# Impact of Integrated Traditional Chinese and Western Medicine Therapy on Overall Survival in Patients with Advanced Hepatocellular Carcinoma: A Postprint Analysis

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## Abstract

Background Integrated traditional Chinese and Western medicine treatment can effectively alleviate symptoms, inhibit tumor metastasis, and prolong survival in patients with hepatocellular carcinoma (HCC). In recent years, with the development of evidence-based medicine, the definitive efficacy of traditional Chinese medicine in treating liver cancer urgently requires support from real-world clinical data. Objective To investigate the survival characteristics of patients with intermediate and advanced HCC and to explore the survival benefits of integrated traditional Chinese and Western medicine treatment for these patients. Methods Clinical data were collected from 291 patients with intermediate and advanced HCC who were hospitalized at Hubei Provincial Hospital of Traditional Chinese Medicine from December 2014 to May 2022, as well as those who visited the hospital from August 2023 to December 2024 and were enrolled in the "Bidirectional Cohort Study of Primary Liver Cancer". Patients were divided into a Western medicine treatment group (167 cases) and an integrated traditional Chinese and Western medicine treatment group (124 cases) based on treatment regimen. Nearest neighbor matching at a 1:1 ratio with a caliper value of 0.05 was employed for propensity score matching (PSM) to select patients; Kaplan-Meier survival curves were constructed to compare differences in 3-year survival and overall survival between the two groups of HCC patients receiving different treatment modalities; and a Cox proportional hazards regression model was utilized to analyze factors influencing survival in HCC patients. Results A total of 210 HCC patients were successfully matched, with 105 cases in each group, including 168 males (80.0%) and 42 females (20.0%), and a mean age of (57.7$±$0.8) years. After matching, no statistically significant differences were observed between the two groups in gender, age, residence, smoking his-

tory, drinking history, viral hepatitis, liver cirrhosis, diabetes, hypertension, or Barcelona Clinic Liver Cancer (BCLC) stage (P>0.05). By the end of follow-up, 166 of the 210 patients (79.0%) had died and 44 (21.0%) remained alive, with a median survival time of 17.29 (95%CI=13.554~21.032) months. The 1-, 3-, and 5-year cumulative survival rates were 51.4%, 20.9%, and 7.3% for the Western medicine treatment group, and 69.8%, 31.7%, and 10.9% for the integrated traditional Chinese and Western medicine treatment group, respectively. Comparisons of 3-year survival and survival until the end of follow-up between the two groups revealed statistically significant differences ( 2 =6.068, P=0.014; 2 =5.171, P=0.023). Multivariate Cox regression model analysis demonstrated that integrated traditional Chinese and Western medicine treatment for intermediate and advanced HCC patients reduced survival risk compared with the Western medicine treatment group (HR=0.642, 95%CI=0.467~0.882, P=0.006). Conclusion Traditional Chinese medicine combined with local tumor therapy and/or targeted/immunotherapy can prolong survival and improve survival rates in patients with intermediate and advanced HCC.

## Full Text

# Analysis of the Impact of Integrated Traditional Chinese and Western Medicine Treatment on Survival in Patients with Intermediate and Advanced Hepatocellular Carcinoma

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**Abstract**

**Background:** Integrated traditional Chinese and Western medicine treatment can effectively relieve symptoms, inhibit tumor metastasis, and prolong survival

in patients with hepatocellular carcinoma (HCC). In recent years, with the development of evidence-based medicine, the therapeutic efficacy of traditional Chinese medicine for HCC urgently requires support from real-world clinical data.

**Objective:** To investigate the survival characteristics of patients with intermediate and advanced HCC and explore the survival benefits of integrated traditional Chinese and Western medicine treatment.

**Methods:** Clinical data were collected from 291 patients with intermediate and advanced HCC who were either hospitalized at Hubei Provincial Hospital of Traditional Chinese Medicine from December 2014 to May 2022, or enrolled in the "Bidirectional Cohort Study of Primary Liver Cancer" at the same hospital from August 2023 to December 2024. Patients were divided into two groups based on treatment regimens: the Western medicine treatment group (167 cases) and the integrated traditional Chinese and Western medicine treatment group (124 cases). Propensity score matching (PSM) was performed using the nearest neighbor method at a 1:1 ratio with a caliper value of 0.05. Kaplan-Meier survival curves were plotted to compare differences in 3-year survival and overall survival between the two groups. A Cox proportional hazards regression model was used to analyze factors influencing patient survival.

**Results:** A total of 210 HCC patients were successfully matched, with 105 cases in each group. The cohort included 168 males (80.0%) and 42 females (20.0%), with a mean age of $(57.7\$\pm0.8) years. After matching, there were no statistically significant differences between
0.05). By the end of follow-up, 166 patients ($79.0^{\{2\}= 6.068, P = 0.014; \chi\{2\}\$=5.171$,
P=0.023). Multivariate Cox regression analysis showed that integrated traditional Chinese and Western medicine treatment reduced the survival risk for intermediate and advanced HCC patients compared with Western medicine treatment alone (HR=0.642, 95%CI=0.467-0.882, P=0.006).

**Conclusion:** Traditional Chinese medicine combined with local tumor treatment and/or targeted/immunotherapy can prolong survival and improve survival rates in patients with intermediate and advanced HCC.

**Keywords:** Hepatocellular carcinoma; Intermediate and advanced stage; Hubei Province; Integrated traditional Chinese and Western medicine treatment; Cohort study; Propensity score matching; Cox regression

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## Introduction

Primary liver cancer (PLC), commonly referred to as liver cancer, is a malignant tumor arising from hepatocytes or intrahepatic bile duct epithelial cells. It ranks as the sixth most common cancer globally and the third leading cause of cancer-related mortality, with hepatocellular carcinoma (HCC) accounting for approximately 90% of PLC cases and a 5-year survival rate of only 21% [1]. According to the National Cancer Center, China reported 367,700 new

HCC cases and 316,500 deaths in 2022, representing 45.3% and 47.1% of global incidence and mortality, respectively, with a 5-year survival rate of merely 12.1% [4]. HCC typically develops on the basis of liver cirrhosis, with chronic hepatitis B virus (HBV) or hepatitis C virus (HCV) infection and long-term heavy alcohol consumption being important pathogenic factors [5], and 80%-90% of PLC cases have a background of hepatitis B-related cirrhosis [6].

Current clinical management of HCC has entered the era of multidisciplinary team-based care, and the advantages and mechanisms of traditional Chinese medicine in HCC treatment have been extensively validated in numerous clinical and experimental studies [7-8]. However, high-level evidence-based medical evidence for comprehensive treatment protocols remains to be further improved. This study focuses on the survival benefits of traditional Chinese medicine combined with Western medicine treatment for intermediate and advanced HCC patients, aiming to enhance the level of evidence and provide references for clinical practice.

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## Methods

**1.1 Study Subjects** Clinical data were collected from 850 HCC patients hospitalized at Hubei Provincial Hospital of Traditional Chinese Medicine from December 2014 to May 2022, and 263 HCC patients enrolled in the "Bidirectional Cohort Study of Primary Liver Cancer" at the same hospital from August 2023 to December 2024.

**Inclusion criteria:** (1) Age $\geq$ 18 years; (2) Diagnosis consistent with the "Guidelines for Diagnosis and Treatment of Primary Liver Cancer (2022 Edition)" [3]; (3) Barcelona Clinic Liver Cancer (BCLC) stage B or C [3]; (4) Complete clinical data including diagnostic information and treatment protocols; (5) Good compliance.

**Exclusion criteria:** (1) Secondary liver cancer; (2) Other pathological types such as intrahepatic cholangiocarcinoma or combined hepatocellular-cholangiocarcinoma; (3) Severe systemic diseases involving the heart, brain, lungs, or other systems; (4) Pregnant or lactating women; (5) Patients receiving only symptomatic supportive care and/or traditional Chinese medicine treatment; (6) Survival period $\leq$ 7 days after diagnosis; (7) Patients deemed unsuitable by investigators. The study protocol was approved by the Ethics Committee of Hubei Provincial Hospital of Traditional Chinese Medicine (approval number: HBZY2023-C87-02).

**1.2 Data Collection and Grouping** **1.2.1 Baseline data collection:** (1) General information: gender, age, residence, smoking history (previous or current smoking), drinking history (previous or current alcohol consumption), viral hepatitis, liver cirrhosis, diabetes, and hypertension; (2) Tumor indicators: BCLC stage, number of tumors, tumor size, portal vein tumor thrombus, and

extrahepatic metastasis; (3) Child-Pugh liver function classification (ascites, hepatic encephalopathy, serum bilirubin, serum albumin, and prolonged prothrombin time).

**1.2.2 Clinical treatment protocols and grouping:** Treatment modalities included hepatectomy, local therapy (transcatheter arterial chemoembolization, hepatic arterial infusion chemotherapy, ablation, and radiotherapy), immunotherapy and/or anti-angiogenic therapy (hereinafter referred to as "targeted/immunotherapy" ), and traditional Chinese medicine treatment. Patients who received hepatectomy and/or local therapy at least once and targeted/immunotherapy for at least one cycle from diagnosis to the end of follow-up were defined as the Western medicine treatment group. Patients in the Western medicine group who additionally took traditional Chinese medicine decoctions for tumor recurrence/metastasis prevention and toxicity reduction for a cumulative period of $ $3 months were defined as the integrated traditional Chinese and Western medicine treatment group.

**1.3 Outcomes and Follow-up** **(1) Outcome measures:** Survival status (alive/dead). Overall survival (OS) was calculated as the time interval from diagnosis to death or the end of follow-up.

**(2) Follow-up indicators:** For the retrospective cohort, electronic medical records of surviving HCC patients were reviewed four times from January 2023 to December 2024. For the bidirectional cohort, follow-up was conducted monthly. The follow-up deadline was December 31, 2024.

**1.4 Quality Control** EpiData 3.1 software was used to establish data entry and verification files. Data entry was performed by hepatology graduate students after unified training. HCC staging was assessed by two attending physicians or higher-level doctors, with discrepancies adjudicated by associate chief physicians or higher-level specialists. All HCC stages in this study refer to BCLC stage at diagnosis. Dedicated data administrators performed data cleaning and verification.

**1.5 Statistical Methods** SPSS 25.0 statistical software was used for analysis. Normally distributed continuous variables were expressed as ($\bar{x}\pm s$). Categorical data were described using relative numbers, with inter-group comparisons performed using $^2$ tests. Based on clinical experience, ten relevant factors were selected: gender, age, residence, smoking history, drinking history, viral hepatitis, liver cirrhosis, diabetes, hypertension, and BCLC stage. A PSM logistic regression model was established using treatment modality as the dependent variable (0=Western medicine group, 1=integrated treatment group) and the ten factors as independent variables to estimate propensity scores. Nearest neighbor matching (1:1 ratio, caliper value=0.05) was used for propensity score matching, dividing patients into Western medicine and integrated treatment groups. Kaplan-Meier survival curves were plotted, and Log-rank tests were used to com-

pare differences in 3-year survival and survival by the end of follow-up between the two groups. Cox proportional hazards regression model was used to analyze factors influencing HCC patient survival, with P<0.05 considered statistically significant.

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## Results

**2.1 General Characteristics** The retrospective liver cancer cohort included 850 patients, and the bidirectional cohort included 263 patients. After excluding 386 patients with BCLC stages A or D, 53 overlapping cases, 299 patients without documented death dates or lost to follow-up, and 84 patients receiving only symptomatic supportive care and/or traditional Chinese medicine treatment, 291 patients were ultimately included (see patient selection flow chart in [Figure 1: see original paper]). The cohort comprised 235 males (80.8%) and 56 females (19.0%), with a mean age of (57.6$±$0.6) years. Patients aged 50-69 years accounted for 66.0% (192/291). There were 167 patients in the Western medicine group and 124 in the integrated treatment group. By the end of follow-up, 209 patients had died and 82 were alive.

**2.2 Baseline Characteristics Before and After PSM** Before PSM, statistically significant differences were observed between the two groups in smoking history, drinking history, underlying liver cirrhosis, and BCLC stage (P<0.05), while no significant differences were found in gender, age, residence, hypertension, diabetes, or viral hepatitis (P>0.05).

A PSM logistic regression model was established with treatment modality as the dependent variable (0=Western medicine group, 1=integrated treatment group) and ten related factors as independent variables: gender (male=0, female=1), age (40-49 years=0, <40 years=1, 50-59 years=2, 60-69 years=3, $ $70 years=4), residence (urban=0, town=1, rural=2), smoking history (no=0, yes=1), drinking history (no=0, yes=1), viral hepatitis (no=0, yes=1), liver cirrhosis (no=0, yes=1), diabetes (no=0, yes=1), hypertension (no=0, yes=1), and BCLC stage (B=0, C=1). Propensity scores were estimated for each patient, and nearest neighbor matching (1:1 ratio, caliper value=0.05) was applied, successfully matching 105 pairs (210 patients total, 105 in each group), as shown in [Figure 2: see original paper].

Among the 210 matched patients, 168 were male (80.0%) and 42 were female (20.0%), with a mean age of (57.7$±$0.8) years. Patients with underlying liver cirrhosis accounted for 76.7% (161/210). BCLC stage distribution was 93 cases (44.3%) in stage B and 117 cases (55.7%) in stage C. Hepatectomy was performed in 25.2% (53/210) of patients, local therapy in 76.7% (161/210), targeted and/or immunotherapy in 51.9% (109/210), and traditional Chinese medicine decoction for $ $3 months in 50% (105/210). After matching, no statistically significant differences were observed between the two groups in gender, age, residence,

smoking history, drinking history, viral hepatitis, liver cirrhosis at first diagnosis, diabetes, hypertension, or BCLC stage (all P>0.05), as shown in .

**2.3 Follow-up and Survival Analysis** By the follow-up deadline, 166 of 210 patients (79.0%) had died and 44 (21.0%) were alive. Overall survival ranged from 1.05 to 124.34 months, with a median survival time of 17.29 months (95%CI=13.554-21.032). The overall 1-, 3-, and 5-year cumulative survival rates were 60.6%, 26.3%, and 9.1%, respectively. The Western medicine group had 1-, 3-, and 5-year cumulative survival rates of 51.4%, 20.9%, and 7.3%, respectively, while the integrated treatment group had rates of 69.8%, 31.7%, and 10.9%. Survival analysis revealed a median survival of 13.05 months (95%CI=8.677-17.427) in the Western medicine group versus 21.96 months (95%CI=13.719-30.204) in the integrated treatment group, with a statistically significant difference ( $^2$=6.068, P=0.014). The difference remained statistically significant by the end of follow-up ( $^2$=5.171, P=0.023), as shown in [Figure 3: see original paper].

**2.4 Multivariate Cox Proportional-Hazards Regression Analysis of Factors Influencing HCC Survival** Using survival time (months) and survival status (0=alive, 1=dead) as dependent variables, and gender (male=0, female=1), age (40-49 years=0, <40 years=1, 50-59 years=2, 60-69 years=3, $ $70 years=4), underlying liver cirrhosis (no=0, yes=1), BCLC stage (B=0, C=1), and treatment modality (Western medicine group=0, integrated treatment group=1) as independent variables, multivariate Cox proportional-hazards regression analysis was performed. After adjusting for confounding factors including gender, age, underlying liver cirrhosis, and BCLC stage, the results showed that compared with patients aged 40-49 years, those aged 50-59 years (HR=2.168, 95%CI=1.274-3.690, P=0.004), 60-69 years (HR=2.273, 95%CI=1.356-3.808, P=0.002), and $ $70 years (HR=2.087, 95%CI=1.075-4.050, P=0.030) had increased survival risk. Patients with underlying liver cirrhosis (HR=1.710, 95%CI=1.168-2.504, P=0.006) and BCLC stage C (HR=2.989, 95%CI=2.129-4.197, P<0.001) also had increased survival risk. In contrast, the integrated treatment group had reduced survival risk compared with the Western medicine group (HR=0.642, 95%CI=0.467-0.882, P=0.006), as shown in .

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## Discussion

HCC is a highly prevalent malignant tumor worldwide. The intermediate and advanced stages present major clinical challenges due to extensive tumor infiltration, declining liver functional reserve, and frequent distant metastasis [9]. While current mainstream Western medicine treatments (such as targeted therapy, transarterial chemoembolization, and immunotherapy) can control tumor progression in the short term, they are associated with high adverse reaction

rates, further liver function impairment, and limited long-term survival benefits [10]. Although traditional Chinese medicine has accumulated rich clinical experience in HCC treatment, large-sample, long-term follow-up real-world cohort studies on survival benefits of integrated treatment for intermediate and advanced HCC patients are lacking, greatly limiting its clinical promotion. Based on our previous retrospective cohort study, this study incorporated bidirectional cohort data to further analyze the survival benefits of traditional Chinese medicine combined with Western medicine for intermediate and advanced HCC patients, aiming to provide higher-level evidence-based medical evidence for clinical practice.

The male-to-female ratio in this study was approximately 4.2:1, with the highest proportion (66%) in the 50-69 age group, consistent with HCC epidemiological data. Previous studies have shown that HCC incidence peaks in the 60-70 age group, with males being the primary affected population [11]. Research suggests that male HCC patients may experience faster disease progression than females [12], or may differ in early symptom recognition and healthcare-seeking behavior, leading to a higher male proportion in intermediate and advanced stages. This gender disparity may be related to higher risk exposure in males, such as smoking [13] and alcohol consumption [14], which increase HCC risk. Additionally, studies have indicated that estrogen may suppress HCC development by upregulating lecithin-cholesterol acyltransferase (LCAT) to maintain cholesterol homeostasis [15], potentially explaining the lower HCC risk in females.

In this study, 72.5% of HCC patients had underlying liver cirrhosis, consistent with previous research [6]. For example, a 10-year follow-up cohort study of 2,079 patients with cirrhosis of various etiologies found that 226 (9.4%) developed HCC during follow-up [16]. These findings underscore the critical importance of timely cirrhosis diagnosis and regular HCC surveillance in high-risk populations for improving prognosis. Combined with the baseline characteristics of this cohort—80.8% male and 77% aged over 50—the results highlight the need for targeted screening of male cirrhosis patients over 50 to improve early detection and survival outcomes.

Approximately 70%-85% of HCC patients have lost indications for curative surgery (such as hepatectomy or liver transplantation) at initial diagnosis and require comprehensive treatment to prolong survival [4]. As a treasure of Chinese civilization, traditional Chinese medicine constitutes an important component of comprehensive HCC treatment [3]. In this study, by the end of follow-up, the integrated treatment group showed higher 1-, 3-, and 5-year cumulative survival rates (69.8%, 31.7%, 10.9%) than the Western medicine group (51.4%, 20.9%, 7.3%), with superior 3-year survival benefit (21.96 months vs. 13.05 months). After adjusting for gender, age, underlying cirrhosis, and BCLC stage, integrated treatment reduced survival risk by 35.8% (HR=0.642, 95%CI=0.467-0.882, P=0.006). These benefits may be attributed to traditional Chinese medicine' s ability to regulate immune cell function in the tumor microenvironment by inhibiting pro-tumor immune cells (such as regulatory T cells

and myeloid-derived suppressor cells) [17-18] while enhancing the cytotoxic capacity of anti-tumor immune cells (such as natural killer cells and cytotoxic T lymphocytes) [19-20]; induce apoptosis by activating the tumor-suppressive TGF-$\beta$/Smad signaling pathway (p-Smad3C) or inhibiting its tumor-promoting signals (p-Smad3L) [21]; and inhibit HCC invasion and metastasis by blocking epithelial-mesenchymal transition (EMT), suppressing matrix degradation, and inhibiting angiogenesis [22]. Studies have shown that traditional Chinese medicine can enhance anti-tumor efficacy, reduce side effects, and decrease drug resistance when combined with immune checkpoint inhibitors (such as PD-1/PD-L1 antibodies) or conventional therapies (chemotherapy, radiotherapy) by regulating the Hippo-YAP pathway and immune microenvironment [23-24].

The survival benefits of integrated treatment for intermediate and advanced HCC have been confirmed by multiple studies, with its core mechanism being synergistic enhancement under the guidance of "Fuzheng Quxie" (strengthening vital Qi and eliminating pathogenic factors) theory [25]. In targeted therapy, Zhang et al. [26] demonstrated that the Yiqi Huayu Jiedu formula combined with sorafenib yielded higher 2-year survival rates than targeted therapy alone in intermediate and advanced HCC. In local ablation therapy, Wang et al. [27] found that patients with high traditional Chinese medicine exposure had lower 2-year recurrence and metastasis rates after microwave ablation than those without traditional Chinese medicine intervention. In conventional medical treatment, Lü et al. [28] showed that Rougan Huaxian Jiedu granules combined with conventional therapy improved 12-month survival rates in intermediate and advanced HCC patients. These findings indicate that traditional Chinese medicine provides important survival protection for intermediate and advanced HCC patients by reducing recurrence and metastasis risk, prolonging survival, and enhancing tolerance to Western medicine treatments.

The modulating effect of patient age on prognosis cannot be ignored. This study found that compared with patients aged 40-49 years, those aged 50-59 years (HR=2.168, 95%CI=1.274-3.690, P=0.004), 60-69 years (HR=2.273, 95%CI=1.356-3.808, P=0.002), and $ $70 years (HR=2.087, 95%CI=1.075-4.050, P=0.030) had increased survival risk. Wang et al. [29] identified a non-linear relationship between age at diagnosis and overall survival in HCC patients through restricted cubic spline analysis, with 60 years identified as a critical inflection point. Age $ $60 years is an unfavorable prognostic factor, consistent with our findings. This may be due to age-related decline in DNA mismatch repair capacity, increased gene mutation rates and tumor mutational burden, heavier comorbidity burden, physical decline, and reduced hepatic drug clearance [29], all of which increase treatment difficulty.

This study also found that underlying liver cirrhosis increased survival risk by 71% in intermediate and advanced HCC patients (HR=1.710, 95%CI=1.168-2.504, P=0.006). A population-based cancer registry study of 9,753 patients found that HCC-specific survival was lower in patients with cirrhosis than in those without (HR=1.259, 95%CI=1.166-1.358, P<0.001) [30], though the risk

magnitude differed from our study, possibly due to different study populations. The adverse prognostic effect of cirrhosis may be related to the formation of a tumor immune barrier (TIB) that inhibits T/NK cell function and induces M2 macrophage polarization, weakening tumor microenvironment regulation [31]. Additionally, cirrhosis-induced metabolic reprogramming (such as enhanced glycolysis) supports tumor growth and drug resistance, promoting HCC progression and treatment resistance.

Disease stage was also identified as a prognostic factor. Compared with BCLC stage B, stage C patients had a 1.989-fold increased survival risk (HR=2.989, 95%CI=2.129-4.197, P<0.001), consistent with the clinical utility of the BCLC staging system. A 2023 Vietnamese retrospective analysis reported median survival of 13.5 months in BCLC stage B patients versus only 4 months in stage C patients [32], confirming that more advanced stage correlates with lower survival rates. Our previous retrospective cohort study of 850 patients also found that 5-year survival rates in BCLC stages B and C were far lower than in stage A [33], highlighting the critical importance of early diagnosis and treatment.

This study has several limitations. As a single-center real-world study, it has relatively short follow-up duration and lacks pathological indicators. Additionally, due to the long time span of the retrospective cohort, data on specific targeted/immunotherapy drugs, treatment cycles, number of local therapy sessions, and duration of traditional Chinese medicine decoction were incomplete for deceased patients, precluding stratified analysis of different treatment combinations and preventing provision of optimized treatment protocol evidence. Furthermore, this study did not standardize herbal formulas, aiming instead to reflect the actual clinical state of syndrome differentiation and treatment, in order to explore the survival benefits of traditional Chinese medicine participation in intermediate and advanced HCC treatment and provide references for clinical decision-making.

The study population comprised intermediate and advanced HCC patients (BCLC stage B or C) diagnosed pathologically or clinically, consistent with the "Guidelines for Diagnosis and Treatment of Primary Liver Cancer (2022 Edition)" [3]. Traditional Chinese medicine interventions were administered on the basis of standard Western medicine treatments (such as targeted therapy and interventional therapy), representing an "integrated comprehensive treatment" scenario where traditional Chinese medicine served as a synergistic adjunct rather than monotherapy. Additionally, the study controlled for baseline differences through PSM, making the results more applicable to clinical scenarios with baseline characteristics similar to this cohort (such as underlying cirrhosis, diabetes, hypertension, and BCLC stage). Clinical application should consider individual patient factors (such as traditional Chinese medicine syndrome patterns and tolerance to Western medicine treatments) for comprehensive decision-making.

In summary, this study, through a "retrospective + bidirectional" cohort design and rigorous confounding control methods, provides references for treatment

decisions in intermediate and advanced HCC patients, clarifies the advantages of integrated treatment in clinical management, and helps clinicians more rationally incorporate traditional Chinese medicine into comprehensive treatment protocols, avoiding misuse or underuse due to insufficient evidence and benefiting more patients. Our findings provide clear direction for future research: subsequent studies should focus on mechanistic investigations (validating traditional Chinese medicine' s regulatory effects on the tumor microenvironment through cellular and animal models), personalized treatment research (developing precise herbal formulas based on traditional Chinese medicine syndrome patterns), optimization of combination protocols (identifying optimal timing for combining traditional Chinese medicine with targeted/immunotherapy), and quality-of-life assessment (using tools such as the EORTC QLQ-HCC scale). Through multidimensional, multicenter research, the integrated treatment system can be continuously improved to promote its high-quality development in the field of liver cancer.

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## Author Contributions

ZHAO Linru was responsible for study conception and design and manuscript writing. TAO Junxiu proposed the main research objectives and revised the manuscript. LUO Baoping was responsible for study implementation. SHI Yufeng and LI Min collected and organized data, performed statistical analysis, and prepared figures and tables. REN Meng was responsible for quality control and review, overall article supervision, and project management.

**Conflict of Interest:** The authors declare no conflict of interest.

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