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Influence of Traditional Chinese Medicine Treatment Duration on Survival in Patients with Primary Liver Cancer: Evidence from Real-World Data

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ABSTRACT

In China, traditional Chinese medicine (TCM) is commonly employed as a therapeutic approach for primary liver cancer (PLC). This study explored how TCM influences patient survival by assessing the correlation between the proportion of treatment time devoted to TCM—termed the treatment-duration ratio (C-TDR, calculated as the duration of TCM therapy divided by the total treatment period, multiplied by 100%)—and the survival outcomes of 1,002 individuals diagnosed with PLC. A total of 1,002 primary liver cancer (PLC) patients treated at the TCM Oncology Department of Changhai Hospital between January 2015 and December 2019 were included in this study. To determine independent prognostic factors for survival at various disease stages and to assess the impact of the TCM treatment-duration ratio (C-TDR) on survival, analyses were performed using univariate and multivariate Cox regression models, as well as propensity score matching (PSM). Cox regression analysis revealed that C-TDR was an independent prognostic factor for overall survival ($P < 0.05$), associated with a 75.67% reduction in the relative risk of death (RR = 0.2433; 95% CI = 0.1747–0.3388). This prognostic significance was also observed across all disease stages ($P < 0.05$). Among the 251 patients in the BCLC-A stage, C-TDR was associated with a 96.09% lower risk of mortality (RR = 0.0391; 95% CI = 0.0151–0.1012), while the 396 patients in BCLC-B experienced an 81.24% reduction in death risk (RR = 0.1876; 95% CI = 0.1112–0.3163). In stage C, comprising 355 patients, the risk of death decreased by 51.36% (RR = 1.0016; 95% CI = 0.9885–1.0149). Significant differences were observed in median overall survival between patients with higher versus lower C-TDR. Furthermore, after propensity score matching, survival outcomes remained significantly improved in the higher C-TDR group across all disease stages. Timely use of traditional Chinese medicine appears to decrease the risk of death and improve survival outcomes in liver cancer."

Keywords: COVID-19, Treatment-duration-ratio, Traditional chinese medicine, Risk of mortality, Primary liver cancer, Survival period

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Introduction

Primary liver cancer (PLC) ranks as the fourth most common malignancy and the second leading cause of cancer-related death worldwide [1]. The global incidence of hepatocellular carcinoma (HCC), the predominant type of PLC, is unevenly distributed, with over 80% of cases occurring in low- to middle-income countries, particularly in East Asia and sub-Saharan Africa [2]. In the United States, the age-adjusted incidence tripled between 1992 and 2010, largely due to high rates of chronic hepatitis C virus infection among individuals born between 1945 and 1965, as well as the growing prevalence of metabolic syndrome, before stabilizing in recent years [3, 4]. Although China represents only 18.4% of the global population, in 2022 it accounted for 466,000 new liver cancer cases and 422,000 deaths, corresponding to 55.4% and 53.9% of global totals, respectively [5, 6]. Overall, PLC has a poor prognosis, with an incidence-to-mortality ratio of approximately 1:0.9, and 5-year survival rates of 15%–19% in North America and 12.1% in China [7–10].

PLC can be classified into three main types: hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (ICC), and a mixed HCC-ICC type, with HCC accounting for roughly 80% of cases [11]. Treatment options depend on disease stage. Early-stage PLC is typically managed with surgical resection, liver transplantation, or radiofrequency ablation [12], while transarterial chemoembolization (TACE) is the standard for intermediate-stage disease [13]. Recently, tyrosine kinase inhibitors (TKIs) and immune checkpoint inhibitors (ICIs) have expanded therapeutic options for advanced liver cancer [14].

Since liver cirrhosis underlies most PLC cases, prognosis is influenced not only by tumor burden but also by liver function and the patient's performance status (PS). While TNM staging is widely used to classify tumor stage based on pathological examination, it does not account for liver dysfunction or PS, both critical in clinical decision-making for HCC [1]. To address this, alternative staging systems such as the Barcelona Clinic Liver Cancer (BCLC) system, Italian Liver Cancer Program, Japanese Comprehensive Staging, and Chinese University Prognostic Index have been proposed [15]. Among these, BCLC staging is widely recognized for its prognostic value as it integrates tumor burden, liver function, and PS, stratifying patients into stages 0, A, B, C, and D [16–20].

PLC staging is typically based on imaging, assessing tumor number, size, location, and vascular invasion, including extrahepatic spread. Very early (BCLC-0) and early-stage (BCLC-A) HCC patients who undergo resection, ablation, or transplantation achieve 5-year overall survival (OS) rates of 50%–75% [21]. For intermediate-stage HCC (BCLC-B), TACE is standard, potentially providing an OS of up to 4 years in optimal candidates. Advanced-stage patients (BCLC-C) may present with cancer-related symptoms and vascular invasion or metastasis, but liver function is usually relatively preserved (Child–Pugh A or B).

Traditional Chinese medicine (TCM) has been widely applied as an adjunct therapy for liver cancer in China [22]. Long-term TCM use has been associated with prolonged survival and improved quality of life [23], yet there is no consensus on the optimal treatment duration [24-28]. Jiedu Granule, a widely used TCM compound containing multiple anti-cancer herbs, is prescribed to "clear heat and remove toxins" according to TCM theory. Previous studies from our team have confirmed the safety and efficacy of Jiedu Granules against PLC [29–33]. However, treatment duration may influence overall survival (OS), leading us to introduce the concept of the treatment-duration ratio of TCM (C-TDR**)**, defined as:

$$\text{C-TDR}=\frac{\text{TCM treatment duration}}{\text{overall treatment duration}}\times 100\% \quad (1)$$

The primary aim of this study was to evaluate the impact of TCM on PLC survival by analyzing the relationship between C-TDR and patient OS.

Materials and Methods

Study design and participants

This study enrolled patients with advanced primary liver cancer (PLC) who received treatment at Changhai Hospital in Shanghai, China, between January 2015 and December 2019. Eligible participants were adults (≥18 years) with PLC confirmed histologically, cytologically, or clinically according to the 2019 Chinese Guidelines for Diagnosis and Treatment of Primary Liver Cancer [24], classified as BCLC stage A to C, with ECOG performance status ≤2 [25], Child–Pugh class A or B, and an expected survival of at least 3 months. Patients were excluded if they had known allergies to TCM or herbal preparations, uncontrolled systemic diseases (e.g., heart, brain, kidney, lung), other incurable malignancies within the past 5 years, history of psychiatric disorders or substance abuse, incomplete clinical data, or were otherwise deemed unsuitable by the investigator.

Written informed consent was obtained from all participants prior to enrollment. The study was approved by the Institutional Review Board of the Chinese Clinical Trial Registry (CHiECRCT-20150073) and conducted in accordance with the principles of the Declaration of Helsinki.

Procedures

This retrospective, real-world study included patients from the liver cancer database who received Traditional Chinese Medicine (TCM) therapy based on Jiedu Granules for a minimum of 3 months, administered twice daily, 30 minutes after meals. All patients concurrently received the best supportive care available, which could include

liver protection, gastrointestinal support, antiviral therapy, and other treatments. Follow-up interventions were individualized based on patient preference and clinical need, including transarterial chemoembolization (TACE), minimally invasive procedures, radiotherapy, targeted therapy, and immunotherapy.

Jiedu Granule (Tianjiang Pharmaceutical Factory, Jiangsu, China; Production License No. Su ZzY20010266) was administered at a dose of 8 g per session (equivalent to 80 g of raw herbal material) twice daily, 30 minutes after meals. The formulation consists of Actinidia valvata root, Salvia chinensis root, Cremastra appendiculata bulb, and Gallus gallus domesticus gizzard membrane in a ratio of 1:1:0.4:0.4. These components are extracted with hot water and lyophilized to produce the final compound. Treatment was continued until patient death or discontinuation due to intolerance [33].

Follow-up began immediately after the end of treatment and continued until the study endpoint on June 30, 2021. Follow-ups were conducted via telephone or during outpatient/inpatient visits for patients who were alive or had withdrawn consent. Survival was assessed every 2 months, and all anticancer therapies administered during the follow-up period were recorded. The primary endpoint was overall survival (OS), defined as the interval from treatment initiation to death.

Patients were categorized into three groups according to BCLC stage: 251 in stage A, 396 in stage B, and 355 in stage C. Within each stage, patients were further divided into high and low TDR groups based on the median C-TDR value **(Figure 1)**. Patients with C-TDR above the median were classified as high TDR, while those below the median were classified as low TDR.

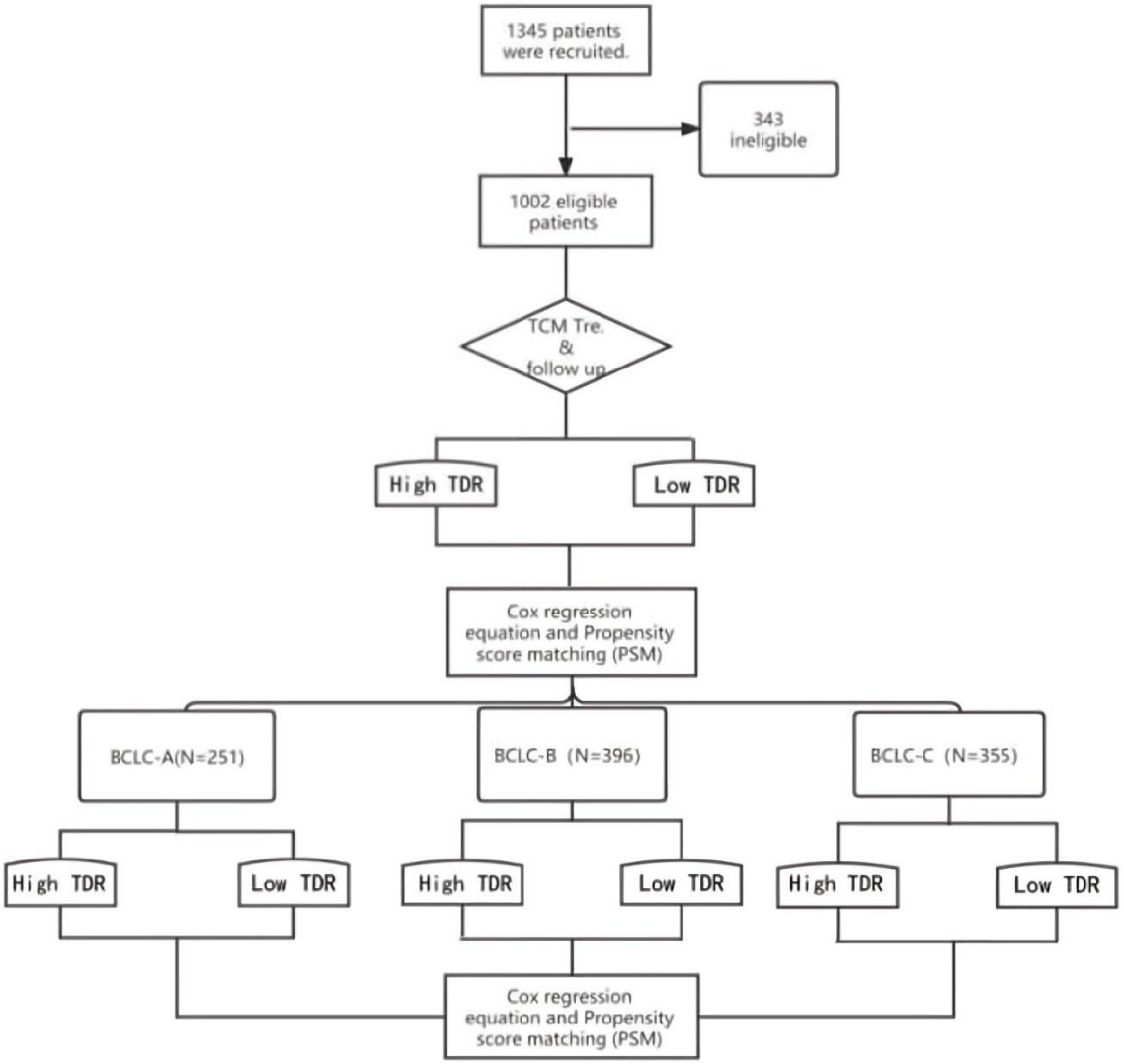


Figure 1. Trial profile. Of the 1,002 patients included in the study, 251 were classified as BCLC stage A, 396 as stage B, and 355 as stage C, forming the basis for subsequent analyses.

Statistical analysis

Survival differences between treatment groups were assessed using Kaplan–Meier analysis and the log-rank test. Subgroup analyses were also conducted. Univariate and multivariate Cox regression models were applied to estimate hazard ratios (HR) or relative risks (RR) along with their 95% confidence intervals (CI) for potential prognostic factors. Two-sided P values <0.05 were considered statistically significant.

Results and Discussion

Demographical and clinical characteristics

Baseline characteristics of the patients are presented in **Table 1**.

Table 1. Baseline of demographic data and patient characteristics.

Variable	BCLC-A (N = 251)	BCLC-B (N = 396)	BCLC-C (N = 355)
Gender			
Male	203 (80.8%)	327 (82.5%)	312 (87.8%) ∗
Female	48 (19.2%)	69 (17.5%)	43 (12.2%) ∗
Age			
≥55 years	121 (48.6%)	187 (47.2%)	259 (72.6%) ∗
<55 years	129 (51.4%)	209 (52.8%)	96 (27.4%) ∗
Hepatitis Status			
Absent	30 (11.9%)	35 (8.8%)	22 (6.1%) ∗
HAV	3 (1%)	1 (0.2%)	2 (0.5%) ∗
HBV	213 (84.8%)	354 (87.1%)	317 (89.2%) ∗
HCV	2 (0.6%)	4 (1%)	12 (3.3%) #
Others	3 (1%)	2 (0.4%)	2 (0.5%) ∗
Child-Pugh Classification			
A	245 (97.6%)	335 (84.5%)	270 (76.0%) ∗
B	6 (2.4%)	61 (15.5%)	85 (24.0%) #
Tumor Type			
Single	218 (86.9%)	167 (42.1%)	100 (28.1%) ∗
Multiple	33 (13.1%)	135 (34.0%)	111 (31.2%) ∗
Massive	0	79 (19.9%)	114 (32.1%) #
Diffuse	0	11 (2.7%)	30 (8.4%) #
Tumor Location			
Right lobe	142 (56.6%)	247 (62.3%)	227 (63.94%) ∗
Left lobe	74 (29.5%)	101 (25.5%)	85 (23.94%) ∗
Both lobes	35 (13.9%)	38 (13.2%)	43 (12.11%) ∗
Tumor Size			
≤3 cm	179 (71.3%)	59 (14.96%)	66 (18.59%) #
3–5 cm	57 (21.7%)	98 (24.7%)	63 (17.75%) #
5–10 cm	15 (0.06%)	163 (41.2%)	126 (35.49%) #
≥10 cm	0	76 (19.2%)	100 (28.17%) #
Tumor Thrombus			
Absent	0	0	171 (48.17%) #
Present	0	0	184 (51.83%) #
Lymph Node Metastasis			
Absent	0	0	245 (69.01%) #
Present	0	0	110 (30.99%) #
Distant Metastasis			
Absent	0	0	263 (74.08%) #
Present	0	0	92 (25.92%) #

Surgical History			
Absent	118 (47.01%)	225 (56.82%)	245 (69.01%) *
Present	133 (52.99%)	171 (43.18%)	110 (30.99%) *

BCLC:Barcelona Clinic Liver Cancer.
P < 0.05 indicates statistical significance.
P > 0.05 indicates no statistical significance.

Survival analysis

Figure 2 presents the overall survival (OS) of 1,002 patients stratified by BCLC stage. Across all patients, the median OS was 33.63 months. When broken down by stage, median survival was 112.27 months for stage A, 37.5 months for stage B, and 14.7 months for stage C. The corresponding 1-, 2-, and 5-year survival rates were 95.29%, 77.23%, and 63.05% for stage A; 84.90%, 50.03%, and 32.24% for stage B; and 57.15%, 18.53%, and 13.72% for stage C, respectively.

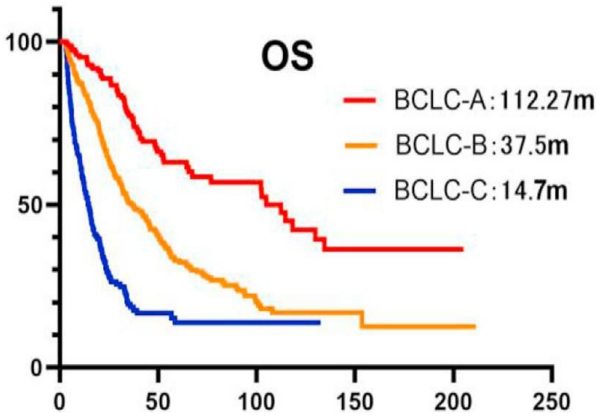


Figure 2. Kaplan–Meier analysis of overall survival (OS) for all 1,002 patients and stratified by BCLC stage. OS: overall survival; mOS: median overall survival; m: months; BCLC: Barcelona Clinic Liver Cancer.

Factors associated with OS

Multivariate Cox proportional hazards analysis revealed several independent predictors of overall survival (OS) among the 1,002 patients with primary liver cancer (PLC) (P < 0.05; **Table 2**). A higher C-TDR was associated with a markedly lower risk of death, reducing mortality by 75.67% (RR [95% CI] = 0.2433 [0.1747–0.3388]). Conversely, several factors were linked to increased mortality: advanced BCLC stage, larger or multiple tumors, aggressive tumor type, and the presence of ascites. Specifically, compared with BCLC-A, patients with BCLC-B had a 104.70% higher risk of death (RR [95% CI] = 2.047 [1.5296–2.7393]), while those with BCLC-C had a 366.93% higher risk (RR [95% CI] = 4.6693 [3.4306–6.3554]). Tumor size also significantly influenced survival: tumors ≥5 cm increased the risk by 36.01% (RR [95% CI] = 1.3601 [1.0947–1.6899]), multiple tumors by 53.46% (RR [95% CI] = 1.5346 [1.146–2.0549]), and massive tumors by 85.75% (RR [95% CI] = 1.8575 [1.1776–2.9299]). Additionally, the presence of ascites was associated with a 71.01% higher risk of death (RR [95% CI] = 1.7101 [1.243–2.3528]) **(Figure 3).**

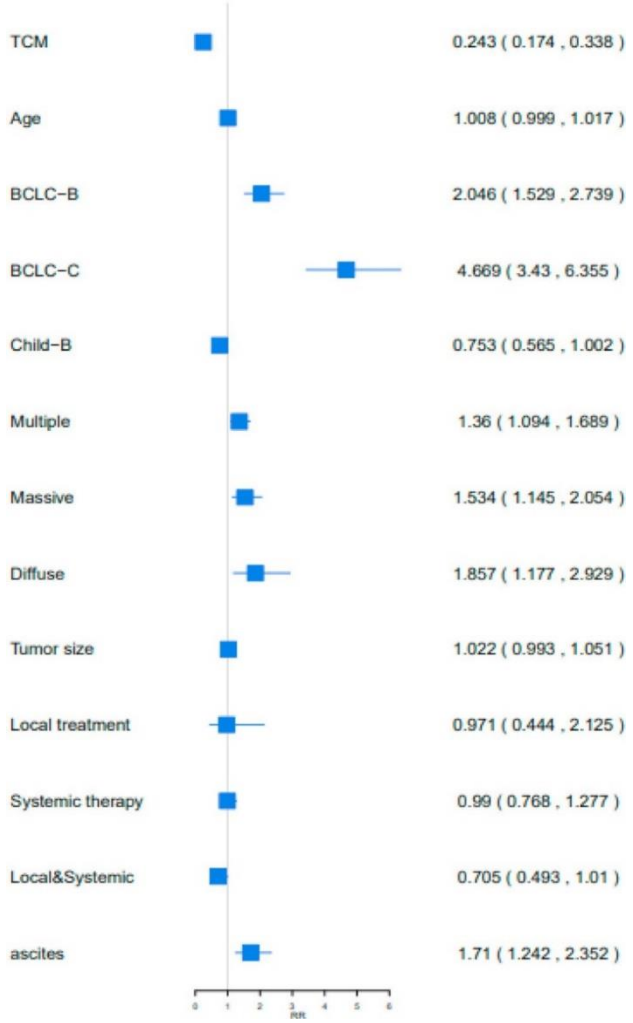


Figure 3. Evaluation of factors influencing overall survival (OS) among 1,002 patients. Abbreviations: TCM, Traditional Chinese Medicine treatment-duration ratio; Local & Systemic, local and systemic anticancer therapies.

Table 2. Results of multivariate Cox regression identifying independent predictors of overall survival in 1,002 patients with primary liver cancer.

Variable	OS RR (95% CI)	P-value	Interpretation of Risk
TDR of TCM	0.2433 (0.1747–0.3388)	0.000 (<0.05) ∗	75.67% reduction in risk ↓
Age	1.0084 (0.9995–1.0175)	0.0656 (>0.05) #	Not significant
BCLC Stage			
BCLC-B vs BCLC-A	2.047 (1.5296–2.7393)	0.000 (<0.05) ∗	104.70% increased risk ↑
BCLC-C vs BCLC-A	4.6693 (3.4306–6.3554)	0.000 (<0.05) ∗	366.93% increased risk ↑
Child-Pugh Classification			
Child-B vs Child-A	0.7533 (0.5658–1.0029)	0.052 (>0.05) #	Not significant
Tumor Characteristics			
Tumor size	1.3601 (1.0947–1.6899)	0.0055 (<0.05) ∗	36.01% increased risk ↑
Multiple tumors	1.5346 (1.146–2.0549)	0.004 (<0.05) ∗	53.46% increased risk ↑
Massive tumors	1.8575 (1.1776–2.9299)	0.0077 (<0.05) ∗	85.75% increased risk ↑
Diffuse tumors	1.0221 (0.9935–1.0514)	0.1315 (>0.05) #	Not significant
Treatment Modalities			
Local treatment	0.9719 (0.4444–2.1259)	0.9432 (>0.05) #	Not significant
Systemic therapy	0.9905 (0.7683–1.2771)	0.9416 (>0.05) #	Not significant

Local + Systemic	0.7057 (0.493–1.0102)	0.0568 (>0.05) #	Not significant
Presence of Ascites	1.7101 (1.243–2.3528)	0.001 (<0.05) ∗	71.01% increased risk ↑

P < 0.05 indicates statistical significance.
P > 0.05 indicates no statistical significance.

Likewise, C-TDR emerged as an independent prognostic factor among the 251 patients in BCLC stage A (P < 0.05); **(Table 3).** In this group, a higher C-TDR was associated with a 96.09% reduction in mortality risk (RR [95% CI] = 0.0391 [0.0151–0.1012]) **(Figure 4).**

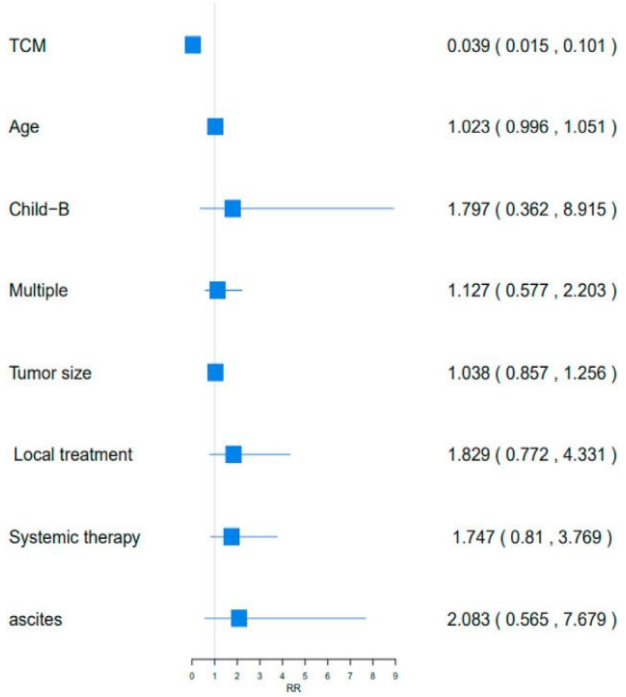


Figure 4. Assessment of prognostic factors for overall survival (OS) in 251 patients with BCLC stage A. Abbreviation: TCM, treatment-duration ratio of Traditional Chinese Medicine.

Table 3. Cox regression analysis identifying predictors of overall survival in 251 patients with BCLC stage A.

Variable	OS Relative Risk (95% CI)	P-value	Risk Interpretation
Traditional Chinese Medicine (TDR of TCM)	0.2433 (0.1747–0.3388)	0.000 (<0.05) ∗	75.67% decreased risk ↓
Age	1.0084 (0.9995–1.0175)	0.0656 (>0.05) #	Not statistically significant
BCLC Stage			
BCLC-B vs BCLC-A	2.047 (1.5296–2.7393)	0.000 (<0.05) ∗	104.70% increased risk ↑
BCLC-C vs BCLC-A	4.6693 (3.4306–6.3554)	0.000 (<0.05) ∗	366.93% increased risk ↑
Child-Pugh Classification			
Child-B vs Child-A	0.7533 (0.5658–1.0029)	0.052 (>0.05) #	Not statistically significant
Tumor Characteristics			
Tumor size	1.3601 (1.0947–1.6899)	0.0055 (<0.05) ∗	36.01% increased risk ↑
Multiple tumors	1.5346 (1.146–2.0549)	0.004 (<0.05) ∗	53.46% increased risk ↑
Massive tumors	1.8575 (1.1776–2.9299)	0.0077 (<0.05) ∗	85.75% increased risk ↑
Diffuse tumors	1.0221 (0.9935–1.0514)	0.1315 (>0.05) #	Not statistically significant
Treatment Modalities			
Local treatment	0.9719 (0.4444–2.1259)	0.9432 (>0.05) #	Not statistically significant
Systemic therapy	0.9905 (0.7683–1.2771)	0.9416 (>0.05) #	Not statistically

			significant
Local + Systemic	0.7057 (0.493–1.0102)	0.0568 (>0.05) #	Not statistically significant
Presence of Ascites	1.7101 (1.243–2.3528)	0.001 (<0.05) ∗	71.01% increased risk ↑

P < 0.05 indicates statistical significance.

P > 0.05 indicates no statistical significance.

In BCLC stage B, three factors were identified as independent predictors of overall survival (OS): C-TDR, tumor type, and the presence of ascites (P < 0.05); **(Table 4).** Among the 396 patients in this group, a higher C-TDR was associated with an 81.24% reduction in mortality risk (RR [95% CI] = 0.1876 [0.1112–0.3163]). Conversely, multiple tumors and ascites were linked to increased risk of death, with multiple tumors conferring a 38.31% higher risk compared to single tumors (RR [95% CI] = 1.3831 [1.0072–1.8992]) and ascites increasing risk by 102.15% (RR [95% CI] = 2.0215 [1.1325–3.6082]) **(Figure 5).**

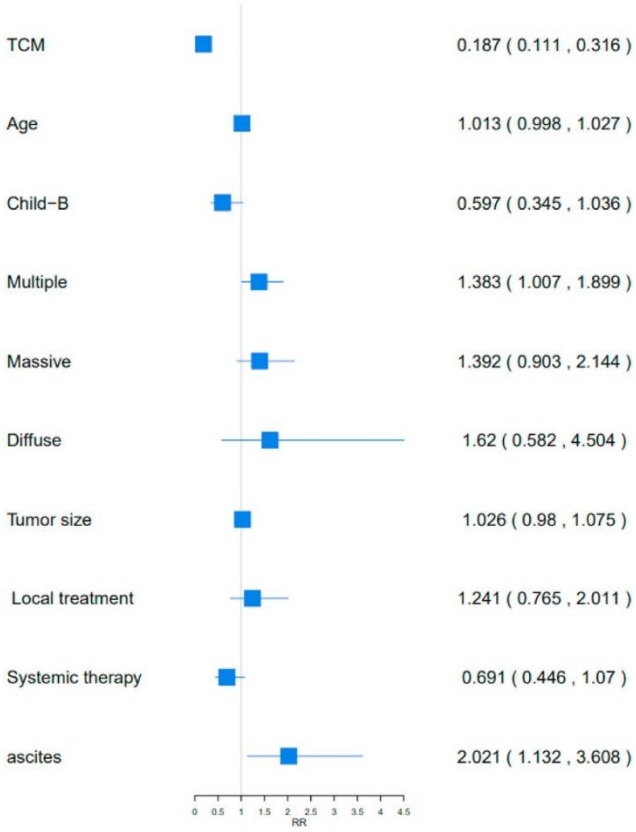


Figure 5. Analysis of prognostic factors for overall survival (OS) in 396 patients with BCLC-B disease

Table 4. Cox regression model evaluating prognostic variables in 396 individuals with BCLC-B.

Variable	OS Relative Risk (95% CI)	P-value	Risk Interpretation
TDR of TCM	0.1876 (0.1112–0.3163)	0.000 (<0.05) ∗	81.24% reduction in risk ↓
Age	1.0132 (0.9989–1.0276)	0.07 (>0.05) #	Not statistically significant
Child-Pugh Classification			
Child-B vs Child-A	0.598 (0.3451–1.0361)	0.0667 (>0.05) #	Not statistically significant
Tumor Characteristics			
Multiple tumors	1.3831 (1.0072–1.8992)	0.045 (<0.05) ∗	38.31% increased risk ↑
Massive tumors	1.3921 (0.9035–2.1449)	0.1337 (>0.05) #	Not statistically significant
Diffuse tumors	1.6204 (0.5829–4.5043)	0.3548 (>0.05) #	Not statistically significant
Tumor size	1.0267 (0.9806–1.0751)	0.2613 (>0.05) #	Not statistically significant
Treatment Modalities			
Local treatment	1.241 (0.7659–2.011)	0.3806 (>0.05) #	Not statistically significant

Systemic therapy	0.691 (0.4461–1.0703)	0.0978 (>0.05) #	Not statistically significant
Presence of Ascites	2.0215 (1.1325–3.6082)	0.0173 (<0.05) ∗	102.15% increased risk ↑

P < 0.05 indicates statistical significance,
#P > 0.05 indicates no statistical significance.

In BCLC stage C, several factors were identified as significant predictors of overall survival (OS), including C-TDR, Child–Pugh score, follow-up treatment, and ascites (P < 0.05); **(Table 5).** Among the 355 patients in this group, higher C-TDR, receiving local treatment, and receiving combined treatment were associated with reductions in mortality risk of 51.36% (RR [95% CI] = 1.0016 [0.9885–1.0149]), 29.53% (RR [95% CI] = 0.7047 [0.5004–0.9924]), and 56.57% (RR [95% CI] = 0.4343 [0.263–0.7173]), respectively. In contrast, diffuse tumor involvement was linked to a 97.49% higher risk of death (RR [95% CI] = 1.0088 [0.9696–1.0495]) **(Figure 6).**

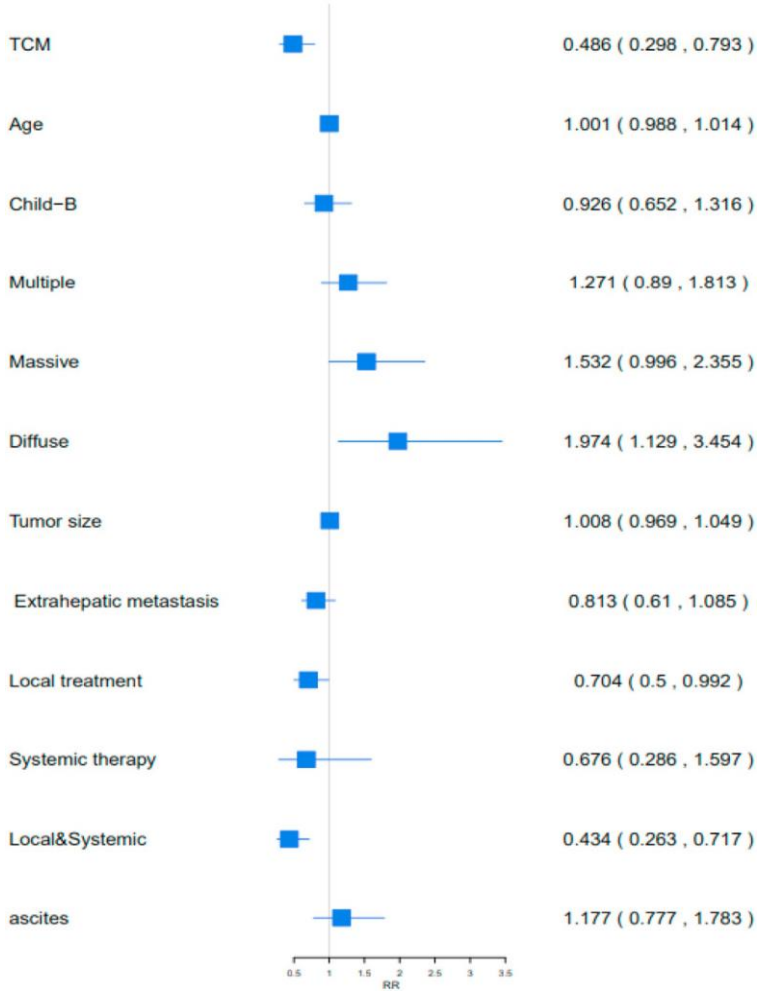


Figure 6. Prognostic factors associated with overall survival (OS) in 355 patients with BCLC stage C. Abbreviations: TCM, treatment-duration ratio of Traditional Chinese Medicine; Local & Systemic, local and systemic therapies.

Table 5. Cox regression analysis of predictors of overall survival in 355 patients with BCLC stage C.

Variable	OS Relative Risk (95% CI)	P-value	Risk Interpretation
Traditional Chinese Medicine (TDR of TCM)	0.1876 (0.1112–0.3163)	0.000 (<0.05) ∗	81.24% reduced risk ↓
Age	1.0132 (0.9989–1.0276)	0.07 (>0.05) #	Not statistically significant
Child-Pugh Classification			
Child-B vs Child-A	0.598 (0.3451–1.0361)	0.0667 (>0.05) #	Not statistically significant

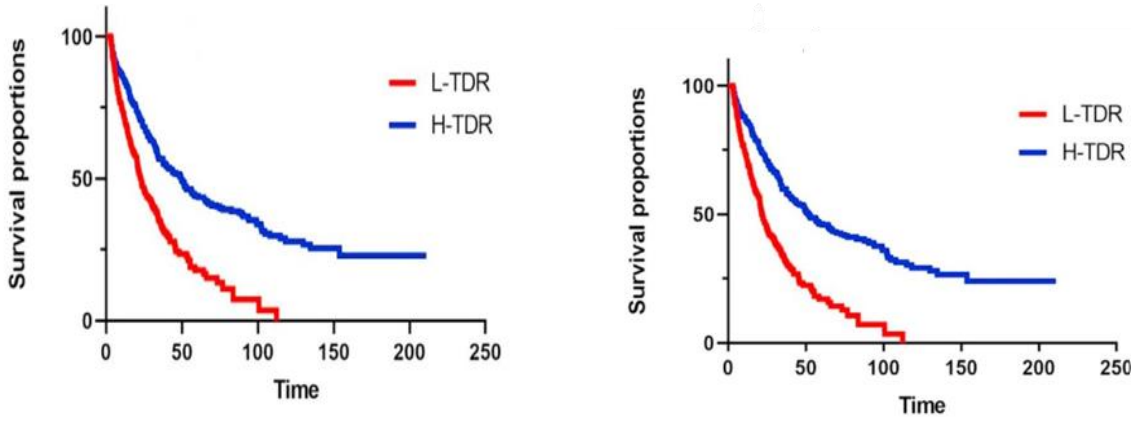
Tumor Characteristics			
Multiple tumors	1.3831 (1.0072–1.8992)	0.045 (<0.05) ∗	38.31% increased risk ↑
Massive tumors	1.3921 (0.9035–2.1449)	0.1337 (>0.05) #	Not statistically significant
Diffuse tumors	1.6204 (0.5829–4.5043)	0.3548 (>0.05) #	Not statistically significant
Tumor size	1.0267 (0.9806–1.0751)	0.2613 (>0.05) #	Not statistically significant
Treatment Modalities			
Local treatment	1.241 (0.7659–2.011)	0.3806 (>0.05) #	Not statistically significant
Systemic therapy	0.691 (0.4461–1.0703)	0.0978 (>0.05) #	Not statistically significant
Presence of Ascites	2.0215 (1.1325–3.6082)	0.0173 (<0.05) ∗	102.15% increased risk ↑

P < 0.05 indicates statistical significance, #P > 0.05 indicates no statistical significance.

Propensity score and survival analysis

Patients were stratified into high and low TDR groups based on the median C-TDR within each BCLC stage. To evaluate survival outcomes and prognostic factors, propensity score matching (PSM) was applied, and subsequent analyses were performed. Across all stages, baseline characteristics were comparable between the H-TDR and L-TDR groups both before and after PSM, with no statistically significant differences (P > 0.05).

Survival analyses demonstrated marked differences between the two groups. Prior to PSM, the median overall survival (OS) in the H-TDR group (n = 501) was 49.2 months, substantially longer than the 22.77 months observed in the L-TDR group (n = 501) (P < 0.05; HR = 0.4628 [0.3879–0.5522]) **(Figure 7a)**. Following PSM, this survival advantage persisted, with median OS of 51.53 months in the H-TDR group versus 21.73 months in the L-TDR group (P < 0.05; HR = 0.4217 [0.3491–0.5094]) **(Figure 7b)**. Corresponding 1-, 2-, and 5-year survival rates were consistently higher in the H-TDR group compared with the L-TDR group: 86.09% versus 70.95%, 59.79% versus 32.25%, and 45.88% versus 16.99%, respective



a) b)

Figure 7. Kaplan–Meier curves comparing overall survival (OS) between patients with high (H-TDR) and low (L-TDR) treatment-duration ratios, before and after propensity score matching (PSM). Panel A: pre-PSM (0 = L-TDR, 1 = H-TDR); Panel B: post-PSM (1 = L-TDR, 2 = H-TDR).

Across all BCLC stages, patients in the H-TDR group experienced consistently longer OS compared with the L-TDR group, both before and after matching. BCLC-A: Before PSM, median OS was 134.47 months for H-TDR (n = 125) versus 40.8 months for L-TDR (n = 126) (P < 0.05; HR = 0.3034 [0.1863–0.4941]). Corresponding 1-, 2-, and 5-year survival rates were 100% vs. 90.1%, 87.8% vs. 61.4%, and 75.7% vs. 38.4%. After PSM, median OS remained 134.47 months in H-TDR (n = 98) versus 40.8 months in L-TDR (n = 98) (P < 0.05; HR = 0.3034 [0.1774–0.5190]), with 1-, 2-, and 5-year survival of 100% vs. 89.9%, 90.0% vs. 59.2%, and 75.5% vs. 37.0%. BCLC-B: Prior to PSM, H-TDR patients (n = 198) had median OS of 49.2 months, compared with 26.77 months for L-TDR (n = 198) (P < 0.05; HR = 0.5441 [0.4151–0.7132]). The 1-, 2-, and 5-year survival rates were 89.1%

vs. 80.2%, 59.5% vs. 36.9%, and 40.8% vs. 18.5%. After PSM, median OS improved to 52.93 months in H-TDR (n = 156) versus 23.67 months in L-TDR (n = 156) ($P < 0.05$; HR = 0.4472 [0.3331–0.6003]), with 1-, 2-, and 5-year survival rates of 90.2% vs. 75.2%, 64.5% vs. 30.2%, and 44.3% vs. 15.2%. BCLC-C: Before PSM, median OS in the H-TDR group (n = 177) was 16.9 months versus 12.27 months in L-TDR (n = 178) ($P < 0.05$; HR = 0.7260 [0.5564–0.9474]), with 1- and 2-year survival rates of 64.2% vs. 50.1% and 21.2% vs. 15.3%. After PSM, H-TDR patients (n = 134) had median OS of 17.4 months, compared with 10.8 months in L-TDR (n = 134) ($P < 0.05$; HR = 0.6207 [0.4613–0.8351]), with 1- and 2-year survival of 66.1% vs. 45.2% and 24.0% vs. 11.9%.

In recent years, integrating Traditional Chinese Medicine (TCM) with conventional Western treatments has become an increasingly accepted approach for managing primary liver cancer (PLC) [22, 23]. TCM offers distinct advantages in both the prevention and management of PLC, including symptom relief and lower rates of adverse reactions. For example, Huaier granule, a widely used TCM preparation, has been shown to significantly extend recurrence-free survival and reduce extrahepatic recurrence in patients with hepatocellular carcinoma (HCC) following curative liver resection [26]. Additionally, a study involving 3,483 PLC patients suggested that adjuvant TCM therapy may prolong median survival and improve overall survival (OS) [27]. However, there remains no global consensus regarding the optimal duration of TCM treatment [22, 23].

This study represents the first and largest real-world analysis in China examining the relationship between the duration of TCM therapy and survival outcomes in PLC. Significant differences were observed among BCLC stages A, B, and C in terms of Child–Pugh class, tumor characteristics (type, location, size, thrombus), and the prevalence of lymph node or distant metastases **(Table 1)**. As expected, survival outcomes varied by stage, with BCLC-C patients exhibiting the poorest prognosis compared with stages A and B **(Figure 2).**

To quantify the impact of TCM duration, we introduced the treatment-duration ratio of TCM (C-TDR), defined as the proportion of overall treatment time during which patients received TCM. A higher C-TDR indicates earlier initiation and longer adherence to TCM therapy. Analyses demonstrated that high C-TDR was an independent predictor of improved OS, indicating that earlier and sustained TCM treatment correlates with longer survival. These results were confirmed using both multivariable Cox regression and propensity score matching (PSM) analyses.

PSM was employed to reduce baseline imbalances between high- and low-C-TDR groups. Propensity scores were calculated using a logistic regression model incorporating variables known to affect PLC prognosis, including BCLC stage, age, sex, Child–Pugh class, tumor characteristics (type, location, size, thrombus), lymph node metastasis, ascites, and distant metastasis [28]. Standardized differences were used to evaluate balance, ensuring comparability between groups and controlling for potential confounders.

This study, initiated in 2015, assessed OS in PLC patients receiving either low or high C-TDR TCM therapy. Previous research has consistently shown that TCM interventions can prolong OS across all disease stages [27–33]. For instance, multicenter randomized trials and cohort studies demonstrated that TCM regimens, including Jiedu granules, effectively extend OS and recurrence-free survival, either alone or combined with therapies such as TACE or sorafenib [29, 32, 33]. Building on these findings, the current study specifically evaluated the effect of C-TDR and confirmed that earlier initiation and longer duration of TCM treatment is associated with improved survival outcomes.

Despite these findings, several limitations should be acknowledged. First, as a retrospective study, selection bias is inevitable. Second, imaging and radiology reports were not independently reviewed, raising the possibility of inaccurate tumor assessments. Third, the analysis did not account for the duration or dosage of concurrent treatments, including targeted therapies and immune checkpoint inhibitors. Finally, further multi-center studies with larger cohorts are needed to better evaluate how patient characteristics influence TCM therapy selection and outcomes.

Conclusion

In conclusion, a high treatment-duration ratio of Traditional Chinese Medicine (C-TDR) is an independent predictor of improved overall survival in patients with primary liver cancer. Early initiation and sustained TCM therapy are associated with a reduced risk of mortality and prolonged survival.

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