ORIGINAL RESEARCH

Analysis of Risk Factors for Pulmonary Infections During Radiotherapy in Lung Cancer Patients

Liyun Guo, MM; Yumei Dong, MM,; Yuexiao Qi, MM; Na Tao, MM; Haixia Song, MM; Lihua Shao, MM; Yaqin Cai, MM; Lijun Xu, MM; Shihong Wei, MM

ABSTRACT

Objective • To investigate the risk factors for lung infection in lung cancer patients undergoing radiotherapy.

Methods • We selected 142 patients with lung cancer who underwent radiotherapy at our hospital from January 2020 to June 2021. The patients were divided into groups according to whether they had pulmonary infection during radiotherapy in our hospital, which was infected group (n=44) and the uninfected group (n=98), respectively. To observe the incidence of lung infection in lung cancer patients during radiotherapy. The distribution of pathogenic bacteria in patients with pulmonary infection was observed. Clinical data of the two groups were collected and compared. The risk factors of lung cancer patients complicated with lung infection were analyzed by binary Logistic regression.

Results • All patients with lung cancer complicated with lung infection underwent relevant examination, and the results showed that they were all complicated infections, and the composition ratio of Klebsiella pneumoniae was the highest (31.82%), followed by Staphylococcus, Pseudomonas, and fungi, which accounted for 27.27%, 22.73%, and 18.18%, respectively. Binary Logistic regression analysis showed that age ≥60 years old, smoking history ≥30 years, radiotherapy duration of combined drug regimen > 2 weeks, pathogenic bacteria combined infection, albumin content < 30 g/L were risk factors for lung cancer patients during radiotherapy.

Conclusion • Age ≥60 years old, smoking history ≥30 years old, radiotherapy duration of combined drug regimen > 2 weeks, pathogenic bacteria combined infection, albumin content < 30 g/L are the risk factors for lung cancer patients during radiotherapy. Clinical prevention and intervention should be based on the aforementioned independent risk factors to decrease the incidence of lung infections, thereby enhancing patient prognosis. (*Altern Ther Health Med.* [E-pub ahead of print.])

Liyun Guo, MM, Chief Physician; **Yumei Dong,** MM, Chief Physician; **Yuexiao Qi,** MM, Chief Physician; **Na Tao,** MM, Chief Physician; **Haixia Song,** MM, Chief Physician; **Lihua Shao,** MM, Chief Physician; **Yaqin Cai,** MM, Chief Physician; **Lijun Xu,** MM, Chief Physician; **Shihong Wei,** MM, Chief Physician; Department of Radiation Oncology, Gansu Provincial Cancer Hospital, Lanzhou, Gansu, China.

Corresponding author: Shihong Wei, MM
E-mail: weishihong100@163.com

INTRODUCTION

Lung cancer is a malignant tumor that develops in the respiratory system of the body. Relevant clinical data show that the population of patients with lung cancer is increasing year by year and developing at a younger age, which seriously affects the survival time and quality of life of patients.[1] At present, the clinical therapeutic effect of lung cancer is mostly accomplished by surgical resection supplemented by chemotherapy or radiotherapy.[2] It should be noted that although chemoradiotherapy can control the progression of tumor lesions in patients during clinical application and to some extent, control their disease conditions, most patients with lung cancer are characterized by functional decline and reduced immune function. They are easily affected by multiple factors in the course of radiotherapy to increase the risk of lung infection, and there are no obvious typical characteristics in the early stage of lung infection. However, a series of adverse reactions caused by pulmonary infection is also an important mechanism for the increase in mortality of patients, which seriously affects the therapeutic effect and prognosis of patients.[3,4] The purpose of this study is to investigate the risk factors for pulmonary infections in lung cancer radiotherapy patients. Conducting a thorough analysis of these associated factors will provide critical information to enhance treatment strategies for lung cancer patients and offer guidance for clinical practice. The relevant research data obtained are reported as follows.

PATIENTS AND METHODS

General Information

A total of 142 patients with lung cancer who received radiotherapy in our hospital from January 2020 to June 2021 were selected. The patients were divided into groups according to whether they had pulmonary infection during radiotherapy in our hospital, which the infected group (n=44) and the uninfected group (n=98). In the infected group, there were 27 males, 17 females, 10 squamous cell carcinoma, 11 adenocarcinoma, 12 small cell lung cancer, 16 peripheral lung cancer, and 28 central lung cancer. In the uninfected group, there were 56 males and 42 females, 27 adenocarcinoma, 30 squamous cell carcinoma, 31 small-cell lung cancer, 47 peripheral lung cancer, and 51 central lung cancer. The comparison of baseline data in 2 groups was all $P > .05$, which confirmed that the comparison between groups was scientific and reasonable.

Inclusion criteria for patients: (1) All clinical examination and diagnosis results of patients meet the diagnostic criteria for lung cancer[5]; The clinical symptoms and relevant examination results of patients with pulmonary infection all meet the relevant contents of Diagnostic Criteria for Nosocomial Infection.[6] (3) Received the chemoradiotherapy intervention program in our hospital and the maintenance time was > 7 days; (4) Patients for whom complete data can be collected. Exclusion criteria: (1) complicated with other malignant tumors; (2) There were signs of pulmonary infection before receiving chemoradiotherapy; (3) patients with combined immune dysfunction; (4) Quit the study due to various factors.

Methods

Detection methods for pathogen distribution confirmation. Before examination, all patients in the infected group received oral cleaning, followed by obtaining sputum samples. The treated and qualified sputum specimens were inoculated in blood AGAR medium (Hangzhou Yidan Company) and cultured for 1 day at a constant temperature of 35°C. VITE2-compact, a Meriere automated microbial identification system, identified the Gran stained colonies.

Detection methods of serum inflammatory factor indexes. All patients included in this study received 5 mL of fasting elbow venous blood in the morning before receiving anti-infection treatment. The obtained blood samples were centrifuged with the parameters set at 3500 r/min with a centrifuge radius of 10 cm for 15 min. The obtained supernatant samples were placed in an automated biochemical analyzer and the serum levels of procalcitonin (PCT), C-reactive protein (CRP), and interleukin-6 (IL-6) were measured. PCT was determined by electrochemical luminescence immunoassay, CRP was determined by transmission turbidimetry, and IL-6 was determined by enzyme-linked immunosorbent assay. Complete the testing in strict accordance with the instructions of the corresponding kit.

Observation Indicators

To observe the incidence of lung infection in lung cancer patients during radiotherapy. The distribution of pathogenic bacteria in patients with pulmonary infection was observed. Serum inflammatory factors were compared between the infected group and the uninfected group. Clinical data of the two groups were collected and compared. Binary *Logistic* regression was used to analyze the risk factors of lung cancer patients complicated with lung infection.

Statistical analysis

All the data in this study were integrated by Statistic Package for Social Science (SPSS) 26.0 analysis (IBM, Armonk, NY, USA) and processing software. The measurement data were expressed by ($\bar{x} \pm s$), the comparison between groups was performed by t test, the rate of counting data was expressed, and the comparison between groups was performed by χ^2 test. The study on the risk factors of lung infection during radiotherapy for lung cancer patients was performed by binary Logistic regression analysis. $P < .05$ meant the difference was statistically significant.

RESULTS

Incidence of lung infection in lung cancer patients during radiotherapy

Out of the 142 patients included in this study, 44 experienced pulmonary infections during radiotherapy, resulting in an infection rate of 30.99%.

Distribution of pathogenic bacteria in patients with lung cancer complicated with lung infection

All patients with lung cancer combined with lung infection underwent relevant examinations, and the results showed that they were all complex infections, and the composition ratio of Klebsiella pneumoniae was the highest (31.82%), followed by Staphylococcus, Pseudomonas, and fungi, accounting for 27.27%, 22.73%, and 18.18%, respectively. See Table 1 for details.

The serum inflammatory factor index levels of the two groups were compared

The levels of serum inflammatory factors, including PCT, CRP, and IL-6, in the infected group increased significantly than those in the uninfected group (all $P < .05$), as shown in Table 2.

Table 1. Distribution and composition of pathogenic bacteria (%)

Pathogenic bacteria	Plant number	proportion
Klebsiella pneumoniae	14	31.82%
Staphylococcus	12	27.27%
Pseudomonas	10	22.73%
fungus	8	18.18%

Table 2. Comparison of serum inflammatory factor indexes between the two groups ($\bar{x} \pm s$)

group	PCT(ng/ml)	CRP(mg/dl)	IL-6(ng/L)
infected group (n=44)	7.34±1.45	28.34±4.52	3.72±1.05
uninfected group (n=98)	0.77±0.19	8.53±1.47	1.64±0.21
t	44.205	39.157	18.864
P value	<.001	<.001	<.001

Comparison of clinical data between the two groups

There was no significant difference in gender between the two groups (all $P > .05$). The comparison of age, smoking history, radiotherapy regimen, radiotherapy duration, combined underlying diseases, albumin content, physical strength before treatment, and distribution of pathogenic bacteria in the two groups was all $P < .05$, as shown in Table 3.

Binary Logistic regression analysis of the risk factors of lung infection in patients with lung cancer during radiotherapy

Factors with $P < .05$ in Table 2 were included as independent variables, and the occurrence of pulmonary infection in patients was included as dependent variables. Binary Logistic regression analysis showed that age ≥60 years old, smoking history ≥30 years, radiotherapy duration of combined drug regimen > 2 weeks, pathogenic bacteria complex infection, albumin content < 30 g/L were risk factors for lung cancer patients during radiotherapy, as shown in Table 4 and Figure 1.

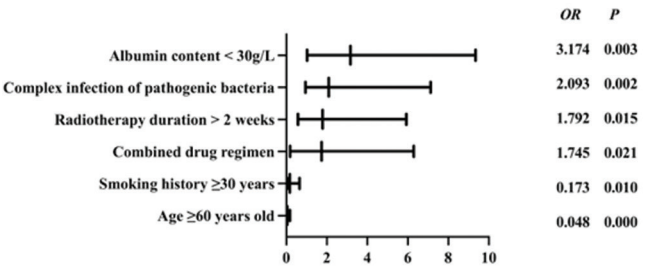
Table 3. Univariate analysis of clinical data differences between the two groups

index	infected group (n=44)	uninfected group (n=98)	t/χ^2	*P* value
Age (years)			14.205	<.001
≥60	33	40		
<60	11	58		
gender			0.070	.791
male	25	58		
female	19	40		
Smoking history (years)			6.836	.009
≥30	27	31		
<30	17	67		
Radiotherapy regimen			7.349	.007
Combination therapy	31	45		
monotherapy	13	53		
Duration of radiotherapy (weeks)			7.408	.006
≤2	18	64		
>2	26	34		
Combined underlying disease (species)			6.493	.011
0	2	26		
1~3	21	53		
≥3	21	19		
Albumin content (g/L)			15.839	<.001
<30	29	32		
≥30	13	66		
Physical condition score before treatment (score)			12.072	.001
<80	30	36		
≥80	14	62		
Pathogenic bacterial infection			34.769	<.001
Individual infection	2	56		
Complex infection	42	42		

Table 4. Risk factors of pulmonary infection in patients with binary *Logistic* lung cancer during radiotherapy

factor	*B*	*S.E.*	*Wald*	*P* value	*OR*	95%*CI*
Age ≥60 years old	3.022	0.662	2.827	.000	0.048	0.013~0.178
Smoking history ≥30 years	1.755	0.679	6.675	.010	0.173	0.046~0.655
Combined drug regimen	0.845	0.633	3.187	.021	1.745	0.184~6.292
Radiotherapy duration > 2 weeks	1.385	0.576	1.194	.015	1.792	0.583~5.925
Complex infection of pathogenic bacteria	2.164	0.842	2.192	.002	2.093	0.943~7.129
Albumin content < 30 g/L	1.431	0.452	2.864	.003	3.174	1.033~9.347

Figure 1. Forest map of risk factors for lung infection during radiotherapy in lung cancer patients



DISCUSSION

Clinical studies have shown that lung cancer frequently occurs in middle-aged and elderly people. Patients with immune dysfunction in this population have a significantly increased risk of lung infection, which is an important factor contributing to poor patient prognosis.[7] Therefore, clarifying and implementing targeted prevention and control measures for the risk factors of pulmonary infection during the treatment of lung cancer patients is of great significance for improving therapeutic effects and patient prognosis.[8] In addition, the progression of lung cancer will seriously affect the functions of various organs in the patient's body. Although chemoradiotherapy can control the progression of tumor lesions, the risk of adverse reactions in patients increases due to various factors during treatment, which will have a serious impact on the body status and thus increase the risk of lung infection.[9,10]

In this study, 146 patients with lung cancer were analyzed to observe the occurrence of lung infection during radiotherapy, and the results showed that 44 patients had lung infections. The distribution of pathogenic bacteria in these patients showed that the proportion of patients with Klebsiella pneumoniae infection was the highest. The mechanism of this phenomenon may be related to the distribution of Klebsiella pneumoniae in the human body. Klebsiella pneumoniae exists widely in the intestinal tract and respiratory system, etc. When patients have obvious lesions in the immune system, antibiotics are needed for treatment, which can easily cause bacterial infection and aggravate the degree of drug resistance of the bacteria in the patients, and then cause the appearance of infection symptoms.[11-13]

In this study, the clinical data of patients with and without infection were compared, and the results showed that age was the risk mechanism of lung infection in patients. The reason may be that the various functions of lung cancer patients ≥60 years old gradually decline with the increase of age, and the immune function of these patients declines. During radiotherapy, the normal play of the ciliary function of the patient's respiratory tract may be hindered, thus affecting the function of the respiratory tract and inducing lung infection.[14] In addition, the duration of smoking history is also an important factor in lung cancer patients complicated with lung infection. Previous studies have shown that smoking is an important mechanism to promote the occurrence and development of lung cancer. For patients who smoke for a long time, continuous smoking will aggravate the dysfunction of lung microenvironment-related functions and seriously affect the normal play of lung functions. Therefore, the probability of infection of lung cancer patients will increase with the extension of smoking

time.[15-17] Previous studies have found that the duration of radiotherapy and chemotherapy is also an important factor causing lung infection in lung cancer patients, and the results of this study also confirmed this point, showing that the longer the duration of radiotherapy, the higher the risk of lung infection. The reason may be that although radiotherapy can effectively kill malignant tumor cells, it will also cause damage to normal cells. Moreover, the longer the radiotherapy duration, the greater the intensity. Patients subjected to high-intensity treatment for a long time may have adverse effects on their gastrointestinal microenvironment homeostasis. They may even lead to adverse complications such as bone marrow suppression.[18] The physical state scale of patients before treatment is an important means to evaluate their physical condition, and the physical condition of patients gets worse and worse with the decrease of the score. In the process of receiving radiotherapy, due to the poor condition of the body, there is a greater risk of invasion by complex pathogens, which may lead to lung infection.[19] The albumin index is a commonly used marker in the clinical evaluation of patients' immune function. Low levels of albumin indicate a decline in patients' immune function, increasing their susceptibility to pathogen invasion and infection.[20]

In addition, in order to further analyze the influence mechanism of lung cancer patients complicated with lung infection during radiotherapy, this study compared the levels of serum inflammatory factors, including PCT, CRP, and IL-6, in the two groups of patients. The results showed that the levels of all indicators in patients with lung cancer complicated with lung infection were abnormally high compared with those in patients without lung infection. It is suggested that the serum levels of PCT, CRP, and IL-6 are significantly changed after the occurrence of lung infection in these patients, which has important reference significance for early clinical identification and diagnosis of lung infection in patients with lung cancer during radiotherapy. PCT is a class of calcitonin propeptide substances. When the body is in a normal state, the level of PCT is extremely low, but when the body has adverse reactions such as infection, a large amount of PCT will be released and show abnormally high expression.[21] Previous studies have shown that the inflammatory response in the body is aggravated by infection, trauma, and other factors, and CRP level, which is also recognized as the most sensitive indicator of the inflammatory response in the body, will also rise abnormally.[22] IL-6 is an inflammatory cytokine with multiple effects, which can be secreted by monocytes, macrophages, T cells, and fibroblasts in the body and participate in the whole inflammatory response. Since lung infection is caused by inflammatory response, which is also involved in the occurrence and development of lung infection, IL-6 can be regarded as an ideal predictor of lung infection.[23]

In conclusion, age ≥60 years old, smoking history ≥30 years old, radiotherapy duration of combined drug regimen > 2 weeks, pathogenic bacteria complex infection, albumin content < 30g/L are risk factors for lung cancer patients during radiotherapy. Clinical prevention and intervention should be carried out according to the above independent risk factors to reduce the complication rate of lung infection and improve the prognosis of patients. In addition, PCT, CRP, and IL-6 showed abnormally high expression in patients with lung cancer complicated with lung infection, suggesting that the above three indicators can provide a certain prediction and diagnosis reference for lung cancer patients with lung infection during radiotherapy. Furthermore, effective medical measures, such as regularly monitoring patients' immune status, developing individualized infection prevention plans, and judiciously using antimicrobial drugs, can help reduce the incidence of pulmonary infections during treatment, thereby improving treatment effectiveness and prognosis.

ETHICAL COMPLIANCE

The ethics committee of Gansu Provincial Cancer Hospital approved this study. Signed written informed consent were obtained from the patients and/or guardians.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

GL and SW designed the study and performed the experiments, YD, YQ and NT collected the data, HS, LS YC and LX analyzed the data, GL and SW prepared the manuscript. All authors read and approved the final manuscript.

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