### **Review Article**

# Exploration of the Integrated Traditional Chinese and Western **Medicine Treatment Model for Primary Liver Cancer Under** the Guidance of the Green Treatment Concept of Tumor



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#### **Abstract**

Unlike the traditional staging treatment of tumors, the core of "Green Tumor Treatment" is to divide the treatment of tumors into three stages: Hegemony (directly targeting the cancer focus), Kingship (supporting the body's vital energy and eliminating pathogenic factors), and Imperialism (improving the internal environment), based on the urgency of the tumor and the patient's physical condition. This approach guides the clinical treatment of tumors. Its treatment system incorporates all minimally invasive and low-damage treatment methods, combining internal and external treatments, traditional Chinese medicine and Western medicine, as well as local and systemic treatments. It aims to maximize treatment outcomes while ensuring the patient's quality of life, which is highly consistent with the treatment goals for primary liver cancer. This review aims to explore the integrated Traditional Chinese and Western medicine treatment model for primary liver cancer under the guidance of the Green Tumor Treatment concept.

#### Introduction

Primary liver cancer (PLC) is a global health challenge. It is estimated that there will be over one million new cases in 2025, posing a serious threat to human health. Studies show that PLC ranks 4th in incidence and 2nd in mortality among malignant tumors in China, and the number of PLC cases in China accounts for 60.5% of the global total.<sup>2</sup> Therefore, the task of prevention and treatment of PLC in China is arduous. According to guidelines, recommended treatments for early-stage PLC include surgical treatments such as hepatectomy and liver transplantation. For intermediate and advanced unresectable PLC, local treatment methods such as Transarterial Chemoembolization (TACE), Hepatic Arterial Infusion Chemotherapy, and tumor ablation are playing an increasingly important role.<sup>3</sup> According to World Health Organization statistics, there are ap-

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proximately 750,000 new PLC cases globally each year. Over 70% of patients are already in advanced stages at the time of diagnosis, losing the opportunity for radical surgery, and even patients who successfully undergo surgery have a recurrence rate of 70%. 4,5 In recent years, the role of targeted immunotherapy in PLC has become increasingly prominent, but the response rate remains below 40%.6 Therefore, in addition to early screening, early detection, and early radical cure, the choice of treatment strategies for preventing postoperative recurrence and treating intermediate to advanced patients is particularly important.

Traditional Chinese medicine (TCM) emphasizes the concept of holism and "individualized treatment". Through multi-dimensional overall regulation-strengthening vital qi (Fu Zheng) to eliminate pathogens (Qu Xie), alleviating complications, harmonizing methods to improve the internal environment, and preventing recurrence—TCM plays an important role throughout the entire course of PLC treatment. Modern medicine emphasizes "focusing on the local and lightly on the whole", showing obvious advantages in surgery. The complementary use of TCM and Western medicine may truly improve therapeutic efficacy.

#### The dilemma of integrated TCM and Western medicine treatment for PLC

With the development of modern medicine, drugs such as anti-hep-

atitis B and C virus agents are playing an increasingly important role in the treatment of infectious liver diseases, while the status of TCM is becoming increasingly marginalized. This bias in academic concepts has caused the development of the discipline of integrated TCM and Western medicine liver disease to gradually lose balance. In terms of professional teams, research on integrated TCM and Western medicine liver disease is mostly completed by TCM practitioners, with fewer Western medicine personnel actively participating in learning and conducting such research, which also limits the depth and breadth of the research.

Problems such as high postoperative recurrence rates in earlystage liver cancer patients, short survival times, and poor quality of life in intermediate and advanced liver cancer patients are prominent. The reason is that modern medicine primarily focuses on "anti-tumor" treatment, neglecting the characteristics of the patients themselves, and lacks a unified understanding of the local lesions versus systemic manifestations of PLC. Traditional TCM has obvious advantages in preventing recurrence, improving complications, and overall regulation, but often overlooks that the tumor is a systemic disease with "prominent local manifestations". Strengthening local treatment, optimizing systemic treatment, and coordinating TCM with Western medicine may improve the overall treatment effect of PLC. A clinical study showed that TACE combined with targeted immunotherapy for advanced hepatocellular carcinoma had significant effects, superior to targeted immunotherapy alone, providing strong evidence for the combined application of local and systemic treatment for PLC.<sup>7</sup>

Currently, a considerable number of PLC patients in China receive integrated TCM and Western medicine treatment, but this is mostly a simple superposition of TCM treatment and Western medicine treatment. The therapeutic effects are not superimposed, and the increased adverse reactions often make it difficult for patients to continue treatment. There is still a lack of effective strategies and plans on how to systematically integrate TCM and Western medicine treatments for PLC to achieve a mutually synergistic model, drawing on each other's strengths to achieve the best efficacy and minimal toxicity.

### The concept of Green Tumor Treatment and three-stage treatment

### The concept of Green Tumor Treatment

Traditional tumor treatment methods include surgery, radiotherapy, and chemotherapy. Due to the low rate of early tumor detection, most patients are already in the intermediate or advanced stages when discovered, losing the chance for radical surgery. Additionally, a significant proportion of patients cannot tolerate surgery or chemoradiotherapy due to advanced age, frailty, or multiple underlying diseases. Faced with such a grim status of tumor treatment, the team proposed the concept of "Green Tumor Treatment" in 2004 for patients who are in intermediate/advanced stages, elderly and frail, have multiple underlying diseases, or cannot tolerate radical surgery or have failed chemoradiotherapy. They pioneered the "Minimally Invasive + TCM" model of "Green Tumor Treatment".

Green Tumor Treatment is guided by TCM theory, inheriting the foundations of traditional TCM internal medicine and modern medicine. It fully utilizes the characteristics of TCM surgery and applies modern minimally invasive techniques, endowing them with "Cold/Heat" properties (Yin/Yang attributes), exploring a new model of tumor treatment. It is a vivid application of integrated TCM and Western medicine in the treatment of malignant

tumors.<sup>8</sup> Its treatment system incorporates all treatment methods that are minimally invasive, low-damage, and sustainable, including minimally invasive therapy, targeted drugs, immune drugs, low-dose chemoradiotherapy, TCM internal treatments, and TCM external treatments. Previous studies have shown that minimally invasive therapy combined with TCM for advanced non-small cell lung cancer can extend patient survival by about one year, alleviate patient suffering, and improve quality of life.<sup>9</sup> Currently, the Green Tumor Treatment model has been implemented in several tertiary hospitals nationwide. Since 2011, the team has held an annual forum on Green Tumor Treatment technology to promote the concept and treatment model across the country.

#### The "control" concept of malignant tumors

The Su Wen Chapter on Great Treatises on the Six Microcosms mentions: "For great accumulation and aggregation, it can be attacked, but stops when more than half is gone; going beyond this leads to death". Regarding the treatment of malignant tumors, TCM emphasizes that one need not pursue the complete elimination of the lesion but should prioritize protecting the patient's vital qi (Righteous Qi). The Union for International Cancer Control points out that tumors have already begun micrometastasis to the blood, tissues, and other organs during the latent period (tumor size approx. 0.5 cm). <sup>10</sup> Therefore, "radical cure" is often an ideal state, and in more cases, "control" should be pursued.

Modern tumor treatments often use aggressive methods to strike the tumor, which may damage the body's normal structure and function or result in a "lose-lose" situation for both the tumor and the body, causing damage to the body's vital qi. Traditional TCM tumor treatment focuses on internal medicine, primarily to enhance efficacy and reduce toxicity, often unaware that "if the disease is shallow but the medicine is deep, it will not hit the target; if the disease is deep but the medicine is shallow, it will not work either". Therefore, in the treatment of malignant tumors, one must avoid "going too far" but also understand the principle that "deep diseases cannot be treated with shallow medicine", focusing on grasping the method and degree of treatment.

#### Three-stage treatment of Green Tumor Treatment

The core of Green Tumor Treatment is to divide tumor treatment into three stages based on the urgency of the tumor condition and the patient's constitution: Hegemony (directly targeting the cancer focus), Kingship (strengthening vital qi and eliminating pathogens), and Imperialism (improving the internal environment). This guides clinical tumor treatment and represents a "Chinese Solution" for tumor treatment. Its characteristic is that the application of TCM and Western medicine is not a rigid "simultaneous" application, but often a "sequential" or "primary/secondary" application.

The three stages are detailed as follows:

- Acute phase (Hegemony stage): At the beginning of treatment, when the tumor burden is high and local compression symptoms are severe, local minimally invasive treatment or TCM external treatment should be the vanguard. The "Elimination" (Xiao) method is dominant, reaching the disease site directly to quickly reduce the local tumor burden and dispel pathogenic factors.
- Chronic phase (Kingship stage): Primarily during the perioperative period, based on systemic syndrome differentiation, TCM "Strengthening Vital Qi and Eliminating Pathogens" (Fu Zheng Qu Xie) is used. The "Tonifying" (Bu) method is dominant, utilizing TCM, low-dose chemoradiotherapy, and biological immune agents. The focus is on adjusting the balance of power

between pathogenic factors and vital qi, stimulating the body's own ability to resist pathogens.

Latent phase (Imperialism stage): When the power of pathogens and vital qi is relatively balanced, the "Harmonizing" (He) method is the main therapeutic principle. This involves improving the internal environment of the body to make it unfavorable for tumor growth, adjusting the cancer constitution, and preventing tumor recurrence.

#### Three-stage treatment of PLC

Studies show that oral TCM combined with interventional therapy for intermediate and advanced liver cancer can effectively improve clinical symptoms and slow liver cancer progression. Early Green Tumor Treatment practices also proved that TCM decoctions can serve as an effective adjuvant treatment strategy, improving long-term survival rates in PLC patients, extending progression-free survival, and improving prognosis. Furthermore, the longer the duration of TCM decoction intake, the more likely patients are to achieve longer survival, reflecting the positive effects of Green Tumor Treatment. 12,13

Compared to other tumors, PLC has a rapid onset, involves abundant Qi and blood locally, and has more prominent manifestations of Cold and Heat, making local treatment more advantageous. TCM can play a unique role in "strengthening vital qi and eliminating pathogens" after local treatment, early intervention in precancerous lesions (inflammation-cancer transformation), and preventing recurrence after early-stage liver cancer surgery.

Specific treatment strategies:

- Acute phase: Focuses on local treatment. It should follow the TCM surgical principle of "Intercept first, then pull out" (先载 后拔). Sequential use of vascular intervention and minimally invasive ablation cuts off the source of tumor Yang Qi (energy), making it unfavorable for tumor growth. Alternatively, TCM external treatment techniques are used to reach the lesion directly, alleviating local problems such as cancer pain and ascites.
- Chronic phase: Uses TCM and targeted immunotherapy to control tumor progression, achieving long-term survival with the tumor.
- Latent phase: TCM participates via the "Harmonizing" method to improve the internal environment and prevent liver cancer recurrence.

### Acute phase: Local treatment — attacking pathogens to reverse disease progression

Intermediate and advanced liver cancer is often accompanied by a large local tumor burden in the liver or distant metastasis, presenting various acute symptoms. At this time, local minimally invasive treatment should be the mainstay, focusing on quickly removing local pathogens, reducing tumor burden, reversing the disease trend, and fighting for time for subsequent treatments. This stage should follow the theory of "Great accumulation... remove six out of ten". Treatment need not pursue "complete eradication of evil" but should emphasize protecting the "protective field" of the tumor and safeguarding the body's vital qi to stimulate the body's own anti-tumor ability. Options include TACE, cryoablation, radiofrequency ablation (RFA), microwave ablation (MWA), and I-125 seed implantation. TCM external treatments, such as acupoint application, moxibustion, and fumigation, can also be selected to reach the lesion directly and alleviate local problems like cancer pain, effusion, and edema.

The Yue Pian Wen (Parallel Prose on Logic) states: "One is pull-

ing (Ba), one is intercepting (Jie). Wherever the disease gathers, if you pull it, the disease will come out on its own without the risk of sinking deeper; wherever the disease passes through, if you intercept it, the evil will be cut off without the worry of erratic transmission". The Inner Canon of the Yellow Emperor says, "Solitary Yin does not grow, solitary Yang does not thrive". Tumors have a Yin body but function as Yang. The treatment strategy should be to destroy its body, damage its Yang, or separate Yin and Yang.

By "cutting off the energy source", the TCM "Intercepting" method cuts off the blood connection between the tumor and the body to separate Yin and Yang, preventing their interaction. Modern medicine can use TACE to rapidly deplete the local Yang Qi of the tumor, forming a situation of "separation of Yin and Yang". Common embolic materials include embolic microspheres and iodized oil to directly cut off the blood supply to liver cancer. Related studies also show that cold-natured Chinese patent medicines such as Huachansu Injection and Compound Kushen Injection show good effects when used in hepatic artery embolization, reflecting the TCM characteristic of "Cold dominates contraction". 14,15 The hepatic artery provides the main blood supply for PLC and is the main source of its Yang Qi. As the degree of malignancy increases, the hepatic artery blood supply gradually increases, which is the modern medical theoretical basis for TACE treatment of PLC. 16

"Firm ones should be whittled, knotted ones should be scattered, and lingering ones should be attacked". Using ablation therapy to directly damage the tumor allows the knotted accumulation to be "pulled out" and the disease to exit. PLC is characterized by "Local Heat Excess". "Treat heat with cold"—cryoablation can be used to restrain it with cold, achieving the state of "Solitary Yin does not grow" and directly destroying the tumor lesion. Clinical studies show that Argon-Helium Knife cryoablation alone or combined with TACE for liver cancer can improve long-term survival and improve the immune function of PLC patients. <sup>17–19</sup>

The tumor body is Yin but functions as Yang; having a tangible form is Yin. Thermal ablation techniques such as RFA and MWA can be used to thermally destroy the body ("Treat cold with heat"), directly burning the tumor so that the Yin evil cannot accumulate, achieving "Solitary Yang does not grow". Clinically, transvascular interventional therapy is often used first to slow tumor growth (making the body Yin while Yang becomes faint), followed by RFA or MWA to destroy the body, thereby improving efficacy and reducing complications, especially for the treatment of large liver cancers. <sup>20,21</sup>

Additionally, recent studies show that composite cryo-thermal ablation for liver cancer cleverly integrates the advantages of high-temperature hyperthermia and deep low-temperature cryotherapy. It achieves goals such as low treatment pain, high safety, low cost, and good efficacy. It is being widely used clinically, and its specific mechanisms await deeper exploration.<sup>22</sup>

I-125 seed implantation, as a supplement to external radiotherapy, has the characteristics of being minimally invasive and precise and has unique advantages for tumors in special locations such as portal vein tumor thrombosis.<sup>23</sup>

"The principle of external treatment is the same as internal treatment; external medicine is the same as internal medicine; the difference lies only in the method". TCM external treatment in tumor therapy can demonstrate the effects of "Simplicity, Convenience, Efficacy, and Low Cost". In the external application of drugs for liver cancer, emphasis should be placed on the use of Qi-moving aromatics, blood-activating and stasis-removing drugs, and hardness-softening and node-dissipating drugs. <sup>24</sup> For example, when tumor progression compresses nerves, causing cancer pain,

TCM external application of warm-Yang, Qi-moving, and blood-activating drugs can be applied to the pain site or corresponding acupoints. Studies show that Clove Pain Relief Ointment (Ding Xiang Zhi Tong Gao), guided by the theory of Warming Yang, can improve the quality of life and Numerical Rating Scale (pain) scores of patients with moderate cancer pain.<sup>25</sup> In clinical application, one should not be restricted to a single drug or formula but should grasp the basic pathogenesis.

During the perioperative period, while rapidly striking the pathogenic Qi, the vital qi is inevitably damaged, leading to a series of clinical symptoms. TCM acupoint application, acupuncture, and auricular acupressure can alleviate adverse reactions such as hiccups and vomiting during the perioperative period. <sup>26–28</sup> In addition, TCM enemas for treating constipation in tumor patients, moxibustion for cancer-related fatigue, and TCM fumigation/application for liver cancer ascites have definite curative effects. <sup>29–32</sup>

## Chronic phase: Simultaneous strengthening of vital qi and elimination of pathogens — systemic regulation

This stage is primarily after local treatment. The pathogenic Qi has been rapidly struck, but the vital qi has also been depleted. Treatment should focus on systemic regulation, using TCM to strengthen vital qi and eliminate pathogens. While restoring the body's vital qi, the remaining pathogens are further removed to alter the balance of power between the body's vital qi and the local pathogenic Qi, ensuring "When vital qi exists within, evil cannot interfere".

In the development of PLC, Spleen and Kidney Yang Deficiency is often the root. Therefore, treatment should focus on warming and tonifying the Spleen and Kidney. If the Spleen and Kidney Yang Qi is vigorous, the Liver is less likely to be damaged. Using "Warming Yang" as the principle ensures that when Yang Qi is vigorous, turbid Yin dissipates naturally. During the perioperative period of PLC, Qi, Blood, and Yang Qi are deficient, so emphasis should be placed on tonifying Qi, Blood, and Yang. The Synopsis of the Golden Chamber states: "If the Spleen is vigorous in all four seasons, it will not be invaded by evil". Strengthening the Spleen can prevent tumor occurrence and disease transmission and treat the tumor by consolidating the foundation. Therefore, attention should also be paid to regulating the Spleen and Stomach to ensure the Qi mechanism of the Middle Burner is unobstructed, Qi and Blood have a source for generation, and vital qi is abundant, enhancing the body's own anti-tumor ability. Analysis of medication used after PLC surgery shows that the main prescriptions mostly utilize modified Liu Jun Zi Tang (Six-Gentlemen Decoction) and Chai Hu Shu Gan San.33

Additionally, there are still residual pathogens in the perioperative period of PLC. Clinically, symptoms such as fever, chills, and abdominal pain are often seen after vascular interventional surgery. This is the "struggle between the Righteous (vital qi) and the Evil". Treatment should take into account the elimination of pathogens. During this process, attention should be paid to the use of Guide Drugs (Yin Jing Yao) to make the TCM treatment focused and potent. Qing Dynasty doctor You Zaijing said: "Without a guide, the army cannot reach the rebel's territory; without a guide, the medicine cannot reach the disease site". Clinically, Honeysuckle (Jin Yin Hua), Gardenia (Zhi Zi), White Peony Root (Bai Shao), Angelica Sinensis (Dang Gui), and Licorice (Gan Cao) can be used together. This adopts the meaning of "rescuing the Liver and defeating fire". Gardenia and Honeysuckle clear Liver fire; White Peony and Angelica soften the Liver and astringe Yin while guiding Gardenia and Honeysuckle to the Liver Meridian; Licorice clears heat, detoxifies, strengthens the Spleen, and harmonizes other drugs. The combination can drain Liver fire without damaging Yin and protect the Spleen and Stomach. Furthermore, slightly toxic drugs and insect-based drugs can be used to eliminate evil. Insect drugs are mostly "flesh and blood sentient products", often enter the Liver Meridian, possess slight toxicity, and are good at moving and searching (zou cuan), and are fierce and specialized in clearing residual evil.

The team previously reflected on regulating the liver cancer immune microenvironment with the method of "Activating Blood, Dissolving Phlegm, and Detoxifying". They believe that besides focusing on the relationship between the body's "Vital Qi" and the tumor cell's "Pathogenic Qi", more attention should be paid to the "Vital Qi" and "Pathogenic Qi" within the immune microenvironment. Representative formulas like Xihuang Pill and Ganjile have been shown to effectively improve the survival of liver cancer patients and improve quality of life.<sup>34</sup>

## Latent phase: Harmonization method — improving the internal environment

Liver cancer is an inflammation-related tumor. Over 80% of Chinese liver cancer patients are associated with chronic Hepatitis B. Stationary Clinically, it often presents as the "Hepatitis – Cirrhosis – Liver Cancer" trilogy. The renowned surgical oncologist Academician Tang Zhaoyou first proposed the concept and related theories of "Subclinical Liver Cancer", termed a "huge progress in human understanding and treatment of liver cancer". In this stage, Western medicine has no other measures besides the use of antiviral drugs. However, even with the widespread promotion of antiviral drugs, the incidence of liver cancer remains high. Therefore, TCM participation in early intervention to advance the treatment window, prevent chronic liver damage, and improve the internal environment is a key link in the prevention and treatment of liver cancer.

In the 1850s, German scholar Rudolf Virchow proposed that a "hostile environment" induces tumors, and the growth of cancer cells requires suitable soil (internal environment).<sup>36</sup> Cancer cells have an instinctual resistance behavior. When attacked by external forces, residual cancer cells will undergo "compensatory accelerated repopulation", thereby promoting tumor recurrence and metastasis. Therefore, special attention should be paid to the regulation of the internal environment during treatment. When the cancer toxin is significant in the early stage, follow "Supplement what is deficient, reduce what is excessive". When the tumor's momentum is gone, use the "Harmonization" (He) method to adjust the constitution to prevent the tumor from "staging a comeback". Formulas like Xiao Chai Hu Tang, Si Ni San, and Yue Ju Wan can be used for harmonization. Wu Fu Yin and Ba Zhen Tang can also be used to treat a deficiency of Qi and Blood in the five viscera. Relevant studies also show that TCM can significantly reduce the risk of recurrence after PLC ablation and prolong recurrence-free survival time.37

Studies suggest that gut microbiota dysbiosis may lead to the occurrence of hepatocellular carcinoma. A series of beneficial attempts have been made through the "Gut–Liver Axis" theory, discovering that regulating intestinal homeostasis is a key breakthrough in treating liver cancer, reflecting the important role of "Treating Pre-disease" (preventive treatment) in the prevention and treatment of liver cancer.<sup>38</sup>

#### **Conclusions**

We have been exploring methods to treat PLC, including the pro-

motion of Hepatitis B vaccines and the use of antiviral drugs, but the reality is unsatisfactory. Some studies predict that by 2040, the number of new liver cancer diagnoses and deaths globally will increase by 55% Changing the status quo of PLC prevention and treatment remains a heavy task with a long way to go. Previous research can still provide us with many ideas, namely that the treatment of PLC cannot rely on a single method or a single line of thought. It requires the cooperation of TCM and Western medicine, focusing on the characteristics of the tumor itself, and even more so on the differences between individuals. The exploration of the integrated TCM and Western medicine model for PLC under the guidance of the Green Tumor Treatment concept requires us to continuously summarize efficacy in clinical practice and provide higher-level evidence-based medical proof through basic research and large-sample multi-center randomized controlled trials.

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#### **Conflict of interest**

The authors have no conflict of interest related to this publication.

#### **Author contributions**

Study concept and design (KWH), drafting of the manuscript (SQZ), critical revision of the manuscript for important intellectual content (YNZ, YZ), and study supervision (BPL). All authors have made significant contributions to this study and have approved the final manuscript.

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