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Treatment of non-small cell lung cancer based on the theory of "lungs as the blood organ"

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Abstract. Lung cancer has become one of the most common types of cancer, with high incidence and mortality rates persistently high. Among them, non-small cell lung cancer (NSCLC) is particularly common, accounting for up to 85% of lung cancer cases. NSCLC seriously endangers the health of people in China and around the world, and its specific causes are related to various factors such as smoking, radiation exposure, air pollution, and genetic factors. In traditional Chinese medicine, NSCLC belongs to the category of lung consolidation. Professor Zhang Wei believes that the lungs not only govern the qi of the body, but also play an important role in the generation and circulation of blood throughout the body, and has extensively expounded the viewpoint of "lungs as the blood organ." This viewpoint is reflected in various functions of the lungs, such as the lungs controlling the hundred vessels, governing the storage of fluids, and controlling the skin and hair. The propulsion of lung qi also provides impetus for the normal circulation of blood. As the lungs serve as the blood organ and are prone to stasis, they are susceptible to the occurrence of "lung consolidation." Therefore, the occurrence of NSCLC may be related to blood stasis in the lungs. Blood stasis is not only the pathological product of lung consolidation, but also the main cause of lung consolidation. It can be inferred that in the treatment of NSCLC, methods such as promoting blood circulation, dredging collaterals, and resolving phlegm and stasis should be adopted.

Keywords: lungs as the blood organ, non-small cell lung cancer, blood stasis, lung consolidation

1. Introduction

Non-small cell lung cancer (NSCLC) is a type of malignant tumor in the lungs excluding small cell lung cancer, mainly divided into various forms such as large cell carcinoma, adenocarcinoma, squamous cell carcinoma, and adenosquamous carcinoma. NSCLC has an extremely high mortality rate, with a three-year survival rate of only about 10% [1]. Currently, clinical treatments include surgical resection and targeted therapy. Targeted therapy involves using specific drugs to selectively kill NSCLC cells [2], thereby reducing damage to normal tissues. In addition to these methods, chemotherapy and radiation therapy are also used in the treatment of NSCLC. Research has shown that the lungs are one of the important sites for platelet production, and they are closely related to both respiratory function and the generation and circulation of blood, which aligns with the viewpoint proposed by Professor Zhang Wei [3] that "lungs serve as the blood organ." Traditional Chinese medicine is an outstanding cultural heritage of China, and studies have found that Chinese medicine has significant efficacy in the treatment of NSCLC. The theory of "lungs as the blood organ" provides a strong basis for explaining NSCLC, and an increasing number of medical professionals are exploring the relationship between this theory and NSCLC, hoping to provide new methods for the treatment of NSCLC.

2. Understanding NSCLC in traditional Chinese medicine

2.1. Etiology and Pathogenesis

In Traditional Chinese Medicine (TCM), NSCLC falls within the category of "lung consolidation," "lung obstruction," and "lung accumulation" [4]. Its clinical manifestations include symptoms such as coughing, bloody sputum, hemoptysis, and dyspnea. As recorded in "Su Wen · Da Qi Lun": "When the lungs are obstructed, there is wheezing and fullness in the chest and abdomen. When the liver is obstructed, there is fullness in the chest and abdomen, and when lying down, there is agitation and inability to

urinate." "Sheng Ji Zong Lu" records: "Accumulation in the lungs causes swelling, fullness, coughing, nasal discharge, and bloody sputum." TCM believes that the onset of NSCLC is due to pathogenic factors residing in the chest, depletion of Zheng Qi (healthy energy), injury to the lungs by pathogenic factors, and obstruction of the lungs by phlegm and stasis. As a result, the normal dissemination and descent of lung qi are hindered, leading to the accumulation of blood stasis and phlegm turbidity [5], thus manifesting symptoms of "lung accumulation."

Lung cancer patients are often diagnosed at an advanced stage, during which their Zheng Qi (healthy energy) is deficient, leading to the manifestation of TCM syndrome of Qi-Yin deficiency [6]. As stated in "Su Wen": "Where pathogens gather, there must be Qi deficiency." TCM syndrome differentiation believes that the lungs are delicate organs, preferring moisture over dryness, and functioning smoothly by descending Qi. The lungs are susceptible to external pathogens, which can damage lung Qi. Patients with lung cancer often require long-term surgery and chemotherapy, which can lead to blood loss, insufficiency of Yin fluids, and Qi escaping with blood, resulting in Qi-Yin deficiency. Prolonged accumulation of NSCLC can damage lung Qi and fluids, leading to deficiency of Zheng Qi and damage to fluids, also resulting in symptoms of Qi-Yin deficiency [7]. The key to the pathogenesis of lung cancer lies in the state of deficiency of Zheng (healthy) Qi and excess of pathogenic factors in the body. NSCLC belongs to primary deficiency with secondary excess. Its fundamental causes lie in deficiency of lung and kidney Qi, depletion of Zheng Qi, and deficiency of Yin fluids [8]. The secondary excess is due to Qi stagnation, blood stasis, and phlegm turbidity obstructing internally, with fluids stagnating in the lungs and forming phlegm, which, when combined with blood stasis, obstructs the meridians and forms tumors, causing the loss of the lung's function of descending and disseminating Qi. As stated in "Danxi Xinfa": "When the lungs are distended and coughing occurs, whether on the left or right, insomnia results from phlegm obstructing Qi, with phlegm combined with blood stasis forming a cavity." This is also the first theory to propose that phlegm and blood stasis share the same origin. Similarly, as recorded in "Xue Zheng Lun": "When blood stagnation persists, it can also transform into phlegm-fluid, leading to hemoptysis and coughing, invariably accompanied by phlegm retention." Thus, it is evident that cases of phlegm and blood stasis occurring together are common in diseases of the lung system.

2.2. Principles and methods of treatment

In the process of TCM syndrome differentiation and treatment, distinguishing between deficiency and excess is particularly important, with the principle of tonifying deficiency and purging excess being consistently applied. As recorded in "Ling Shu · Jing Mai" [9]: "When there is excess, purge it; when there is deficiency, tonify it; when there is heat, disperse it; when there is cold, retain it; when there is collapse, moxibust it. Neither excess nor deficiency, follow the channels to treat." Lung cancer in TCM diagnosis belongs to primary deficiency with secondary excess, and treatment needs to fully consider the diagnosis and treatment strategy of reinforcing the healthy Qi, attacking the pathogenic factors, and combining tonification and purging. Wang Ruiping et al. [10] believe that the cause of lung cancer is deficiency of both the spleen and lungs. In TCM, the spleen belongs to the Earth element and the lungs belong to the Metal element. When the Earth does not generate Metal, lung Qi becomes deficient. Therefore, treatment often involves the method of nourishing the Earth to generate Metal. As recorded in "Su Wen · Yin Yang Ying Xiang Da Lun": "The spleen generates flesh, and flesh generates the lungs." Therefore, in the treatment of NSCLC, strengthening the spleen and regulating the stomach can ensure the abundance of the source of Qi and blood, thereby assisting lung Qi and replenishing lung Qi on the basis of tonifying the Earth. Jiang Wenwen et al. [11] believe that the Qi-Yin deficiency type is extremely common among various types of lung cancer. "Su Wen" states: "Where pathogens gather, there must be Qi deficiency." The cause of lung cancer lies in deficiency of healthy Qi, invasion of pathogenic factors into the lungs leading to damage to fluids, obstruction of fluid distribution, accumulation of phlegm in the lungs, insufficient Qi propulsion, sluggish blood circulation, blood stasis. Prolonged obstruction by phlegm and blood stasis in the lungs leads to the formation of tumors, which further damage fluids and healthy Qi, exacerbating Qi-Yin deficiency. Therefore, treatment should focus on nourishing Qi and nourishing Yin, leveraging the advantages of reinforcing the healthy Qi and solidifying the foundation. Clinical findings have shown that the method of nourishing Qi and nourishing Yin can significantly prolong the survival period of lung cancer patients, reduce serum tumor markers, improve clinical symptoms, and enhance immune function [12]. Wu Mianhua et al. [13] adopt the method of eliminating stasis and resolving phlegm to treat lung cancer, as lung cancer is often diagnosed in the middle to late stages, with the basic pathogenesis being the mutual accumulation of phlegm and stasis. Research has shown that the clinical use of the method of eliminating stasis and resolving phlegm to treat lung cancer is effective. Some practitioners believe that the treatment of NSCLC should involve anti-cancer detoxification, regulating Qi and resolving depression, warming Yang, and promoting circulation methods.

2.3. Traditional Chinese medicine treatment for NSCLC

In recent years, research has found that Traditional Chinese Medicine (TCM) adjuvant therapy for NSCLC has shown significant efficacy, effectively prolonging the survival period of NSCLC patients. Currently, Western medicine treatments for lung cancer often include surgery, chemotherapy, radiotherapy, targeted therapy, and immunotherapy to alleviate patient suffering and improve their quality of life. When applying Western medicine treatments for NSCLC, using Chinese herbal medicine as an adjuvant therapy has significant advantages. Jiao Jin et al. [14] found that the use of Qishe Benefiting Lung Decoction on the basis of chemotherapy can effectively improve the quality of life of lung cancer patients. This decoction mainly consists of 18 Chinese herbal medicines including Astragalus, Codonopsis, Dioscorea, Coix seed, Cornus, Ostrea gigas, Houttuynia cordata, and Fagopyrum tataricum. Among them, Astragalus and Codonopsis tonify the spleen and benefit the lungs, supplement Qi, detoxify,

and promote tissue regeneration and fluid production [15]; Dioscorea and Coix seed can tonify the spleen and kidneys, permeate dampness and drain pus, and Ostrea gigas can soften hardness, disperse nodules, and calm the mind; Houttuynia cordata and Fagopyrum tataricum together clear heat, detoxify, transform phlegm, and eliminate pus. Clinical verification results show that Qishe Benefiting Lung Decoction combined with chemotherapy for treating NSCLC is significantly effective compared to the control group, and it can effectively improve TCM syndromes in patients. Qiao Xiaoyan et al. [16] found that the Decoction for Strengthening the Spleen and Benefiting the Kidneys has good efficacy in treating NSCLC while also alleviating patient pain and improving their survival time. The ingredients of the Decoction for Strengthening the Spleen and Benefiting the Kidneys [17] include Astragalus, Coix seed, Ligustrum, Poria, Eucommia bark, Atractylodes, Vine of Cissus, Rehmannia, Licorice, Goji berry, Polygonatum, Chinese date, and American ginseng. This decoction has the effects of nourishing Yin and tonifying the kidneys, supplementing Yin and nourishing blood, tonifying the spleen and benefiting Qi, nourishing essence and filling the marrow, eliminating dampness and reducing swelling, inhibiting tumor cell proliferation, and promoting cell apoptosis. Clinical studies have proven that the Decoction for Strengthening the Spleen and Benefiting the Kidneys has a good effect on improving sleep quality, enhancing immune function, and inhibiting the proliferation of lung cancer cells.

It can be seen that Chinese herbal medicine has significant advantages in enhancing the immune function of NSCLC patients, promoting tumor cell apoptosis, inhibiting tumor angiogenesis, blocking the cell cycle, and reducing cell toxicity. TCM has achieved significant results in theoretical and clinical research on NSCLC treatment. In the future, the combination of chemotherapy and Chinese medicine treatment for NSCLC will remain a hot topic, requiring further research.

3. Lungs as the organ of blood

Throughout history, many medical practitioners have regarded the lungs as the organ of Qi, responsible for governing Qi and respiration. The lungs are considered to have the function of regulating the overall Qi of the human body, as stated in "Su Wen · Five Organs' Generation": "All Qi belongs to the lungs." Furthermore, the function of the lungs in governing Qi is divided into governing the overall Qi of the body and the Qi of respiration. In addition to this, the lungs also play a role in promoting dissemination and descent and in regulating the water pathways. However, based on extensive research and literature review, Professor Zhang Wei proposed the theory of "lungs as the organ of blood" [18]. Starting from this theory, Professor Zhang Wei conducted a large number of clinical practice analyses and data surveys, achieving a series of results in clinical treatment [19]. There are early records in ancient medical texts regarding the lungs producing blood and the lungs being the organ of blood. As stated in "Bencao Shu Gou Yuan · Shanguo Section": "The lung Yin descends into the heart and produces blood; when the blood vessels are moistened, Yin within Yang descends first." And in "Bencao Shu Gou Yuan · Shancao Section": "The lung Yin descends into the stomach, which is where Qi transforms into blood [20]." From this, it can be inferred that besides being the organ of Qi and governing the overall Qi of the body, the lungs also play a crucial role in the generation of blood in the human body. The theoretical basis for the lungs as the organ of blood mainly includes: the lungs produce blood, and the lungs participate in the process of blood generation in the human body; the lungs circulate blood, and lung Qi propels the normal circulation of blood in the human body's vessels. The relationship between Qi and blood is closely intertwined, which ancient medical practitioners recognized early on. With the continuous development of medicine into modern times, modern medicine also acknowledges the close relationship between the lungs and the generation of blood.

3.1. Production of blood by the lungs

The lungs participate in the process of blood generation in the human body. Relevant literature can also be found in the "Huangdi Neijing" (Yellow Emperor's Inner Canon). In the "Lingshu · Yingwei Shenghui," it is recorded: "The middle burner is also within the stomach. After emerging from the upper burner, what is received here secretes dregs and steams fluids, refining their essence. It then ascends to the lung meridians, where it transforms into blood." In the "Huangdi Neijing · Lingshu," it is stated: "Humans receive Qi from grains. Grains enter the stomach and are passed on to the lungs. The five Zang organs and six Fu organs all receive Qi. The clear portion becomes Ying (nourishing Qi), while the turbid portion becomes Wei (defensive Qi). Ying resides within the meridians, while Wei circulates outside the meridians. Ying continuously circulates, and after fifty degrees, it returns to the major meeting point. Yin and Yang mutually penetrate each other..." After eating and drinking, the spleen and stomach receive, transform, and transport the food and drink. Under the transformation of the spleen's Qi, the food and drink are converted into refined substances and dregs. The dregs are then expelled from the body, while the refined substances, under the influence of spleen Qi, ascend to the heart and lungs, where they combine with lung Qi to complete the formation of blood and nourishing Qi. The lungs govern Qi, and Qi can produce blood. As recorded in "Su Wen · Liujie Cangxiang Lun": "The lungs are the root of Qi." The "Huangdi Neijing" states: "Formed blood cannot be produced spontaneously; it is generated from formless Qi" [21]. Both blood and Qi are derived from the subtle transformation of the human body. Qi leads the blood, and blood is the mother of Qi. In terms of Yin and Yang, Qi is Yang, and blood is Yin. Yin and Yang are interdependent and inseparable. As recorded in the "Nanjing" (Classic of Difficult Issues): Qi governs warming, and blood governs moistening. Only when the Qi of the human body is sufficient and the blood circulates normally can life exist.

The Lungs Govern the Regulation of Water Passages, Disseminating and Distributing Body Fluids throughout the Body, Ensuring the Normal Circulation of Body Fluids. Physiologically, the lungs prefer moisture and dislike dryness. Only when the body's fluids are sufficient can the lungs maintain their moist state and function normally. Since fluids and blood share the same

origin, fluids can transform into blood, and blood can transform into fluids. As recorded in the "Lingshu · Jue Qi": "Nourishing Qi secretes its fluids, which are then distributed through the vessels and transformed into blood" [22]. As stated in the "Shanghan Lun · Bian Taiyang Bing Mai Zheng Bing Zhi": "Those deficient in blood should not be induced to sweat." This fully reflects the theoretical basis of the unity of fluids and blood. Furthermore, the convergence of hundreds of vessels occurs within the lungs. The blood throughout the body converges in the lungs for gas exchange and is then distributed throughout the body. As stated in the "Su Wen · Jingmai Bielun": "The Qi of the vessels flows through, the Qi of the vessels returns to the lungs, the lungs face the hundreds of vessels, and transmit essence to the skin and hair. The Qi point forms the Cun, which determines life and death." The Cun point is the part where the hand Taiyin lung meridian circulates, and pulse diagnosis specifically targets the Cun point. This indicates the close relationship between the lungs and the blood vessels. In recent years, Borges et al. [23] have discovered a close connection between the lungs and the generation of platelets. Modern research has also confirmed that the lungs are the main site of platelet production and possess significant hematopoietic potential [24].

3.2. The lungs propel blood circulation in the meridians

As stated in the "Su Wen · Jingmai Bielun": "Food Qi enters the stomach, turbid Qi returns to the heart, and essence is transmitted through the vessels. The Qi of the vessels flows through, the Qi of the vessels returns to the lungs, the lungs face the hundreds of vessels, and transmit essence to the skin and hair." The lungs govern Qi and control respiration [25]. Qi can be categorized into ancestral Qi, defensive Qi, and nutrient Qi, among which the formation of ancestral Qi relies on the lungs. Ancestral Qi plays a role in promoting blood circulation. Therefore, insufficient ancestral Qi often leads to blood stasis and various diseases. As mentioned in the "Du Yi Sui Bi · Qixue Jingshen Lun": "Ancestral Qi is the combination of nutrient and defensive Qi, originating from the lungs, accumulating in the Qi Sea, circulating within the Qi vessels, and moving with breath." The lungs inhale fresh air from the natural environment and exhale the stale Qi produced by the body's metabolism. The circulation of Qi and blood depends on the gas exchange function of the lungs [26]. The lungs govern the circulation of blood with the heart, assisting the heart in transporting blood throughout the body. As recorded in the "Du Yi Sui Bi · Qixue Jingshen Lun": "Ancestral Qi is the active Qi. All breathing, speech, voice, and limb movements, as well as the strength of tendons, are functions of ancestral Qi [27]." Qi and blood complement each other. Insufficient lung Qi can lead to impaired blood circulation, resulting in symptoms such as respiratory difficulties and coughing. In severe cases, it can lead to blood stasis and the mutual formation of phlegm and blood stasis, thereby triggering the onset of lung cancer.

4. The relationship between NSCLC and "lungs as the source of blood"

Currently, in clinical practice, the basic treatment principles mainly focus on reinforcing Qi, nourishing Yin, clearing heat, detoxification, and resolving phlegm and masses. Professor Zhang Wei [18] suggests that in the treatment of pulmonary diseases, not only should the concept of "lungs as the organ of Qi" be considered, but also the notion of "lungs as the source of blood" should be fully taken into account. Strategies such as promoting blood circulation, resolving stasis, tonifying the lungs, regulating Qi to supplement blood, resolving phlegm, and dispersing masses to expel pathogens can be employed in the treatment of NSCLC.

4.1. Blood activation and stasis resolution in NSCLC

The term "blood activation and stasis resolution" is first recorded in the "Huangdi Neijing". It states, "When the blood and Qi do not harmonize and counterflow within the flesh, it leads to the formation of abscesses and swellings." Thus, as early as the Pre-Qin to Han Dynasty period, China had the concept of blood stasis, including basic treatment methods such as "dispersing what is congealed, attacking what is retained, reducing what is firm, and eliminating what is obstructive". Throughout the long-term clinical practice of treating lung cancer, Chinese medicine has summarized numerous prescriptions for blood activation and stasis resolution, which have been clinically proven effective. For example, the "Shennong Bencao Jing" records many Chinese medicinal materials for blood activation and stasis resolution, such as Yuanhu, Chuanxiong, Danshen, Niuxi, and Sumu. However, the most influential book on blood activation and stasis resolution in later generations is the "Jin Kui Yao Lue". It records in the "Jin Kui Yao Lue" that Guizhi Fuling Wan, Dahuang Taichong Wan, and Biejia Jian Wan can all activate blood and resolve stasis [28]. The occurrence of lung cancer is triggered by multiple factors. In the early stages, it is often due to deficiency of righteous Qi, invasion of external pathogens, stagnation of Qi leading to blood stasis, and the formation of blood clots. Early-stage lung cancer patients may present with symptoms such as coughing, dyspnea, sputum, hemoptysis, hoarseness, and fixed chest pain [29]. Blood stasis is a consistent factor in the development of NSCLC. In the treatment of such diseases, Chinese medicine often uses classic prescriptions like Xuefu Zhuyu Tang. Professor Zhang Hong often uses modified Xuefu Zhuyu Tang in the treatment of NSCLC. The main ingredients of Xuefu Zhuyu Tang include Taoren, Honghua, Danggui, Shengdihuang, Niuxi, Chuanxiong, Jiegeng, Chishao, Zhike, Gancao, and Chaihu [30]. This prescription is often used to treat chest congestion due to blood stasis, Qi stagnation, and pain. Honghua, Chuanxiong, Chishao, and Niuxi can activate blood circulation and relieve pain; Shengdi and Danggui nourish blood and Yin, clear heat, and activate blood; Jiegeng and Zhike can widen the chest and promote Qi circulation; Chaihu can soothe the liver and relieve depression. Modern medical research has found that starting from the concept of "lungs as the source of blood" and using drugs to activate blood circulation and resolve stasis can significantly reduce blood viscosity,

enhance immune function, and inhibit the proliferation of lung cancer cells in the treatment of NSCLC.

4.2. Heat-clearing and detoxifying therapy in NSCLC

The "Yi Zong Jin Jian" records, "Boils and carbuncles originate from the generation of heat toxins, which obstruct the meridians and cause stagnation of Qi and blood." Many medical practitioners believe that the fundamental cause of NSCLC is the invasion of heat toxins, which damage Yin fluids [31]. The lungs prefer moisture and dislike dryness; therefore, damage to Yin fluids inevitably leads to the occurrence of lung diseases. Traditional Chinese medicine believes that fluids and blood originate from the same source, so damage to fluids inevitably leads to damage to blood. Accumulation of heat toxins in the lungs develops into tangible evils, which is one of the reasons for the occurrence of lung cancer. In recent years, medical workers have found that formulas with heat-clearing and detoxifying properties have a good effect in treating lung cancer [32]. The use of heat-clearing and detoxifying drugs can treat lung inflammation, thereby playing a therapeutic role in lung cancer. It is precisely because the "lungs are the source of blood" that the lungs need the nourishing effects of blood and fluids. Heat-clearing and detoxifying therapy for NSCLC can reduce the burning of fluids by heat toxins and reduce damage to the lungs.

5. Conclusion and prospects

Lung cancer is one of the most common malignant tumors in China, with the highest incidence and mortality rates. Western medicine often uses methods such as surgical resection and chemotherapy to treat non-small cell lung cancer, which may cause certain damage to the body during the treatment process. This article explores and summarizes the experience of treating non-small cell lung cancer from the perspective of promoting blood circulation and removing blood stasis, starting from the concept of "the lungs as the source of blood" proposed by Professor Zhang Wei. "The lungs as the source of blood" determines that the lungs have the characteristics of easy stasis, which can easily lead to poor blood circulation and trigger a series of diseases. Clinical verification has shown that treating lung cancer from the perspective of "the lungs as the source of blood" has a good effect. Treating lung cancer is a lengthy process, and it is necessary to strengthen patients' awareness of prevention, strive for early detection and treatment, and achieve a combination of traditional Chinese and Western medicine, leveraging the strengths of both. Traditional Chinese medicine emphasizes a holistic approach and individualized treatment based on syndrome differentiation. It is hoped that in the future, the fundamental mechanisms of non-small cell lung cancer will be further elucidated, providing new insights for the use of traditional Chinese medicine in its treatment.

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