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# Advances in the treatment of cancer-related fatigue in patients with advanced gastric cancer

*Xiaohong Ma[1], Ruyi Yang[2*], Kai Fang[1]*

[1]School of Medicine, Qinghai University, Xining, China
[2]Department of Traditional Chinese Medicine, Affiliated Hospital of Qinghai University, Xining, China

*Corresponding Author. Email: yangruyi202110@163.com

**Abstract.** Cancer-Related Fatigue (CRF) is one of the most common manifestations of Cancer-Related Distress (CRD). CRF in patients with advanced gastric cancer is a complex condition involving multiple contributing factors. It is closely associated with cancer cachexia caused by the tumor itself and is also related to various adverse effects following chemotherapy, targeted therapy, immunotherapy, and surgical treatment. In addition, psychosocial factors such as anxiety and depression significantly exacerbate patients' experience of fatigue. Current diagnostic and therapeutic strategies for CRF in advanced gastric cancer emphasize multidisciplinary comprehensive intervention. Western medical treatment primarily focuses on etiological management, while integrated traditional Chinese and Western medicine demonstrates unique advantages in holistic regulation. This integrative approach not only helps delay disease progression but also improves the quality of life of patients with advanced gastric cancer. This article aims to review the relevant etiological factors of CRF in advanced gastric cancer and recent research progress in etiological treatment through integrated traditional Chinese and Western medicine.

**Keywords:** advanced gastric cancer, cancer-related fatigue, etiology, integrated traditional Chinese and Western medicine, review

## 1. Introduction

Fatigue is one of the most common manifestations of Cancer-Related Distress (CRD) [1]. The 2023 edition of the National Comprehensive Cancer Network (NCCN) defines Cancer-Related Fatigue (CRF) as a distressing, persistent sense of exhaustion or physical weakness caused by cancer or its treatment that is disproportionate to recent activity, interferes with daily functioning, and cannot be relieved by rest, with symptoms typically lasting for more than two weeks [2]. Early symptoms of gastric cancer are often subtle, and most patients are diagnosed at a locally advanced or advanced stage. Cancer-related fatigue in patients with advanced gastric cancer not only has a high incidence but also results from the combined effects of tumor-associated hypermetabolism, impaired nutritional absorption caused by gastric cancer, and multiple treatment-related factors such as surgery and chemotherapy. Its pathogenesis is complex and refractory, posing a serious threat to patients' quality of life. Studies have shown that approximately 60% of patients with malignant tumors experience varying degrees of cancer-related fatigue [3]. This substantial symptom burden leads to loss of

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independence in daily activities, reduced treatment adherence, and the development of severe anxiety, depression, and cognitive impairment. Ultimately, it significantly undermines patients' will to survive and their sense of dignity in life. This article focuses on cancer cachexia, adverse effects associated with chemotherapy, targeted therapy, immunotherapy, and surgical treatment, as well as psychosocial factors, in order to systematically explore the etiological mechanisms of cancer-related fatigue in advanced gastric cancer and to identify effective intervention strategies.

## 2. Cancer cachexia

Cancer cachexia is a wasting syndrome characterized primarily by anorexia or reduced food intake, weight loss, and depletion of adipose tissue and skeletal muscle. It disrupts the homeostasis of pro-inflammatory responses, neuroendocrine regulation, and nutritional metabolism, resulting in abnormalities in energy, protein, and lipid metabolism, and ultimately leading to cancer-related fatigue [4]. Therefore, improving cachexia in patients with gastric cancer is of critical importance for the management of cancer-related fatigue.

Early nutritional support should be implemented in clinical practice. Oral supplementation with Eicosapentaenoic Acid (EPA), which has anti-inflammatory and metabolic regulatory properties, can help stabilize body weight, improve appetite, and enhance quality of life. Ghrelin and its analogues, circulating orexigenic hormones associated with growth hormone release, not only stimulate appetite but also enhance muscle protein synthesis and exert protective effects against muscle atrophy [5]. Novel histone deacetylase inhibitors such as AR-42 promote muscle cell proliferation and hypertrophy by upregulating follistatin expression. In addition, moderate exercise combined with enteral nutrition can provide essential energy and protein support. Fish oil, which possesses anti-catabolic and anti-inflammatory properties, is recommended as a nutritional supplement, while megestrol acetate is widely used clinically as an appetite stimulant.

In Traditional Chinese Medicine (TCM), cancer cachexia is classified under the categories of "consumptive deficiency" (xulao) and "flaccidity syndrome" (weizheng). The *Plain Questions: Discussion on the True Organs of the Jade Mechanism* (*Suwen·Yujizhenzang Lun*) describes a condition characterized by severe skeletal emaciation, muscle wasting, chest fullness, and labored breathing, which closely resembles the clinical manifestations of cachexia [6]. TCM treatment of cancer cachexia focuses on deficiency as the root, with the fundamental principle of strengthening vital qi and eliminating pathogenic factors. Sun Yan [7] and colleagues emphasized that "the spleen and stomach constitute the foundation of acquired constitution", and administered a spleen-strengthening and stomach-nourishing herbal paste composed of 24 medicinal ingredients, including Codonopsis pilosula (Dangshen), Atractylodes macrocephala (Baizhu), Poria cocos (Fuling), and Dolichos lablab (Baibiandou). After treatment, nutritional indicators—including body mass index, serum total protein, serum albumin, subjective global assessment scores, and Karnofsky Performance Status scores—were significantly improved compared with the control group. Based on the TCM principle that "regulating qi is primary and the spleen and stomach are fundamental", a randomized controlled trial involving 200 patients with cancer-related fatigue demonstrated that patients receiving mild moxibustion at acupoints Danzhong (CV17), Zhongwan (CV12), Qihai (CV6), and bilateral Zusanli (ST36), combined with acupuncture at bilateral Xuehai (SP10), bilateral Waiguan (SJ5), and Taichong (LR3), showed significantly reduced fatigue scores on the Revised Piper Fatigue Scale compared with baseline ($p < 0.01$). Furthermore, immune indicators such as $CD3^+$ T cells and $CD4^+$ T cells were significantly improved ($p < 0.05$), and overall quality of life was markedly enhanced [8]. In addition, emerging TCM injectable preparations have demonstrated therapeutic potential. Kangai Injection regulates the tumor microenvironment, inhibits tumor angiogenesis, and alleviates chemotherapy- and radiotherapy-induced bone marrow suppression and immune

injury. Aidi Injection enhances immune function, inhibits various tumor cells, and exerts anti-fatigue, anti-hypoxia, and antitumor effects. Kangai Injection has also been shown to improve mitochondrial function in cardiomyocytes, increase ATP levels, and restore energy metabolism in animal models. These novel TCM injectable agents may alleviate fatigue symptoms in patients with advanced gastric cancer by restoring food intake and enhancing immune function [9].

For patients with advanced gastric cancer experiencing cancer-related fatigue caused by cachexia, Western medicine emphasizes daily nutritional supplementation, oral nutritional support, enteral nutrition via nasogastric tube, and parenteral nutrition, all of which provide rapid clinical benefits. In contrast, TCM primarily focuses on tonifying deficiency, using herbal paste formulations to strengthen foundational vitality, regulating the triple burner through principal acupoint therapy combined with syndrome-based acupoint selection, and employing novel TCM injections to restore appetite and alleviate cancer-related fatigue. These approaches have demonstrated favorable safety and efficacy profiles.

## 3. Treatment-related adverse effect

### 3.1. Surgical treatment

Surgical intervention may provide survival benefits for patients with advanced gastric cancer. Palliative gastrectomy can be performed to relieve acute complications such as bleeding and obstruction, while experimental cytoreductive surgery aims to prolong survival. In addition, conversion therapy may achieve R0 resection following effective preoperative chemotherapy. Although surgical resection improves survival outcomes in patients with gastric cancer, reconstruction of the digestive tract is inherently invasive and induces neuroendocrine alterations, inflammatory responses, and persistent postoperative pain. These changes often result in impaired digestive and absorptive function, sleep disturbances, and an increased likelihood of fatigue.

Perioperative pain management is routinely implemented in patients with advanced gastric cancer and may include opioid analgesics, nonsteroidal anti-inflammatory drugs, and local anesthetics to alleviate persistent postoperative pain and reduce fatigue. However, postoperative digestive and absorptive dysfunction is unavoidable. The National Comprehensive Cancer Network recommends lifelong monitoring of postoperative nutritional status and management of potential nutritional complications, including deficiencies in vitamin B12, iron, zinc, calcium, and vitamin D, along with routine supplementation of multivitamin and mineral complexes [10].

From the perspective of traditional Chinese medicine, patients with advanced gastric cancer often present with preexisting impairment of spleen and stomach function, as well as deficiencies of qi, blood, yin, and yang. Surgical trauma further damages the spleen and stomach of the middle burner, exacerbating deficiencies of qi, blood, yin, and yang, and thereby contributing to fatigue. In one study, patients in the treatment group who received Shenqi Yichang Decoction demonstrated significantly lower Piper Fatigue Scale scores and significantly higher Functional Assessment of Cancer Therapy–General (FACT-G) scores compared with the control group. This formula contains medicinal ingredients such as Panax ginseng (Renshen), Astragalus membranaceus (Huangqi), Coix lacryma-jobi (Shengyiyiren), Actinidia chinensis root (Tengligen), Akebia trifoliata (Bayuezha), and Sophora flavescens (Kushen), which promote recovery of postoperative gastrointestinal function, enhance immune function, tonify qi and blood, and alleviate fatigue symptoms [11]. In terms of external TCM therapies, based on the principle that "meridians govern the regions they traverse", transcutaneous electrical acupoint stimulation applied to bilateral Zusanli (ST36), Neiguan (PC6), and Hegu (LI4) significantly reduced Numeric Rating Scale (NRS) pain scores in the treatment group compared with the

control group. Furthermore, gastrointestinal motility indicators were significantly improved, demonstrating effects in promoting meridian circulation, relieving pain, enhancing gastrointestinal motility, and alleviating fatigue [12]. Additional studies have shown that auricular acupressure at points including the sympathetic, subcortex, small intestine, large intestine, stomach, endocrine, and spleen points, combined with acupoint herbal application, can facilitate recovery of gastrointestinal function, provide analgesia, promote early postoperative rehabilitation, and reduce cancer-related fatigue in patients with gastric cancer [13].

Surgical treatment remains an important therapeutic option for patients with advanced gastric cancer. However, as an invasive intervention, it inevitably leads to postoperative pain and digestive dysfunction, both of which contribute to cancer-related fatigue. Western medical approaches such as analgesic therapy and nutritional support provide rapid and effective relief but are associated with notable adverse effects and increased economic burden. In contrast, traditional Chinese medicine interventions—including transcutaneous electrical acupoint stimulation, auricular acupressure, acupoint herbal application, and herbal decoctions—have demonstrated significant clinical efficacy with fewer adverse effects. Integrated treatment combining traditional Chinese and Western medicine offers a comprehensive approach that alleviates fatigue symptoms while supporting postoperative recovery in patients with advanced gastric cancer.

## 3.2. Chemotherapy

Treatment for advanced gastric cancer primarily involves neoadjuvant chemotherapy and postoperative chemotherapy. Fatigue is the most common symptom associated with chemotherapy for malignant tumors. While chemotherapy targets and eliminates cancer cells, it also causes substantial damage to normal tissues and physiological functions. During chemotherapy, unavoidable adverse effects such as bone marrow suppression, gastrointestinal reactions, and neurotoxicity often occur, leading to anemia, infection, nausea, vomiting, and loss of appetite, all of which may induce or exacerbate fatigue [14].

Chemotherapy regimens for advanced gastric cancer are typically based on platinum agents combined with fluorouracil-based drugs. Platinum-based regimens are a major contributing factor to chemotherapy-induced anemia. Clinical management mainly includes blood transfusion, administration of Erythropoietin (EPO), and supplementation with hematopoietic substrates such as iron [15]. Short-acting and long-acting recombinant human granulocyte colony-stimulating factor are commonly used to prevent and treat neutropenia and reduce the risk of infection. Oral leukocyte-elevating agents, such as Leucogen tablets, batyl alcohol tablets, and vitamin B4, may also be administered. Chemotherapy-Induced Nausea and Vomiting (CINV) can result in disturbances of fluid and electrolyte balance, acid–base imbalance, dehydration, anorexia, malnutrition, and cachexia, and in severe cases may threaten life [16]. Western medical management focuses on symptomatic antiemetic therapy, including 5-Hydroxytryptamine (5-HT) receptor antagonists represented by the "setron" class of drugs, neurokinin-1 receptor antagonists such as rolapitant and aprepitant, glucocorticoids, and dopamine receptor antagonists such as metoclopramide [17].

According to traditional Chinese medicine theory, chemotherapy in advanced gastric cancer tends to damage vital qi, resulting in dysfunction of the zang-fu organs, deficiency of qi and blood, and imbalance of yin and yang. Therefore, the primary therapeutic principle is to tonify qi and nourish blood in order to alleviate adverse effects such as bone marrow suppression and fatigue following chemotherapy. One study found that treatment with Shuyu Pill resulted in significantly higher total effective rates in TCM syndrome scores, Piper Fatigue Scale scores, Karnofsky Performance Status scores, and sleep improvement compared with the control group [18]. Many scholars believe that chemotherapy-induced consumptive deficiency arises from the toxic effects of chemotherapeutic agents, leading to a state characterized by deficiency of vital qi and persistence of pathogenic factors. This imbalance persists throughout the disease course. In patients with leukopenia,

moxibustion applied to acupoints Guanyuan (CV4), Qihai (CV6), Shenque (CV8), and Zusanli (ST36) has been shown to improve immune function by increasing $CD4^+$ and $CD8^+$ T-cell levels, thereby alleviating deficiency-related fatigue symptoms [19]. Chemotherapy-related toxicity also damages the spleen and stomach, impairing their transport and transformation functions and causing upward rebellion of stomach qi, resulting in nausea, vomiting, and poor appetite. Based on syndrome differentiation, modified Banxia Xiexin Decoction, Lizhong Pill, or Liujunzi Decoction may be prescribed. These treatments can be combined with moxibustion at Zusanli (ST36), Neiguan (PC6), and Zhongwan (CV12) to protect gastric function, relieve nausea and vomiting, restore vital energy, improve nutritional intake, and effectively reduce cancer-related fatigue in patients with advanced gastric cancer [20].

The various adverse effects associated with chemotherapy for advanced gastric cancer frequently induce or aggravate fatigue. Western medicine recommends symptomatic management, including oral antiemetic drugs, recombinant human granulocyte colony-stimulating factor injections, oral leukocyte-elevating agents, blood transfusion, and iron supplementation. Traditional Chinese medicine, in contrast, employs herbal compound formulations with demonstrated efficacy and minimal adverse effects to tonify qi and nourish blood, protect gastric function, alleviate nausea and vomiting, and restore constitutional vitality. These treatments, combined with external therapies such as moxibustion, effectively mitigate chemotherapy-related adverse effects and reduce fatigue symptoms.

### 3.3. Immunotherapy

Immunotherapy has become one of the standard treatment modalities for advanced gastric cancer, and a variety of therapeutic strategies have been developed, including immune checkpoint inhibitors, adoptive cell therapy, chimeric antigen receptor T-cell therapy, and tumor vaccines [21]. Among these, immune checkpoint inhibitors—by targeting the Programmed Cell Death Protein 1 (PD-1/PD-L1) pathway or Cytotoxic T-Lymphocyte-Associated Antigen-4 (CTLA-4)—activate T-cell-mediated immune responses to eliminate tumor cells and have emerged as a key therapeutic approach in advanced gastric cancer. However, these therapies may also induce thyroid dysfunction, including hypothyroidism and thyrotoxicosis, which are common contributors to fatigue in affected patients [22].

While immunotherapy enhances antitumor immune responses, excessive activation of the immune system may lead to a range of immune-related adverse events. For example, bone marrow suppression may occur, increasing the risk of secondary infections. In addition, immunotherapy may induce gastrointestinal adverse reactions such as colitis, diarrhea, nausea, and vomiting, which impair nutritional intake and absorption. Over time, these effects may result in weight loss, malnutrition, and even cachexia [23]. Certain immunotherapeutic agents may also potentiate the toxicity of concurrent chemotherapy or targeted therapy, further reducing treatment tolerability.

Beyond these effects, immunotherapy may involve multiple organs and endocrine systems, including the heart, lungs, adrenal glands, and thyroid, leading to immune-related adverse events manifested clinically as mental fatigue, generalized weakness, somnolence, and other fatigue-related symptoms. Therefore, careful monitoring and prompt management of these adverse effects are essential during clinical treatment. The primary management strategies for immunotherapy-related adverse events include corticosteroids and other immunosuppressive agents, combined with appropriate supportive care, which can effectively alleviate fatigue symptoms in patients with advanced gastric cancer undergoing immunotherapy [24].

According to traditional Chinese medicine theory, as stated in the *Huangdi Neijing*, "excess yin leads to impairment of yang". TCM considers pathogenic factors such as cold and dampness to be associated with higher fatigue severity scores. Cold-damp pathogens tend to impair yang qi, resulting in slowed metabolic

activity and symptoms such as aversion to cold, lethargy, and mental fatigue. Furthermore, the heavy and turbid nature of dampness can obstruct the movement of qi, leading to symptoms including limb heaviness, fatigue, and dysfunction of the spleen and stomach, which may become chronic and difficult to resolve. Clinical therapies such as herbal hot compresses and moxibustion are commonly employed to restore the balance of yin and yang and promote energy metabolism, thereby effectively alleviating fatigue symptoms [25]. Huang Xiaona and colleagues reported that WD-3 Mixture, a spleen-strengthening herbal compound formula, increased the abundance of intestinal microbiota and improved the gut microecological environment in patients with gastric cancer, thereby enhancing the efficacy of immunotherapy and alleviating post-treatment fatigue. Their study also demonstrated that this formulation effectively improved gastrointestinal symptoms such as dry mouth, taste alterations, and dysphagia in patients undergoing immunotherapy for advanced gastric cancer, significantly reducing fatigue symptoms [26].

Fatigue resulting from immune-related adverse events such as hypothyroidism is common in patients with advanced gastric cancer receiving immunotherapy. Western medical management primarily involves symptomatic treatment with immunosuppressive agents and corticosteroids. In contrast, traditional Chinese medicine attributes these symptoms to cold-damp pathogenic factors impairing yang qi and slowing metabolism. Therapeutic approaches such as herbal hot compresses, moxibustion, and spleen-strengthening herbal compound formulations are used to promote energy metabolism and effectively alleviate fatigue symptoms.

### 3.4. Targeted therapy

At present, targeted therapy for advanced gastric cancer primarily focuses on molecular targets such as Human Epidermal growth factor Receptor 2 (HER2), Fibroblast Growth Factor Receptor 2 (FGFR2), and the transmembrane protein CLDN18.2 [27].

Trastuzumab is the first-line targeted agent for HER2-positive advanced gastric cancer. Trastuzumab deruxtecan (DS-8201a) and disitamab vedotin have been approved for second-line and third-line treatment of HER2-positive gastric cancer, respectively, and have been shown to improve survival outcomes in patients with advanced gastric cancer. However, these agents may also cause adverse effects such as pancytopenia and pneumonia, which contribute to fatigue. Antiangiogenic agents such as bevacizumab and apatinib mesylate inhibit tumor cell proliferation and metastasis but are associated with toxicities including proteinuria and hypertension. If not properly controlled, these complications may progress to nephrotic syndrome, resulting in symptoms such as fatigue and loss of appetite [28]. Western medical management recommends regular monitoring of blood pressure and liver and renal function throughout antiangiogenic therapy. Potent angiotensin II receptor blockers, such as irbesartan, may be used to lower blood pressure and reduce proteinuria, thereby alleviating fatigue symptoms.

In traditional Chinese medicine, proteinuria falls within the category of "turbid urine" and is attributed primarily to dysfunction of the spleen and kidney. Deficiency of spleen qi impairs the spleen's ability to retain essential substances, while kidney qi deficiency leads to downward leakage of vital essence. In addition, pathological factors such as dampness and blood stasis further contribute to urinary protein loss. Jingui Shenqi Pill, as described in Zhang Zhongjing's *Jingui Yaolue* (*Essential Prescriptions from the Golden Cabinet*), has been shown to reduce 24-hour urinary protein excretion, improve qualitative proteinuria, and alleviate TCM syndrome manifestations, with a favorable safety profile. Its therapeutic principles include warming and tonifying the spleen and kidney, promoting blood circulation, and eliminating damp turbidity, thereby reducing proteinuria and alleviating fatigue symptoms [29]. Astragalus is a commonly used herb in traditional Chinese medicine formulations for cancer-related fatigue. It has demonstrated multiple pharmacological effects,

including regulation of lipid and glucose metabolism, anti-inflammatory and antioxidant activity, antifatigue effects, vascular endothelial protection, blood pressure reduction, improvement of renal microcirculation, and protection of renal cells. These properties make it effective in reducing proteinuria and relieving fatigue [30]. Acupuncture therapies targeting acupoints such as Renying (ST9), Taichong (LR3), Quchi (LI11), Fengchi (GB20), Zusanli (ST36), and Neiguan (PC6), combined with specialized techniques such as abdominal acupuncture, ocular acupuncture, and buccal acupuncture, have been shown to inhibit vascular smooth muscle proliferation, regulate the renin–angiotensin system, and modulate Nitric Oxide (NO) levels. These effects contribute to blood pressure reduction, inhibition of myocardial hypertrophy, and protection of ischemic myocardium, thereby alleviating fatigue caused by adverse effects of targeted therapy in patients with advanced gastric cancer [31].

Adverse effects such as hypertension and proteinuria frequently occur following targeted therapy in patients with advanced gastric cancer, impairing physiological function and contributing to fatigue. Western medical management typically involves long-term antihypertensive therapy; however, such treatment may be associated with rebound hypertension after discontinuation, hypotension, and drug resistance, which limit its clinical applicability. Compared with conventional Western pharmacotherapy, single-herb treatments such as Astragalus, compound herbal formulations, and acupuncture offer advantages including lower cost, greater patient acceptance, and fewer adverse effects. Therefore, integrated traditional Chinese and Western medicine provides an effective approach for managing fatigue caused by adverse effects of targeted therapy in advanced gastric cancer.

## 4. Psychosocial factor

During the course of treatment, patients with advanced gastric cancer often experience significant psychological distress due to factors such as adverse drug reactions, changes in dietary structure, and the high financial burden of treatment. In addition, the cancer itself, surgical trauma, and adjuvant therapies can impair patients' functional abilities, physical condition, and mental status, resulting in both physical and psychological fatigue.

Studies have shown that psychological resilience—defined as an individual's capacity for self-regulation and adaptation in the face of adversity—plays a crucial role in patients with advanced gastric cancer. Optimism, social support, and self-efficacy are all positively correlated with psychological resilience. In other words, higher levels of these factors enhance resilience and enable patients to cope more effectively with disease-related stress [32]. Targeted psychosocial interventions for patients with advanced gastric cancer can help alleviate psychological stress, improve self-management efficacy, enhance immune function, and ultimately relieve cancer-related fatigue. Among specific intervention strategies, cognitive behavioral therapy helps patients identify and modify maladaptive cognitive and behavioral patterns, thereby alleviating emotional distress. Multiple studies have confirmed its effectiveness in reducing fatigue and improving quality of life in cancer patients. Mindfulness-based stress reduction encourages patients to focus on present-moment experiences with a nonjudgmental attitude, reducing anxiety and stress. Clinical evidence indicates that it can significantly alleviate cancer-related fatigue and improve sleep quality. Furthermore, comprehensive approaches—including health education, peer support, and family involvement—can strengthen patients' understanding of their condition, enhance their initiative and confidence in treatment, and promote personal growth, thereby reducing fatigue at a holistic level [33].

According to the *Huangdi Neijing Suwen*, "In the courageous, qi flows freely; in the fearful, it stagnates and leads to disease". Traditional Chinese medicine holds that psychological distress in patients with advanced

gastric cancer primarily affects the middle jiao. Emotional disturbances disrupt the ascending and descending movement of qi, leading to disharmony between the liver and spleen and impaired digestive and transformative functions of the spleen and stomach. Clinically, this manifests as fatigue-related symptoms such as depression, sallow complexion, and slowed physical activity. Under the guidance of TCM emotional regulation theory, therapeutic approaches—including verbal counseling, emotional redirection, and five-tone therapy—are employed to regulate emotional states, relieve qi stagnation, restore physiological balance, and improve digestive and systemic function. Traditional therapeutic exercises have also been shown to be effective in cancer rehabilitation. Tai Chi can improve fatigue and quality of life, Baduanjin enhances sleep quality, and Liuzijue is particularly effective in regulating emotional states. These traditional exercise methods integrate movement and stillness while simultaneously cultivating physical and mental well-being, providing comprehensive benefits and effectively alleviating fatigue in patients with advanced gastric cancer [34].

Given current limitations in medical knowledge and the complexity of the disease, patients with advanced gastric cancer may have limited tolerance for pharmacological treatments targeting psychological disorders due to their adverse effects. Therefore, the key to management lies in effective communication, emotional support, and practical problem-solving. Integrated traditional Chinese and Western medical approaches, combined with exercise and psychosocial interventions as nonpharmacological therapies, can alleviate cancer-related distress and treatment-related burden. These strategies help regulate liver qi, harmonize qi and blood, reduce patient suffering, and potentially delay disease progression.

## 5. Conclusion and future perspectives

Fatigue is an inevitable consequence in patients with advanced gastric cancer, arising from cancer cachexia, treatment-related adverse effects, and psychosocial factors. It exerts profound and far-reaching negative effects on patients' quality of life and survival. At present, a variety of interventions are available, including pharmacological and nonpharmacological comprehensive management, exercise interventions, and psychological therapies. However, as a multidimensional and multifactorial symptom, cancer-related fatigue remains difficult to manage optimally, and significant challenges persist in identifying the most effective treatment strategies. Therefore, it is essential to leverage the complementary strengths of integrated traditional Chinese and Western medicine in addressing the etiology and treatment of cancer-related fatigue in advanced gastric cancer. Future research should focus on elucidating the biological mechanisms underlying their synergistic effects and establishing standardized systems for evaluating therapeutic efficacy. Such efforts aim to alleviate patient suffering, reduce treatment-related adverse effects and economic burden, and ultimately improve quality of life. Looking ahead, emerging technologies—including mobile health–based wearable devices, artificial intelligence, and remote monitoring systems—offer promising tools for the dynamic and real-time assessment of objective indicators such as physical activity levels, sleep quality, and heart rate variability. When integrated with subjective fatigue assessment scales, these technologies may enable the development of predictive and management models for cancer-related fatigue, thereby facilitating its long-term and individualized management. At the same time, it is important to actively evaluate the synergistic efficacy and safety of combining traditional Chinese medicine formulations with targeted therapy and immunotherapy. Establishing a patient-centered, multidisciplinary collaborative care model—integrating oncology, traditional Chinese medicine, nutrition, rehabilitation, and psychological services—will be critical. Future treatment goals should extend beyond prolonging survival to significantly enhancing patients' quality of life, enabling them to live with greater vitality, dignity, and well-being.

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