The impact of hematological and radiation parameters on clinical prognosis of esophageal cancer patients treated with definitive chemoradiotherapy

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Abstract

Purpose:

The aims of the study were to conduct a survival analysis of thoracic esophageal squamous cell carcinoma (ESCC) patients treated with radical chemoradiotherapy and to identify prognostic variables from among the hematological and radiotherapy parameters.

Methods:

Cases of ESCC receiving definitive chemoradiotherapy at Jiangsu Cancer Hospital between January 2018 and September 2020 were screened. Cox proportional hazards model was used to assess the impact of hematologic and dosimetric parameters on overall survival (OS). The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing absolute neutrophil count (ANC) by absolute lymphocyte count (ALC) in the week prior to radical radiotherapy. Variables associated with radiation were gathered according to dose-volume histograms (DVH). X-tile software was used to determine the optimal cut-off values for pre-treatment NLR and post-treatment ALC nadir. Associations between lymphopenia and dose-volume parameters were analyzed using multivariate logistic regression.

Results:

The study comprised a total of 100 ESCC patients. The median follow-up of surviving patients was 33.9 months (interquartile range, 29.2-41.1), with 1-year and 3-year OS rates of 87% and 62.5%, respectively. Multivariate Cox regression analysis demonstrated a significant survival benefit in patients with lower baseline NLR ($\leq 2.2$), higher ALC nadir (>0.24*10^9/L), lighter lymphopenia (value dropped<1.82*10^9/L), and lower mean lung dose (<10.75Gy). Dose-volume parameters of the heart and lungs were correlated with radiation-induced lymphopenia (RIL) ($p < 0.05$).

Conclusion:

In ESCC patients treated with definitive radiotherapy, baseline NLR, ALC nadir, degree of lymphopenia and mean lung dose (MLD) are independent prognostic factors for OS. Optimization of radiation parameters in the heart and lungs can be effective in avoiding RIL.

Introduction

Worldwide, there were an estimated 604,000 new cases and 544,000 fatalities of esophageal cancer in 2020 [1] and there were about 320,000 new cases of esophageal cancer (EC) in China, making it the fourth leading cause of cancer death in China [2]. Squamous cell carcinoma was present in 90% of these cases in China [3]. Although concurrent chemoradiotherapy has somewhat improved the local control rate and survival rate of inoperable locally advanced esophageal squamous cell carcinoma (ESCC) to some extent [4][5], the prognosis of some patients is still not very satisfactory. Therefore, studies exploring the
The correlation between biological indicators and tumor prognosis has attracted extensive attention from scholars. In recent years, the important role of immune and inflammatory responses in the tumor microenvironment has been gradually discovered. Systemic inflammatory response promotes vascular proliferation, DNA damage and tumor invasion through up-regulation of cytokines [6]. Among many inflammatory indicators, studies have confirmed the significant correlation between neutrophil-to-lymphocyte ratio (NLR) and malignancy, which can provide important information for prognosis [7–9]. Absolute neutrophil counts (ANC) reflect the tumor-induced inflammatory response, while absolute lymphocyte counts (ALC) reflect the level of anti-tumor immunity, so NLR can be used as an indicator of whether the two are balanced. Radiation can suppress host immunity by killing immune cells, in particular cytotoxic T lymphocytes [10]. Radiation-induced lymphopenia (RIL) is a common hematologic toxicity because peripheral lymphocytes are known to be the most radiosensitive cells. ALC nadir has been proven to be correlated with poor survival in a wide variety of malignancies, such as glioblastoma, cervical and non-small cell lung cancer (NSCLC) [11–13]. The aim of this study was to explore the impact of peripheral hematologic indicators and radiation parameters on OS in ESCC patients receiving radical chemoradiotherapy and to determine the relationship between lymphopenia and radiation parameters.

**Patients And Methods**

**Patient Selection**

We retrospectively analyzed the medical records of 100 patients who underwent radical chemoradiotherapy at Cancer Hospital affiliated of Nanjing Medical University from January 2018 to September 2020. The specific inclusion criteria were: (1) 18 to 75 years of age; (2) histologically confirmed esophageal squamous cell carcinoma; (3) clinical stage IIA to IVA (American Joint Committee on Cancer, 8th edition); (4) The primary esophageal focus was limited to the thoracic segment; (5) Eastern Cooperative Oncology Group (ECOG) performance status ≤ 2; (6) completed radical intensity-modulated radiotherapy (IMRT) no less than 50Gy; (7) no serious hematopoietic, cardiac, pulmonary, hepatic or renal dysfunction; and adequate bone marrow function; (8) had retrievable full blood counts and radiation parameters (cardiac, lung and whole body dose). Primary exclusion criteria included patients who underwent surgery or lacked complete information on complete blood counts and dose-volume histogram (DVH) or had an immature follow-up period.

**Definitive concurrent chemoradiotherapy**

Radiotherapy was conducted using a Varian linear accelerator. All 100 cases were treated with involved-field radiotherapy (IFi) using the IMRT technique. Target volumes were defined in accordance with the International Commission on Radiation Units (ICRU) and Measurements Report #62. The gross tumor volume (GTV) was defined as including primary tumor and all metastatic lymph nodes (the short diameter of the lymph node local in the tracheoesophageal sulcus ≥ 5mm, in the mediastinum ≥ 1 cm,
and biopsy-confirmed metastatic lymph nodes). The clinical target volume (CTV) included a 3-cm cephalad and caudal margin beyond GTV (without giving prophylactic irradiation). The planning target volume (PTV), defined by a 1-cm margin around CTV, was established. The field next to the spinal cord could be slightly adjusted to avoid excessive exposure. Dose limitations for the critical organs were as follows: (1) the V20 (percentage of the total lung volume receiving over 20 Gy) of lung was ≤ 25%; (2) the V30 of heart was ≤ 40%; (3) the V30 of liver was ≤ 30%; and (4) the maximum spinal cord dose was ≤ 45 Gy.

Concurrent chemotherapy was conducted on the first day of radiotherapy: paclitaxel (175 mg/m$^2$), continuous intravenous drip for 3 hours, day 1; cisplatin (25 mg/m$^2$), i.v. drip., days 1 to 3. Cycles were duplicated every 4 weeks, for 2 courses altogether.

**Dosimetric analysis**

Critical organs were outlined on each axial section of the simulated CT scan. For example, for the heart, the superior side starts at the level of the inferior border of the pulmonary artery and extends down through the midline to the apical part of the heart. DVH of the organs at risk (OARs) were subsequently generated using the treatment planning system.

**Data Collection**

The following clinical characteristics were obtained: of age, gender, tumor site, tumor length, stage, ECOG performance status, etc. ALC and ANC were recorded within the one week before definitive chemoradiotherapy (dCRT). The nadir of ALC was the lowest, appearing within two months after the dCRT started. The NLR was calculated by dividing the ANC by the ALC. The following radiotherapy-related variables were assessed based on the DVH: mean heart dose (MHD), mean lung dose (MLD), V30 of heart, and V20 of lung.

**Statistical analysis**

Categorical variables were descriptively analyzed by frequency and proportion. Median and inter-quartile range (IQR) were used to summarize continuous variables. X-tile 3.6.1 software (Yale University, New Haven, CT, USA) was used to determine the best critical value of pretreatment NLR and ALC nadir. On this basis, the receiver operating characteristics (ROC) curve was used to determine the cut-off points for radiation parameters with ALC nadir as the state variable. Survival curves were plotted using the Kaplan-Meier method, with log-rank tests used to compare OS in subgroups, and hazard ratios (HR) were estimated using Cox regression models. SPSS 25.0 was used for data analysis.

**Results**

**Baseline characteristics**
Of the 100 thoracic ESCC patients enrolled in our study, the majority were male (72%). Their baseline characteristics are listed in Table 1. The median age of all subjects was 65 years (range, 45–76). For the majority of patients, the tumor was in clinical stage III (55%), followed by clinical stage a (27%), and only 18 subjects in clinical stage b (18%). The median length of the tumor was 5 cm (range, 1–8), and the tumor of 54 cases located in upper thoracic segment. The overwhelming of patients (93%) received radiotherapy with a prescribed dose more than 60 Gy.
Table 1

Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>65 (45-76)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>72 (72%)</td>
</tr>
<tr>
<td>Female</td>
<td>28 (28%)</td>
</tr>
<tr>
<td>ECOG performance score</td>
<td></td>
</tr>
<tr>
<td>0~1</td>
<td>93 (93%)</td>
</tr>
<tr>
<td>2</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>Clinical stage (AJCC 6th)</td>
<td></td>
</tr>
<tr>
<td>b</td>
<td>18 (18%)</td>
</tr>
<tr>
<td></td>
<td>55 (55%)</td>
</tr>
<tr>
<td>a</td>
<td>27 (27%)</td>
</tr>
<tr>
<td>Tumor length (cm)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>50 (50%)</td>
</tr>
<tr>
<td>≥5</td>
<td>50 (50%)</td>
</tr>
<tr>
<td>Tumor location</td>
<td></td>
</tr>
<tr>
<td>Upper 25cm</td>
<td>54 (54%)</td>
</tr>
<tr>
<td>Middle 25-30cm</td>
<td>30 (30%)</td>
</tr>
<tr>
<td>Lower 30m</td>
<td>13 (13%)</td>
</tr>
<tr>
<td>Multiple primary</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Prescribed RT dose (Gy)</td>
<td></td>
</tr>
<tr>
<td>60</td>
<td>7 (7%)</td>
</tr>
<tr>
<td>60</td>
<td>93 (93%)</td>
</tr>
</tbody>
</table>

AJCC, American Joint Committee on Cancer

Overall survival and optimal cut-off values

As of April 1, 2022, the median follow-up for surviving patients was 33.9 months (IQR, 29.2–41.1, 95% CI [30.7–37.0]). In the entire patient cohort, the median OS did not reach, with the 1-year and 3-year OS rates
were 87.0% and 62.5%, respectively. The median progression-free survival (PFS) was 35.8 months, with the 1-year and 3-year PFS rates of 77.0% and 49.1%, respectively. (Fig. 1)

In order to dichotomize the haematologic indicators, we determined the optimal cut-off values of 2.2 for pretreatment NLR, 0.24*10^9/L for ALC nadir, and 1.82*10^9/L for change in lymphocyte count pre- and post-treatment, based on X-tile 3.6.1 software (Yale University, New Haven, CT, USA). The critical value of ALC nadir was subsequently used as a state variable in the ROC curve analysis to identify the cut-off values of the relevant radiation parameters (Fig. 2). Consequently, the predictors of avoiding ALC nadir below 0.24*10^9/L were heart V30 ≤ 11.4%, MHD ≤ 7.75 Gy, lung V20 ≤ 19.25% and MLD ≤ 10.75 Gy.

**The predictive significance of cut-off values**

With reference to Figs. 3 and 4, the Kaplan-Meier curves for OS revealed that patients in the lower baseline NLR group, the higher ALC nadir group, the group with greater lymphocyte count change values and the lower cardiopulmonary radiation parameters had longer OS. Table 2 summarises the analysis of the factors associated with OS. Univariate analysis based on the COX regression model indicated that ECOG score, tumour length, ALC nadir and cardiopulmonary radiation parameters were associated with OS. The results of the multivariate analysis showed that the independent indicators of OS include ECOG score (HR = 6.759, 95%CI = 2.599–17.579, p = 0.000), baseline NLR (HR = 2.979, 95%CI = 1.235–7.187, p = 0.015), degree of LC change (HR = 3.116, 95%CI = 1.329–7.305, P = 0.009) and MLD (HR = 3.020, 95%CI = 1.382–6.597, P = 0.006).
### Table 2
Univariate and multivariate Cox regression analysis of factors associated with OS

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th></th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td></td>
<td>HR (95%CI)</td>
<td>P</td>
<td>HR (95%CI)</td>
<td>P</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
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<tr>
<td>65 vs ≥ 65</td>
<td>0.758 (0.383–1.509)</td>
<td>0.426</td>
<td>/</td>
<td>NS</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
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<tr>
<td>Male vs Female</td>
<td>1.113 (0.517–2.395)</td>
<td>0.784</td>
<td>/</td>
<td>NS</td>
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<tr>
<td>ECOG</td>
<td></td>
<td></td>
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<tr>
<td>0 ~ 1 vs 2</td>
<td>0.219 (0.090–0.536)</td>
<td>0.001</td>
<td>0.148 (0.057–0.385)</td>
<td>0.000</td>
</tr>
<tr>
<td>Tumor location</td>
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<tr>
<td>Upper vs Middle</td>
<td>0.919 (0.311–2.821)</td>
<td>0.833</td>
<td>/</td>
<td>NS</td>
</tr>
<tr>
<td>Lower vs Middle</td>
<td>0.648 (0.516–4.620)</td>
<td>0.437</td>
<td>/</td>
<td>NS</td>
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<tr>
<td>Clinical stage</td>
<td></td>
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<tr>
<td>II ~ III vs IVa</td>
<td>0.541 (0.169–1.729)</td>
<td>0.300</td>
<td>/</td>
<td>NS</td>
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<tr>
<td>Tumor length, cm</td>
<td></td>
<td></td>
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<tr>
<td>5 vs ≥ 5</td>
<td>0.331 (0.154–0.714)</td>
<td>0.005</td>
<td>/</td>
<td>NS</td>
</tr>
<tr>
<td>Pretreatment NLR</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>≤2.2 vs 2.2</td>
<td>0.515 (0.239–1.109)</td>
<td>0.090</td>
<td>0.336 (0.139–0.809)</td>
<td>0.015</td>
</tr>
<tr>
<td>ALC Nadir (*10⁹/L)</td>
<td></td>
<td></td>
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<tr>
<td>≤0.24 vs 0.24</td>
<td>2.907 (0.149–0.794)</td>
<td>0.012</td>
<td>/</td>
<td>NS</td>
</tr>
<tr>
<td>LC change value (*10⁹/L)</td>
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<tr>
<td>≤1.82 vs 1.82</td>
<td>0.505 (0.239–1.065)</td>
<td>0.073</td>
<td>0.321 (0.137–0.752)</td>
<td>0.009</td>
</tr>
<tr>
<td>Heart V30 (%)</td>
<td></td>
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<tr>
<td>11.4 vs ≥ 11.4</td>
<td>0.380 (0.171–0.845)</td>
<td>0.018</td>
<td>/</td>
<td>NS</td>
</tr>
<tr>
<td>MHD (Gy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.75 vs ≥ 7.75</td>
<td>0.341 (0.148–0.787)</td>
<td>0.012</td>
<td>/</td>
<td>NS</td>
</tr>
<tr>
<td>Lung V20 (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19.25 vs ≥ 19.25</td>
<td>0.346 (0.150–0.798)</td>
<td>0.013</td>
<td>/</td>
<td>NS</td>
</tr>
</tbody>
</table>

LC: lymphocyte count;
Multiple Logistic regression analysis of lymphopenia

The prevalence of grade 1–2, grade 3 and grade 4 lymphopenia was 9%, 45% and 46% respectively in the whole patient cohort. To further attain more insights into the effect of relevant radiation parameters on lymphopenia, a multiple logistic regression analysis was performed. The results are presented in Table 3, where increased cardiopulmonary exposure dose are risk factors for the development of lymphopenia.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Multiple Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR(95%CI) P</td>
</tr>
<tr>
<td>Heart V30(%)</td>
<td>2.727(1.078–6.899)</td>
</tr>
<tr>
<td>MHD(%)</td>
<td>19.091(2.102–173.375)</td>
</tr>
<tr>
<td>Lung V20(%)</td>
<td>2.231(0.880–5.657)</td>
</tr>
<tr>
<td>MLD(%)</td>
<td>12.133(1.359–108.364)</td>
</tr>
</tbody>
</table>

(A) Heart V30; (B) MHD; (C) Lung V20; (D) MLD

LC: lymphocyte count; △LC: percentage decline in lymphocyte count.

Correlation of lymphopenia with acute radiation side effects

In this study, no grade 3–4 acute radiation side effects were observed. The incidences of grade 1–2 radiation skin reaction, radiation esophagitis and radiation pneumonia in patients during radiotherapy were 41%, 75% and 46%, respectively. Based on the results of the ROC analysis, change in lymphocyte counts before and after radiotherapy was somewhat predictive of grade 2 radiation pneumonitis, but the overall predictive value was faint (Supplementary file).

Discussion
With the development of radiotherapy technology and the continuous optimization of chemotherapy regimens, dCRT has become essential in inoperable locally advanced ESCC, but there are still certain patients whose prognosis needs further improvement. This study investigated the impact of peripheral blood indicators during radiotherapy, including baseline NLR, ALC nadir and degree of lymphopenia, on OS in ESCC patients. We also examined the correlation between RIL and radiation parameters to provide a reference for better optimization of radiotherapy planning to mitigate radiation-induced immunosuppression in the future.

Systemic inflammatory responses play an important role in tumourigenesis, progression and metastasis\(^6\). NLR, a marker of the systemic inflammatory response, is straightforward, easy to obtain, and valuable in determining the treatment outcome and predicting the prognosis of cancer patients. Patients in this retrospective study with lower NLR status had a more significant survival benefit compared to those with high baseline NLR values. Furthermore, it was established by a multivariate COX regression analysis that baseline NLR was one of the independent prognostic factors for patients with ESCC.

A recent study on radiotherapy for esophageal cancer reported the presence of lymphopenia in 15.4% of patients prior to radiotherapy\(^{14}\), 8% in our study, and showed that patients with concomitant lymphopenia prior to treatment had a significantly worse survival than those without lymphopenia (\(p = 0.070\)). The reasons for the malignant tumors accompanying lymphopenia prior to anti-tumour therapy are currently ambiguous and may be related to either the direct induction of T lymphocyte apoptosis by malignancy via the FAS/FASL pathway or the increase in infiltrating lymphocytes from the peripheral blood circulation into the malignant tissues due to a collective immune response caused by cancer progression, resulting in peripheral lymphopenia. Of course, the nutritional status of the organism itself should not be ignored.

Lymphocytes are the most radiosensitive hematopoietic cells and are typically depleted by radiation using a 50% lethal dose of 1 to 2Gy\(^{15}\). Treatment-related haemocytopenia and immunosuppression in thoracic malignancies usually predict a poorer survival outcome. Our findings also reveal that patients with lower ALC nadir and heavier lymphopenia during radiotherapy generally accompanied by an unsatisfactory prognosis. Furthermore, with the development of immunotherapy, radiation-induced haematological toxicity may have a more profound impact. While most previous studies exploring radiation-related haematological toxicity have focused on myelosuppression, we already know that radiotherapy can produce complex and long-lasting changes to the systemic immune system. For instance, the activity of lymphocytes in patients with Hodgkin's lymphoma continues to be affected even though their counts recover to normal after radiotherapy\(^{16–17}\). In addition to immunosuppressive effects, immunostimulating roles have also been documented for radiotherapy. Radiotherapy exerts strong and substantial anti-tumor effect by boosting the immunogenicity of cancer cells\(^{18}\). Furthermore, the radiation-induced modulation of the tumor microenvironment can promote the recruitment of immune cells in the tumor, as well as enhance the tumor cell detection and eradication by immune cells\(^{19}\).
Preclinical studies demonstrated that PD-L1 expression was upregulated in the tumor microenvironment after radiotherapy\cite{20-21}. Therefore, with the increasing development of immunotherapy, eliminating the immunosuppressive effects of radiotherapy is essential to achieving the optimal combined anti-tumour effect\cite{22}.

Thoracic malignancies that are encompassed in the radiation portal, such as esophagus, lung, and left-sided breast cancers, frequently get radiation close to the heart. Previous studies have highlighted the detrimental consequences of lung or heart radiation dose-volumes in lung cancer radiotherapy. Combined with our research findings, the higher doses of radiation of the heart and lungs would result in severe lymphopenia. A randomized Phase III clinical trial (RTOG 0617) also revealed the potential for radiation to act as a risk factor reducing immune function.

The range of radiotherapy targets for EC is broad, including cervical, mediastinal and upper abdominal lymph nodes, and may contain multiple OARs. In clinical practice, the radiation target volume of oesophageal cancer, particularly whether elective nodal irradiation (ENI) or involved field irradiation (IFI) is still the subject of ongoing debate. However, previous studies have confirmed that ENI did not alter the failure patterns and survival outcomes of locally advanced esophageal cancer patients treated with radical radiotherapy\cite{25-28}. IFI has a smaller radiation target volume compared to ENI, and in our retrospective study that included patients all with IFI, the incidence of grade 4 lymphocytopenia was 46%, which is lower than in previous studies of concurrent radiotherapy\cite{29}. All things considered, IFI may be a better option for reducing the incidence of RIL.

The study did have several limitations. Firstly, as a single-centre retrospective study, there was some selection bias. Secondly, because the patients included all received dCRT, it was not possible to explore whether the presence or absence of concurrent chemotherapy during radiotherapy had a significant effect on the incidence of RIL in patients. Finally, because of sample size limitations, we did not include additional radiation parameters for analysis. Other than that, in our study, the dosimetric parameters of the heart reflected the statistically significant differences in the univariate analysis only, but not in the multivariate Cox regression. We believe that there are two possible reasons: (1) when the variables of the heart and lung were simultaneously entered into the Cox regression, an interaction occurred between them, which interfered with the outcome; and/or (2) the relative contribution of radiation received by the heart to the outcome was likely to be relatively small compared with that of the lung in ESCC patients receiving radical radiotherapy.

**Conclusion**

Our study shows that higher baseline NLR and RIL are significantly associated with adverse outcomes in EC patients. ALC nadir during radiotherapy is predicted by the radiation parameters of the heart and lungs, and safeguarding the immune system by continuously improving the radiotherapy plan may be a significant future path to enhance the prognosis of the EC population.
Abbreviations

ESCC: esophageal squamous cell carcinoma; OS: on overall survival; NLR: neutrophil-to-lymphocyte ratio; ANC: absolute neutrophil count; ALC: absolute lymphocyte count; LC: lymphocyte count; DVH: dose-volume histograms; RIL: radiation-induced lymphopenia; MLD: mean lung dose; NSCLC: non-small cell lung cancer; AJCC: American Joint Committee on Cancer; ECOG: Eastern Cooperative Oncology Group; IMRT: intensity-modulated radiotherapy radiotherapy; IFI: involved-field radiotherapy; ICRU: International Commission on Radiation Units; GTV: gross tumor volume; CTV: clinical target volume; PTV: planning target volume; dCRT: definitive chemoradiotherapy; MHD: mean heart dose; IQR: inter-quartile range; ROC: receiver operating characteristics; HR: hazard ratios; PFS: progression-free survival; OARs: organs at risk; ENI: elective nodal irradiation;

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Nanjing Medical University (No. 2018-084). All patients signed informed consents prior to enrollment.

Consent for publication

Not applicable.

Conflict of Interest

The authors declare that they have no competing interests.

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Author Contributions

HL and SS analyzed the data and were major contributors to writing the manuscript. JY and GZ were major contributors to the trial design and the enrollment of patients. QW, YF, RZ, DG, ZZ, YG, and TW are responsible for the enrollment, efficacy, and safety records of the patients. All authors contributed to the article and approved the submitted version.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.
Acknowledgments

Not applicable.

References


**Figures**

**Figure 1**

Survival curves of enrolled patients
Figure 2

ROC curve analysis to identify the cut-off values of the relevant radiation parameters

(A) Heart V30; (B) MHD; (C) Lung V20; (D) MLD
Figure 3

Kaplan–Meier curves of overall survival for subgroup populations (hematological parameters)

LC: lymphocyte count; △LC: percentage decline in lymphocyte count.
Figure 4

Kaplan–Meier curves of overall survival for subgroup populations (radiation parameters)

Supplementary Files

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- Supplementaryfile.docx