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Anxiety is a risk prognosis factor for hepatocellular carcinoma with portal vein tumor thrombus who underwent hepatic arterial infusion chemotherapy: a propensity score-matching cohort study

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Abstract

Background Increasing evidence indicates that psychological factors play a role in tumor progression. This study aims to explore the impact of anxiety disorder on the prognosis of hepatocellular carcinoma (HCC) patients with portal vein tumor thrombus (PVTT) who underwent hepatic arterial infusion chemotherapy (HAIC).

Methods A propensity score-matching cohort study was conducted in 68 HCC patients with PVTT who underwent HAIC between January 2020 and December 2023. The anxiety situation was evaluated using the Hamilton Anxiety Rating Scale before HAIC. The objective response rate, overall survival (OS), progression-free survival, and adverse events were compared between the different anxiety score groups. Using Cox proportional hazards models for univariate and multivariate analysis to explore the risk factors of OS.

Results No statistical difference was found in the tumor response, treatment-related adverse events, and PFS between the two groups before and after PSM. Compared with low anxiety scores patients, the OS of obvious anxiety patients was shorter (hazard ratio [HR] = 1.606; 95%CI: 0.868–2.973; $P = 0.116$). The univariate and multivariate analysis showed that BMI (HR = 1.174, 95%CI: 1.044–1.320; $P = 0.007$), high anxiety score (HR = 2.769, 95%CI: 1.289–5.947; $P = 0.007$), and serum ammonia (HR = 1.059; 95%CI: 1.032–1.086; $P < 0.001$) were independent risk factors of OS.

Conclusions Our study reveals that elevated anxiety scores in HCC patients with PVTT correlated with poor prognosis, indicating that it's a potential prognostic marker. The high anxiety score, BMI, and serum ammonia were independent risk factors of OS.

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Keywords Anxiety, Hepatocellular carcinoma, Hepatic artery infusion chemotherapy, Prognosis, Serum ammonia

Background

Portal vein tumor thrombus (PVTT) is a common complication in hepatocellular carcinoma (HCC) associated with poor prognosis and treatment challenges [1, 2]. While Western guidelines recommend sorafenib as the primary treatment for HCC with PVTT, Eastern countries offer more aggressive options, including surgery, radiotherapy, and transarterial chemoembolization [3, 4]. Recent advancements in surgical techniques, radiotherapy, and systemic therapies have expanded the treatment options and improved the prognosis of HCC patients with PVTT [5].

Recent studies have highlighted the significant prevalence of psychiatric disorders, particularly anxiety and depression, among HCC patients [6]. A large cohort study found that 18.6% of HCC patients had a psychiatric diagnosis after cancer diagnosis, with depression (58.3%) and anxiety (53.0%) being most common [7]. The prevalence of anxiety symptoms in hepatic cancer patients was estimated at 29.1%, while depression symptoms were found in 21.5% [8]. Interestingly, anxiety and depression were associated with increased overall survival rates in HCC patients [9]. However, anxiety disorders significantly impact quality of life, particularly causing insomnia [10]. These findings underscore the importance of early evaluation and treatment of psychological disorders in HCC patients.

Comprehensive education and care programs can effectively reduce anxiety and depression, improve quality of life, and prolong survival in HCC patients who underwent surgical resection [11]. Psycho-oncological interventions have shown promise in reducing psychological burden and improving quality of life for HCC patients [12]. The COVID-19 pandemic has further impacted mental health in HCC patients, with chronic disease, gender, and age being key predictors of depression, anxiety, and stress levels [13]. However, the impact of anxiety disorder on the survival of HCC patients with PVTT who underwent hepatic arterial infusion chemotherapy (HAIC) remain unknown.

Therefore, this study aims to explore the impact of anxiety disorder on the postoperative prognosis of HCC patients with PVTT who underwent HAIC. Unlike previous studies, we conducted a systematic evaluation of anxiety status and conducted in-depth analysis of its relationship with anxiety levels and disease progression. The propensity score matching (PSM) model was used to balance the bias of other factors for anxiety disorders. Through survival analysis, this study attempts to reveal the impact of anxiety status on the prognosis of HCC patients with PVTT who underwent HAIC.

Methods

Patients selection

This is a retrospective cohort study to evaluate the effect of anxiety disorder on tumor response and survival of HCC patients complicated with portal vein tumor thrombus after HAIC. The subjects were HCC patients with PVTT who received HAIC treatment in Chongqing University Jiangjin Hospital from January 2020 to December 2023. The Cheng's Classification was used to classify the extent of HCC associated with PVTT (Type I tumor thrombus invades the portal vein branch of liver lobe or liver segment; Type II tumor thrombus invades the left or right branch of the portal vein; Type III tumor thrombus invades the main portal vein; Type IV tumor thrombus invades the superior mesenteric vein) [14]. This study adhered to the guidelines of the Declaration of Helsinki and was approved by the Institutional Review Board of Chongqing University Jiangjin Hospital (KY20240812-001). This study was registered in the Chinese Clinical Trial Registry (ChiCTR2500095127).

The inclusion criteria were as follows: (1) age over 18 years; (2) patients who had been pathologically or clinically diagnosed with HCC; (3) complete clinical data and medical history; (4) patients has received a primary school education or above to ensure the accuracy of the questionnaire evaluation; (5) All patients and their families signed informed consent prior to treatment to allow for the retrospective review and reporting of medical records.

The exclusion criteria were as follows: (1) previous history of mental illness or autoimmune disease; (2) with other malignant tumors; (3) severe cardiovascular, cerebrovascular, pulmonary, liver, renal diseases or other organ failure; (4) follow up for less than 3 months or only baseline data available.

Data collection

General clinical information of the included patients was collected from an electronic medical record system, including gender, age, chronic disease, viability, smoking and drinking history, anxiety situation, liver cirrhosis history, and tumor condition. Each patient participated in consistent follow-ups, either through outpatient visits or phone calls. These follow-ups were scheduled to occur monthly following treatment. Survival data were determined on December 31, 2024.

The progression-free survival (PFS) was defined as the interval from the start of HAIC until tumor progression or death from any cause. The overall survival (OS) was measured from the time of initial HAIC treatment to any cause of death. The tumor response after 6 weeks from

initial treatment was based on the modified Response Evaluation Criteria in Solid Tumors (mRECIST) [15]. The treatment related adverse events were classified in accordance with the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE version 5.0) [16].

Anxiety scale

The anxiety status of the included patients was evaluated using the Hamilton Anxiety Scale (HAMA) [17]. The HAMA consist of psychological and somatic symptoms, including 14 elements. Psychological symptoms include anxious mood, tension, fear, insomnia, reduced intellect, depressed mood, and behavior at interview. Somatic symptoms include muscular, sensory, cardiovascular, respiratory, gastrointestinal, genitourinary, and autonomic nerve. Each item is rated on a scale of 0 (not present) to 4 (severe), where a total score more than 17 is defined as a high anxiety score which indicating obvious anxiety [18]. If the psychological symptoms score is greater than the somatic symptoms score, it is considered psychic anxiety, otherwise it's considered as somatic anxiety. Perform HAMA scoring before HAIC for each patent, and all patients received routine psychological counseling after assessing anxiety. All assessments were independently completed by 2 trained assessors.

Propensity score matching

To balance the baseline feature bias between the patients with different anxiety scores, one-to-one propensity score matching was conducted. Propensity scores for all patients were calculated using logistic regression analysis, taking into account baseline characteristics such as gender, age, body mass index (BMI), chronic disease, smoking history, and drinking history. The matching technique employed was the one-to-one nearest-neighbor approach with an optimal caliper of 0.05 [19].

Statistics analysis

Statistical analysis was performed using SPSS 23.0 and STATA/MP 16.0. For continuous data, either the Student's t-test or the Mann-Whitney U test was employed for comparisons. Categorical data were analyzed through chi-squared tests or Fisher's exact test. Survival data were determined using the Kaplan-Meier method and subsequently assessed using log-rank tests. Using Cox proportional hazards models for univariate and multivariate analysis to explore the risk factors of OS. A two-tailed *P*value under 0.05 was considered to indicate statistical significance.

Results

Baseline characteristics

Between January 2020 and December 2023, a total of 89 eligible patients with HCC and PVTT who received HAIC treatment were reviewed. After screening based on the inclusion and exclusion criteria, 68 patients for subsequent analysis were finally determined: 37 patients in the low anxiety scores group and 31 patients in the high anxiety scores group. The patients in the low anxiety scores group mainly were somatic anxiety, while the patients in the high anxiety scores group mainly were psychogenic anxiety ($P < 0.001$). To balance the baseline feature bias between the patients with different anxiety scores, gender, age, BMI, chronic disease, smoking history, and drinking history were considered as covariates for propensity scores. After PSM, 29 pairs of patients were evaluated (Fig. 1). The equilibrium test and kernel density map revealed that the differential baseline characteristics of the two groups after PSM were balanced and the matching effect was good (Fig. 2). Table 1 provides a detailed comparison of the baseline characteristics between the two groups before and after PSM.

Tumor response and safety

All the patients completed the follow-up as scheduled. As of the follow-up time, 15 patients died (40.5%) in the low anxiety scores group, and 18 patients (62.5%) died in the high anxiety scores group. A total of 25 patients (67.6%) experienced tumor progression in the low anxiety scores group, and 22 patients (71.0%) experienced tumor progression in the high anxiety scores group. No statistical differences were found in the death rate and disease progression rate between the two groups before and after PSM.

After 6 weeks from initial HAIC treatment, 2 patients achieved complete response, 24 patients achieved partial response, 7 patients kept stable disease, and 4 patients experienced progressive disease in the low anxiety scores group. The objective response rate (ORR) was 70.3% (26/37) and the disease control rate (DCR) was 89.2% (33/37) in the low anxiety scores group. And, 1 patients achieved complete response, 20 patients achieved partial response, 7 patients kept stable disease, and 3 patients experienced progressive disease in the high anxiety scores group. The ORR was 67.7% (21/31) and the DCR was 90.3% (28/31) in the high anxiety scores group. No statistical difference was found in the tumor response between the two groups before and after PSM.

None of the patients discontinued the treatment because of treatment related adverse events. The incidence of treatment related adverse events in the low anxiety scores group was 43.2% (16/37) and that was 25.8% (8/31) in the high anxiety scores group. No statistical

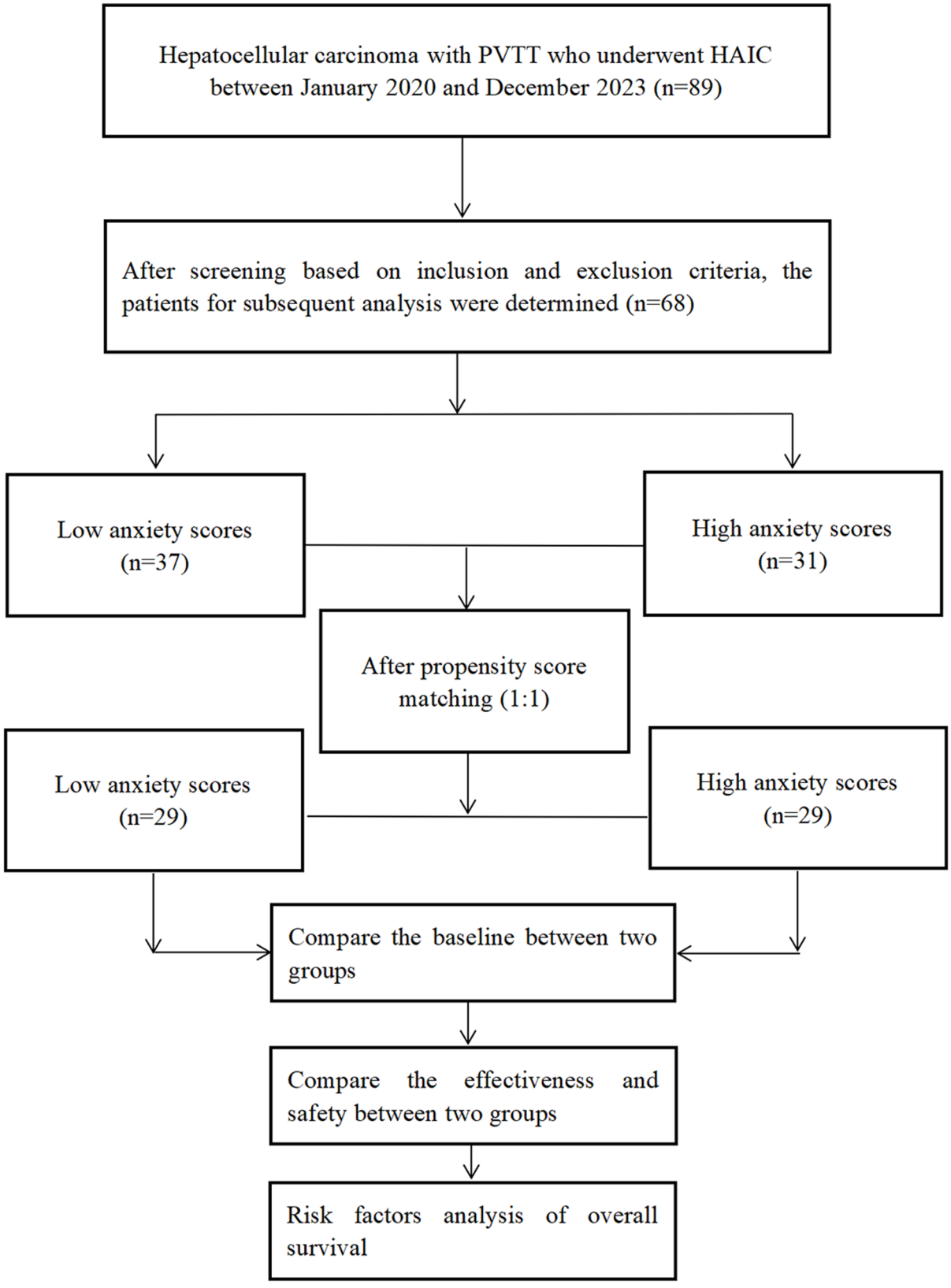

Fig. 1 Research flowchart

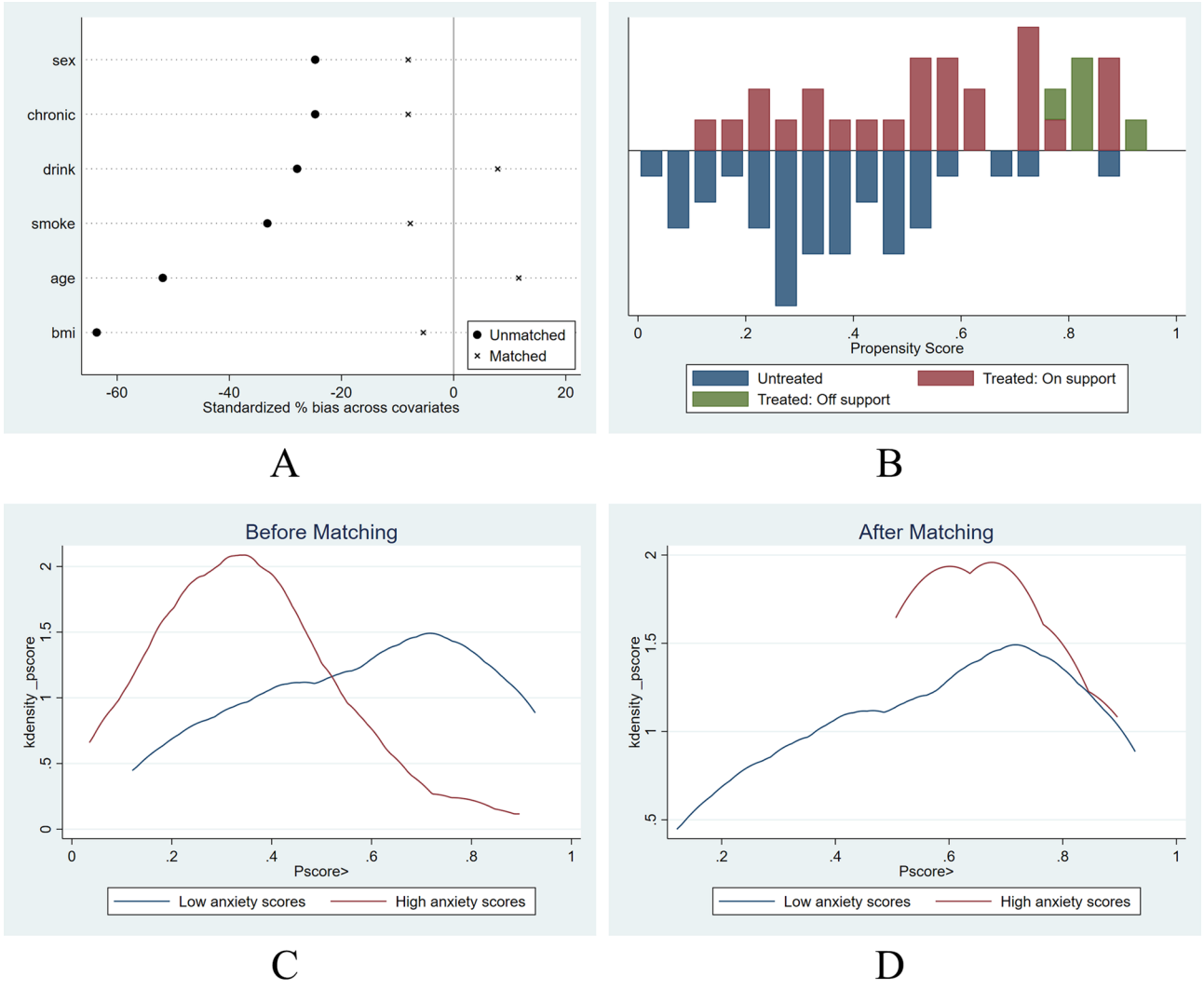

Fig. 2 The results of propensity score matching; (**A**) The standardized deviation of difference features decreased significantly after matching; (**B**) After matching, the two groups have a preferable common value range; (**C**) The kernel density map before propensity score matching; (**D**) The kernel density map after propensity score matching. BMI, body mass index

difference was found in the treatment related adverse events between the two groups before and after PSM.

Table 2 provides a detailed comparison of the tumor response and safety of the two groups before and after PSM.

Survival analysis

Before PSM, the median PFS in the low anxiety scores group was 8.1 months, whereas it was 6.1 months in the high anxiety scores group (hazard ratio [HR] = 1.280; 95%CI: 0.720–2.274; $P = 0.394$; Fig. 3A). The median OS in the low anxiety scores group was not calculated due to less than half of the deaths, whereas it was 8.4 months in the high anxiety scores group (HR = 2.470; 95%CI: 1.223–4.987; $P = 0.009$; Fig. 3B). After PSM, the median PFS in the low anxiety scores group was 9.5 months, whereas it was 5.7 months in the high anxiety scores group (HR = 1.606; 95%CI: 0.868–2.973; $P = 0.116$; Fig. 3C). The median OS in the low anxiety scores group also was not calculated due to less than half of the deaths, whereas it was 8.4 months in the high anxiety scores group (HR = 2.086; 95%CI: 1.010–4.311; $P = 0.034$; Fig. 3D).

Risk factor analysis of OS

The result of the univariate Cox proportional hazards models analysis revealed that BMI, anxious type, high anxiety score, albumin-bilirubin ratio, and serum ammonia were the risk factors of OS for HCC patients with PVTT who initially underwent HAIC. The factors with $P < 0.1$ in univariate analysis were included into multivariate Cox proportional hazards models analysis. The result showed that BMI (HR = 1.174, 95%CI: 1.044–1.320; $P = 0.007$), high anxiety score (HR = 2.769, 95%CI: 1.289–5.947; $P = 0.007$), and serum ammonia (HR = 1.059;

Table 1 The baseline characteristics of hepatocellular carcinoma with portal vein tumor thrombus underwent HAIC

Variables	Before PSM			After PSM		
	Low anxiety scores ($n=37$)	High anxiety scores ($n=31$)	*P*	Low anxiety scores ($n=29$)	High anxiety scores ($n=29$)	*P*
Gender, n (%)			0.226			1.000
male	21 (56.8)	22 (71.0)		20 (69.0)	20 (69.0)	
female	16 (43.2)	9 (29.0)		9 (31.0)	9 (31.0)	
Age, Mean ± SD	57.5 ± 11.7	62.3 ± 9.0	0.070	62.5 ± 9.3	62.3 ± 9.2	0.932
BMI(kg/m^2), Mean ± SD	21.3 ± 2.6	22.9 ± 3.1	0.019*	22.8 ± 3.2	22.7 ± 2.8	0.839
Chronic disease, n (%)	23 (62.2)	23 (74.2)	0.291	20 (69.0)	21 (72.4)	0.773
Drinking history, n (%)	15 (40.5)	15 (48.4)	0.516	13 (44.8)	13 (44.8)	1.000
Smoking history, n (%)	18 (48.6)	21 (67.7)	0.113	18 (62.1)	19 (65.5)	0.785
Anxious type, n (%)			<0.001*			<0.001*
psychic anxiety	7 (18.9)	20 (64.5)		5 (17.2)	19 (65.5)	
somatic anxiety	30 (81.1)	11 (35.5)		24 (82.8)	10 (34.5)	
Anxiety score, Median (Q1, Q3)	14 (13, 15)	19 (18.5, 20)	<0.001*	15 (13, 16)	19 (18, 20)	<0.001*
Viral hepatitis, n (%)	13 (35.1)	17 (54.8)	0.103	12 (41.4)	15 (51.7)	0.430
Cirrhosis, n (%)	25 (67.6)	17 (54.8)	0.282	18 (62.1)	16 (55.2)	0.594
ECOG score, n (%)			0.988			0.570
0	25 (67.6)	21 (67.7)		21 (72.4)	19 (65.5)	
1	12 (32.4)	10 (32.3)		8 (27.6)	10 (34.5)	
Cheng's classification, n (%)			0.866			0.764
I-II	28 (75.8)	24 (77.4)		21 (72.4)	22 (75.9)	
III-IV	9 (24.3)	7 (22.6)		8 (27.6)	7 (24.1)	
Child-Pugh class, n (%)			0.341			0.291
A(5–6)	16 (43.2)	17 (54.8)		11 (37.9)	15 (51.7)	
B(7–9)	21 (56.8)	14 (45.2)		18 (62.1)	14 (48.3)	
ALBI, n (%)			0.632			0.286
1(≤-2.60)	23 (62.2)	21 (67.7)		15 (51.7)	19 (65.5)	
2(-2.60~-1.39)	14 (37.8)	10 (32.3)		14 (48.3)	10 (34.5)	
Tumor>5 cm, n (%)	26 (70.3)	21 (67.7)	0.822	23 (79.3)	19 (65.5)	0.240
Number of tumors>3, n (%)	25 (67.6)	21 (67.7)	0.988	17 (58.6)	21 (72.4)	0.269
Tumor capsule, n (%)	11 (29.7)	7 (22.6)	0.506	10 (34.5)	6 (20.7)	0.240
AFP>400, n (%)	19 (51.4)	19 (61.3)	0.411	16 (55.2)	19 (65.5)	0.421
TB(umol/L), Median (Q1, Q3)	15.9 (11.3, 18.9)	14.9 (10.6, 20.8)	0.868	12.5 (11.1, 20.5)	14.6 (10.5, 20.8)	0.852
Albumin(g/L), Median (Q1, Q3)	36.1 (32.8. 42.5)	36.2 (31.9, 39.9)	0.805	33.4 (31.3, 36.1)	36.2 (31.4, 39.5)	0.150
ALT(U/L), Median (Q1, Q3)	45 (42, 58)	37 (27, 69)	0.241	44 (42, 50)	37 (26, 72)	0.213
AST(U/L), Median (Q1, Q3)	68 (36, 91)	76 (54.5, 111.5)	0.187	68 (48, 86)	76 (57, 114)	0.756
Serum Ammonia, Median (Q1, Q3)	54 (38, 65)	57 (47.5, 68)	0.166	54 (40, 61)	57 (49, 69)	0.175

HAIC, hepatic artery infusion chemotherapy; PSM, Propensity score matching; BMI, Body Mass Index; ALBI, Albumin-bilirubin; TB, Total bilirubin; ALT, Alanine asninotrasferase; AST, Aspartic transaminase; AFP, Alpha-fetoprotein; SD, Standard deviations

95%CI: 1.032–1.086; $P<0.001$) were independent risk factors of OS. The comprehensive findings were presented in Table 3.

Discussion

Most HCC patients with PVTT endure different levels of anxiety, which can not only accelerate tumor progression but also significantly impact their health-related quality of life [6]. The impact of anxiety situation on the survival of HCC patients with PVTT remains unknown. The important finding of this study was that nearly half (31/68, 45.6%) of HCC patients with PVTT had anxiety scale scores greater than 17 points, which indicated obvious anxiety. The main clinical manifestations of obvious anxiety patients were psychological anxiety symptoms. Compared with low anxiety scores patients, the overall survival of obvious anxiety patients was shorter. To accurately explore the impact of anxiety factors on curative effects, this study used PSM to balance the relevant factors affecting anxiety, such as gender, age, BMI, chronic disease, smoking history, and drinking history. The PSM results showed that the differences in the relevant factors affecting anxiety between the two groups were significantly reduced after matching. After PSM, there was still a statistically significant difference in overall survival between the two groups. The risk factors

Table 2 Comparison of effectiveness and safety between the groups

Variables	Before PSM			After PSM		
	Low anxiety scores (*n* = 37)	High anxiety scores (*n* = 31)	*P*	Low anxiety scores (*n* = 29)	High anxiety scores (*n* = 29)	*P*
Tumor response			0.957			0.114
complete response, n (%)	2 (5.4)	1 (3.2)		2 (6.9)	1 (3.4)	
partial response, n (%)	24 (64.9)	20 (64.5)		22 (75.9)	18 (62.1)	
stable disease, n (%)	7 (18.9)	7 (22.6)		1 (3.4)	7 (24.1)	
progressive disease, n (%)	4 (10.8)	3 (9.7)		4 (13.8)	3 (10.4)	
ORR, n (%)	26 (70.3)	21 (67.7)	0.822	24 (82.8)	19 (65.5)	0.134
DCR, n (%)	33 (89.2)	28 (90.3)	0.878	25 (86.2)	26 (89.7)	0.686
Death, n(%)	15 (40.5)	18 (62.5)	0.150	14 (48.3)	17 (58.6)	0.430
Disease progression, n(%)	25 (67.6)	22 (71.0)	0.762	20 (69.0)	22 (75.9)	0.557
Treatment related adverse events, n(%)	16 (43.2)	8 (25.8)	0.134	4 (13.8)	7 (24.1)	0.315

PSM, Propensity score matching. ORR, Objective response rate; DCR, Disease control rate

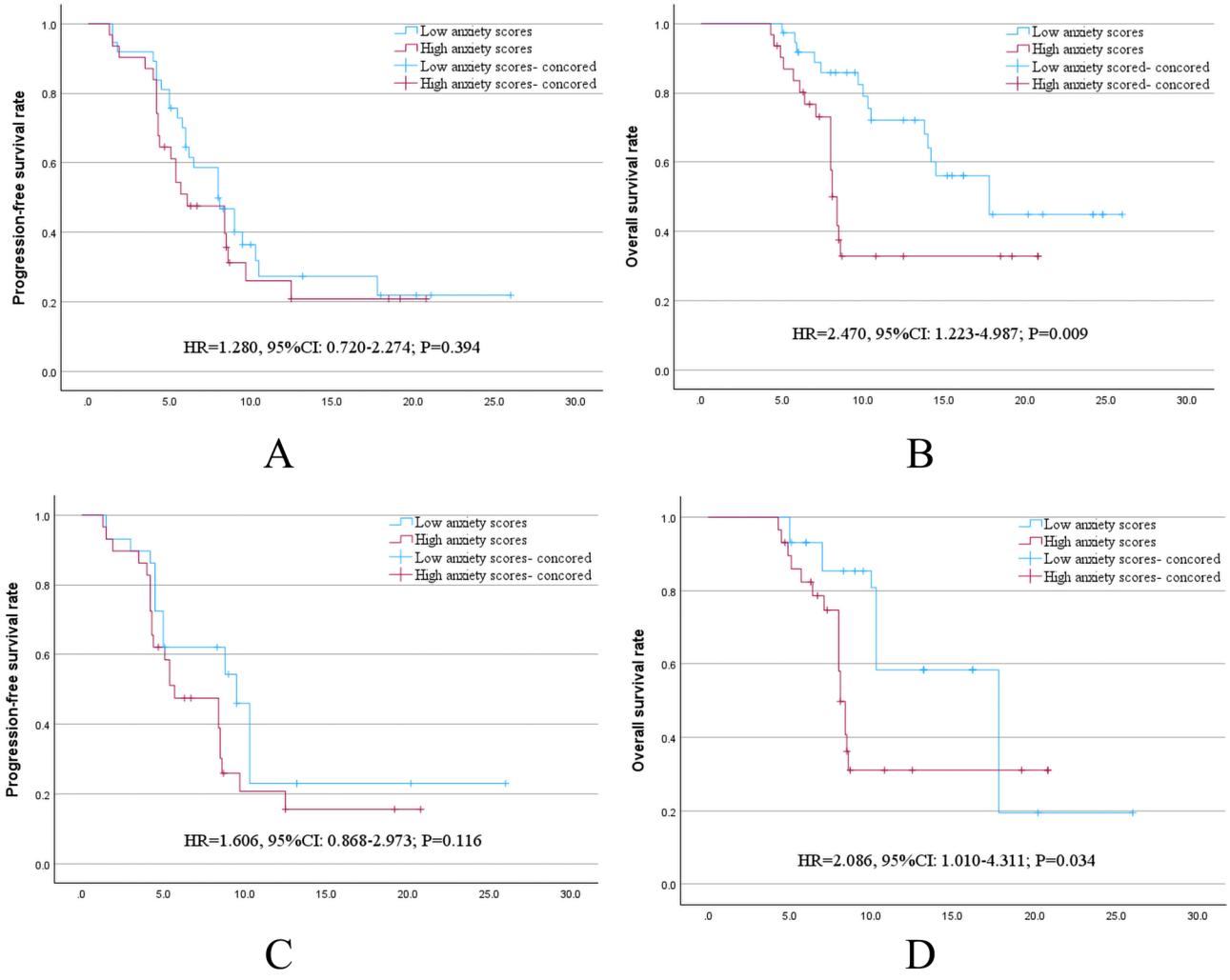

Fig. 3 Kaplan–Meier curves of survival outcome between two groups; (**A**) Comparison of progression free survival between the two groups before propensity score matching; (**B**) Comparison of overall survival between the two groups before propensity score matching; (**C**) Comparison of progression free survival between the two groups after propensity score matching; (**D**) Comparison of overall survival between the two groups after propensity score matching. HR, hazard ratio

Table 3 Risk factors analysis of overall survival for hepatocellular carcinoma with portal vein tumor thrombus underwent hepatic artery infusion chemotherapy

	Univariate analysis				Multivariate regression analysis			
	Hazard ratio (HR)	95%CI		*P* value	Hazard ratio (HR)	95%CI		*P* value
		lower	upper			lower	upper	
Gender	1.481	0.703	3.120	0.301				
Age	1.012	0.981	1.044	0.439				
BMI	1.180	1.051	1.325	0.005#	1.174	1.044	1.320	0.007*
Chronic disease	0.920	0.445	1.901	0.821				
Drinking history	0.899	0.451	1.795	0.763				
Smoking history	1.563	0.767	3.186	0.219				
Anxious type	2.605	1.274	5.327	0.009#	1.516	0.624	3.685	0.359
Anxiety score>17	2.470	1.223	4.987	0.012#	2.769	1.289	5.947	0.007*
Viral hepatitis	1.253	0.633	2.482	0.518				
Cirrhosis	1.150	0.555	2.383	0.706				
ECOG score	1.190	0.584	2.424	0.632				
PVTT classification	0.679	0.293	1.572	0.366				
Child-Pugh class	1.538	0.764	3.096	0.227				
ALBI	2.065	1.038	4.105	0.039#	2.113	0.807	5.532	0.127
Tumor>5 cm	1.303	0.605	2.809	0.499				
Tumor number>3	1.086	0.516	2.285	0.827				
Tumor capsule	0.665	0.287	1.537	0.339				
AFP>400	1.216	0.609	2.428	0.580				
TB	1.028	0.988	1.070	0.172				
Albumin	0.938	0.870	1.012	0.098#	1.008	0.920	1.105	0.863
ALT	1.003	0.989	1.016	0.696				
AST	0.996	0.988	1.004	0.351				
Serum Ammonia	1.048	1.024	1.072	<0.001#	1.059	1.032	1.086	<0.001*

BMI, Body Mass Index; PVTT, Portal vein tumor thrombus; ALBI, Albumin-bilirubin; TB, Total bilirubin; ALT, Alanine asninotrasferase; AST, Aspartic transaminase; AFP, Alpha-fetoprotein; HR, Hazard Ratio

Variables with a *p*-value less than 0.1 from the univariate analysis are included into the multivariate regression analysis

* The *p*-value is statistically significant

analysis of OS showed that anxious type and anxiety score were risk factors. It indicated that psychological anxiety symptoms may be associated with poor prognosis. It may increase overall survival time by improving psychological anxiety symptoms and reducing anxiety scores. Given the correlation between anxiety and prognosis, especially psychological anxiety, it is recommended to implement comprehensive psycho-oncological interventions for HCC patients with PVTT who underwent HAIC, including mindfulness training, meditation, and moderate exercise. Previous studies have shown that the psycho-oncological interventions can reduce anxiety levels and may prolong survival [11, 20]. In the future, randomized controlled trials need to be conducted to verify its effectiveness. Besides, there is a problem worth thinking about, which is how anxiety affects OS when no difference is noted in response rates or PFS. Although anxiety does not significantly affect tumor response or PFS, it may aggravate systemic inflammatory response through neuroendocrine pathways (such as activation of the thalamus pituitary adrenal axis), thereby accelerating liver failure or multiple organ dysfunction [21]. In addition, patients with anxiety may have shorter survival time due to reduced treatment compliance or immunosuppression. More research is needed to confirm these hypotheses.

The other important finding of this study was that serum ammonia was an independent risk factor for OS. Although the serum ammonia was not directly related to anxiety scores, a high level of serum ammonia was associated with poor prognosis. A retrospective cohort study reported that 21.3% of cancer patients exhibited hyperammonemia on admission [22]. These patients had an average survival period of 41.6 days and a significant association with liver metastases. Increased ammonia levels correlate with higher hepatocellular carcinoma occurrence in cirrhotic individuals, and hyperammonemia in HCC patients predicts poorer survival [23, 24]. The potential mechanism is that elevated ammonia levels coincide with increased glutaminolysis and β-catenin-mediated ammonia production, which promote cancer stem cell properties and activate mTORC1 signaling [25]. Some studies have confirmed that ammonia's stimulation of lipogenesis via sterol regulatory element-binding

protein activation further contributes to enhanced tumor growth [26]. In addition, hyperammonemia is closely related to acute-on-chronic liver failure and may directly lead to multiple organ dysfunction, and baseline ammonia levels are associated with 30-day mortality and liver-related complications [27, 28]. Therefore, the correlation between ammonia metabolism and the occurrence, development and prognosis of liver cancer has attracted more and more attention. Our study also confirmed that serum ammonia was an independent risk factor for HCC patients with PVTT undergoing HAIC treatment. Monitoring fluctuations in serum ammonia levels in HCC patients throughout their clinical treatment is crucial.

The highlights of this study include the following points: (1) The correlation between anxiety situation and prognosis of liver cancer who underwent HAIC therapy was studied; (2) Propensity score matching was conducted to balance the relevant factors affecting anxiety between the two groups and enhance the evidence strength of the results; (3) BMI, high anxiety score, and serum ammonia were independent risk factors of OS for HCC patients with PVTT undergoing HAIC treatment.

This article also has some limitations. Due to its retrospective design and the development of new technologies, despite of propensity score matching, the study had a limited sample size and brief follow-up duration. Consequently, randomized controlled trials involving larger groups and extended follow-up periods are needed to confirm these results. In addition, the diagnosis of anxiety disorder was determined by HAMA scoring. The somatic symptoms, such as gastrointestinal, are easily confused with clinical symptoms of liver cancer. It leads to a generally high score for HCC patients. Therefore, some researches considering more anxiety scales are needed to confirm the results of this study. Besides, in this study, traditional tumor factors such as tumor size, tumor number, and AFP levels did not show significant prognostic value, which may be related to the small sample size and high tumor heterogeneity in PVTT patients. Meanwhile, all included patients received HAIC combined with TKI and ICI, whose standardized treatment may partially offset the differential effects of tumor characteristics. More studies are needed to explore the impact of tumor characteristics on prognosis.

Conclusion

Our study reveals that elevated anxiety scores in HCC patients with PVTT correlated with poor prognosis, indicating that it's a potential prognostic marker. The high anxiety score, BMI, and serum ammonia were independent risk factors of OS.

Abbreviations

BMI	Body mass index
DCR	Disease control rate
HAIC	Hepatic arterial infusion chemotherapy
HAMA	Hamilton Anxiety Scale
HCC	Hepatocellular carcinoma
HR	Hazard ratio
ORR	Objective response rate
OS	Overall survival
PFS	Progression-free survival
PSM	Propensity score matching
PVTT	Portal vein tumor thrombus

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Author contributions

All authors contributed to the study conception and design. Material preparation was performed by Hua-guo Feng and Ling Lu. Data collection and analysis were performed by Shuang-quan Liu, Jiu-ling Zheng, and Yan-han Liu. The first draft of the manuscript was written by Hao-yang Tan and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

All data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

This study adhered to the guidelines of the Declaration of Helsinki and was approved by the Institutional Review Board of Chongqing University Jiangjin Hospital (KY20240812-001). This study was registered in the Chinese Clinical Trial Registry (ChiCTR2500095127). The patient's informed consent form before treatment complied with the requirements of the Institutional Review Committee of Chongqing University Jiangjin Hospital.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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