConvTRT2(≥60 Gy)).

Results: There was similar efficacy among the contemporary radiotherapy regimens for PFS of LS-SCLC. HypoTRT and HyperTRT significantly improved the OS of LS-SCLC compared with ConvTRT1 (<60 Gy), while not improving the OS of LS-SCLC compared with ConvTRT2 (≥60 Gy). There was no significant difference between HypoTRT and HyperTRT, between ConvTRT1(<60 Gy) and ConvTRT2(≥60 Gy), respectively. HyperTRT developed the highest odds of acute radioactive esophagitis compared to ConvTRT1(<60 Gy) and ConvTRT2(≥60 Gy). There was no significant difference in the incidence of acute radioactive esophagitis between HypoTRT and HyperTRT, ConvTRT1(<60 Gy), ConvTRT2(≥60 Gy), respectively and between ConvTRT1 and ConvTRT2. There was no statistically significant difference among radiotherapy regimens for the incidence of acute radioactive pneumonia.

Conclusion: The current radiotherapy regimens are similar in efficacy and toxicity for LS-SCLC, except for ConvTRT1(<60 Gy). Given the lower costs and convenient logistics management of HypoTRT comparatively, it is an acceptable alternative for LS-SCLC.

KEYWORDS

effectiveness, limited-stage small cell lung cancer, network meta-analysis, radiotherapy regimens, toxicity
1  |  INTRODUCTION

It is estimated that lung cancer ranks second among common tumors and is the main cause of tumor death. In 2020, there were more than 2 million newly diagnosed lung cancers and 1.8 million deaths from lung cancer, accounting for approximately one tenth (11.4%) of the tumors diagnosed and one fifth (18%) of the deaths.1 In the United States, there are about 30,000 patients with small cell lung cancer (SCLC) every year, with a 5-year overall survival rate of 6%.2 This deadly neuroendocrine tumor with a short doubling time and early metastasis is difficult to treat for oncologists.3 For limited-stage small cell lung cancer (LS-SCLC), the standard treatment is concurrent chemoradiotherapy at present.4–6 However, the optimal dose and fractionations of radiotherapy are still controversial.

Hyper/ConvTRT have been recommended by the NCCN on the basis of clinical efficacy in separate clinical trials,7–11 but it is not clear which treatment is better. Turrisi et al12 and Faivre-Finn C et al7 reported that the hyperfractionated, twice-daily radiotherapy (BID) demonstrated superior survival when compared to the conventionally fractionated thoracic radiotherapy. Yet, this result was not widely accepted due to inconvenient operation and potential severe esophagitis and granulocytopenia.13 The latest two prospective studies reported that hypofractionated radiotherapy (HypoTRT) seemed to contribute to improve OS than HyperTRT.14,15 In 2020, two meta-analyses revealed that twice-daily thoracic radiotherapy appeared to be better than once-daily for LS-SCLC with better antitumor effects (OS) and similar adverse effects. However, neither did the two studies strictly distinguish HypoTRT and ConvTRT in once-daily thoracic radiotherapy group, nor did they consider the effect of total doses in ConvTRT group.

So, the primary objective of this network meta-analysis was to compare the value of the current radiotherapy regimens as estimated by PFS and OS for HypoTRT, HyperTRT, and ConvTRT. The secondary objective was to compare the adverse events and relative toxicity of radiotherapy regimens mentioned above. Network meta-analysis can indirectly compare A and B therapies through a common comparator, such as C therapy that has been compared to A and B therapies in different studies.16

2  |  MATERIALS AND METHODS

2.1  |  Search strategy

PubMed, Embase, Web of Science, and the Cochrane Library were comprehensively searched for studies that evaluated radiotherapy regimens for LS-SCLC. The search work ended in January 2022. The following search terms were used: small cell lung cancer, radiotherapy, hypofractionated, hyperfractionated, conventionally fractionated radiotherapy, twice-daily, and once-daily etc. The study was confined to English publications focusing on humans.

2.2  |  Inclusion and exclusion criteria

Inclusion criteria: (1) All patients were ones with LS-SCLC; (2) the studies compared at least two thoracic radiotherapy regimens; (3) the studies provided the data of survival and/or adverse effects of radiotherapy. Exclusion criteria: Single arm studies, case reports, repeated publications, studies with unclear efficacy indicators, and without control group, conference abstracts without full-text and registered clinical studies with incomplete key data were excluded.

2.3  |  Interventions and subjects

Interventions: HypoTRT, HyperTRT, and ConvTRT. ConvTRT was divided into ConvTRT1(<60 Gy) and ConvTRT2(≥60 Gy) on the basis of the minimum total radioactive dose in the group. Subjects: Patients with LS-SCLC diagnosed by pathology, regardless of gender, race, and nationality.

2.4  |  Data extraction and quality assessment

The data extraction was conducted by two investigators independently. Any disagreements were discussed and reached an agreement with the participation of the third researcher. The following data were extracted: the first author, publication year, country, sample size, median age of participants, chemotherapy regimen, radiotherapy regimen, follow-up time, adverse reactions (esophagitis and pneumonia), and survival data (PFS,OS). HR was first extracted from multivariate analysis, if not, HR from univariate analysis. Once HR was missing, HR was estimated from Kaplan–Meier curve with the method recommended by Tierney et al17 and Parmar.18 The studies were evaluated according to NOS scale and 6–9 points were high-quality literature. The study obtained approval from the Ethics Committee of Xi’an Chest Hospital.

2.5  |  Statistical analysis

WinBUGS 14.0 and Stata 14.0 were used for data analysis. The estimated risk ratio (RR) was used to summarize the relationship between interventions and esophagitis or pneumonia. The prognostic role of interventions was
| Study                     | Country   | No. of patients | Arm                          | Median age (years) |
|--------------------------|-----------|-----------------|------------------------------|-------------------|
| Gregory M. M. (2003)     | America   | 122             | HypoTRT 40 Gy/15f            | 63                |
|                          |           | 92              | Conv TRT 50 Gy/25f           |                   |
| Catherine S. Bettington (2013) | Australia | 38              | HypoTRT 40 Gy/15f            | 66.5              |
|                          |           | 41              | HyperTRT 45 Gy/30f           | 61                |
| Bjørn H. Gronberg (2015)  | Norway    | 84              | HypoTRT 42 Gy/15f            | 63                |
|                          |           | 73              | HyperTRT 45 Gy/30f           | 63                |
| Bo Qiu (2021)            | China     | 85              | HypoTRT 65 Gy/26f            | 58                |
|                          |           | 92              | HyperTRT 45 Gy/30f           | 58                |
| Jing Zhang (2017)        | China     | 31              | HypoTRT 55 Gy/22 f           | 59                |
|                          |           | 31              | Conv TRT 60 Gy/30 f          | 57                |
| Joanna Socha (2015)      | Poland    | 100             | HypoTRT 42 Gy/15f            | 59                |
|                          |           | 82              | Conv TRT 44–60 Gy/22-30f     | 59                |
| Michael Yan (2021)       | Canada    | 63              | HypoTRT 40 Gy/15f            | 68.5              |
|                          |           | 110             | HyperTRT 45 Gy/30f           | 65.7              |
| Sondos Zayed (2020)      | Canada    | 56              | HypoTRT 40 Gy/15f, 45 Gy/15f, 45 Gy/20f | 63.3 |
|                          |           | 61              | ConvTRT 60 Gy/30f, 66 Gy/33f | 68.2              |
| Dan Han (2015)           | China     | 63              | HyperTRT 45 Gy/30f           | 58                |
|                          |           | 80              | ConvTRT 60 Gy/30f            | 55                |
| Abhilash Gazula (2014)   | America   | 26              | HyperTRT 45 Gy/30f           | 59                |
|                          |           | 19              | ConvTRT 50-66.6 Gy/25-37f   | 65                |
| Andrew L. Turrisi (1999) | America   | 211             | HyperTRT 45 Gy/30f           | 61                |
|                          |           | 206             | ConvTRT 45 Gy/25f            | 63                |
| By James A. Bonner(1999) | America   | 130             | HyperTRT 45 Gy/30f           |                   |
|                          |           | 132             | ConvTRT 50.4 Gy/25f          |                   |
| Corinne Faivre-Finn (2017) | UK        | 274             | HyperTRT 45 Gy/30f           | 62                |
|                          |           | 273             | ConvTRT 66 Gy/33f            | 63                |
| John M. Watkins (2009)   | America   | 54              | HyperTRT ≥ HyperTRT 45 Gy/30f| 62                |
|                          |           | 17              | ConvTRT ≥ 59.4G/28f         | 59                |
| Marianna Christodoulou (2018) | Netherlands | 29           | HyperTRT 45 Gy/30f           | 73                |
|                          |           | 38              | ConvTRT 66 Gy/33f            |                   |
| By Noah C. Choi (1998)   | America   | 24              | HyperTRT ≥ 45 Gy/30-36f      | 60                |
|                          |           | 19              | ConvTRT ≥ 56 Gy/28           |                   |
| Natsuo Tomita (2009)     | Japan     | 37              | HyperTRT 45 Gy/30f           | 58                |
|                          |           | 61              | ConvTRT ≥ 54 Gy/27f         | 66                |
|                          |           | 29              | ConvTRT < 54 Gy/27f         | 70                |
| David Schreiber (2015)   | America   | 2821            | HyperTRT 45 Gy/30f           | 65                |
|                          |           | 996             | ConvTRT 45 Gy/25f            |                   |
|                          |           | 11,116          | ConvTRT 46-59.4 Gy/23-33f    |                   |
|                          |           | 5095            | ConvTRT 60-61.2 Gy/30-34f    |                   |
|                          |           | 5017            | ConvTRT 62-72 Gy/31-40f      |                   |
| Steven E. Schild (2004)  | America   | 130             | HyperTRT 48 Gy/32f           | 62.5              |
|                          |           | 131             | ConvTRT 50.4 Gy/28f         | 63                |
| Median follow-up (months) | Quality score of literature | Study design | Radioactive Esophagitis | Radioactive pneumonitis | PCI | CTregimen |
|--------------------------|-----------------------------|--------------|------------------------|------------------------|-----|-----------|
| 14.8                     | 7                           | Retrospective|                        |                        | 21  | CAV/CEV/EP |
| ≥ 12                     | 8                           | Retrospective|                        |                        | 19  | EP/EC     |
| 81                       | 7                           | Prospective  | 26                     | 5                      | 69  | EP/EC     |
|                          |                             |              | 24                     | 3                      | 61  |           |
| 24.3                     | 9                           | Prospective  | 58                     | 55                     | 63  | EP        |
|                          |                             |              | 63                     | 49                     | 67  |           |
| 30                       | 7                           | Retrospective| 8                      | 7                      | 46  | EP/EC     |
|                          |                             |              | 10                     | 12                     | 48  |           |
| 31                       | 8                           | Retrospective| 24                     | 2                      | 52  | EP/EC     |
|                          |                             |              | 15                     | 5                      | 37  |           |
| 20.4                     | 8                           | Retrospective|                        |                        | 41  | Not mentioned |
|                          |                             |              |                        |                        | 80  |           |
| 162                      | 9                           | Retrospective| 51                     | 22                     | 30  | Not mentioned |
|                          |                             |              | 51                     | 30                     | 42  |           |
| 27.14                    | 7                           | Retrospective|                        |                        |     | EP        |
| 30                       | 7                           | Retrospective| 20                     | 2                      |     | EP/EC/CPT-P/CPT-C |
|                          |                             |              |                        |                        | 11  | 7         |
|                          |                             |              |                        |                        | 90  | 39        |
|                          |                             |              | 130                    | 38                     |     | EP        |
| 39                       | 7                           | Prospective  | 16                     | 8                      |     | EP        |
|                          |                             |              | 7                      | 6                      |     |           |
| 45                       | 7                           | Prospective  | 206                    | 56                     |     | EP        |
|                          |                             |              | 182                    | 55                     |     |           |
| 26.2                     | 7                           | Retrospective| 11                     | 2                      |     | EP        |
|                          |                             |              | 4                      | 1                      |     |           |
|                          |                             |              |                        |                        |     | EP        |
|                          |                             |              |                        |                        |     |           |
|                          |                             |              |                        |                        |     |           |
|                          |                             |              |                        |                        |     |           |
| 88.8                     | Prospective                 | 16           | 11                     | 0                      |     | EP        |
|                          |                             |              | 3                      | 0                      |     |           |
|                          |                             |              |                        |                        |     |           |
|                          |                             |              |                        |                        |     |           |
|                          |                             |              |                        |                        |     |           |
evaluated by both adjusted and unadjusted hazard ratios (HRs) and their 95% confidence intervals (CIs) of OS/PFS on behalf of survival from the primary studies. The rank probability for each treatment was estimated and illustrated visually using bar diagram. The consistency of the network was evaluated by Lumley method using Stata 14.0. Publication bias was assessed by funnel diagram.

3 | RESULTS

3.1 | Studies identification and characteristics of eligible studies

Of the 693 potentially relevant articles, 658 articles were excluded by title and abstract in the initial screening stage, leaving only 35 for full-text evaluation. In the rest articles, the articles were excluded those did not include extractable survival data or the regimens of interest (HyperTRT and ConvTRT were mixed into a group). Finally, 19 articles were included in this study, reporting the results of eight prospective studies7,8,12,14,15,19–21 and 11 retrospective ones22–32 (Figure 1).

Table 1 provided the characteristics of the included studies. Specific details about the total dose and fraction of each radiotherapy regimen were presented. The patients received at least one cycle of concurrent chemotherapy during radiotherapy. Our study included 28,189 patients. They came from America, Poland, Australia, Norway, China, Canada, UK, Netherlands, and Japan. PFS, OS, radioactive esophagitis, and radioactive pneumonia were reported in 14, 19, 11, and 11 studies, respectively. The scores of these all studies were ≥7 points by NOS scale.

3.2 | Meta-analysis

3.2.1 | Radiotherapy regimen and PFS of LS-SCLC

Fourteen studies were included in our PFS analysis. The plot of network is shown in Figure 2A. Compared to ConvTRT(1,2), HyperTRT, and HypoTRT seemed to show better for PFS of LS-SCLC. However, these differences were not statistically significant (HR = 1.00, 95%CI: 0.86–1.15; HR = 0.99, 95%CI: 0.86–1.13; HR = 0.93, 95%CI: 0.79–1.09; HR = 0.92, 95%CI: 0.79–1.08), as seen by the overlapping confidence intervals in Figure 3. HypoTRT were not superior to HyperTRT for PFS of LS-SCLC (HR = 0.94, 95%CI:0.82–1.07). There was no significant difference between ConvTRT1 and ConvTRT2 for PFS of LS-SCLC (HR = 1.01, 95%CI:0.84–1.22) (Figure 3).

3.2.2 | Radiotherapy regimen and OS of LS-SCLC

Nineteen studies reported the effect of radiotherapy on OS of LS-SCLC. The plot of network is shown in Figure 2B.
Zhou et al. HyperTRT and HypoTRT significantly improved OS of LS-SCLC compared to ConvTRT1, with statistical significance (HR = 0.82, 95% CI: 0.80–0.85; HR = 0.80, 95% CI: 0.71–0.91). HyperTRT and HypoTRT were beneficial to OS of LS-SCLC than ConvTRT2, but there was no significant difference (HR = 0.90, 95% CI: 0.79–1.03; HR = 0.88, 95% CI: 0.75–1.04). Compared with ConvTRT1, ConvTRT2 did not improve OS of LS-SCLC (HR = 0.92, 95% CI: 0.80–1.05) (Figure 4).

3.2.3 | Effect of radiotherapy regimen on acute radioactive esophagitis

Acute radioactive esophagitis was reported in 11 studies. The plot of network is shown in Figure 2C. Compared to ConvTRT(1, 2), patients receiving HyperTRT had the highest odds of developing acute radioactive esophagitis with statistical significance (HR = 1.32, 95% CI: 1.08–1.60; HR = 1.12, 95% CI: 1.01–1.25). Patients receiving HypoTRT
were more likely to develop acute radioactive esophagitis than patients receiving ConvTRT1 (HR = 1.48, 95%CI: 1.26–1.74). Patients receiving HypoTRT were equally likely to develop acute radioactive esophagitis than patients receiving ConvTRT2 (HR = 1.00, 95%CI: 0.54–1.83). There was no significant difference in the incidence of acute radioactive esophagitis between HypoTRT and HyperTRT (HR = 0.89, 95%CI:0.49–1.61), ConvTRT1 and ConvTRT2 (HR = 0.92, 95%CI:0.50–1.72), respectively (Figure 5).

3.2.4 | Effect of radiotherapy regimen on acute radioactive pneumonia

We included data from 11 studies to evaluate acute radioactive pneumonia. The plot of network is shown in Figure 2C. Patients receiving different radiotherapy regimen did not seemed to have statistically different incidence of acute radioactive pneumonia (HR = 0.45, 95%CI:0.28–2.50; HR = 0.98, 95%CI:0.61–1.57; HR = 0.99, 95%CI:0.70–1.39; HR = 1.00, 95%CI: 0.72–1.40; HR = 0.33, 95%CI: 0.06–1.79; HR = 0.33, 95%CI:0.06–1.73) (Figure 6).

3.3 | Probability ranking diagram

The ranking probability map was plotted by calculating the ranking probability of each radiotherapy regimen. The ranking first probability value of ConvTRT1, ConvTRT2, HyperTRT, and HypoTRT for PFS were 0.174, 0.126, 0.100, and 0.600, respectively. For OS, the ranking first probability values of ConvTRT1, ConvTRT2, HyperTRT, and HypoTRT were 0, 0.037, 0.345, and 0.617, respectively. The ranking first probability values for ConvTRT1, ConvTRT2, HyperTRT, and HypoTRT were 0.998, 0.2, 0, and 0, respectively in the incidence of acute radioactive esophagitis. In the incidence of acute radioactive pneumonia, the ranking first probability values for ConvTRT1, ConvTRT2, HyperTRT, and HypoTRT were 0.256, 0.078, 0.291, and 0.375, respectively. (Figure 7).

3.4 | Consistency test

The loop consistency was analyzed for the four outcomes. The results showed that there were two closed loops in every outcome, without inconsistencies with $P > 0.05$. (Table 2).

3.5 | Publication bias

The funnel diagram of OS showed a biased distribution, suggesting that there was a certain publication bias. The funnel diagram was relatively symmetrical in PFS, acute radioactive esophagitis, and acute radioactive pneumonia, suggesting that there was less publication bias in the results. In addition, some scattered points were distributed at the bottom of the funnel diagram, suggesting that the results might be affected by the small samples (Figure 8).

4 | DISCUSSION

It has been reported that the median survival time of LS-SCLC is 15–20 months, suggesting that the tumor is extremely malignant. For LS-SCLC that is not suitable for surgery, the current standard treatment is concurrent

**FIGURE 5** RR of acute radioactive esophagitis outcomes. RR<1 indicates better outcomes compared to control.
However, there is much debate about the optimal dose and fractionations of radiotherapy regimen. This was the first network meta-analysis of the contemporary radiotherapy regimens used in LS-SCLC that are recommended or not by the 2020 NCCN guidelines to determine the optimal scheme.

Several conclusions could be drawn from the research. First, the contemporary radiotherapy regimens had similar efficacy for PFS of LS-SCLC and therefore could all be acceptable options for treatment. Second, HypoTRT and HyperTRT significantly improved the OS of LS-SCLC compared with ConvTRT1(<60 Gy), while not improving the OS of LS-SCLC compared with ConvTRT2(≥60 Gy). There was no significant difference between HypoTRT and HyperTRT, between ConvTRT1(<60 Gy) and ConvTRT2(≥60 Gy), respectively. Third, HyperTRT developed the highest odds of acute radioactive esophagitis compared to ConvTRT1(<60 Gy) and ConvTRT2(≥60 Gy). HypoTRT were more likely to develop acute radioactive esophagitis than ConvTRT1(<60 Gy). There was no significant difference in the incidence of acute radioactive esophagitis between HypoTRT and HyperTRT, between HypoTRT and ConvTRT2, respectively. Fourth, there was no statistically significant difference among radiotherapy regimens for incidence of acute radioactive pneumonia. Finally, the first ranked treatments in term of longer survival (for PFS and OS) and lower risk for acute radioactive esophagitis and acute radioactive pneumonia were HypoTRT, HypoTRT, ConvTRT1(<60 Gy), and HypoTRT, respectively.

HyperTRT and ConvTRT2(≥60 Gy) have been recommended by the NCCN on the basis of clinical
efficacy in separate clinical trials. Our data supported the recommendation made by the NCCN. Our data did not support the results of these previous meta-analysis which revealed twice-daily thoracic radiotherapy appeared to be better than once-daily for LS-SCLC with better antitumor effects (OS) and similar adverse effects. One caveat to consider was that neither did the two studies strictly distinguish HypoTRT and ConvTRT in once-daily thoracic radiotherapy group, nor did they consider the effect of total doses in ConvTRT group. In addition, Lin Yang’s study did not include a prospective study. On the basis of these results, it was reasonable to assume that HyperTRT might be equivalent ConvTRT2(≥60 Gy). So, HyperTRT and ConvTRT2(≥60 Gy) can be used for LS-SCLC, which are in line with the NCCN guidelines.

We also found that HypoTRT had similar effectiveness in improving OS compared with HyperTRT and ConvTRT2(≥60 Gy). However, HypoTRT has additional benefits compared with HyperTRT and ConvTRT2. First, HypoTRT can increase the treatment rate, reduce medical expenses, and make patient more comfortable. According to the research report, the cost is 31.7% lower when low fractionated whole breast irradiation (WBI) compared with traditional fractionated whole breast in the United States. A study in Asia also showed that the total cost of hypofractionated WBI was reduced by about one third than conventional fractionated WBI. From a logistical point of view, HypoTRT is easier to manage for both patients and treatment professionals. Second, The higher toxicity rates observed in the Turrisi trial have made people persistently hesitate to BID treatment generally adopted. Similar toxicity shown in this network meta-analysis made HypoTRT possible. Lastly, the start of chemotherapy until the end of radiotherapy(SER)is an important predictor of survival in patients with LS-SCLC27. Extending ser 1 week can reduce OS by 1.83% in rapidly proliferating tumors such as SCLC. Prolonging the total duration of radiotherapy will accelerate repopulation of tumor cells, which is unfavorable to treating tumor. HypoTRT may solve some problems about accelerated repopulation caused by prolonged radiotherapy schedules, such as Hyper/ConvTRT.

Acute radioactive esophagitis is the most common complication in patients with LS-SCLC receiving radiotherapy. Acute radioactive pneumonia is another treatment-related complication. Therefore, in addition to efficacy, we compared adverse events such as acute radioactive esophagitis and pneumonia. Our analysis suggested that contemporary regimens might be equivalent for the incidences of acute radioactive esophagitis and pneumonia except for ConvTRT1(<60 Gy). Thus, radiotherapy doctors can focus on the patient’s preference and tolerance when deciding the radiotherapy regimen.

One of the strengths of our study was that we compared the contemporary radiotherapy regimens from all of the available studies which provided these data. We also compared efficacy between ConvTRT1(<60 Gy) and
ConVTRT2(≥60 Gy), which revealed that ConvTRT1(<60 Gy) was significantly inferior to ConVTRT2(≥60 Gy) in improving OS of LS-SCLC. Understanding the efficacy of current radiotherapy regimen is of vital importance for radiotherapy doctors’ decision-making. Considering the similar efficacy of these regimens except for ConvTRT1(<60 Gy), it is important to evaluate other aspects of treatment to help determine the optimum regimen. Both the cost of treatment regimen and the convenience of operation should be important factors in decision-making.

This study had several limitations. First, the studies included in this network meta-analysis were not all prospective studies, but some retrospective ones. Second, other treatments in the included study might be different. There were differences in chemotherapy regimen, timing of radiotherapy and chemotherapy, treatment after recurrence and so on. Third, most of the included studies did not distinguish between the two recurrence patterns including local recurrence and distant metastasis, but expressed by PFS. Therefore, the difference between the two relapse patterns was not discussed in this study.

5 CONCLUSION

Overall, HypoTRT, HyperTRT, and ConVTRT2(≥60 Gy) regimens fared similarly with regard to efficacy and toxicity, thus providing radiotherapy doctors with flexibility in choosing regimens tailored to patient preference and tolerability. Our analysis suggested that HypoTRT was an acceptable option for LS-SCLC patients today with the benefit of reducing costs and convenient logistics management. Our analysis does not replace the need for comparison with RCT trials.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Jiupeng Zhou and Quanli Dou made contributions to conception and design, publication search, quality evaluation, data collection, statistics, and manuscript writing. Yongfeng Zhang and Heng Liu made contributions to statistics and editors, and Hui Guo contributed to conception, design, statistics, and editing.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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