

## **Study on the effect of chemotherapy on physical status of patients with non-small-cell lung cancer.**

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### **Abstract**

**This study is to investigate the effect of chemotherapy on living quality, anxiety and immunity of patients with non-small-cell lung cancer. 78 patients with non-small-cell lung cancer treated with chemotherapy in hospital were selected randomly. The clinical effect of chemotherapy on patients was evaluated every two cycles. The living quality, anxiety and immunity of patients with lung cancer were graded. Before chemotherapy, the scores of living quality functional fields, fatigue and dyspnoea were high. There were 53.8% patients with anxiety. The score of SAS was  $52.36 \pm 6.42$ . After two cycles of chemotherapy, dyspnoea was obviously improved, while insomnia and loss of appetite were obviously increased. There were 73.1% patients with anxiety and the score of SAS was  $52.36 \pm 6.18$ , which were significantly increased compared with before chemotherapy. After four cycles of chemotherapy, the scores of body, role, emotion and social function were obviously reduced, while nausea and vomiting, loss of appetite, constipation and financial difficulty were worse. There were 80.8% patients with anxiety. The score of SAS was  $55.27 \pm 6.42$ . Compared with two cycles of chemotherapy, the difference was not statistically significant. Compared with before chemotherapy, the number of CD8<sup>+</sup> was decreased, and the ratio of CD4<sup>+</sup>/CD8<sup>+</sup> was increased. The physical status of part patients was relieved after chemotherapy, but their anxiety was quite obvious and their immunity and living quality were decreased. Medical worker should be timely evaluated patients' living quality and emotional changes, provide a good job of health and prevention, and actively carry out psychological counselling for patients.**

**Keywords:** Lung cancer, Chemotherapy, Quality of life, Anxiety, Immunity.

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### **Introduction**

At present, the whole world is faced with the same enemy, lung cancer, which has been the main cause of death of human with malignant tumor. According to different biological behaviour, lung cancer can be divided into small cell lung cancer and Non-Small-Cell Lung Cancer (NSCLC). The prevalence of non-small-cell lung cancer is up to more than 80% [1,2]. Now the lung cancer is advocated to adopt comprehensive multi-disciplinary treatment that is mainly based on the stage of NSCLC. The treatment includes surgery, radiotherapy, chemotherapy, immunotherapy, traditional Chinese medicine, etc. [3]. Surgery is the first choice and the fundamental method for treating lung cancer. But about 65%~70% cases in the stages III, IV were not suitable to be done surgery. Even if the patients could be done surgery, about 70% cases would be recurrent and had cancer cell metastasis after surgery. Radiotherapy is only a local treatment, and cannot effectively solve the problem of cancer cell metastasis in the whole body. Therefore the radiotherapeutic effect has certain limitations in clinical practice. Chemotherapy in comprehensive treatment

has been the first treatment for NSCLC. However, chemotherapy can not only kill tumor cells, but also kill normal cells and immune (resistant) cells. If only chemotherapy was performed in patients, it would bring about many symptoms, such as vomit, hair loss, anorexia, the reduction of blood cells, the decrease of immunity, and mental disease like depression [4-6]. To take positive measures to improve patients' physical status, it is necessary to accurately control the effect of chemotherapy on physical status of patients with non-small-cell lung cancer. By combining many relevant materials with several years' clinical experience, this research studied the physical status of 78 cases with non-small-cell lung cancer after chemotherapy.

### **Materials and Methods**

#### ***Clinical materials***

There were 78 cases in the observation group, including 48 male patients, 30 female patients, aged 38~70 years old, average age  $58.2 \pm 3.9$  years old. There were no statistical

differences in gender, age, and clinical manifestation of patients which were comparable (Table 1).

### **Inclusion and exclusion criteria**

**Inclusion criteria:** 1. patients were pathologically diagnosed with primary bronchial lung cancer for the first time and had not been treated with chemotherapy; 2. according to the international stage standard of lung cancer of NCCN in 2009, the patients were diagnosed in the stage III or IV; 3. physical score of KPS was not less than 70; 4. time of expected survival was more than 3 months; 5. the patients were willing to accept a questionnaire survey.

**Exclusion criteria:** 1. patients have history of mental illness; 2. after explained, patients still did not understand the questionnaire items; 3. patients had received an anti-anxiety treatment; 4. patients have a history of alcohol or drug dependence.

### **Methods**

**Chemotherapy protocols:** First-line chemotherapy for non-small-cell lung cancer was given two kinds of drug protocols containing platinum (platinum+gemcitabine or vinorelbine, paclitaxel, pemetrexed, etc.). If the disease moved on, the patients would be given second-line chemotherapy (docetaxel, pemetrexed and so on). The rest were continuing the original protocol. After chemotherapy, the physical status of patients was evaluated every 2 cycles.

Before chemotherapy, the general material of patients were recorded, including gender, age, BMI, KPS score, pathological types, lung cancer stages, chemotherapy protocols, degree of education, having or not having basic diseases, etc. EORTC QLQ-C30 [7] and Self-rating Anxiety Scale (SAS) [8] were adopted to investigate the status of patients before and after 2 cycles of chemotherapy in one week as well as after 4 cycles of chemotherapy in one week. Then the patients were explained how to answer the questionnaire survey. In the EORTC QLQ-C30 scales, the higher the score of function areas and overall body status got, the better the function status and living quality of the patients were. On the contrary, the higher the score of symptom fields got, the more the symptoms or problems of patients were [7]. In the SAS scale, according to Chinese norm, boundary value of SAS is 50. If the score of SAS is not less than 50, it would indicate that the patients have anxiety.

**Evaluation of immunity:** The limosis venous blood of patients was taken in the morning before chemotherapy and on the 14<sup>th</sup> day after 4 cycles of chemotherapy. The limosis venous blood was detected by FACSCalibur (a type of flow cytometry). The detection method was the whole blood dissolving blood cells+monoclonal antibody (CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, and NK cells) (provided by the Kurt immunological technique agency in China). The experimental results were analysed by Cellouest software to examine the activity of T-lymphocyte subsets and NK cells.

### **Statistical method**

The SPSS 16.0 statistical package for windows was adopted to analyse the data. The comparison of measurement data between all groups before chemotherapy adopted t to examine. One-factor analysis of variance was used to analyse the average number between all groups. Count data was tested by chi-square.

### **Results**

#### **Impact on quality of life**

The score comparison of patients with lung cancer in all aspects of living quality was shown in Table 2. There was no statistical significance in cognitive function, fatigue and diarrhoea. Compared with before chemotherapy, after 2 cycles of chemotherapy, the scores of physical function, role function and social function in function fields were reduced, the scores of pain, nausea and vomiting in symptom fields increased, the scores of insomnia, appetite loss, abnormal stool and economic conditions also increased, and the score of overall living quality decreased. Compared with before chemotherapy, after 4 cycles of chemotherapy, the scores of physical function, role function, emotional function, social function in the function fields were significantly decreased, the scores of pain, nausea and vomiting in the symptom fields increased, the scores of insomnia, appetite loss, abnormal stool and economic conditions in the symptom fields improved, and the score of overall quality of life reduced.

#### **Influence of anxiety**

Before and after 2 cycles of chemotherapy and after 4 cycles of chemotherapy, the number of patients with anxiety in 78 cases was respectively 42 cases (53.8%), 57 cases (73.1%), 63 cases (80.8%). The score of SAS was respectively  $46.54 \pm 5.46$ ,  $52.36 \pm 6.18$ ,  $55.27 \pm 6.42$ . The comparison of anxiety score between before chemotherapy and after 2 cycles of chemotherapy has statistical significance. The comparison between after 4 cycles of chemotherapy and before chemotherapy has statistical significance, too. But the comparison between after 2 cycles and 4 cycles of chemotherapy has no statistical significance.

#### **Influence of immunity**

Before chemotherapy, the differences among CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, CD4<sup>+</sup>/CD8<sup>+</sup> ratio, and NK cells have no statistical significance. After chemotherapy, CD3<sup>+</sup>, CD4<sup>+</sup>, NK cells have no evident changes. Compared with before chemotherapy, the number of CD8<sup>+</sup> was reduced ( $P=0.019$ ). Compared with before chemotherapy, the ratio of CD4<sup>+</sup>/CD8<sup>+</sup> was increased ( $P=0.015$ ) (Table 3).

**Table 1.** Comparison of pre-treatment baseline.

	Value
Total number of patients	78

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Age (year)		58.2 ± 3.9		3	8
Gender	Male	48	TNM stage	IIIa	20
	Female	30		IIIb	23
KPS score	1	49	IV		35
	2	21			

Table 2. Compare of scores for EORTC QLQ-C30 in different periods of chemotherapy (Mean ± SD).

	Baseline	2 cycles	4 cycles	F	P
Functioning scales					
Physical	76.08 ± 11.32	72.1 ± 11.28	66.10 ± 16.25	6.982	0.001
Role	65.89 ± 23.21	60.31 ± 18.75	49.75 ± 21.48	7.48	0.001
Emotion	62.33 ± 23.11	60.66 ± 20.87	47.36 ± 18.42	8.11	0.001
Cognitive	60.32 ± 31.09	65.09 ± 21.84	65.22 ± 18.91	0.039	0.059
Social	63.16 ± 24.15	56.74 ± 18.04	42.31 ± 12.96	19.89	0.001
Symptom scales					
Fatigue	51.27 ± 23.98	50.62 ± 21.32	58.24 ± 17.91	1.769	0.146
Pain	24.80 ± 20.64	31.39 ± 20.98	39.11 ± 23.42	4.908	0.02
Nausea and vomiting	23.94 ± 18.02	26.89 ± 15.36	35.21 ± 16.29	8.96	0.001
Specific items reflecting symptoms and economic conditions					
Dyspnoea	49.78 ± 33.92	38.42 ± 25.49*	41.59 ± 26.02	2.533	0.059
Insomnia	36.81 ± 29.03	46.11 ± 24.32*	47.66 ± 23.92	3.384	0.032
Appetite loss	36.94 ± 25.65	48.01 ± 26.59*	69.27 ± 24.33	15.98	0.003
Constipation	30.31 ± 20.32	36.77 ± 27.95	45.82 ± 30.35	3.543	0.039
Diarrhoea	33.29 ± 23.78	34.99 ± 26.02	35.29 ± 25.86	0.172	0.758
Financial impact	40.31 ± 30.16	43.18 ± 32.13	56.82 ± 34.15	3.667	0.031
Global quality of life	58.56 ± 20.99	53.82 ± 17.26	46.19 ± 14.78	7.054	0.001

Note: \*Compare before chemotherapy with after 2 cycles, P<0.05; Compare after 2 cycles with after 4 cycles, P<0.05; Compare before chemotherapy with after 4 cycles, P<0.05.

Table 3. Comparison of the immunologic function.

	CD3+ (%)	CD4+ (%)	CD8+ (%)	CD4+/CD8+ (%)	NK cells (%)
Before chemotherapy	63.82 ± 11.9	34.78 ± 6.21	25.72 ± 7.33	1.62 ± 0.86	24.12 ± 9.02
After 4 cycles of chemotherapy	61.94 ± 10.8	35.92 ± 7.45	23.17 ± 6.26	1.99 ± 0.97	21.83 ± 9.85
P	0.235	0.374	0.019	0.015	0.186

Discussion

The quality of life means the state of daily life, including the ability to accomplish daily life, such as physical activity, psychological activity, social life and satisfaction degree of patients to their own function as well as the control of disease [9]. The quality of life in the treatment of cancer was gradually showing its importance, as the important criteria for evaluating curative effect [10]. With chemotherapy going on, the

dyspnoea of patients was improved significantly, but pain, appetite loss, insomnia, nausea and vomiting, and financial difficulties were gradually increased, and social function was decreased. Among them, appetite loss, and nausea and vomiting were related to lung cancer and the side effects of chemotherapy drugs and pain killers. The untoward reaction of chemotherapy drugs and patients' emotional reaction in the treatment of lung cancer could lead to decrease of quality of sleep [11]. The physical status of patients with lung cancer and

repeated treatment in hospital brought about obstruction of family life and social activities, and influence of social value. The economic expenses of patients with lung cancer were positively correlated with the severity of the disease [12]. Expensive medical expenses and the limited economic ability of patients has been a pair of prominent contradictions in the treatment.

Anxiety is inner unrest or unfounded fear that lacks obviously objective reasons [13-15]. Anxiety is the most common psychological characteristics in patients with lung cancer, but it is also easy to be ignored and underestimated by medical worker [16]. Excessive anxiety has a negative effect on the cancer outcome and quality of life of patients. The study found that with chemotherapy going on, anxiety of the patients with lung cancer was gradually increased. It was taken into consideration that it was related to symptom aggravation, poor physical status, short life span of prognosis and deterioration of economic conditions.

The immune function of the body is closely related to the occurrence and development of tumor. When the immune function of the host is low or suppressed, the incidence of tumor is increased. When tumor is growing, the immune function of patients would be further inhibited. In general, cellular immunity plays an important role in anti-tumor response, which is mainly derived from T cell subsets and NK cells. Class I restrictive T cells are mostly CD8<sup>+</sup> cells, T-Lymphocytes. It can also secrete lymphatic factors that enable tumor cells to be directly dissolved. Class II restrictive T cells are mostly CD4<sup>+</sup> T-helper cells (Th). It produces lymphatic factors, which activate other effector cells to produce inflammatory reactions and mediate their effect. T cell subsets can be detected in the peripheral blood and infiltrating cells around tumor. NK cells are a special subgroup of lymphocytes, which are large granular lymphocytes, null cells. NK cells, class III T lymphocytes, are not dependent on thymus, antibodies, without MHC restriction and presensitization, which can secrete cytotoxic factors to kill tumor cells. NK cells as the first line of defense take on the task of innate immunity. The experimental results of the study showed that compared with before chemotherapy, CD3<sup>+</sup>, CD4<sup>+</sup>, the ratio of CD4<sup>+</sup>/CD8<sup>+</sup>, and NK cells after chemotherapy were reduced, which revealed that chemotherapy has an inhibiting effect on cellular immunity. Therefore, killing tumor cells and protection of the body's immunity play the same important role in the process of tumor treatment.

### Conflict of Interest Statement

All co-authors have seen and agree with the contents of the manuscript and there is no conflict of interest.

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