Clinical Research Progress of Cancer Cachexia Treated by Chinese and Western Medicine

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through these two approaches, with the aim of providing reference for clinical treatment.

1. Introduction

Cachexia, a chronic metabolic disorder syndrome associated with weight loss, inflammation, and/or anorexia [1], is most prevalent in malignant tumors. Studies indicate that 50% to 80% of cancer patients develop cachexia [2], while approximately 30% of cancer-related deaths are directly attributed to this condition [3]. Cancer cachexia (CC) typically manifests through skeletal wasting and visceral muscle loss, accompanied by appetite loss, significant weight reduction, fatigue, and other catabolic symptoms. This debilitating condition not only complicates treatment planning and reduces quality of life but also diminishes therapeutic outcomes and shortens survival periods, profoundly impacting the lives of cancer patients.

2. Understanding cancer cachexia in Traditional Chinese Medicine

Traditional Chinese Medicine (TCM) has not established a specific medical term for cancer-related cachexia. Current research predominantly categorizes it under the "deficiency syndrome" and "atrophy syndrome" [4,5], describing a condition marked by organ dysfunction and deficiency of qi, blood, yin, and yang. The Su Wen: Jade Mechanism and True Treasury records: "With bony emaciation, sunken flesh, chest fullness, labored breathing, and physical collapse, death within six months is expected" [6]. Most scholars attribute this to spleen deficiency and impaired spleen-stomach harmony, which disrupts qiblood production and leads to muscle wasting, often accompanied by appetite loss, limb fatigue, loose stools, and a pale swollen tongue. Those classifying cachexia as atrophy syndrome note symptoms like sallow complexion, limb weakness, muscle wasting, and weight loss, suggesting damage to internal organs and skeletal malnutrition. The Nei Jing defines atrophy syndrome as both physical and visceral atrophy, attributing its root cause to fundamental organ deficiencies. Impaired organ function and depletion of qi-blood fluids result in inadequate nourishment of tendons and muscles, causing muscle weakness, emaciation, and atrophy [7]. Some researchers emphasize the imbalance between nutritive and defensive qi as the key pathogenesis. As essential life forces, insufficient defensive qi leads to thin skin, lax pores, and weakened muscles. The atrophy of adipose tissue can directly lead to cachexia and weight loss. When both nutritive and defensive qi are deficient, the body loses its nourishing capacity, resulting in organ malnutrition and impaired mental clarity [8]. Studies indicate that "cancer toxins" are a key pathogenic factor in cancer-related cachexia, with the primary mechanism being "toxin-induced deficiency" [9]. Based on traditional theories like "the spleen governs flesh and limbs while the kidney controls bones and marrow," some scholars propose that spleen-kidney deficiency deprives body fluids of their source and weakens musculoskeletal support. They suggest using spleen-tonifying and kidneynourishing methods to address skeletal muscle atrophy in cancer cachexia [10]. According to traditional

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Abstract: Cancer cachexia, a complex metabolic disorder syndrome, is characterized by skeletal and muscular wasting, anorexia, and immune dysfunction. Patients with advanced cancer often develop this condition, which significantly compromises quality of life. In traditional Chinese medicine (TCM), it is classified as "deficiency fatigue," associated with organ decline and deficiencies in qi-blood-yin-yang balance. This article starts from the perspective of recent treatments of cancer cachexia using both traditional Chinese and Western medicine, and studies the diagnosis and treatment of cancer cachexia

Chinese medicine, the occurrence of cancer cachexia is closely related to the three organs of the lung, spleen and kidney. Moreover, the relevant treatments for tumor patients, such as radiotherapy, chemotherapy and surgery, will inevitably affect the spleen and stomach functions of the patients. When the spleen and stomach's transportation and transformation functions are out of balance, symptoms such as abdominal distension, poor appetite and anorexia will occur. The patients' eating function will be impaired. If this situation persists and recurs for a long time, it will develop into cancer cachexia. Whether categorized as "deficiency syndrome" or "atrophy syndrome," cancer cachexia fundamentally manifests as deficiency disorders. Prolonged chemotherapy and drug-induced damage often disrupt spleen-stomach harmony, impairing blood and qi production. This leads to malnutrition, bone erosion, and ultimately disease progression.

3. Understanding cancer cachexia in Western medicine

Western medicine predominantly attributes cancer-related cachexia to metabolic abnormalities in the three major nutrients. Additionally, systemic inflammatory responses mediated by tumor tissues themselves or cytokines induced by the body contribute to cachexia development. These mechanisms lead to skeletal muscle atrophy and adipose tissue breakdown, thereby exacerbating cachexia. The browning of white adipose tissue (WAT) may be central to fat and muscle loss in cachectic patients [11]. The activation of white fat browning leads to an increase in light brown adipose tissue, which, under the induction of local factors, performs functions similar to those of brown fat (producing heat and consuming energy). This, in turn, affects the tumor microenvironment, causing fat loss and muscle loss, and promoting the occurrence of cancer cachexia. Studies indicate that imbalances between triglyceride synthesis and breakdown participate in adipose breakdown during cachexia. Notably, activated hormonesensitive esterase (HSL) has been identified as a key mechanism enhancing fat breakdown in cachectic patients. Although no significant hormonal changes are observed in tumor cachectics, molecular mechanisms at membrane receptor or post-receptor levels may induce HSL upregulation, triggering lipolysis [12]. Multiple studies demonstrate that cachexia development is closely associated with cytokine actions from both tumor cells and host cells. Tumor necrosis factor α (TNF- α) promotes skeletal muscle consumption through multiple pathways, including activation of nuclear factor κB. At the same time, these inflammatory mediators can cause an increase or decrease in hypothalamic activity, leading to anorexia and weight loss. Leptin, secreted by the arcuate nucleus of the hypothalamus, can act on the central nervous system to suppress the patient's appetite. After entering the bloodstream, it can regulate sugar, fat and energy metabolism, prompting the patient's body to reduce food intake, increase energy release, and inhibit the synthesis of fat cells, thereby resulting in weight loss. Research further reveals a strong connection between cachexia and gut microbiota, where dysbiosis induces inflammatory responses that inhibits the hypothalamic appetite center, which leads to the production of anorexia, and the long-term cycle leads to the production of cancer cachexia [13].

4. Treatment of cancer cachexia in Traditional Chinese Medicine

4.1 Chinese herbal decoction

4.1.1 Pay attention to spleen and stomach, benefit qi and activate blood

The spleen and stomach, being the foundation of postnatal constitution, govern the limbs and muscles while serving as the source of qi and blood production. Ancient physicians placed great emphasis on their crucial role in developing deficiency syndromes. The Ling Shu: Ben Shen states: "When spleen qi deficiency occurs, limbs become inactive and internal organs malfunction." The Treatise on the Origins and Symptoms of Various Diseases notes: "Those with weak spleen and stomach often suffer from fluid retention," indicating that deficiency syndromes correlate with these organ weaknesses. Modern pharmacology reveals that Shenling Baizhu San, which tonifies qi and strengthens the spleen, regulates lipid metabolism through multiple targets, inhibits inflammation, corrects metabolic disorders, and alleviates cancer cachexia [14]. Chen Jiangfeng et al. [15] through network pharmacology and molecular docking techniques, it is inferred that the potential mechanism by which the Sijunzi Decoction regulates cancerous cachexia may mainly lie in regulating the metabolism of glucose, lipids and proteins, preventing cell proliferation, promoting tumor cell apoptosis, inhibiting angiogenesis, thereby suppressing tumors. It mainly exerts its therapeutic effect on cancerous cachexia through the PI3K-Akt and Wnt signaling pathways. Song Na et al. [16] observed 63 advanced cancer patients using modified Tiaowei Xingpi Fang, finding better improvement in TCM syndrome scores, appetite loss, and abdominal

distension compared to the progesterone-controlled group, with significantly fewer adverse reactions. Zhao Qiongqiong et al. [17] combined Xiao Jian Zhong Decoction with conventional Western medicine for cancer cachexia. After 4 weeks of treatment, by comparing the clinical effective rate, weight change, hemoglobin, serum albumin and other indicators of the two groups of patients, the results showed that it could significantly improve the symptoms of fatigue and anorexia of the patients, increase weight, correct anemia, and had no obvious side effects.

4.1.2 Harmonizing Ying and Wei, sweet and warm to relieve the center

Scholars have proposed that the deficiency of Yingwei (vital energy) forms the pathological basis of malignant disease constitution, based on the theory that "deficiency leads to insufficient defensive qi, while overexertion causes depletion of nutritive qi." They further deduce the progression of malignant disease constitution through impaired circulation of Yingwei, and emphasize that disrupted circulation rhythms exacerbate energy consumption in this condition. Therefore, harmonizing Yingwei serves as the fundamental principle, with sweet-warm Jianzhong being a crucial therapeutic approach. Wu Oians Medical Mirror states: "While recognizing Zhang Zhongjings use of Guizhi Decoction for treating typhoid fever, few realize its application in managing consumptive diseases. Understanding Guizhi Decoctions therapeutic value for consumptive conditions reveals the essence of Zhang Zhongjings medical philosophy" [18], emphasizing that consumptive diseases should be treated through Yingwei imbalance theory, with prescriptions modified from Guizhi Decoction according to syndrome differentiation [8]. Modern TCM expert Wang Zhongqi demonstrated remarkable efficacy in treating advanced lung cancer with malignant disease constitution using modified Xiao Jianzhong Decoction through the Yingwei harmony method [19]. Sun Chunxia et al. [20] developed a formula combining Yingwei harmonization with qi-tonifying exterior-strengthening herbs for postoperative breast cancer patients, achieving significant improvement in TCM syndrome patterns. Huangqi Jianzhong Decoction may inhibit white adipose tissue browning by promoting macrophage M1 polarization and inhibiting M2 polarization, thereby delaying fat consumption in cancerous mice and improving their malignant disease constitution [21].

4.1.3 Anti-cancer detoxification, benefit qi and nourish yin

In all stages of cancer progression—whether early, intermediate, or advanced—patients with tumorrelated cachexia typically exhibit malignant tumors. Treatment strategies should prioritize addressing critical factors: those with weakened constitutions require tonification therapy, while improved physical conditions necessitate focused pathogen elimination and cancer treatment. The pathogenesis of cachexia primarily involves deficiency of qi-blood-yin-yang and chronic debilitation. Professor Zhou Zhongying, a renowned traditional Chinese medicine expert, proposed the "cancer toxin" theory based on long-term clinical experience. It holds that cancer toxins are generated on the basis of dysfunction of the internal organs and stagnation of qi and blood, induced by various internal and external factors, and they are a kind of specific pathogenic factor leading to cancer. He posits that cancer toxins constitute the root cause of tumor development, advocating anti-cancer detoxification as the primary approach supplemented by qi-tonifying and constitution-supporting therapies. Gao Zhen et al. [22] observed 30 late-stage cancer cachexia patients using the Cancer Detoxification Formula, The control group was given the best supportive treatment, while the treatment group was given the Xiaoai Jiedu Formula on this basis. The observation lasted for 42 days. The results showed that the addition of the Xiaoai Jiedu Formula could significantly improve the quality of life score of patients with advanced tumor cachexia, reduce the level of inflammatory factors, and improve the quality of life of patients. Jia Yingjie et al. [23] divided 40 mice into the healthy group, the model group, the Xiaoyan Decoction group, and the medroxyprogesterone acetate group. Through modeling, mice other than the healthy group were established as lung cancer cachectic mice. After 14 days of continuous administration, in the lung cancer cachectic mice treated with Xiaoyan Decoction, the weight of the gastrocnemius muscle was significantly higher than that of the medroxyprogesterone acetate group. The levels of serum TNF- α , IL-6, and the expressions of MAFbx and MURF-1 mRNA were significantly higher in the Xiaoyan Decoction group than in the medroxyprogesterone acetate group. Xiaoyan Decoction may improve the cachectic state of lung cancer by reducing inflammatory responses, improving muscle protein degradation, and increasing the weight of the gastrocnemius muscle in mice. Experimental studies indicate Baoyuan Detoxification Decoction can delay cancer-related muscle atrophy by suppressing TNF-α, IL-6, and the ubiquitin-proteasome (UPP) pathway [24]. Zhang Min et al. [25] conducted a clinical trial combining Compound Bamao Capsules with thalidomide for cancer treatment. In patients with cachexia, the results showed that the combination of these drugs could reduce the level of inflammatory cytokines and improve the quality of life.

4.1.4 Double supplementation of spleen and kidney to protect the righteous qi

Cancer is an immune system disorder. Both the cancer itself and cancer treatment can lead to a decline in the patient's immune function. Patients with cachexia predominantly occur in advanced-stage cancer patients, characterized by prolonged illness-induced physical weakness and impaired organ function. The compromised spleen-stomach digestive system fails to nourish muscles and limbs, while insufficient kidney essence and yang deficiency impair skin warmth maintenance, leading to progressive weight loss and skeletal atrophy [26]. Zhang Meiling et al. [27] divided cachectic-stage cancer patients into control and treatment groups. The control group received nutritional support therapy, while the treatment group supplemented with Shuyi decoction. The treatment group showed greater efficacy in alleviating symptoms like fatigue and regulating weight loss, possibly through reduced inflammatory factor levels. Experimental studies demonstrated that C57 mice treated with Jianpi Yishen Formula (a traditional Chinese medicine formula) exhibited significantly improved cachexia compared to methylprednisolonetreated groups, with enhanced median survival potentially linked to reduced TNF-α and Activin-A levels [28]. Xu Kai et al. [29] employed a dual-spleen-kidney supplementation approach for stage IV lung cancer cachexia. The Western medicine group was given medroxyprogesterone acetate dispersible tablets, while the traditional Chinese medicine group was given the modified formula of Xiaojunzi Decoction combined with Liwei Dihuang Decoction on the basis of medroxyprogesterone acetate dispersible tablets. The results showed that the TCM treatment group demonstrated better quality of life, improved nutritional status, and clinical symptom relief than Western medicine-only groups, while also reducing cachexia-associated cytokine levels.

4.2 Acupuncture and other therapies

Zhou Xuetao et al. [30] divided 109 patients with advanced lung cancer and cachexia into a control group and an experimental group. The control group received standard nutritional support therapy, while the experimental group received "Laoshizhen" (a traditional Chinese herbal formula) in addition to standard care. Specifically, acupoints such as Shangquan(CV13), Zhongquan, Xiaquan, both sides of Tianqiu(S25), both sides of Daheng(SP15), Qihai(CV6), Guanyuan, and both sides of Zusanli are selected. These points work together to tonify the spleen and stomach, regulate the qi circulation in the middle jiao, and enhance the body's defenses while eliminating pathogenic factors. After two weeks of treatment, the experimental group showed significantly higher levels of iliac muscle index, lean body mass, and quality of life scores compared to the control group, demonstrating improved nutritional status with fewer adverse reactions. Hu Qingqing et al. [31] conducted a comparative study between moxibustion combined with herbal decoction and medroxyprogesterone acetate for treating spleen-kidney deficiencytype cancer cachexia. Moxibustion was administered at bilateral Zusanli (ST36) and Yongquan (SP5) acupoints. Results indicated that the moxibustion-herbal decoction group outperformed the Western medicine-only group in TCM syndrome scores, cellular immune function, and body weight, effectively improving cancer cachexia. Another study revealed that acupuncture-treated patients exhibited better weight loss control and BMI improvement compared to palliative chemotherapy groups, demonstrating acupunctures efficacy in enhancing BMI and mitigating weight reduction in cancer cachexia patients [32].

5. Treatment of cancerous cachexia in Western medicine

Current Western medical treatment for cancer-related cachexia primarily involves nutritional support, psychological counseling, exercise therapy, and pharmacological interventions [33]. Patients with cachexia often experience prolonged loss of appetite, making appetite stimulation an effective approach to improve nutritional status. Clinically, glucocorticoids and progesterone preparations are widely used as effective appetite stimulants. A systematic review demonstrated that therapeutic doses of medroxyprogesterone acetate significantly enhanced appetite in advanced cancer patients, with more patients showing marked weight gain and improved KPS scores. These indicators—weight gain, appetite improvement, and elevated KPS scores—serve as comprehensive quality-of-life metrics for cancer patients [34]. Additionally, dexamethasone, a long-acting and cost-effective glucocorticoid, has shown notable efficacy in alleviating fatigue, anorexia, and depressive symptoms in advanced cachexia patients [35]. However, prolonged glucocorticoid use may cause adverse effects such as hyperglycemia, immune dysfunction, and impaired protein catabolism leading to muscle atrophy, thereby accelerating cachexia progression [36]. Metabolic disorders constitute a key etiological factor in cancer-related cachexia. These medications primarily regulate bodily functions through mechanisms including transcription factor suppression, cytokine blockade, and anabolic promotion. Current pharmacological recommendations primarily include fish oil and nonsteroidal anti-inflammatory drugs (NSAIDs) such as thalidomide. Fish

oil has been shown to improve appetite, muscle mass, and body weight in patients with advanced-stage tumors. EPA inhibits IL-6 gene activation by blocking MK-κB, thereby reducing IL-6 production [37]. For pre-cachectic patients, nutritional counseling, enhanced dietary intake, and oral nutritional supplements are recommended. In advanced cancer cachexia cases where oral nutrition fails to meet requirements, parenteral nutrition should be considered to provide high-energy, high-protein, and high-fat diets [38]. Additionally, studies demonstrate that moderate aerobic and resistance training can help prevent cancer cachexia, reverse muscle wasting, and prolong survival [39,40].

6. Conclusion

Given the complex pathogenesis of cancer-related cachexia involving multi-organ and systemic metabolic disturbances, anti-cachexia drug therapies have shown limited progress. To date, no specialized drugs targeting tumor-related cachexia have been approved for market release, and there remains a lack of established standard treatment protocols. Early diagnosis and timely intervention are therefore critical. Traditional Chinese Medicine (TCM), guided by holistic concepts and syndrome differentiation theory, combines internal and external therapies to improve cachexia conditions and prolong survival in cancer patients. However, current understanding of TCMs therapeutic mechanisms remains incomplete, and these approaches lack large-scale clinical trials and evidence-based medical support, necessitating further research. Additionally, numerous studies indicate that integrated TCM-Western medicine approaches can achieve better clinical outcomes in both preventing and treating cancer-related cachexia.

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