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## Detection of the serum endothelin content in patients with acute lung injury and its value of severity evaluation

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### ABSTRACT

**Objective:** To observe the correlation of serum endothelin content in patients with acute radiation lung injury and with the degree of inflammatory reaction and the lung functional level.

**Methods:** 68 Patients with non-small cell lung cancer who received the radiotherapy in treatment from May 2013 to October 2015 in our hospital were selected as the object of study. 25 patients who had acute radiation induced lung injury within 24 months of the radiotherapy were rolled in the radiation induced lung injury group (RILI group), and the rest of 43 without acute lung injury were rolled in the negative control group (NC group). The contents of endothelin, tumor necrosis factor  $\alpha$ , interleukin-1 $\beta$ , interleukin-6 in serum and the partial pressure of oxygen in artery, partial pressure of carbon dioxide in artery, vital capacity, forced expiratory volume in one second, maximal ventilatory volume, and diffusion capacity for carbon monoxide were tested.

**Results:** The content of serum endothelin of the patients in the RILI group [(69.3  $\pm$  7.5) pg/mL] were all obviously higher than that of the NC group [(24.1  $\pm$  2.9) pg/mL]; the content of the serum tumor necrosis factor  $\alpha$  [(49.6  $\pm$  5.1) ng/mL vs. (22.7  $\pm$  3.1) ng/mL], interleukin-1 $\beta$  [(29.4  $\pm$  3.3) ng/mL vs. (15.7  $\pm$  1.8) ng/mL], interleukin-6 [(163.4  $\pm$  20.3) pg/mL vs. (89.4  $\pm$  10.2) pg/mL] and the partial pressure of carbon dioxide in artery [(49.2  $\pm$  5.2) mmHg vs. (40.3  $\pm$  4.8) mmHg] were all obviously higher than that of the NC group, which were positively correlated with the serum endothelin content. But the partial pressure of oxygen in artery [(68.4  $\pm$  7.8) mmHg vs. (87.3  $\pm$  9.5) mmHg], vital capacity [(1203.4  $\pm$  136.5) mL vs. (2034.8  $\pm$  238.5) mL], forced expiratory volume in one second [(38.4  $\pm$  4.1)% vs. (58.3  $\pm$  6.2)%], maximum minute ventilation [(33.7  $\pm$  3.8) L/min vs. (66.1  $\pm$  7.9) L/min] and diffusing capacity of the lungs for carbon monoxide [(79.3  $\pm$  8.9)% vs. (86.7  $\pm$  9.4)%] were obviously lower than that of the NC group, which were negatively correlated with the serum endothelin content.

**Conclusion:** The elevated content of the endothelin in the serum of patients with acute radiation induced lung injury could assess the degree of inflammatory reaction and the lung functional level.

## 1. Introduction

Lung cancer is the malignant tumor in the first place of its occurrence rate and death rate in the world at present. Over 90% of the type of lung cancer is non-small cell lung cancer. For the past few years, with the continuous development of the radiotherapy technique, radiotherapy had become the most important way for the treatment of the non-small cell lung cancer, which could put off the growth of the tumor and lengthen the patients' life time<sup>[1–3]</sup>. However, it will cause the damage of the normal lung tissues when the lung cancer cells are killed by the radiotherapy, and lead to the clinical symptoms, such as

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The study protocol was performed according to the Helsinki declaration and approved by the Ethics Committee of the hospital. The patients who were rolled in the groups had obtained informed consent.

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radiation induced lung injury cough, fever, dyspnea, and decline of lung function<sup>[4–6]</sup>. The total occurrence rates are still over 15%, though the radiotherapy technique had been continually improved and the occurrence rate of the lung cancer had decreased<sup>[7]</sup>. This disease essentially belongs to the aseptic inflammation and is difficult to get completely reversed and cure. To find out the disease and accurately evaluate and treat it at early stage would be conducive to improve the prognosis of patients<sup>[8,9]</sup>. Some studies had reported that there was close relations between the acute radiation induced lung injury and the changes in serum endothelin content<sup>[10,11]</sup>, but the change conditions of the endothelin content in serum of the patients with acute radiation induced lung injury hadn't been reported. In the present study, the detection of the serum endothelin content in patients with acute lung injury and its value of severity evaluation of acute lung injury were analyzed.

## 2. Materials and methods

### 2.1. Cases materials

68 Patients with non-small cell lung cancer who received the radiotherapy in treatment from May 2013 to October 2015 in our hospital and were conformed to the following inclusion and exclusion criteria were selected as the objects of study. The inclusion criteria: the patients in the period of TNM III with ages of 30–70, who couldn't receive surgery, and expected life time of over 6 months, with normal lung function, more than 50% vital capacity in one second, normal hepatorenal function and bone marrow hematopoietic function, and no other coexisting malignant tumors and distant metastasis in lung cancer were found. The exclusion criteria: the patients with functional injury of liver and kidney, who had chronic complications of diabetes, coronary heart disease *etc.* were excluded from the study. This study was approved by the Ethics Committee of the hospital, and the patients who were rolled in the groups had obtained informed consent.

In the process of the radiotherapy, the following criterion was used to judge the occurrence of acute radioactive lung injury: the clinical symptoms are cough, fever and dyspnea, and through chest CT scanning, the homogeneous density flake-like obscured shadow and its border inside the lung lobes were found in accord with that in the radiotherapy; the symptoms still exist after one week regular treatment of the antibiotics, that were diagnosed to be the acute radiation induced lung injury after excluded pulmonary infection. The endpoint of observation was that the time of the occurrence of the acute radiation induced lung injury or 24 weeks after the radiotherapy, the patients with acute radiation induced lung injury were rolled in the radiation induced lung injury group (RILI group), and the other patients were rolled in the negative group (NC group).

### 2.2. Experimental method

The clinical index of patients in the RILI group was tested after the corresponding clinical symptoms of the lung injury appeared, and the clinical index of the patients in the NC group was tested after 24 weeks of the radiotherapy. 5–10 mL of the peripheral venous blood samples of patients in the two groups were collected at corresponding time, and serum samples were obtained by centrifugal separation after holding

under the indoor temperature condition, then the enzyme-linked immunosorbent assay kits (produced by Shanghai Westang Bio-tech CO., Ltd.) were used to test the contents of endothelin, tumor necrosis factor  $\alpha$ , interleukin-1 $\beta$ , interleukin-6; 2–5 mL of the peripheral venous blood samples were collected to tested the partial pressure of oxygen in artery (PaO<sub>2</sub>) and partial pressure of carbon dioxide in artery (PaCO<sub>2</sub>) by the blood gas analyzer, and the volume of forced expiratory volume in one second (FEV1), maximum minute ventilation (MVV), and diffusing capacity of the lungs for carbon monoxide (DLCO).

### 2.3. Statistical analysis

The software of SPSS19.0 version was used to enter and analyze the data. The measurement data were expressed as mean  $\pm$  SD and analyzed by *t*-test; the enumeration data were expressed by frequency form and analyzed by *Chi*-square test; the correlations between the above two variables were tested by Pearson's correlation analysis. *P* < 0.05 was regarded as the criterion that the differences were statistically significant.

## 3. Results

### 3.1. General materials of cases

25 Patients with occurrence of acute radiation induced lung injury in the 68 cases were rolled in the RILI group, which included 19 males and 6 females, whose ages were (38  $\pm$  4) years, BMI indexes were (22.5  $\pm$  2.6) kg/m<sup>2</sup>, and the contents of ALT were (14.6  $\pm$  1.7) IU/L, AST were (17.1  $\pm$  1.5) IU/L, SCr were (68.3  $\pm$  7.2)  $\mu$ mol/L, and BUN were (3.8  $\pm$  0.5) mmol/L before the treatment; The 43 patients who hadn't got the acute radiation induced lung injury within 24 weeks of the radiotherapy were rolled in the NC group, which included 33 males and 10 females, whose ages were (36  $\pm$  4) years, BMI indexes were (21.8  $\pm$  2.3) kg/m<sup>2</sup>, and the contents of ALT were (15.1  $\pm$  1.6) U/L, AST were (16.7  $\pm$  1.9) IU/L, SCr were (65.8  $\pm$  6.8)  $\mu$ mol/L, and BUN were (3.6  $\pm$  0.4) mmol/L before the treatment. According to statistic analysis, the genders, ages, BMI indexes, and the contents of ALT, AST, Scr, BUN had no differences (Table 1).

**Table 1**

General materials of patients in RILI group and NC group.

General material	RILI group (n = 25)	NC group (n = 25)	P
Gender (M/F)	19/6	33/10	< 0.05
Ages (years)	38 $\pm$ 4	36 $\pm$ 4	< 0.05
BMI (kg/m <sup>2</sup> )	22.5 $\pm$ 2.6	21.8 $\pm$ 2.3	< 0.05
ALT (IU/L)	14.6 $\pm$ 1.7	15.1 $\pm$ 1.6	< 0.05
AST (IU/L)	17.1 $\pm$ 1.5	16.7 $\pm$ 1.9	< 0.05
Scr ( $\mu$ mol/L)	68.3 $\pm$ 7.2	65.8 $\pm$ 6.8	< 0.05
BUN (mmol/L)	3.8 $\pm$ 0.5	3.6 $\pm$ 0.4	< 0.05

### 3.2. Contents of serum endothelin and inflammatory factors

The content of serum endothelin of the patients in the RILI group [(69.3  $\pm$  7.5)] vs. (24.1  $\pm$  2.9) pg/mL were all obviously higher than that of the NC group; Similar to variation tendency

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