

# Social Support, Quality of Life, and Financial Toxicity Among Patients with Hepatocellular Carcinoma

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**Background & Aims:** Despite the significant hepatocellular carcinoma (HCC) patient population, gaps exist in understanding their survivorship journey.

**Methods:** Patients diagnosed with HCC at all stages were recruited at Sun Yat-sen University Cancer Center from August 1, 2023, to December 30, 2023. The comprehensive score for financial toxicity (COST) was used to assess financial toxicity, the Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep) was used to assess quality of life (QOL), and the Social Support Rating Scale (SSRS) was used to assess social support. Separate multiple linear regression models were performed to assess the association among social support, FT, and QOL.

**Results:** Of the 250 approached HCC patients, 239 completed the survey and were included in this study. Most respondents were male (192 [80.3%]), of Han nationality (235 [98.3%]), and married (214 [89.5%]). Higher social support ( $\beta$ , 0.13; 95% CI, 0.01 ~ 0.26;  $P = 0.048$ ) was independently associated with lower FT (higher COST score). Lower FT ( $\beta$ , 0.74; 95% CI, 0.49 ~ 0.99;  $P < 0.001$ ) and social support ( $\beta$ , 1.47; 95% CI, 0.73 ~ 2.21;  $P < 0.001$ ) were independently associated with higher QOL. Social support not only directly affected the QOL ( $b = 0.62$ ,  $P < 0.001$ , 95% CI [0.33–0.90]) but also indirectly affected the QOL through FT ( $b = 0.14$ , 95% CI [0.03–0.28]).

**Conclusion:** The findings of this survey study suggest that social support was associated with higher QOL and lower FT in HCC patients. Future investigations focusing on targeted social support interventions may enhance QOL and reduce FT in HCC patients.

**Keywords:** social support, quality of life, financial toxicity, hepatocellular carcinoma, cross-sectional survey

## Introduction

Hepatocellular carcinoma (HCC) stands as a pressing global health challenge characterized by a rising incidence and mortality rate.<sup>1,2</sup> Although the overall survival of HCC patients was improved accompanied by the emergence of immunotherapies recently, research on HCC survivorship remains limited.

Vital facets of HCC survivorship encompass enhancing overall survival, navigating the array of long-term adverse effects from HCC treatment, and comprehending their impact on patient-reported outcomes like quality of life (QOL) and financial toxicity (FT). Despite patients with early-stage HCC typically being asymptomatic, individuals across all stages and treatment modalities often endure diminished QOL relative to the general or cirrhotic populations.<sup>3–5</sup> The term FT has been used to describe both the objective financial burdens of medical care as well as the subjective distress.<sup>6</sup> Several researches have reported that FT was associated to decreased QOL in other cancers such as lung cancer, colorectal

cancer, breast cancer, and so on,<sup>7–9</sup> but FT is yet to be reported in HCC patients. In addition, HCC patients commonly contend with chronic liver diseases like HBV infection, HCV infection, steatohepatitis, and alcoholic hepatitis. In China, approximately 80% of HCC patients are infected with HBV,<sup>10</sup> and they are recommended to take antiviral drugs for whole life long.<sup>11,12</sup> Beyond HCC, the treatment of chronic liver diseases like antivirals for HBV and liver protectants further compounds FT among HCC patients, which may cause higher FT for them compared to other cancers.

Cancer can also disrupt the social fabric of patients,<sup>13</sup> which may in turn influence the support they receive during their illness.<sup>14,15</sup> It is reported that social support could ameliorate the negative psychological repercussions of cancer diagnosis and treatment.<sup>16,17</sup> In our investigation, we employed the Social Support Rating Scale (SSRS),<sup>18,19</sup> besides subjective support (perceived support or emotional assistance), objective support (actual support received, such as financial support) and utilization of support (effective use of social support) are also included into the dimensions of SSRS. Thus, delving into the impact of social support on FT and various QOL dimensions beyond emotional well-being holds significance.

In this study, we aim to (1) report the presence and degree of FT experienced by HCC patients and identify demographic and clinical risk factors for FT, (2) pinpoint demographic and clinical risk factors for different dimensions of QOL in HCC patients, and (3) investigate the association among social support, FT and QOL.

## Methods

### Study Design and Participants

We have investigated 239 patients diagnosed with HCC at Sun Yat-sen University Cancer Center from August 1, 2023, to December 30, 2023, a convenience sampling method was used in this study. Inclusion criteria encompassed: 1) Histologically or radiologically confirmed HCC diagnosis; 2) Age  $\geq$  18 years; 3) Primary school education or higher; 4) Awareness of their HCC diagnosis; 5) Willingness to participate in this study. Exclusion criteria involved: 1) History of mental illness; 2) Severe systemic infections, severe anemia, or cachexia; 3) Patients with communication barriers. This research received approval from the Ethics Committee Board of Sun Yat-sen University Cancer Center (Approval number B2023-261-01). Participants were briefed face-to-face on questionnaire completion procedures and guidelines. They independently completed the questionnaire, with certain sections filled by investigators based on medical records or consultation with participants. All questionnaires were distributed and reviewed promptly post-collection to rectify any oversights, ensuring data integrity. Out of 250 distributed surveys, 239 valid responses were obtained, yielding an impressive response rate of 95.6%.

The questionnaire comprised the Comprehensive Score for Financial Toxicity (COST) measure, the Social Support Rating Scale (SSRS), and the Functional Assessment of Cancer Therapy-Hepatobiliary (FACT-Hep). The COST tool, validated with 11 items, gauges cancer patients' financial toxicity (lower scores indicating higher FT).<sup>20</sup> The SSRS,<sup>18,19</sup> devised by Shuiyuan Xiao, was employed to evaluate social relationships across three dimensions through ten items: objective support (actual support received), subjective support (perceived support or emotional assistance), and utilization of support (effective use of social support). The FACT-Hep is an extension of the FACT-G (Functional Assessment of Cancer Therapy-General, consisting of 27 items) with an added liver-specific module- "additional concerns" (comprising 19 items closely related to physical health issues in patients with liver cancer), resulting in a 46-item self-assessment scale.<sup>21</sup> It includes five dimensions: physical well-being, social/family well-being, emotional well-being, functional well-being, and additional concerns, all rated on a 5-point scale (0–4 points), with higher scores indicating a higher quality of life (QOL) in that aspect for the patient.

### Statistical Analysis

Participant demographic and clinical characteristics are summarized using frequencies and percentages. Scores on the QOL scale, COST tool, and social support measure are summarized using medians and interquartile ranges (IQRs). Multivariable linear regression analysis, incorporating significant factors from univariate analysis ( $P < 0.05$ ), was performed to identify the independent risk factors associated with QOL and FT. Constructing a deeper understanding of the relationships among social support, FT, and QOL, structural equation models (SEM) were crafted using The AMOS 24.0 software. The verification of the impact of social support on the interplay between FT and QOL was

examined through bootstrapping analyses with 5000 samples. The effect size for each indirect effect was assessed using completely standardized indirect effect beta values.<sup>22</sup> The indirect effect was considered significant if the 95% bias-corrected confidence intervals did not include 0. A two-tailed P value of <0.05 was deemed statistically significant. Statistical analyses were conducted using SPSS version 26.0 or R version 4.2.2 (R Foundation, Vienna, Austria).

## Results

### Patient Demographics and Characteristics

Of the 250 patients with HCC approached for participation, 239 (95.6%) completed the survey and were included in this study. The average age of the respondents was 50.5 (standard deviation [SD], 11.1) years, the majority were male (192 [80.3%]), of Han nationality (235 [98.3%]), married (214 [89.5%]), and possessed social basic medical insurance (202[84.5%]). Approximately half of the patients reported a household income of ¥2000–4000/month/person (101 [42.3%]), and had an educational level below high school (122 [51.0%]). The predominant occupation before illness was peasantry (62 [25.9%]), followed by service (53 [22.2%]), and worker (43 [18.0%]). Not coincidentally, the most residence of patients was rural (81 [33.9%]). For work status currently, around half of the patients were employed on sick leave (112 [46.9%]), notably, 88 (36.8%) patients were unemployed, much higher than that (13 [5.4%]) before illness. Details are described in Table 1.

**Table 1** Patient Demographics and Characteristics

Variables	Value (N = 239)
<b>Sex</b>	
Male	192(80.3)
Female	47(19.7)
<b>Age (years)</b>	
<65	211(88.3)
≥65	28(11.7)
Median (SD)	50.5(11.1)
<b>Nationality</b>	
The Han nationality	235(98.3)
Minority nationality	4(1.7)
<b>Residence</b>	
City	68(28.5)
County	40(16.7)
Township	50(20.9)
Rural	81(33.9)
<b>Education</b>	
<High school	122(51.0)
High school/ technical secondary school/ junior college	98(41.0)
Bachelor's degree	19(7.9)
<b>Marital status</b>	
Married	214(89.5)
Single	13(5.4)
Divorced	8(3.3)
Widowed	4(1.7)

(Continued)

**Table 1** (Continued).

Variables	Value (N = 239)
<b>Work status currently</b>	
Employed, Full-time/part-time,	35(14.6)
Change in employment, full-time/part-time,	4(1.7)
Employed, on sick leave	112(46.9)
Unemployed	88(36.8)
<b>Household income (¥/month/person)</b>	
<2000	44(18.4)
≥2000, <4000	101(42.3)
≥4000	94(39.3)
<b>Medical insurance</b>	
Social basic medical insurance	202(84.5)
Commercial medical insurance	8(3.3)
Private	15(6.3)
Others	14(5.9)
<b>Time since diagnosis (months)</b>	
<6	183(76.6)
≥6	56(23.4)
<b>Times of hospitalizations in the past year</b>	
<5	195(81.6)
≥5, <10	38(15.9)
≥10	6(2.5)
<b>Comorbidity (chronic disease)</b>	
No	87(36.4)
Yes	152(63.6)
<b>Type of therapy</b>	
Surgery	73(30.5)
Ablation	9(3.8)
TACE	12(5.0)
HAIC	10(4.2)
Immunotherapy + targeted therapy + interventional therapy	135(56.5)
<b>Stage at diagnosis</b>	
I	56(23.4)
II	39(16.3)
III	110(46.0)
IV	34(14.2)
<b>Family history of cancer</b>	
No	184(77.0)
Yes	55(23.0)

(Continued)

**Table 1** (Continued).

Variables	Value (N = 239)
<b>Costs in the hospitalization (¥)</b>	
<20,000	83 (34.7)
≥20,000, <40,000	104 (43.5)
≥40,000, <60,000	41(17.2)
≥60,000	11(4.6)
<b>Occupation before illness</b>	
Retiree	29(12.1)
Professional technical personnel	16(6.7)
Worker	43(18.0)
Serviceman	2(0.8)
Administrator	9(3.8)
Service crew	53(22.2)
Homemaking service operators	4(1.7)
Peasantry	62(25.9)
Unemployed	13(5.4)
Student	1(0.4)
Others	7(2.9)

Around half of the patients had stage III disease at diagnosis (110 [46.0%]) and received combination therapy of immunotherapy, targeted therapy, and interventional therapy (135 [56.5%]). A majority of patients had a family history of cancer (184 [77.0%]) and were accompanied with chronic disease such as diabetes and hypertension (152 [63.6%]). Most patients were diagnosed less than 6 months (183 [76.6%]) and had been hospitalized fewer than 5 times in the past year (195 [81.6%]). Hospitalization costs for 104 patients (43.5%) ranged between ¥20000 and 40000.

## Financial Toxicity Analysis

The median COST score was 19 (IQR, 10–25), and high FT was defined as a COST score below the cohort's median (<19). Univariate analysis of the COST score ([Supplementary Table 1](#)) revealed several demographic and clinical factors that were associated with higher FT, including residence in rural ( $\beta$ , -4.56; 95% CI, -7.49 ~ -1.63;  $P = 0.003$ ), unemployment currently ( $\beta$ , -6.17; 95% CI, -9.72 ~ -2.61;  $P < 0.001$ ), private in medical insurance ( $\beta$ , -6.19; 95% CI, -11.01 ~ -1.38;  $P = 0.012$ ), treatment of hepatic arterial infusion chemotherapy (HAIC) ( $\beta$ , -8.50; 95% CI, -14.53 ~ -2.47;  $P = 0.006$ ) or combination treatment ( $\beta$ , -4.15; 95% CI, -6.74 ~ -1.55;  $P = 0.002$ ), higher disease stage (stage III vs stage I:  $\beta$ , -13.09; 95% CI, -19.53 ~ -6.64;  $P < 0.001$ ; stage IV vs stage I:  $\beta$ , -17.44; 95% CI, -25.97 ~ -8.90;  $P < 0.001$ ), occupation of peasantry ( $\beta$ , -4.68; 95% CI, -8.62 ~ -0.73;  $P = 0.021$ ) and unemployment before illness ( $\beta$ , -7.05; 95% CI, -12.90 ~ -1.1;  $P = 0.019$ ). Overall social support ( $\beta$ , 0.16; 95% CI, 0.02 ~ 0.30;  $P = 0.025$ ) and higher household income (¥2000–4000/month/person vs <¥2000/month/person:  $\beta$ , 3.93; 95% CI, 0.79 ~ 7.06;  $P = 0.015$ ; ≥¥4000/month/person vs <¥2000/month/person:  $\beta$ , 8.11; 95% CI, 4.93 ~ 11.2;  $P < 0.001$ ) were associated with lower FT.

Multivariate analysis ([Table 2](#)) suggested that unemployment currently ( $\beta$ , -4.17; 95% CI, -7.65 ~ -0.69;  $P = 0.02$ ), and treatment of HAIC ( $\beta$ , -7.65; 95% CI, -13.55 ~ -1.7;  $P = 0.012$ ) or combination treatment ( $\beta$ , -3.93; 95% CI, -7.09 ~ -0.78;  $P = 0.015$ ) were independently associated with higher FT. Overall social support ( $\beta$ , 0.13; 95% CI, 0.01 ~ 0.26;  $P = 0.048$ ) and higher household income (¥2000–4000/month/person vs <¥2000/month/person:  $\beta$ , 3.20; 95% CI, 0.09 ~ 6.30;  $P = 0.045$ ; ≥¥4000/month/person vs <¥2000/month/person:  $\beta$ , 7.62; 95% CI, 4.53 ~ 10.7;  $P < 0.001$ ) were independently associated with lower FT.

Based on the above analysis, the following were identified as the independent risk factors for high financial toxicity: (1) unemployment currently, (2) treatment of HAIC and combination treatment, (3) lower overall social support (score < 36 [median]), (4) household income < ¥2000/month/person. Within our cohort, 11.7% ( $n = 28$ ) of patients had zero risk

**Table 2** The Multivariate Analysis of Risk Factors for Financial Toxicity (COST Score)

Variables	b	S.E	t	P	$\beta$ (95% CI)
<b>Overall social support</b>	0.13	0.07	1.99	0.048	0.13 (0.01 ~ 0.26)
<b>Work status currently</b>					
Employed, Full-time/part-time,					0.00 (Reference)
Change in employment, full-time/part-time,	0.58	4.74	0.12	0.903	0.58 (-8.71 ~ 9.86)
Employed, on sick leave	-0.81	1.68	-0.48	0.629	-0.81 (-4.11 ~ 2.48)
Unemployed	-4.17	1.77	-2.35	0.020	-4.17 (-7.65 ~ -0.69)
<b>Household income (¥/month/person)</b>					
<2000					0.00 (Reference)
≥2000, <4000	3.20	1.59	2.02	0.045	3.20 (0.09 ~ 6.30)
≥4000	7.62	1.58	4.83	<0.001	7.62 (4.53 ~ 10.72)
<b>Type of therapy</b>					
Surgery					0.00 (Reference)
Ablation	-2.48	2.99	-0.83	0.407	-2.48 (-8.33 ~ 3.37)
TACE	-3.48	2.69	-1.29	0.197	-3.48 (-8.76 ~ 1.79)
HAIC	-7.65	3.01	-2.54	0.012	-7.65 (-13.55 ~ -1.75)
Immunotherapy + targeted therapy + interventional therapy	-3.93	1.61	-2.44	0.015	-3.93 (-7.09 ~ -0.78)

**Abbreviation:** CI, Confidence Interval.

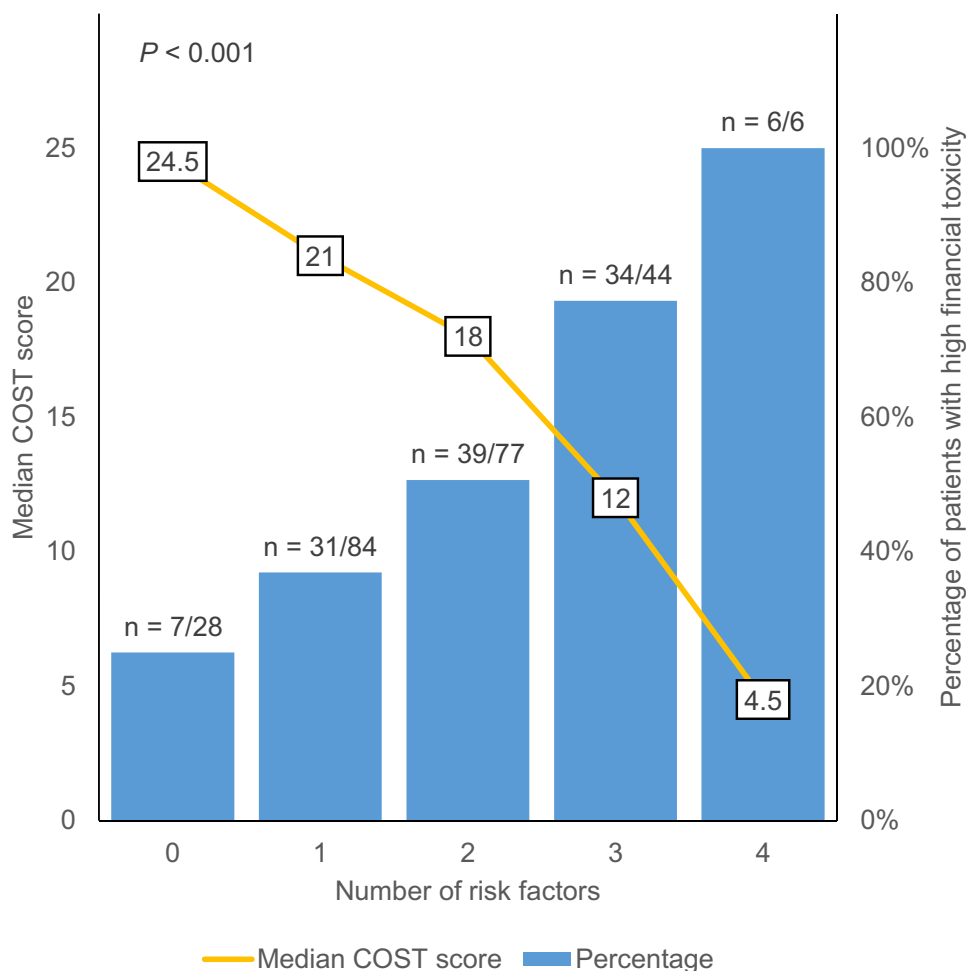
factors, 35.1% (n = 84) had one, 32.2% (n = 77) had two, 18.4% (n = 44) had three, and 2.5% (n = 6) had all four risk factors. The relationship between high FT and the median COST score, stratified by the number of risk factors, is illustrated in [Figure 1](#). As the number of risk factors increased from zero to four, the percentage of patients with high FT increased from 25.0% (n = 7/28) to 36.9% (n = 31/84) to 50.6% (n = 39/77) to 77.3% (n = 34/44) and to 100% (n = 6/6), respectively ( $P < 0.001$ ). As expected, the median COST score decreased as the number of risk factors increased. The median COST score for those with zero risk factors was 24.5 (range: 7–35), one risk factor was 21 (range: 3–41), two risk factors was 18 (range: 1–41), three risk factors was 12 (range: 0–27), and four risks was 4.5 (range: 0–13).

## Quality of Life Analysis

The median overall QOL score was 111 (IQR, 97–124). Univariate analysis results for overall QOL are provided in [Supplementary Table 2](#). The multivariate analysis ([Table 3](#)) revealed that time since diagnosis is longer than 6 months ( $\beta$ , -7.12; 95% CI, -12.73 ~ -1.5;  $P = 0.014$ ), and stage II ( $\beta$ , -9.3; 95% CI, -15.10 ~ -3.5;  $P = 0.002$ ) or stage III ( $\beta$ , -8.35; 95% CI, -16.41 ~ -0.2;  $P = 0.043$ ) disease were independently associated with lower overall QOL. Lower FT (higher COST score) ( $\beta$ , 0.74; 95% CI, 0.49 ~ 0.99;  $P < 0.001$ ) and overall social support ( $\beta$ , 1.47; 95% CI, 0.73 ~ 2.21;  $P < 0.001$ ) were independently associated with higher overall QOL.

Overall QOL comprises five parts, including physical well-being, social/family well-being, emotional well-being, functional well-being, and additional concerns. To explore how demographic and clinical factors influence overall QOL across these domains, we conducted further univariate and multivariate analyses of the five components. Univariate analysis results for physical well-being ([Supplementary Table 3](#)), social/family well-being ([Supplementary Table 4](#)), emotional well-being ([Supplementary Table 5](#)), functional well-being ([Supplementary Table 6](#)), and additional concerns ([Supplementary Table 7](#)) are provided in the supplementary.

The multivariate analysis ([Table 4](#)) revealed that high school/technical secondary school/junior college education ( $\beta$ , -1.71; 95% CI, -3.01 ~ -0.41;  $P = 0.011$ ) and stage II ( $\beta$ , -2.09; 95% CI, -4.10 ~ -0.08;  $P = 0.043$ ), stage III ( $\beta$ , -2.98; 95% CI, -4.56 ~ -1.40;  $P < 0.001$ ) or stage IV ( $\beta$ , -5.07; 95% CI, -7.18 ~ -2.97;  $P < 0.001$ ) disease were independently associated with worse physical well-being, and lower FT ( $\beta$ , 0.17; 95% CI, 0.10 ~ 0.24;  $P < 0.001$ ) was independently associated with better physical well-being. Objective support ( $\beta$ , 0.18; 95% CI, 0.02 ~ 0.35;  $P = 0.033$ ) and subjective



**Figure 1** The bar graph represents the percentage of patients with high financial toxicity [Comprehensive Score for Financial Toxicity (COST) <19] and the line graph represents the median COST score stratified by the number of risk factors. Lower median COST score indicates higher financial toxicity. As the number of risk factors increased from zero to four, the percentage of patients with high FT increased from 25.0% (n = 7/28) to 36.9% (n = 31/84) to 50.6% (n = 39/77) to 77.3% (n = 34/44) and to 100% (n = 6/6), respectively ( $P < 0.001$ ).

support ( $\beta$ , 0.24; 95% CI, 0.16 ~ 0.33;  $P < 0.001$ ) were independently associated with better social/family well-being. Time since diagnosis longer than 6 months ( $\beta$ , -1.2; 95% CI, -2.36 ~ -0.03;  $P = 0.045$ ) was independently associated with worse emotional well-being, and lower FT ( $\beta$ , 0.13; 95% CI, 0.08 ~ 0.19;  $P < 0.001$ ) was independently associated with better emotional well-being. Time since diagnosis longer than 6 months ( $\beta$ , -2.44; 95% CI, -3.93 ~ -0.95;  $P = 0.002$ ) was independently associated with worse functional well-being, and lower FT ( $\beta$ , 0.11; 95% CI, 0.04 ~ 0.18;  $P = 0.003$ ), overall social support ( $\beta$ , 0.14; 95% CI, 0.05 ~ 0.23;  $P = 0.003$ ), and Bachelor's degree education ( $\beta$ , 2.48; 95%

**Table 3** The Multivariate Analysis of Risk Factors for Overall QOL

Variables	b	S.E	t	P	$\beta$ (95% CI)
<b>COST score</b>	0.74	0.13	5.83	<0.001	0.74 (0.49 ~ 0.99)
<b>Overall social support</b>	1.47	0.38	3.87	<0.001	1.47 (0.73 ~ 2.21)
<b>Time since diagnosis (months)</b>					
<6					0.00 (Reference)
$\geq 6$	-7.12	2.86	-2.49	0.014	-7.12 (-12.73 ~ -1.51)

(Continued)

**Table 3** (Continued).

Variables	b	S.E	t	P	$\beta$ (95% CI)
<b>Stage at diagnosis</b>					
I					0.00 (Reference)
II	-3.41	3.75	-0.91	0.364	-3.41 (-10.77 ~ 3.94)
III	-9.30	2.96	-3.14	0.002	-9.30 (-15.10 ~ -3.50)
IV	-8.35	4.11	-2.03	0.043	-8.35 (-16.41 ~ -0.29)

**Abbreviation:** CI, Confidence Interval.

CI, 0.08 ~ 4.88;  $P = 0.044$ ) were independently associated with better functional well-being. Employment on sick leave ( $\beta$ , -3.95; 95% CI, -7.61 ~ -0.29;  $P = 0.035$ ) or unemployment currently ( $\beta$ , -4.89; 95% CI, -8.80 ~ -0.98;  $P = 0.015$ ) and treatment of HAIC ( $\beta$ , -7.38; 95% CI, -13.76 ~ -1.0;  $P = 0.024$ ) or combination treatment ( $\beta$ , -4.12; 95% CI, -6.94 ~ -1.30;  $P = 0.005$ ) were independently associated with worse additional concerns, and lower FT ( $\beta$ , 0.22; 95% CI, 0.08 ~ 0.36;  $P = 0.002$ ) and overall social support ( $\beta$ , 0.18; 95% CI, 0.03 ~ 0.32;  $P = 0.017$ ) were independently associated with better additional concerns.

In summary, lower FT was independently associated with improved physical well-being, emotional well-being, functional well-being, and additional concerns; social support was independently associated with improved social/family well-being, functional well-being, and additional concerns (Figure 2).

## Association Among Social Support, Financial Toxicity, and Quality of Life

As previously discussed, social support was found to be independently associated with FT and QOL, while FT was independently associated with QOL. Thus, mediation analyses were performed to ascertain whether social support indirectly influenced QOL through FT. The structural equation model (SEM) was constructed (Figure 3), and the Bootstrap sampling test method was employed to conduct a study on the effect of social support between FT and QOL with 5000 sampling iterations. The results showed that the total effect of social support on QOL was 0.76 ( $P < 0.001$ , 95% CI [0.45–1.06]), the direct effect of social support on QOL was 0.62 ( $P < 0.001$ , 95% CI [0.33–0.90]), and the indirect effect of social support on QOL through FT was 0.14 (95% CI [0.03–0.28]), accounting for 18.4% of the total effect.

## Discussion

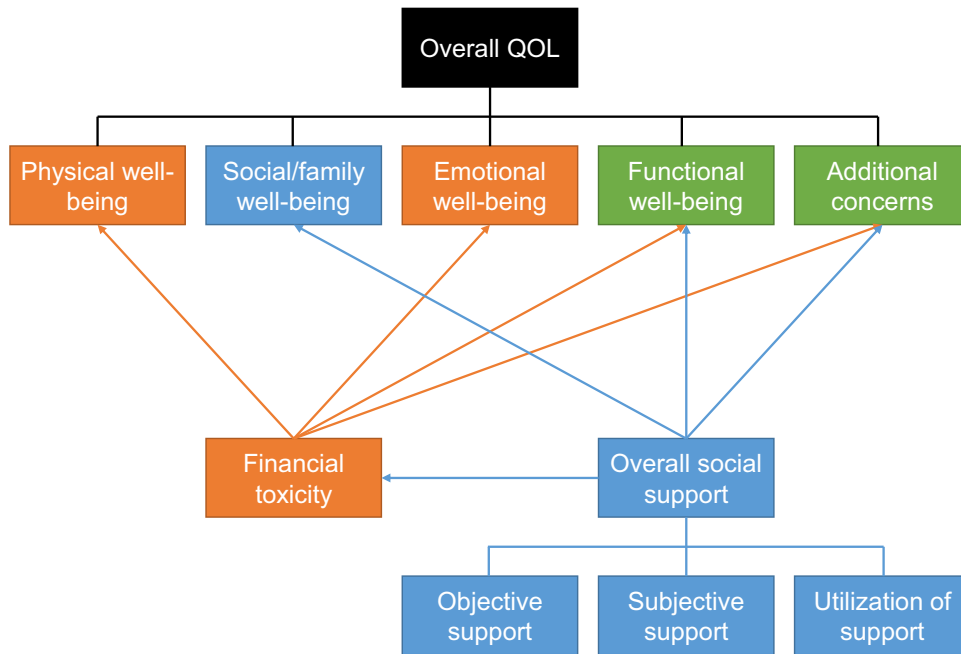
### Financial Toxicity in Hepatocellular Carcinoma Patients

This research marks the inaugural exploration into FT in HCC patients. The median COST score was 19 in our cohort, a figure lower than that observed in other cancer types such as lung cancer (median COST score: 24–29),<sup>23–25</sup> colorectal cancer (median COST score: 21–24.5),<sup>26</sup> and breast cancer (median COST score: 28),<sup>27</sup> indicating higher FT. Notably, HCC patients commonly contend with chronic liver diseases like HBV infection, HCV infection, steatohepatitis, and alcoholic hepatitis. In China, approximately 80% of HCC patients are infected with HBV,<sup>10</sup> and they are recommended to take antiviral drugs for whole life long.<sup>11,12</sup> Beyond HCC, the treatment of chronic liver diseases like antivirals for HBV and liver protectants further compounds FT among HCC patients, which may cause higher FT for them compared to other cancers.

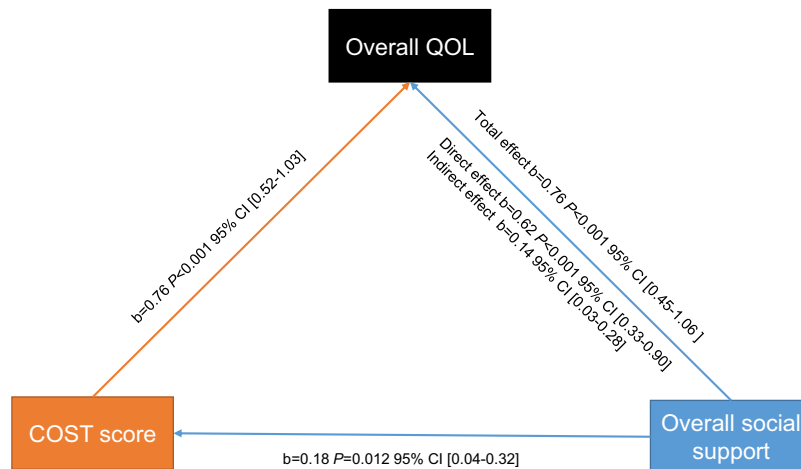
This study illuminates that unemployment and lower household income stand as independent factors associated with higher FT, echoing findings in other cancer studies.<sup>28</sup> Moreover, we identified treatment of HAIC and combination treatment were independently associated with higher FT. HAIC and combination treatment were palliative treatment for median or advanced stage HCC, requiring patients for multiple hospitalizations, which interrupted the normal life of HCC patients and consequently resulted in higher FT. Noteworthy is the revelation that social support emerged as a pivotal factor in mitigating FT within our study.

**Table 4** Multivariate Analysis of Risk Factors for Physical Well-Being, Social/Family Well-Being, Emotional Well-Being, Functional Well-Being, and Additional Concerns

	Physical Well-Being		Social/Family Well-Being		Emotional Well-Being		Functional Well-Being		Additional Concerns	
	$\beta$ (95% CI)	P	$\beta$ (95% CI)	P	$\beta$ (95% CI)	P	$\beta$ (95% CI)	P	$\beta$ (95% CI)	P
<b>COST score</b>	0.17 (0.10 ~ 0.24)	<0.001			0.13 (0.08 ~ 0.19)	<0.001	0.11 (0.04 ~ 0.18)	0.003	0.22 (0.08 ~ 0.36)	0.002
<b>Overall social support</b>							0.14 (0.05 ~ 0.23)	0.003	0.18 (0.03 ~ 0.32)	0.017
<b>Objective support</b>			0.18 (0.02 ~ 0.35)	0.033						
<b>Subjective support</b>			0.24 (0.16 ~ 0.33)	<0.001						
<b>Education</b>										
<High school	0.00 (Reference)						0.00 (Reference)			
High school/ technical secondary school/ junior college	-1.71 (-3.01 ~ -0.41)	0.011					0.68 (-0.63 ~ 1.99)	0.313		
Bachelor's degree	0.45 (-1.92 ~ 2.83)	0.709					2.48 (0.08 ~ 4.88)	0.044		
<b>Work status currently</b>										
Employed, Full-time/part-time									0.00 (Reference)	
Change in employment, full-time/part-time									-5.36 (-15.21 ~ 4.48)	0.287
Employed, on sick leave									-3.95 (-7.61 ~ -0.29)	0.035
Unemployed									-4.89 (-8.80 ~ -0.98)	0.015
<b>Time since diagnosis (months)</b>										
<6					0.00 (Reference)		0.00 (Reference)			
≥6					-1.20 (-2.36 ~ -0.03)	0.045	-2.44 (-3.93 ~ -0.95)	0.002		
<b>Type of therapy</b>										
Surgery									0.00 (Reference)	
Ablation									1.04 (-5.51 ~ 7.59)	0.756
TACE									-0.09 (-5.94 ~ 5.76)	0.976
HAIC									-7.38 (-13.76 ~ -1.00)	0.024
Immunotherapy + targeted therapy + interventional therapy									-4.12 (-6.94 ~ -1.30)	0.005
<b>Stage at diagnosis</b>										
I	0.00 (Reference)									
II	-2.09 (-4.10 ~ -0.08)	0.043								
III	-2.98 (-4.56 ~ -1.40)	<0.001								
IV	-5.07 (-7.18 ~ -2.97)	<0.001								



**Figure 2** The effect of social support and financial toxicity on different dimensions of quality of life (QOL).



**Figure 3** The direct and indirect effect of social support on quality of life (QOL): total effect of social support on QOL was 0.76 ( $P<0.001$ , 95% CI [0.45–1.06]), the direct effect of social support on QOL was 0.62 ( $P<0.001$ , 95% CI [0.33–0.90]), and the indirect effect of social support on QOL through FT was 0.14 (95% CI [0.03–0.28]), accounting for 18.4% of the total effect.

Building on the work of Melinda et al, it is evident that unmet physical, social, and medical needs are associated with lower QOL, with only unmet social needs correlating with higher FT in lung cancer patients.<sup>25</sup> The provision of social support effectively addresses patients’ social needs, underscoring its significant impact on FT.

We have identified four risk factors independently associated with FT as described above. As the number of risk factors increased from zero to four, the percentage of patients with high FT increased accordingly. As expected, the median COST score exhibited a decline with an increasing number of risk factors (Figure 1).

### Quality of Life in Hepatocellular Carcinoma Patients

Longer time since diagnosis, higher stage disease, higher FT, and less social support were identified as independent factors associated with lower overall QOL in this study. Beyond overall QOL, our investigation delved into factors

influencing diverse dimensions of QOL, encompassing physical well-being, social/family well-being, emotional well-being, functional well-being, and additional concerns (liver-specific module).

Our findings indicate that lower FT was independently associated with better physical well-being, emotional well-being, functional well-being, and additional concerns, except for social/family well-being. FT intensifies feelings of anxiety, depression, and fatigue due to increased medical interventions, leading to compromised emotional well-being.<sup>29,30</sup> Patients with cancer are also more likely than individuals without cancer to experience loss of income because of decreased productivity and job loss and are more likely to miss work, take unexpected sick days or unpaid leave, and miss opportunities for promotion and raises,<sup>31,32</sup> resulting in worse functional well-being. Additionally, patients with higher FT may be less able to focus on the day-to-day clinical management,<sup>33</sup> delay or forgo necessary medical care and prescriptions,<sup>34</sup> and have higher rates of adverse events because of lower capacity to manage them, thereby compromising physical well-being and raising additional concerns.

We found that social support was independently associated with social/family well-being, functional well-being, and additional concerns. Conversely, the absence of an independent association between social support and emotional well-being was unexpected, especially given previous reports linking social support to emotional QOL in other cancer survivor populations.<sup>35,36</sup> The reasons may be as follows: firstly, a different QOL tool would have a different outcome,<sup>37,38</sup> we employed a liver-specific QOL tool (FACT-Hep) in this study; secondly, we found longer time since diagnosis and FT were independently associated with the emotional well-being in the multivariable analysis, these two factors may contribute more to the impact of emotional well-being than social support; thirdly, social support was independently associated with FT, which may indirectly affect emotional well-being.

As mentioned above, social support was not only independently associated with QOL but also FT, and FT was the independent factor associated with QOL. To elucidate the interplay between social support, FT, and QOL, we employed a structural equation model with mediation analysis. This approach allows us to disentangle direct effects (eg, how social support independently improves QoL) from indirect effects (eg, how social support alleviates FT, which in turn enhances QoL). The Bootstrap method (5000 resamples) was used to calculate confidence intervals for these effects, as it is robust to non-normal data distributions and provides reliable estimates even in smaller samples. For total effect, Social support improved QoL by 0.76 units; for direct effect, 81.6% of this improvement (0.62 units) occurred independently of FT reduction; for indirect effect, the remaining 18.4% (0.14 units) operated through reducing FT. The Bootstrap 95% CI for the indirect effect ([0.03–0.28]) excluded zero, confirming its significance. The 18.4% mediation proportion suggests that interventions targeting both social support and FT may amplify QoL improvements compared to isolated approaches.

Most independent factors associated with FT and QOL are immutable (eg, disease stage, treatment methods, time since diagnosis, income, and work status), social support remains a modifiable factor that medical professionals can guide and enhance.<sup>35</sup> Medical professionals can guide patients to actively seek social support, strengthen the utilization of social support, and educate family members and friends to provide social support for patients, which may significantly bolster patients' QOL and alleviate FT burdens.

## Strengths and Limitations

Our study has several other strengths including a very high response rate of 95.6%, thereby ensuring the representativeness of our study population among HCC patients at our institution. Furthermore, the provision of standardized instructions and face-to-face interactions during questionnaire completion facilitated high-quality data collection, with immediate post-collection scrutiny to rectify any omissions or errors promptly.

Conversely, our study has certain limitations. Being cross-sectional in nature, it fails to capture the evolving patient experiences over time, necessitating longitudinal investigations for a comprehensive understanding of patient trajectories. Moreover, our study overlooks the perspectives of caregivers concerning QOL, FT, and social support, crucial for a holistic comprehension of the survivorship journey.

## Conclusions

We found that unemployment, lower household income, treatment of HAIC or combination treatment, and lower social support were independently associated with higher FT. Lower FT was independently associated with better physical well-

being, emotional well-being, functional well-being, and additional concerns, except for social/family well-being. Social support was independently associated with social/family well-being, functional well-being, and additional concerns. Social support not only affected the QOL directly but also indirectly through FT. The interplay between social support, FT, and QOL offers insights to tailor interventions effectively, mitigating FT burdens, and enhancing QOL for HCC patients.

## Abbreviations

HCC, hepatocellular carcinoma; COST, The comprehensive score for financial toxicity; FACT-Hep, the Functional Assessment of Cancer Therapy-Hepatobiliary; FT, financial toxicity; HAIC, hepatic arterial infusion chemotherapy; IQRs, interquartile ranges; QOL, quality of life; SD, standard deviation; SEM, structural equation models.

## Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further information is available from Yaojun Zhang upon request.

## Ethics Approval Statement

This study was conducted according to the ethical guidelines of the 1975 Declaration of Helsinki. This research was approved by the institutional review board of Sun Yat-sen University Cancer Center (Approval number B2023-261-01). Informed consent was obtained from all subjects involved in the study.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no conflicts of interest in this work.

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