

Original Article

Comparison of three-dimensional conformal radiotherapy with intensity modulated radiotherapy in the treatment of locally advanced non-small cell lung cancer: retrospective analysis of 250 cases

Xiaoxia Liu¹, Jianhua Chen², Zhijia Li³, Yike Liu⁴, Yunxiao Wang³, Yan Zhang³, Xiu Jin³, Rui Liu³, Lei Fan³, Zhongchao Huo³, Haitao Li²

Departments of ¹Medical Immunology, ²Laboratory Medicine, Medical College of Hebei University of Engineering, Handan 056038, Hebei Province, China; ³Department of Oncology, Affiliated Hospital of Hebei University of Engineering, Handan 056002, Hebei Province, China; ⁴Operating Room of The First Hospital of Yongnian District, Handan City, Hebei Province, China

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Abstract: To investigate the clinical efficacy and adverse reactions of intensity modulated radiotherapy compared with three-dimensional conformal radiotherapy in the treatment of patients with locally advanced non-small cell lung cancer, 250 cases of locally advanced non-small cell lung cancer treated with radiotherapy from January 2014 to May 2017 in our hospital were selected for the retrospective analysis, among which 141 patients in the study group received intensity modulated radiotherapy and 109 patients in the control group received three-dimensional conformal radiotherapy. The dose of the radiotherapy in the two groups was basically the same, and the efficacy and adverse reactions were under observation. The effective rate of treatment in the study group was 71.6% and 57.6% in the control group, with the difference being statistically significant ($P < 0.05$). Besides, the radiation pneumonia incidence of the study group was significantly lower than that in the control group ($P < 0.05$), but no significant difference was found in the incidence of radiation esophagitis ($P > 0.05$). The incidence of recurrence of lesions, chylous leakage, infection and the incidence of cumulative radiation lung injury was decreased in patients. Compared with three-dimensional conformation radiotherapy, intensity modulated radiotherapy has a better therapeutic effect on locally advanced non-small cell lung cancer, and the incidence of adverse reactions and recurrence is relatively lower.

Keywords: Non-small cell lung cancer, intensity modulated radiotherapy, three-dimensional conformal radiotherapy

Introduction

Lung cancer is considered as one of the most malignant tumors worldwide. Non-small cell lung cancer (NSCLC) accounts for 80% of lung cancers, which included all types of lung cancers except for small cell lung cancer [1]. Similar to other malignancies, early diagnosis and early treatment are the keys to improve prognosis. However, most NSCLC were found to be locally advanced or even with distant metastasis. At this time, radical surgery could not be performed and comprehensive treatment based on radiotherapy and chemotherapy was necessary. Based on the radiation therapy in three-dimensional conformal radiotherapy (3DCRT),

intensity modulated radiotherapy (IMRT) adjusts the dose intensity of the radiation field accordingly to improve the radiation dose in the target tumor and reduce the irradiation of the peripheral normal tissues and organs. Previous studies have shown the dosimetry advantage of IMRT in esophageal cancer, lung cancer, nasopharyngeal cancer and other cancers [2-4]. In the present study, 250 patients with stage III NSCLC received radiotherapy in our hospital were retrospectively studied, among which 141 patients received IMRT in the study group and 109 patients received 3DCRT in the control group. The clinical efficacy and adverse radiation reactions were analyzed.

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Table 1. Comparison of clinical baseline characteristics (n)

Clinical baseline characteristics		Study group (n=141)	Control group (n=109)	P value
Age	< 60	64	49	0.549
	≥ 60	77	60	
Gender	Male	79	57	0.782
	Female	62	52	
Differentiation	Medium and high	55	44	0.315
	Low and none	86	65	
Clinical stage	Stage IIIa	67	42	0.120
	Stage IIIb	74	67	
Pathological type	Squamous cell carcinoma	50	47	0.256
	Adenomatous carcinoma	62	31	
	Others	29	31	

Inclusion criteria: (1) patients between 20 and 70 years old; (2) patients whose pathological diagnosis of NSCLC was clear with clinical stage III; distant metastasis was excluded by relevant imageological examination before radiotherapy; (3) no obvious surgical indications after multidisciplinary consultation. Exclusion criteria: (1) patients with chronic bronchitis, emphysema and other basic diseases; (2) those

Table 2. Comparison of clinical efficacy (n)

	CR	PR	SD	PD	Effective
Study group (n=141)	36	65	25	15	101
Control group (n=109)	14	48	32	14	34
χ^2 value					3.682
P value					0.044

who failed to complete the radiotherapy plan. All patients were between 41 and 68 years old, with an average age of 57.2±6.1 years. No significant statistical differences were found in clinical baseline characteristics such as gender, degree of differentiation, clinical stage, and pathological type (**Table 1**).

Table 3. Comparison of adverse reactions between the two groups (n)

	Radiation esophagitis		Radiation pneumonia	
	I-II	III-IV	I-II	III-IV
Study group (n=141)	86	9	74	13
Control group (n=109)	66	16	66	14
χ^2 value	0.201		4.402	
P value	0.707		0.036	

Radiotherapy plan

The radiotherapy plans of all patients were designed in the radiotherapy planning system. Primary lung lesions, positive lymph nodes and peripheral lymphatic drainage areas were the main composition of Planning Target Volume (PTV). Requirements for radiotherapy plan design: 1) the total prescription dose of all patients was 56-62 Gy given in 28-31 times, and a single dose was 2 Gy, irradiated by the 6MV X-ray of the linear accelerator. 2) at least 90% of PTV received more than 95% of the prescription dose, and the PTV volume greater than 110% of the prescription dose was ≤ 20%. 3) the maximum dose of normal organs requires the spinal cord ≤ 45 Gy, normal lung V20 ≤ 30%, V30 ≤ 20%, esophagus ≤ 30%, and heart ≤ 50%. 4) after 2/3 of the total prescription dose of this radiotherapy, an enhanced chest CT examination was performed again, and the target area was repositioned if the tumor shrank significantly to reduce the exposure to normal tissues.

Materials and methods

Clinical materials

In total, 250 patients with lung cancer who received radiotherapy in Affiliated Hospital of Hebei University of Engineering from January 2014 to May 2017 were selected. All the study procedures involving human participants were in accordance with the ethical standards of the Affiliated Hospital of Hebei University of Engineering ethics committee and obey the regulations of the 1972 Helsinki declaration and its ethical standards. All participants and their families signed informed consent forms before carrying out the study.

Observation indexes

Enhanced chest CT examination was performed before and one month after the end of radio-

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Table 4. Comparison of lesion recurrence rate, chylous leakage and infections incidence [n (%)]

Group	Case	Recurrence rate	Chylous leakage	Infection	Incidence rate
Control group	109	18 (16.5)	15	15	30 (27.9)
Study group	141	8 (5.6)	3	5	8 (5.6)
χ^2 value	-	6.554	-	-	6.012
P value	-	0.012	-	-	0.009

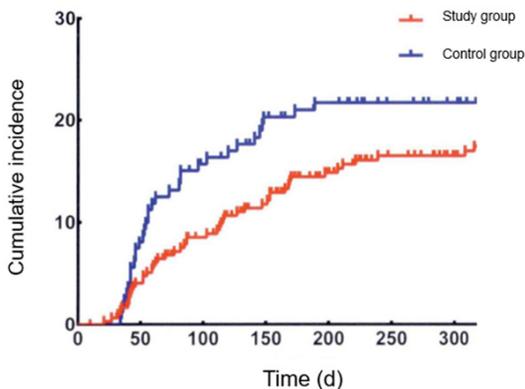


Figure 1. Comparison of the cumulative incidence of radiation-induced lung injury between the two groups.

therapy, according to RECIST1.1 efficacy evaluation criteria [5-7]: (1) CR: no new lesions showed up and all target lesions disappeared; (2) PR: the maximum diameters of the target lesions reduced by least 30% compared with the baseline data; (3) SD: non-PR/PD; (4) PD: new lesions appeared or the maximum diameters of target lesions increased by more than 20%. The treatment was considered as effective with PR and CR. Toxic and side effects of radiotherapy refer to RTOG acute radiation response standard [6-10].

Statistical analysis

The statistical analysis was conducted with SPSS 20.0 software. Enumeration data such as clinical efficacy, number of cases of adverse reactions were expressed as “n”. The two groups were compared under χ^2 test, and $P < 0.05$ was considered statistically significant.

Results

Clinical efficacy

One month after the radiotherapy, the efficacy was reviewed. The effective rate of IMRT for lo-

cally advanced NSCLC in the study group was 71.6%, while the rate for 3DCRT in the control group was 57.6%. The effective rate of IMRT was significantly higher than that of 3DCRT ($P < 0.05$, **Table 2**).

Adverse reactions

In both groups, radiation esophagitis, radiation pneumonia and other injuries occurred in different degrees during radiotherapy (**Table 3**). The incidence of I-II and III-IV radiation esophagitis in the IMRT was 60.9% and 6.5%, and the incidence of I-II and III-IV radiation esophagitis in the three-dimensional conformation radiotherapy was 60.7% and 14.8%. No significant statistical difference was found in the incidence of radiation esophagitis ($P > 0.05$). The incidence of I-II and III-IV radiation pneumonia was 52.5% and 9.8% during IMRT, while the incidence of I-II and III-IV radiation pneumonia was 61.0% and 13.6% during three-dimensional conformation radiotherapy. The difference in the incidence of radiation pneumonia was significantly different ($P < 0.05$).

Comparison of lesion recurrence, chylous leakage and infections incidence

The recurrence rate, chylous leakage and infection rate of the study group were lower than that of the control group ($P < 0.05$). Eighteen cases recurred in half a year with a recurrence rate of 16.5% in the control group. Only 8 patients relapsed in the study group with a recurrence rate of 5.6%. There were 15 cases of chylous leakage and infection in the control group, 3 cases of chylous leakage and 5 cases of infection in the study group. See **Table 4** for details. Therefore, the incidence of radioactive pneumonia was significantly different ($P < 0.05$).

Comparison of radiation-induced lung injury

In the control group, the cumulative incidence of radiation-lung injury was 21.7% over time, while for the study group the incidence was 17.8%. In summary, the study group had a lower recurrence rate and a lower cumulative incidence of radioactive lung injury, suggesting a better therapeutic effect (**Figure 1**).

Discussion

Radiotherapy dose is related to the effects of killing tumor cells. Appropriately increasing radiotherapy dose can lead to more efficiency in killing tumor cells, but the excessive increase will add up to the toxic and side effects of radiotherapy [11-16]. Therefore, how to increase the radiation intensity of the target tumor area while reducing the irradiation of peripheral normal tissues is the continuous focus of clinical treatment. The high-dose radiation area of IMRT is highly consistent with the tumor target area, increasing the radiation dose of primary lung lesions while reducing that of peripheral normal organs and tissues.

A study explored a small sample of 50 patients with stage III NSCLC under concurrent chemoradiotherapy, and found that its effective rate of 60% of IMRT was higher than the 48% of three-dimensional conformation radiotherapy with no statistically significant difference [9]. Among the 250 patients with stage III NSCLC included in the research, 141 received IMRT and 109 received 3DCRT. While the effective rate of IMRT was significantly higher than that of 3DCRT, the incidence of radiation pneumonia was significantly lower than that of 3DCRT. The total effective rate of radiotherapy in this study was 65.0%, similar to the 57.5% total effective rate as reported by a previous study [10]. However, a large-sample and multicenter prospective study is in need to further validate its effect on the long-term efficacy, namely patients' survival time. There were retrospective studies confirming that there was no significant difference between the two treatments in terms of survival [17-21]. Some single-center studies have shown that intensity modulated radiation therapy compared with 3DCRT can prolong patient's survival time [22-24]. For instance, a researcher has found that intensity-modulated radiotherapy can prolong survival time in comparison with 3DCRT in a retrospective analysis of 496 patients with locally advanced NSCLC [13]. However, biases existed in the patient selection of these researches, namely choosing patients with a positive result, which were more favorable for the experiment [25-27]. Intensity modulated radiation therapy in our study measured the incidence of lesion recurrence, chylous leakage and infection compared with three-dimensional conformal radiation

therapy. It is found that intensity modulated radiation therapy can lower the recurrence rate and lower cumulative incidence of radiation-induced lung injury at the same time. Studies have proved the efficiency of intensity modulated radiation therapy in treating locally advanced NSCLC [28-30]. Therefore, differences between the two radiotherapies on survival time require more cases to draw a cautious conclusion.

To conclude, compared with 3DCRT, intensity modulated radiotherapy has better short-term efficacy and relatively low adverse reactions in treating locally advanced NSCLC. As a small-sample retrospective study, the level of evidence in evidence-based medicine is limited. Therefore, the efficacy of intensity modulated radiotherapy in treating locally advanced NSCLC needs to be further clarified with a large-sample and multicenter prospective study with randomized controlled trials.

Disclosure of conflict of interest

None.

Address correspondence to: Zhongchao Huo, Department of Oncology, Affiliated Hospital of Hebei University of Engineering, No. 83 Cong Tai Road, Handan 056002, Hebei Province, China. E-mail: zhongchaohuo6563@163.com; Haitao Li, Department of Laboratory Medicine, Medical College of Hebei University of Engineering, Handan 056038, Hebei Province, China. E-mail: haiwengzhiliao6@126.com

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