

# Relationship between depression and blood cytokine levels in lung cancer patients

Wen-Juan Liu<sup>1</sup>, Xiao-Dan Wang<sup>2</sup>, Wei Wu<sup>3</sup>,  
Xiao Huang<sup>1\*</sup>

> **Objective:** To study the correlation between depression and blood cytokine levels in lung cancer patients.

**Methods:** 92 patients with advanced lung cancer were evaluated for depression using the scoring index of depression self-rating scale. Lack of depression (n=24), mild depression (n=45), and moderate depression (n=23) were found in the cohort. Meanwhile, 40 healthy subjects were selected as the control group. The levels of IL-10, IL-6, IL-8, and TNF- $\alpha$  in each group were detected by sandwich enzyme-linked immunosorbent assays, and their correlation with the degree of depression was analyzed.

**Results:** The levels of IL-10, IL-6, IL-8, and TNF- $\alpha$  were all higher than those in the control group ( $P < 0.05$ ). Moreover, the depression statuses of patients with lung cancer were positively correlated with IL-10, IL-6, and TNF- $\alpha$  levels ( $r = 0.705, 0.301, \text{ and } 0.446, P < 0.01$ ); however, the level of IL-8 was not relevant ( $r = 0.136, p > 0.05$ ).

**Conclusion:** Serum levels of IL-10, IL-6, and TNF- $\alpha$  are associated with depression scoring in patients with lung cancer. <

**Key words:** cytokines, depression, lung cancer.



<sup>1</sup>MD, Department of Psychological Medicine, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai (200032), China.

<sup>2</sup>Department of Respiratory Medicine, Zhongshan Hospital, Fudan University, Shanghai 200032, China.

<sup>3</sup>Department of Pharmacy, Zhongshan Hospital, Fudan University, Shanghai 200032, China.

\*Corresponding author  
huangxiao320@126.com

of the immune system to identify and kill tumor cells, thereby affecting the curative effect of chemotherapy drugs that increase the frequency of adverse reactions, ultimately leading to shortened survival time [3, 4]. Studies have shown that patient depression and quality of life are related to changes in the levels of certain cytokines in the body [5]. However, the mechanisms involved have not yet been fully elucidated. By investigating IL-10, IL-6, IL-8, and TNF $\alpha$  serum levels, this study preliminarily discusses the relationship of these cytokines and lung cancer patients with depression [6].

## Materials and Methods

### General information

A total of 92 patients (59 males and 33 females) with advanced lung cancer, aged 38–72 years, with a median age of 58 years old, were recruited from May 2014 to May 2016. The pathological types were: 29 cases of squamous carcinoma, 54 cases of adenocarcinoma, and 9 cases of other types. The clinical staging was: 10 stage IIIA patients, 26 IIIB patients, and 56 patients at stage IV. The Self-Rating Depression Scale (SDS) score index made it possible to define three groups of patients: 24 patients had no depression, 45 had mild depression, 23 had moderate depression, and no patients had severe depression. The exclusion criteria were the following: other serious physical and mental illnesses; brain metastases upon the evaluation of depression; severe cognitive and intellectual disabilities; junior middle school culture; and patients with difficulty with communication.

## Introduction

Lung cancer is one of the most common malignant tumors. In recent years, the incidence and mortality of global lung cancer have increased, especially in China and other economically advanced countries [1]. Moreover, depression is common in patients with advanced cancer who suffer from mental illness while suffering from physical pain [2]. To improve patient life quality, prolonging the survival time is the aim of advanced cancer treatment. Furthermore, the patient quality of life may be affected by depression, anxiety, and other negative emotions, which interfere with treatment adherence and eventually reduce the ability

## Method

### Depression score

We used the SDS after the patient was diagnosed for the first time. Depression was assessed according to the SDS score index (score index = score/highest score 80 points): SDS score less than 50% = not depression; 50%–60% = mild depression; 60%–70% = moderate depression, and >70% = severe depression. At the same time, 40 healthy individuals with no depression were assessed using SDS and were used as the control group.

### Cytokine detection

Fasting venous blood (5 mL) was collected from the patients in the morning. Blood samples were then centrifuged at 4000 rpm/min for 10 min. After discarding cell pellets, serum were kept at  $-70^{\circ}\text{C}$  until further use. The IL-10, IL-6, IL-8, and TNF- $\alpha$  serum levels were detected and quantified by using double-antibody sandwich ELISA. ELISA kits were purchased from Biosome (XX, XX, USA).

### Statistical analysis

We used the SPSS 19.0 software for statistical analysis. The mean and standard deviation of ELISA data were calculated and the variance and t-test were used for significance analysis. Pearson correlation coefficient was used to analyze the correlation between the levels of cytokines and depression.  $P < 0.05$  was considered statistically significant.

## Results

### Changes in serum cytokine levels.

The levels of IL-10, IL-6, IL-8, and TNF- $\alpha$  in patients with different degrees of depression were statistically different from those in the control group ( $P < 0.05$ ). Moreover, statistically significant differences existed in the IL-10 levels of patients with depression ( $P < 0.05$ ). A statistically significant difference was found between IL-6 and TNF- $\alpha$  levels in patients without depression compared with those with mild depression and moderate depression ( $P < 0.05$ ). Additionally, no statistically significant difference was found between mild and moderate depression ( $P > 0.05$ ). Lastly, no statistically significant difference existed between the IL-8 levels of patients with depression ( $P > 0.05$ ) (Table 1).

### Correlation analysis between the degree of depression and cytokine levels

Pearson correlation analysis showed that, in patients with lung cancer, the IL-6, IL-10, and TNF- $\alpha$  levels and degree of depression are positively correlated ( $r = 0.705, 0.301, 0.446$ , respectively;  $P < 0.01$ ). By contrast, IL-8 level and the degree of depression showed no obvious correlation ( $r = 0.136, P > 0.136$ ).

## Discussion

Cancer is a common disease that severely threatens human life and causes physical, psychological, and spiritual trauma to patients [7].

Depression is a common mental disorder with various causes. It manifests with significant and lasting low mood as its main clinical feature. Serious depression can be marked by suicidal thoughts and behavior. Moreover, depression is highly common in cancer patients, with an incidence of 39%–55% in patients with lung cancer in China. Anxiety and depression are common in patients with malignant tumors. However, effective methods to improve the mental state of patients have not been fully recognized and implemented [8–11]. The patient quality of life may be affected by depression, anxiety, and pain. This may reduce patient satisfaction and interfere with treatment adherence, possibly leading to an increased fatality rate. Thus, the medical staff should take effective treatment measures to fight depression [12, 13]. Unfortunately, the incidence of depression is high, and, although it is closely related to the prognosis, it is often neglected in clinical work.

In recent years, along with advances in social medicine and medical technology in fields such as surgery, radiotherapy, and chemotherapy, the use of biologics for treating malignant tumors has led to major progress, and the 5-year survival rate of patients with tumors has clearly improved. The issue of depression in cancer patients is getting increasing attention [14–16]. Interestingly, several studies have confirmed that cytokines, neurotransmitters, and hormones are related through extensive and close-contact networks, often when inflammation processes are present. The levels of the inflammatory cytokines IL-10, IL-6, IL-8, and TNF- $\alpha$  were therefore analyzed in the present study. Our results in lung cancer patients with depression show that IL-6, IL-10, and TNF- $\alpha$  levels are higher than those in healthy individuals, with an increasing trend when depression is more severe. IL-6, IL-10, and TNF- $\alpha$  levels were found to be closely related to the degree of lung cancer and of depression, and one can hypothesize that they participate in the development of lung cancer and depression [17–23].

Patients with lung cancer and depression are in a state of immune activation. IL-1 $\beta$ , IL-6, IL-10, TNF- $\alpha$  could act through the hypothalamus pituitary adrenal axis (HPA) involved in the pathogenesis of depression [8, 9]. IL-6, IL-10, an increased level of TNF- $\alpha$  activity can induce the secretion of adrenal hormone releasing hormone by the hypothalamus [24–26], resulting in excessive HPA activity and leading to depressive symptoms and depression in patients with lung cancer. IL-8 level was found to be relatively elevated in lung cancer patients as compared to healthy individuals, but but no significant correlation with depression level was found.

Patient Group	Number	IL-10	IL-6	IL-8	TNF- $\alpha$
No depression	24	68.36 $\pm$ 8.83	49.37 $\pm$ 3.63	27.35 $\pm$ 1.93	162.95 $\pm$ 5.56
Mild depression	45	105.8 $\pm$ 11.78	51.35 $\pm$ 2.95	37.36 $\pm$ 1.57	169.91 $\pm$ 9.7
Moderate depression	23	106,63 $\pm$ 9.83	51.65 $\pm$ 2.32	37.89 $\pm$ 1.55	175.9 $\pm$ 10.33
Healthy individuals	40	59.05 $\pm$ 8.32	39,97 $\pm$ 3.03	26.06 $\pm$ 1.71	150.33 $\pm$ 9.96

**Table 1.** Serum cytokine levels in each group. (mean  $\pm$  sd, pg/mL).

In conclusion, this study shows that levels of IL-10, IL 6, and TNF  $\alpha$  are more elevated in lung tumor patients than in healthy individuals and that they can be positively correlated to the depression scoring index. Our work suggests a strong interplay between anti-tumor immunity, inflammation process and elements from the nervous system.  $\diamond$

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#### CONFLICT OF INTERESTS

The authors have no potential conflict of interests.

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