Journal of Hepatocellular Carcinoma

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Factor Analysis of the Effect of Hepatitis B-Related Liver Cancer Treatment Efficacy

Shuai-Wei Liu[1,2,*], Yan Zhou[1,2,*], Xue Yan Feng[1,2,*], Long Hai[1,2], Wan-Long Ma[1,2], Li Na Ma[1,2], Xiang-Chun Ding[1,2], Xia Luo[1,2]

[1]Department of Infectious Diseases, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, 750004, People's Republic of China; [2]Infectious Disease Clinical Research Center of Ningxia, Yinchuan, Ningxia, 750004, People's Republic of China

*These authors contributed equally to this work

Correspondence: Xia Luo; Xiang-Chun Ding, Email 516723708@qq.com; 13619511768@163.com

Background and Aim: Drug-eluting bead transcatheter arterial chemoembolization (DEB-TACE) is commonly used to treat unresectable hepatitis B-related primary liver cancer, but its therapeutic effect is influenced by various factors. This study analyzes the clinical factors related to the overall survival (OS) and progression-free survival (PFS) of patients with hepatitis B-related hepatocellular carcinoma (HCC) treated with DEB-TACE to provide reference data for individualized treatment.

Methods: In this retrospective study, 128 patients with hepatitis B-related primary liver cancer who received DEB-TACE treatment and being followed up (range of follow-up: 4–39 months) were included. The relationships between clinical characteristics, tumor markers, inflammatory factors, blood biochemical parameters, and OS and PFS were analyzed. Statistical methods, including Kaplan-Meier analysis, the Log rank test, and Cox regression analysis, were used to evaluate independent factors affecting patient prognosis.

Results: Factors such as tumor size, tumor number, vascular invasion, extrahepatic metastasis, stage (CNLC and BCLC), and alpha-fetoprotein (AFP) level significantly affected OS and PFS ($P < 0.05$). In particular, patients with a tumor diameter >5 cm, multiple tumors, portal vein invasion, and extrahepatic metastasis had significantly shorter OS and PFS. Preoperative inflammatory factors (eg, white blood cell count, absolute neutrophil count, procalcitonin, and C-reactive protein) and blood biochemical parameters (eg, aspartate aminotransferase (AST), total bilirubin (TBIL), albumin (ALB)) were closely related to patient prognosis. Multivariate Cox regression analysis revealed that age, Child-Pugh score, BCLC stage, TBIL, ALB, CRP, and AFP were independent prognostic factors for OS.

Conclusion: This study highlights the significance of tumor clinical characteristics and preoperative inflammatory factors in predicting the prognosis of patients with hepatitis B-related HCC treated with DEB-TACE. By comprehensively evaluating these clinical and biological markers, more personalized treatment plans can be developed for liver cancer patients, thereby improving treatment outcomes and survival rates.

Keywords: DEB-TACE, HBV-related hepatocellular carcinoma, overall survival, progression-free survival, prognostic factors

Introduction

Primary liver cancer, commonly referred to as hepatocellular carcinoma (HCC), ranks among the most prevalent and lethal malignancies worldwide. According to the Global Cancer Report of 2022, while the incidence of liver cancer is lower than that of breast, lung, stomach, and colorectal cancers, it has the second highest mortality rate globally.[1] In China, about 400,000 new cases are reported annually, accounting for nearly 50% of new cases worldwide, with a five-year survival rate of only 12.1–14.1%, significantly lower than that of other cancer types.[2] Hepatitis B virus (HBV) infection is the leading cause of primary liver cancer, particularly in Asian countries, where HBV-related cases comprise up to 60%.[3] Despite advancements in early screening and therapeutic technologies that have improved the management of liver cancer, the disease often progresses insidiously with subtle early symptoms. Consequently, the majority of patients are diagnosed at intermediate or advanced stages, by which

Received: 25 January 2025
Accepted: 15 May 2025
Published: 5 June 2025

time the optimal window for surgical intervention is frequently missed. Surgical resection remains the first-line treatment for liver cancer; however, about 70% of patients are not candidates for curative surgery at the time of diagnosis.[4] For patients with unresectable liver cancer, selecting effective local treatment strategies to enhance survival outcomes poses a considerable challenge. Transcatheter arterial chemoembolization (TACE), a commonly employed local treatment modality, is extensively used in such cases. TACE combines localized chemotherapy with vascular embolization by injecting microspheres containing chemotherapeutic agents and embolic substances into the tumor-feeding artery, thereby achieving a dual therapeutic effect and demonstrating promising efficacy.[5]

In recent years, drug-eluting bead transcatheter arterial chemoembolization (DEB-TACE), an advanced version of TACE, has become an important treatment modality for unresectable liver cancer patients owing to its relatively high drug adsorption capacity and slow, sustained drug release characteristics. DEB-TACE enables more precise delivery of chemotherapeutic agents while minimizing injury to healthy liver tissue, thereby enhancing both the safety and therapeutic efficacy of the intervention.[6] Despite its proven clinical effectiveness, the determinants of DEB-TACE's short-term efficacy remain insufficiently understood, particularly in patients with hepatitis B-related hepatocellular carcinoma. To address this gap, the present study retrospectively analyzed clinical data from 128 patients diagnosed with hepatitis B-associated primary liver cancer who underwent DEB-TACE. The objective was to identify the key factors influencing short-term treatment outcomes, thereby offering a theoretical foundation for clinical decision-making and supporting the development of individualized therapeutic strategies.

Materials and Methods

Study Design and Subjects

In this retrospective analysis, 128 patients with hepatitis B-related primary liver cancer who underwent DEB-TACE treatment at the General Hospital of Ningxia Medical University between September 2019 and March 2023 were included. All patients met the following inclusion criteria:[7] (1) diagnosis of primary liver cancer confirmed by imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI); (2) history of HBV infection or positive HBV DNA test; (3) age above 18 years; (4) first-time diagnosis of primary liver cancer with TACE administered via catheter; (5) presence of measurable lesions; (6) CNLC stage IIb, IIIa, or IIIb, Child-Pugh class A or B, and an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2; (7) eligibility for surgical or ablative treatments that were not undertaken due to advanced age, severe cirrhosis, or similar factors in CNLC stage I or IIa cases; (8) incomplete obstruction of the main portal vein or, if completely obstructed, presence of compensatory intrahepatic collateral circulation; (9) informed consent obtained from patients and their families; and (10) normal mental status with the ability to cooperate with treatment and follow-up procedures. Exclusion criteria were: (1) age over 80 years; (2) extensive liver cancer metastasis rendering TACE unfeasible; (3) severe coagulation disorders; (4) serious infections; (5) coexistence of other malignancies or multi-organ dysfunction; and (6) history of prior antitumor therapy. This retrospective cohort comprised 107 male and 21 female patients, with a mean age of 56.06 ±10.33 years. The study was approved by the Medical Ethics Committee of General Hospital of Ningxia Medical University (approval number: KYLL-2025-0039).

Observation Indicators

Comprehensive data were collected for all patients, encompassing tumor characteristics (including tumor diameter, number, distribution, alpha-fetoprotein levels, CNLC stage, BCLC stage, presence of lymph node metastasis, major vascular invasion, and liver cancer metastasis), comorbid conditions (such as cirrhosis, hypertension, diabetes, and coronary heart disease), postoperative embolism syndrome manifestations (including fever, nausea, vomiting, abdominal pain, and anorexia), as well as preoperative biochemical parameters (transaminases, bilirubin, albumin, creatinine, blood urea nitrogen, and cholinesterase). Additionally, routine blood tests, coagulation profiles, inflammatory markers, and HBV DNA levels were documented.

Surgical Procedure

All surgeries were performed in the digital subtraction angiography room. Preoperative liver cancer patients were evaluated for tumor status through upper abdominal CT or MRI based on the Guidelines for the diagnosis and treatment of primary liver cancer.[8] Following anesthesia, standard disinfection procedures were conducted, and the femoral artery was punctured using the Seldinger technique, after which a 5F sheath was introduced. Under X-ray fluoroscopic guidance, a catheter was super-selectively advanced to the celiac trunk artery for angiography to identify the tumor's arterial blood supply and any accessory hepatic arteries. Subsequently, a microcatheter was used to embolize the tumor's feeding arteries.[9] In the DEB-TACE group, DC® drug-eluting microspheres (BioCompatibles, UK) with diameters of 100–300 μm or 300–500 μm served as both drug carriers and embolic agents. These microspheres were loaded with idarubicin hydrochloride (10 mg, Nanjing Pharmaceutical Co., Ltd., batch number: 2404071) and mixed with a high-concentration contrast agent at ratios of 1:1, 1:1.1, or 1:1.2. The resulting mixture of embolic agent and chemotherapeutic drug was then pulse-injected into the tumor's feeding vessels via the microcatheter. The embolization endpoint was the complete disappearance of tumor staining on angiography. After surgery, the microcatheter was removed, the wound was compressed, hemostasis was achieved, and the wound was bandaged.

Follow-up, Observation, and Evaluation Indicators

Follow-up was conducted over the telephone or by reviewing the outpatient reexamination medical records of the patients to understand the recurrence and survival status of the patients. One month postoperatively, patients were followed up at intervals of 2–3 months, with patient death defined as the endpoint of follow-up; all surviving patients were followed until March 2023.

The patients underwent enhanced CT or MRI of the abdomen every 1–3 months after the surgery to assess treatment efficacy. The efficacy was assessed according to the modified Response Evaluation Criteria in Solid Tumors (mRECIST): (1) Progression-free survival (PFS): the time from randomization (or start of treatment in single-arm trials) to tumor progression or death due to any other cause (whichever occurs first). (2) Overall survival (OS): the time from randomization (or start of treatment in single-arm trials) to death due to any cause.[10]

Statistical Analysis

All statistical analyses were performed using SPSS version 25.0. Continuous variables were expressed as mean ±standard deviation ($\overline{X} \pm s$), and comparisons between groups were conducted using either the independent samples *t*-test or the Mann–Whitney *U*-test, depending on data distribution. Categorical variables were compared using the Chi-square test. Survival curves were constructed using the Kaplan-Meier method, and the Log rank test was employed to assess the influence of various clinical characteristics on the OS and PFS. The proportional hazards assumption for the Cox regression model was evaluated using the Schoenfeld residual test (global test p-value = 0.25), and Kaplan-Meier curves were observed to not intersect, supporting model validity. Linearity between continuous variables and the log hazard was confirmed through Martingale residual plots. Accordingly, Cox proportional hazards regression analysis was applied. Statistical significance was defined as a two-sided P-value of less than 0.05.

Results

Multiple Tumors and Vascular Invasion Reduce Patient Prognosis

In this study, 128 patients diagnosed with hepatitis B virus-related hepatocellular carcinoma (HBV-HCC) were included, comprising 107 males (83.5%) and 21 females (16.5%), with a mean age of 56.06 ±10.33 years. Tumor characteristics revealed that 57 patients (44.5%) had tumors measuring ≤5 cm, while 71 patients (55.5%) had tumors >5 cm in diameter; 54 patients (42.2%) presented with a single tumor, and 74 patients (57.8%) had multiple tumors. All patients received DEB-TACE treatment and were followed up for a period ranging from 4 to 39 months. Analysis of the impact of tumor characteristics on survival prognosis demonstrated statistically significant differences ($P < 0.05$) in OS and PFS based on several factors: tumor size >5 cm, the presence of multiple tumors (>2), the coexistence of multiple tumors with the largest exceeding 5 cm, portal vein invasion, CNLC stage, BCLC stage, alpha-fetoprotein (AFP) levels, lymph node

metastasis, and extrahepatic metastasis (Table 1). Patients classified as CNLC stage III and BCLC stage C exhibited significantly shorter OS compared to those at earlier stages ($P < 0.05$), underscoring the advanced stage as a critical indicator of poor prognosis. Additionally, elevated AFP levels (>400 ng/mL) were linked to increased tumor aggressiveness, potentially reflecting a more active biological behavior of the malignancy. The median PFS of patients with lymph node and extrahepatic metastases was reduced by about 50%, highlighting distant metastasis as a pivotal risk factor for treatment failure.

Table 1 The Effect of Patient Tumor Characteristics on the Prognosis and Survival of Patients

Parameters	N	Overall Survival (OS, N = 128)	F/Z	P value	Progression-Free Survival (PFS, N = 128)	F/Z	P value
Tumor size (cm, x±s)							
≤ 5 cm	57	26.72±18.33	19.308	0.000	8.46±9.88	6.061	0.015
> 5 cm	71	14.10±14.175			4.89±8.44		
Tumor site [case (%)]							
Unilobular tumor	54	25.07±16.27	9.583	0.002	8.80±9.49	7.657	0.007
Multilobular tumor	74	15.84±17.04			4.78±6.93		
Tumor and Tumor size > 5 cm							
YES	47	13.91±15.17	8.905	0.003	4.55±6.47	4.073	0.046
NO	81	23.19±17.61			7.59±9.07		
Tumor distribution							
Left liver side	19	19.26±13.25	0.656	0.521	7.68±9.53	1.594	0.207
Right liver side	68	21.26±17.78			7.28±8.22		
Bilateral	41	17.37±18.14			4.59±7.73		
CNLC stage [case (%)]							
Stage I	43	28.37±15.42	12.889	0.000	10.16±10.12	6.382	0.000
Stage II	41	22.17±18.19			6.54±8.72		
Stage III	38	7.68±9.07			2.84±2.51		
Stage IV	6	17.17±22.99			2.67±2.25		
BCLC stage							
Stage A	42	27.95±15.48	15.606	0.000	10.31±1019	8.658	0.000
Stage B	42	22.07±17.19			5.95±6.95		
Stage C	44	9.61±13.96			3.32±5.85		
Tumor marker AFP							
Positive	97	17.92±16.53	4.473	0.036	6.04±7.64	1.100	0.296
Negative	31	23.35±18.59			7.84±10.15		
Tumor marker AFP Level							
< 7	31	25.35±18.59	3.382	0.037	7.84±10.15	2.022	0.137
≥ 7 and < 400	44	20.75±16.06			7.61±9.37		
≥ 400	53	15.57±16.69			4.74±5.60		
Portal vein invasion							
Yes	32	5.75±6.10	35.470	0.000	2.52±2.11	10.32	0.002
No	96	24.38±17.30			7.79±9.16		
Hepatic vein invasion							
Yes	8	10.13±15.51	2.666	0.105	3.13±3.04	1.392	0.240
No	120	20.36±17.26			6.70±8.51		
Lymph node metastasis							
Yes	22	11.55±14.65	6.190	0.014	3.36±3.09	3.809	0.053
No	106	21.42±17.35			7.12±8.90		
Extrahepatic metastasis							
Yes	21	6.67±6.93	16.039	0.000	2.95±2.66	4.646	0.033
No	107	22.28±17.55			7.17±8.86		

Complications, Postembolization Syndrome, Preoperative Biochemistry, and Routine Blood Tests Influence the Prognosis and Survival of Patients

Regarding liver function and accompanying diseases, the Child-Pugh classification, combined with cirrhosis, diabetes, coronary heart disease, hypertension, and post-TACE syndromes, such as nausea, vomiting, fever, poor appetite, and abdominal pain, did not significantly affect the PFS or OS of patients ($P > 0.05$) (Table 2).

The results of preoperative blood biochemistry analysis revealed that patients with abnormal aspartate aminotransferase (AST), total bilirubin (TBIL), albumin (ALB), white blood cell (WBC), neutrophil absolute value (NEUT#), and procalcitonin (PCT) levels had significantly shorter OS than patients with normal levels of the above indicators ($P < 0.05$). Patients with abnormal levels of cholinesterase (ChE) and C-reactive protein (CRP) had significantly shorter OS and PFS than patients with normal levels of the above indicators ($P < 0.05$). These results suggested that AST, ChE, TBIL, ALB, WBC, NEUT#, PCT, ChE, and CRP may be important factors influencing OS. Further binary logistic regression analysis indicated that patients with higher platelet counts (PLTs) had longer OS ($P < 0.05$) (Tables 3 and 4).

Table 2 Effect of Liver Function and Complications on the Prognosis and Survival of Patients

Parameters	N	Overall Survival (OS, N = 128)	F	P value	Progression-free Survival (PFS, N = 128)	F	P value
Liver function score							
A	71	22.06±15.95	1.523	0.222	7.04±8.09	1.015	0.365
B	50	17.08±18.25			6.24±9.07		
C	7	14.86±21.86			2.43±2.15		
Liver Cirrhosis							
Yes	124	19.70±17.47	0.004	0.950	6.50±8.31	0.031	0.860
No	4	20.25±11.12			5.75±9.50		
Hypertension							
Yes	22	19.59±15.69	0.001	0.970	9.23±10.57	2.954	0.088
No	106	19.75±17.66			5.91±7.70		
Diabetes							
Yes	14	22.50±18.88	0.406	0.525	6.93±8.66	0.046	0.830
No	114	19.38±17.13			6.42±8.31		
Coronary heart disease							
Yes	3	22.00±32.97	0.053	0.818	2.67±1.23	0.644	0.424
No	125	19.66±16.97			6.57±8.39		
Fever							
Yes	46	19.70±17.91	0.000	0.991	6.39±8.07	0.007	0.931
No	82	19.73±17.02			6.52±8.50		
Nausea							
Yes	29	17.17±15.25	0.813	0.369	4.90±5.12	1.359	0.246
No	99	20.46±17.83			6.94±9.01		
Vomit							
Yes	16	19.44±15.31	0.005	0.945	6.06±6.16	0.045	0.832
No	112	19.76±17.60			6.54±8.60		
Poor appetite							
Yes	20	20.80±17.20	0.092	0.762	5.65±6.53	0.233	0.630
No	108	19.52±17.36			6.63±8.62		
Celialgia							
Yes	66	17.89±17.15	1.527	0.219	5.41±6.93	2.270	0.134
No	62	21.66±17.34			7.61±9.49		

Table 3 Effect of Preoperative Biochemical and Routine Blood Tests on Patient Prognosis and Survival

Parameters	N	Overall Survival (OS, N = 128)	t	P value	Progression-Free Survival (PFS, N = 128)	t	P value
AST							
Normal	92	22.43±17.54	8.568	0.004	7.16±8.61	2.253	0.136
Abnormal	36	12.78±14.63			4.72±7.31		
ALT							
Normal	100	20.86±17.70	2.011	0.159	6.48±8.59	0.000	0.993
Abnormal	28	15.64±15.27			6.46±7.39		
AST/ALT							
Normal	63	20.38±17.25	0.181	0.671	5.67±6.69	1.180	0.280
Abnormal	65	19.08±17.41			7.26±9.62		
Total bilirubin							
Normal	81	22.36±17.99	5.324	0.023	7.15±8.55	1.445	0.232
Abnormal	47	15.17±15.08			5.32±7.84		
Direct bilirubin							
Normal	40	18.58±17.03	0.254	0.615	5.90±8.44	0.278	0.599
Abnormal	88	20.24±17.46			6.74±8.29		
Indirect bilirubin							
Normal	106	19.53±17.40	0.074	0.785	6.70±8.34	0.436	0.510
Abnormal	22	20.64±17.01			5.41±8.28		
Albumin							
Normal	94	22.48±17.47	9.648	0.002	7.11±8.71	2.049	0.155
Abnormal	34	12.09±14.39			4.74±6.92		
Creatinine							
Normal	79	21.15±17.26	1.425	0.235	7.15±8.87	1.366	0.245
Abnormal	49	17.41±17.23			5.39±7.29		
Urea nitrogen							
Normal	109	19.18±17.43	0.703	0.403	6.13±7.93	1.291	0.258
Abnormal	19	22.79±16.49			8.47±10.28		
Cholinesterase							
Normal	57	23.82±18.12	6.035	0.015	8.25±9.54	4.794	0.030
Abnormal	71	16.42±15.94			5.06±6.93		
Coagulation PT							
Normal	36	15.47±13.76	3.076	0.082	4.97±4.75	1.649	0.201
Abnormal	92	21.38±18.27			7.07±9.30		
Coagulation PTA							
Normal	93	20.43±17.03	0.575	0.45	6.68±8.10	0.197	0.658
Abnormal	35	17.83±18.02			5.94±8.94		
Leukocyte							
Normal	51	17.14±16.33	7.053	0.009	6.37±8.14	0.053	0.819
Abnormal	43	25.82±18.12			6.74±8.82		
Neutrophil absolute value							
Normal	100	18.10±16.81	4.112	0.045	6.79±8.59	0.648	0.422
Abnormal	28	25.50±17.98			5.36±7.26		
Hemoglobin							
Normal	88	20.94±16.96	1.419	0.236	6.82±8.58	0.474	0.493
Abnormal	40	17.03±17.88			5.73±7.74		
Platelet							
Normal	62	17.94±16.83	1.284	0.259	7.02±8.74	0.505	0.479
Abnormal	66	21.39±17.64			5.97±7.92		

(*Continued*)

Table 3 (Continued).

Parameters	N	Overall Survival (OS, N = 128)	t	P value	Progression-Free Survival (PFS, N = 128)	t	P value
C-reactive protein							
Normal	74	26.64±16.66	35.828	0.000	8.92±9.93	17.060	0.000
Abnormal	54	10.24±13.21			3.13±3.92		
Procalcitonin							
Normal	104	21.93±17.69	9.737	0.002	7.03±8.79	2.477	0.118
Abnormal	24	10.13±11.35			4.08±5.33		
HBV DNA							
Normal	69	18.13±17.45	1.268	0.262	6.52±9.20	0.004	0.947
Abnormal	59	21.58±17.03			6.42±7.21		

Notes: Normal range note: AST (17–59 U/L), ALT (<50 U/L), total bilirubin (3–22 μmol/L), direct bilirubin (0–5 μmol/L), indirect bilirubin (0–19 μmol/L), biochemical albumin (35–50 g/L), creatinine (58–110 μmol/L), blood urea nitrogen (3.2–7.1 mmol/L), cholinesterase (5900–12,220 <50 U/L), coagulation PT (9.4–12.5s), coagulation PTA (75–157%), blood routine albumin (3.5–9.5 × 10–9/L), blood routine neutrophil absolute value (1.8–6.3 × 10–9/L), hemoglobin (130–175 g/L), platelet count (125–350 × 10–9/L), and hepatitis B DNA (<1 × 10–2 IU/mL).

Table 4 Binary Logistic Regression Analysis of the Effect on Survival Outcomes

Parameters	B	Standard Error	Wald	df	Sig.	Exp(B)	95.0% Exp(B) CI	
							Lower	Upper
AST	−0.014	0.017	0.655	1	0.418	0.987	0.955	1.020
ALT	0.043	0.024	3.032	1	0.082	1.043	0.995	1.095
AST/ALT	0.932	0.745	1.564	1	0.211	2.538	0.589	10.932
Total bilirubin	−0.088	0.180	0.239	1	0.625	0.916	0.643	1.303
Direct bilirubin	0.112	0.137	0.673	1	0.412	1.119	0.856	1.463
Indirect bilirubin	0.112	0.210	0.287	1	0.592	1.119	0.742	1.688
Albumin	−0.082	0.077	1.130	1	0.288	0.922	0.793	1.071
Creatinine	−0.004	0.022	0.027	1	0.870	0.996	0.954	1.041
Urea nitrogen	0.207	0.165	1.566	1	0.211	1.230	0.889	1.701
Cholinesterase	0.000	0.000	0.039	1	0.843	1.000	1.000	1.000
Coagulation PT	0.220	0.216	1.031	1	0.310	1.246	0.815	1.904
Coagulation PTA	0.007	0.030	0.058	1	0.809	1.007	0.949	1.069
Leukocyte	−0.692	0.375	3.431	1	0.065	0.501	0.240	1.043
Neutrophil absolute value	1.015	0.518	3.845	1	0.050	2.759	1.000	7.609
Hemoglobin	−0.020	0.016	1.495	1	0.211	0.980	0.949	1.012
Platelet	0.014	0.005	7.420	1	0.006	1.014	1.004	1.025

Cox Regression Analysis

Based on the results of multivariate Cox regression analysis, we further identified the independent prognostic factors affecting the OS and PFS of patients. The results indicated that patient age, Child-Pugh score, BCLC stage, TBIL, indirect bilirubin, ChE, PT, PLT, CRP, PCT, AFP, and postoperative fever were significant predictors of OS, with abnormalities in these parameters being strongly associated with a reduced OS duration ($P < 0.05$). In contrast, other variables, including sex, the presence of comorbid conditions, and HBV DNA status, did not demonstrate a statistically significant impact on patient prognosis in this study (Table 5).

Table 5 Cox Regression Analysis of Factors Affecting Overall Survival Time

Characteristic	N	Hazard.Ratio	X95.CI_lower	X95.CI_upper	P.value
Gender		1.616	0.490	5.332	0.431
male	107				
female	21				
Age (56.06±10.33)		1.066	1.012	1.124	0.017
Liver Cirrhosis		0.059	0.003	1.021	0.052
Yes	85				
No	9				
Hypertension		0.776	0.225	2.675	0.688
Yes	22				
No	106				
Diabetes		1.142	0.301	4.334	0.846
Yes	14				
No	114				
CHD		0.518	0.045	5.929	0.597
Yes	3				
No	125				
Tumor distribution		1.839	0.819	4.131	0.140
Left liver side	19				
Right liver side	68				
Bilateral	41				
Tumor site		0.646	0.086	4.845	0.671
Unilobular	54				
Multilobular	74				
Tumor Num		2.039	0.399	10.423	0.392
≤ 5	57				
>5	71				
Tumor number >3 and Tumor size > 5 cm		1.643	0.219	12.353	0.629
Yes	47				
No	81				
Portal vein invasion		0.313	0.081	1.200	0.090
Yes	32				
No	96				
Hepatic vein invasion		1.701	0.209	13.860	0.620
Yes	8				
No	120				
Lymph node metastasis		3.113	0.698	13.871	0.136
Yes	22				
No	106				
Extrahepatic metastasis		0.663	0.159	2.766	0.573
Yes	21				
No	107				
Liver function score		4.113	1.634	10.352	0.003
A	71				
B	50				
C	7				
CNLC stage		0.554	0.218	1.405	0.214
I	43				
II	41				
III	38				
IV	6				

(*Continued*)

Table 5 (Continued).

Characteristic	N	Hazard.Ratio	X95.CI_lower	X95.CI_upper	P.value
BCLC Stage		6.141	1.628	23.172	0.007
A	42				
B	42				
C	44				
AST Num		0.993	0.978	1.008	0.338
AST		0.446	0.083	2.397	0.347
Normal	92				
Abnormal	36				
ALT Num		1.020	0.984	1.057	0.282
ALT		1.219	0.172	8.653	0.843
Normal	100				
Abnormal	28				
AST/ALT Num		1.965	0.675	5.716	0.215
AST/ALT		1.452	0.571	3.687	0.433
Normal	63				
Abnormal	65				
Total bilirubin Num		0.738	0.561	0.970	0.029
Total bilirubin		2.724	0.675	10.991	0.159
Normal	81				
Abnormal	47				
Direct bilirubin Num		1.120	0.885	1.418	0.345
Direct bilirubin		0.883	0.223	3.500	0.860
Normal	40				
Abnormal	88				
Indirect bilirubin Num		1.538	1.069	2.213	0.020
Indirect bilirubin		0.187	0.017	1.995	0.165
Normal	106				
Abnormal	22				
Albumin Num		0.927	0.792	1.085	0.346
Albumin		0.186	0.032	1.079	0.061
Normal	94				
Abnormal	34				
Creatinine Num		0.975	0.910	1.044	0.468
Creatinine		0.959	0.193	4.780	0.960
Normal	79				
Abnormal	49				
Urea nitrogen Num		1.054	0.733	1.514	0.778
Urea nitrogen		0.572	0.116	2.821	0.493
Normal	109				
Abnormal	19				
Cholinesterase Num		0.999	0.998	0.999	0.000
Cholinesterase		0.055	0.012	0.256	0.000
Normal	57				
Abnormal	71				
Coagulation PT Num		1.000	0.625	1.600	0.999
Coagulation PT		0.283	0.086	0.931	0.038
Normal	36				
Abnormal	92				
Coagulation PTA Num		0.978	0.922	1.036	0.448
Coagulation PTA		1.027	0.218	4.840	0.973

(*Continued*)

https://doi.org/10.2147/JHC.S519397

Table 5 (Continued).

Characteristic	N	Hazard.Ratio	X95.CI_lower	X95.CI_upper	P.value
Normal	93				
Abnormal	35				
Leukocyte Num		0.854	0.404	1.803	0.679
Leukocyte		0.285	0.052	1.567	0.149
Normal	51				
Abnormal	43				
Neutrophils Num		0.889	0.367	2.153	0.794
Neutrophils		1.713	0.387	7.578	0.478
Normal	100				
Abnormal	28				
Hemoglobin Num		0.995	0.962	1.030	0.787
Hemoglobin		0.783	0.246	2.493	0.678
Normal	88				
Abnormal	40				
Platelet Num		1.008	1.001	1.015	0.032
Platelet		0.234	0.080	0.687	0.008
Normal	62				
Abnormal	66				
C-reactive protein		5.357	2.042	14.052	0.001
Normal	74				
Abnormal	54				
Procalcitonin		0.120	0.028	0.511	0.004
Normal	104				
Abnormal	24				
HBV DNA		0.948	0.370	2.426	0.911
Normal	69				
Abnormal	59				
Tumor marker AFP		0.234	0.080	0.687	0.008
Positive	97				
Negative	31				
Fever		3.928	1.657	9.309	0.002
Normal	46				
Abnormal	82				
Nausea		1.265	0.287	5.567	0.756
Normal	29				
Abnormal	99				
Vomit		0.834	0.142	4.896	0.841
Normal	16				
Abnormal	112				
Poor appetite		1.485	0.407	5.422	0.550
Normal	20				
Abnormal	108				
Celialgia		0.866	0.425	1.766	0.692
Normal	66				
Abnormal	62				

Survival Curve Analysis

Further analysis using Kaplan-Meier survival curves demonstrated that AFP, ALB, AST, ChE, presence of extrahepatic metastasis, hepatic vein invasion, leukocyte count, lymph node metastasis, PCT, TBIL, tumor size, solitary tumor status, and portal vein invasion were all significantly associated with OS ($P < 0.05$). Specifically, patients who were AFP-

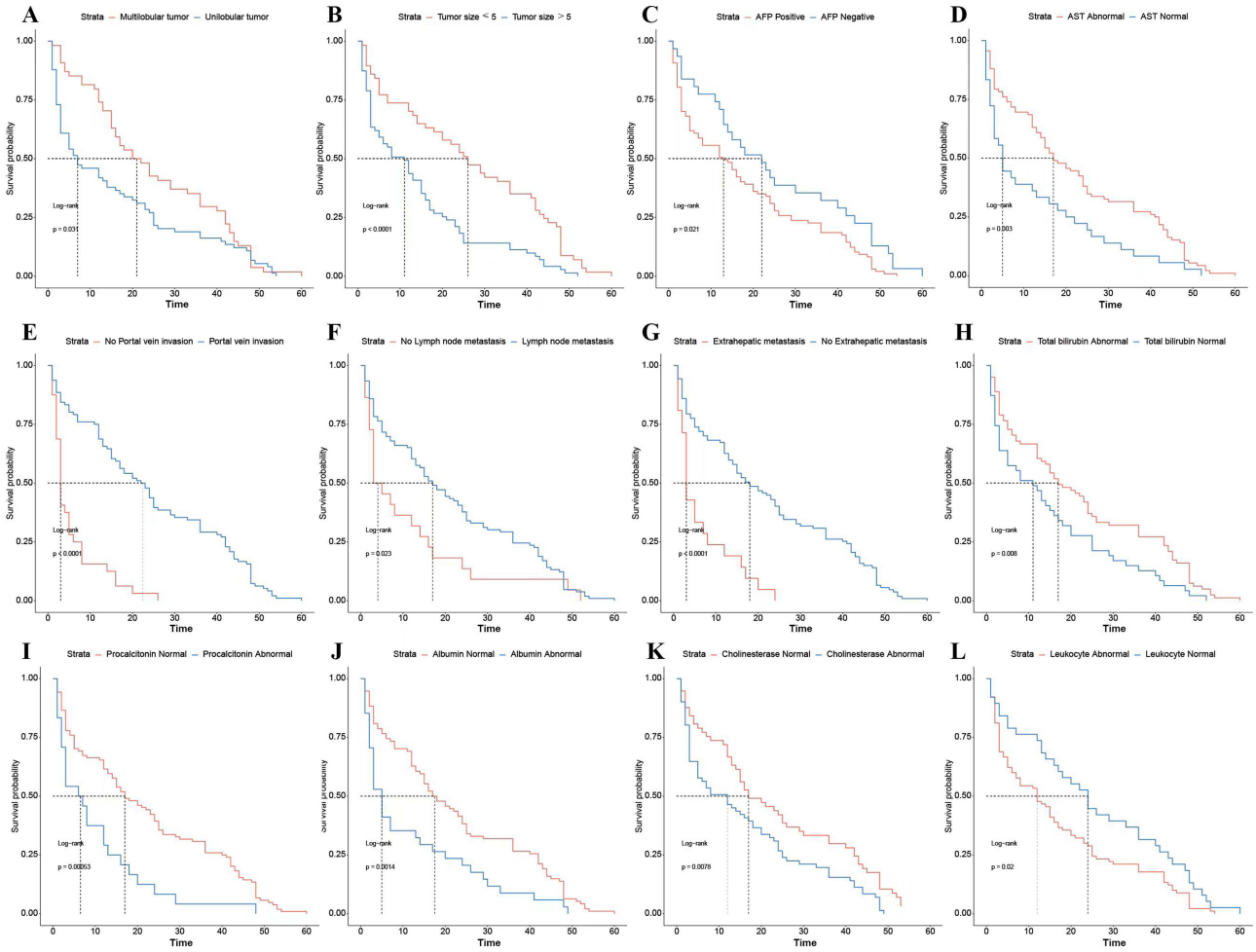

Figure 1 K-M curves influencing the survival time of patients after D-TACE ((**A**) Multilobular tumor; (**B**) Tumor size; (**C**) AFP; (**D**) AST; (**E**) Portal vein invasion; (**F**) Lymph node metastasis; (**G**) Extrahepatic metastasis; (**H**) Total bilirubin; (**I**) Procalcitonin; (**J**) Albumin; (**K**) Cholinesterase; (**L**) Leukocyte).

negative, exhibited normal levels of AST, WBC, ALB, TBIL, and PCT, had a solitary tumor, and lacked extrahepatic metastasis, hepatic vein invasion, and portal vein invasion, demonstrated significantly prolonged OS compared to those with abnormalities in these parameters (Figure 1).

Complications and Safety Analysis

No patients experienced serious complications following surgery, and the treatment was generally well-tolerated. A small number of patients developed mild liver function impairment, fever, nausea, or localized pain postoperatively; however, these symptoms were effectively managed and resolved within a short duration. The findings indicate that D-TACE demonstrates a high safety profile in patients with unresectable HBV-related liver cancer.

Discussion

Transcatheter arterial chemoembolization (TACE) is the preferred nonsurgical palliative treatment method for primary liver cancer in clinical practice. The mechanism of action involves obstructing the tumor's blood supply while delivering chemotherapeutic agents to kill or inhibit tumor cells; however, this approach does not directly or completely eradicate tumor cells.[11] Drug-eluting microspheres represent a novel class of embolic materials, offering advantages such as non-degradability, the ability to maintain high local drug concentrations within the tumor, and reduced systemic drug exposure. Several studies have demonstrated that, in patients with unresectable HCC, drug-eluting microspheres provide superior short-term efficacy and safety compared to conventional TACE.[12] Nevertheless, this method incurs higher costs

than traditional TACE. Therefore, it is essential for clinicians to adopt a rational surgical strategy based on a comprehensive assessment of the patient's overall condition, tumor characteristics, and financial considerations.

In this study, we investigated the factors influencing PFS and OS in patients with primary liver cancer undergoing DEB-TACE treatment for the first time, including various factors, such as the general conditions of patients, underlying comorbidities, tumor characteristics, and preoperative clinical indicators. The results indicated that sex and the presence of underlying comorbidities did not have a significant impact on the PFS or OS of patients undergoing DEB-TACE. In contrast, tumor characteristics such as CNLC stage, tumor diameter, number of lesions, presence of vascular invasion, lymph node metastasis, and extrahepatic metastasis were found to significantly influence OS, consistent with findings from previous studies.[11,13] Among clinical indicators, factors including AFP, AST, ChE, TBIL, ALB, WBC, NEUT, PCT, and CRP emerged as potential determinants of OS. Multifactor Cox regression analysis further identified age, Child-Pugh score, BCLC stage, TBIL, IBIL, ChE, prothrombin time (PT), platelet count (PLT), CRP, PCT, AFP, and postoperative fever as independent risk factors for OS.[11] While tumor volume and stage are well-established prognostic factors in liver cancer, the role of inflammation in tumor progression has been relatively underexplored. The tumor microenvironment is rich in inflammatory factors and immune cells that contribute to the initiation and progression of malignant tumors. In recent years, there has been a growing body of research and literature supporting the prognostic significance of inflammatory markers in liver cancer and other malignancies.[14] The binary logistic regression analysis, multifactor Cox regression analysis, and Kaplan-Meier method employed in this study indicated that common inflammatory factors, such as WBCs, neutrophils, PCT, and CRP, are closely related to the PFS and OS of primary liver cancer patients undergoing DEB-TACE and can serve as preoperative predictive indicators along with tumor characteristics, the Child-Pugh score, tumor stage, etc.

Previous studies have primarily focused on evaluating the efficacy and safety of various treatment modalities for patients with primary liver cancer. With ongoing advancements in medical technology, the emphasis has increasingly shifted toward precision and personalized oncologic therapies, necessitating more thorough preoperative assessments tailored to individual patients. Global clinical research has demonstrated that the postoperative survival of patients with primary liver cancer is influenced by a combination of clinicopathological factors, sociodemographic characteristics, medical history, and imaging findings.[2,5,7,10,15–17] In recent years, considerable progress has been made in constructing predictive models using machine learning, which have been extensively applied in areas such as disease diagnosis, onset prediction, treatment efficacy evaluation, survival analysis, and recurrence prediction.[11–13,18] Despite these advancements, the prognostic evaluation framework for primary liver cancer remains underdeveloped, primarily due to the disease's complexity, poor curability, frequent postoperative complications, generally unfavorable prognoses, and high recurrence and metastasis rates. In particular, research focusing on predictive models for TACE is limited. Current models rely on only a few prognostic indicators, such as tumor size, tumor count, degree of differentiation, lymph node involvement, AJCC stage, and alpha-fetoprotein levels.

Limitations

This was a single-center retrospective study with a relatively small sample size and did not consider machine learning algorithms to construct the final predictive model.

All patients in this study had primary liver cancer based on hepatitis B, and a certain selection bias might have occurred in the population.

Due to the fact that liver reserve function tests have only recently been initiated locally, the results of this study lack indicators pertaining to liver reserve function.

The prognostic model developed in this study was constructed using clinical index variables and did not include molecular typing parameters, such as gene mutations or characteristics of the immune microenvironment.[19] Although the model demonstrated a certain degree of predictive efficacy, incorporating established molecular features—such as TP53 mutations and PD-L1 expression—may enhance the precision of prognostic stratification.[11–13,18] Future research may improve model accuracy and clinical utility by integrating multi-omics data, thereby enabling a more comprehensive and individualized prediction framework.

Conclusion

This study included commonly used clinical indicators closely associated with the occurrence and progression of primary liver cancer, such as routine blood tests, biochemical parameters, and coagulation profiles, which are standard inflammatory markers, along with tumor-related indicators, including tumor diameter, number, stage classification, and the presence of distant and lymph node metastases. The study confirmed the clinical utility of these variables in predicting PFS and OS in patients undergoing DEB-TACE.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. No datasets were generated or analyzed during the current study.

Ethics Approval and Informed Consent

The study protocols were approved by the Medical Ethics Committee of General Hospital of Ningxia Medical University (approval number: KYLL-2025-0039, Yinchuan, China) and all methods were performed in accordance with the principles expressed in the Declaration of Helsinki. All patients provided written informed consent to participate.

Consent for Publication

All patients provided written informed consent to publish. All images in this article have been approved by me and I have signed an informed consent form.

Acknowledgments

We would like to express our gratitude to the Clinical Medicine Center for its support of this work.

Author Contributions

S.W.L. and Y.Z. wrote the manuscript drafts and performed formal analysis. X.Y.F. helped interpret data and study design. L.H.H. and W.L.M. aided analytical design. L.N.M. performed the acquisition of data. X.C.D. and X.L. provided interpretation. All authors reviewed the manuscript. 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.

Funding

This work was supported by Ningxia Natural Science Foundation (Grant No.: 2024AAC05090).

Disclosure

The authors declare no competing interests in this work.

References

1. Ye JZ, Chen JZ, Li ZH, et al. Efficacy of postoperative adjuvant transcatheter arterial chemoembolization in hepatocellular carcinoma patients with microvascular invasion. *World J Gastroenterol*. 2017;23(41):7415–7424. doi:10.3748/wjg.v23.i41.7415
2. Xia Y, Tang W, Qian X, et al. Efficacy and safety of camrelizumab plus apatinib during the perioperative period in resectable hepatocellular carcinoma: a single-arm, open label, Phase II clinical trial. *J Immunother Cancer*. 2022;10(4). doi:10.1136/jitc-2022-004656
3. Park JW, Chen M, Colombo M, et al. Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. *Liver Int*. 2015;35(9):2155–2166. doi:10.1111/liv.12818
4. Liu X, Xia F, Chen Y, et al. Chinese expert consensus on refined diagnosis, treatment, and management of advanced primary liver cancer (2023 edition). *Liver Res*. 2024;8(2):61–71. doi:10.1016/j.livres.2024.05.001
5. Ding J, Wen Z. Survival improvement and prognosis for hepatocellular carcinoma: analysis of the SEER database. *BMC Cancer*. 2021;21(1):1157. doi:10.1186/s12885-021-08904-3

6. Zhang XP, Wang K, Wei XB, et al. An eastern hepatobiliary surgery hospital microvascular invasion scoring system in predicting prognosis of patients with hepatocellular carcinoma and microvascular invasion after R0 liver resection: a large-scale, multicenter study. *Oncologist*. 2019;24(12):e1476–e1488. doi:10.1634/theoncologist.2018-0868
7. Xiaohong S, Huikai L, Feng W, Ti Z, Yunlong C, Qiang L. Clinical significance of lymph node metastasis in patients undergoing partial hepatectomy for hepatocellular carcinoma. *World J Surg*. 2010;34(5):1028–1033. doi:10.1007/s00268-010-0400-0
8. Zhou J, Sun H, Wang Z, et al. Guidelines for the diagnosis and treatment of primary liver cancer (2022 Edition). *Liver Cancer*. 2023;12(5):405–444. doi:10.1159/000530495
9. Chen X, Lu Y, Shi X, et al. Development and validation of a novel model to predict regional lymph node metastasis in patients with hepatocellular carcinoma. *Front Oncol*. 2022;12:835957. doi:10.3389/fonc.2022.835957
10. Zheng Y, Zhang X, Lu J, Liu S, Qian Y. Association between socioeconomic status and survival in patients with hepatocellular carcinoma. *Cancer Med*. 2021;10(20):7347–7359. doi:10.1002/cam4.4223
11. Chiu CC, Lee KT, Lee HH, et al. Comparison of models for predicting quality of life after surgical resection of hepatocellular carcinoma: a prospective study. *J Gastrointest Surg*. 2018;22(10):1724–1731. doi:10.1007/s11605-018-3833-7
12. Ho WH, Lee KT, Chen HY, Ho TW, Chiu HC. Disease-free survival after hepatic resection in hepatocellular carcinoma patients: a prediction approach using artificial neural network. *PLoS One*. 2012;7(1):e29179. doi:10.1371/journal.pone.0029179
13. Noh B, Park YM, Kwon Y, et al. Machine learning-based survival rate prediction of Korean hepatocellular carcinoma patients using multi-center data. *BMC Gastroenterol*. 2022;22(1):85. doi:10.1186/s12876-022-02182-4
14. Molla MD, Akalu Y, Geto Z, Dagnew B, Ayelign B, Shibabaw T. Role of caspase-1 in the pathogenesis of inflammatory-associated chronic noncommunicable diseases. *J Inflamm Res*. 2020;13:749–764. doi:10.2147/JIR.S277457
15. Lin E, Zou B, Zeng G, et al. The impact of liver fibrosis on microvascular invasion and prognosis of hepatocellular carcinoma with a solitary nodule: a Surveillance, Epidemiology, and End Results (SEER) database analysis. *Ann Translat Med*. 2021;9(16):1310. doi:10.21037/atm-21-3731
16. Zhang K, Tao C, Wu F, Wu J, Rong W. A practical nomogram from the SEER database to predict the prognosis of hepatocellular carcinoma in patients with lymph node metastasis. *Ann Palliat Med*. 2021;10(4):3847–3863. doi:10.21037/apm-20-1876
17. Hai L, Liu S, Ma L, Ding X, Bai X, Luo X. Comparative study of the short-term efficacy and safety between DEB-TACE and C-TACE in the treatment of unresectable hepatocellular carcinoma, a retrospective study. *Technol Cancer Res Treat*. 2024;23:15330338241250315. doi:10.1177/15330338241250315
18. Shi HY, Lee KT, Lee HH, et al. Comparison of artificial neural network and logistic regression models for predicting in-hospital mortality after primary liver cancer surgery. *PLoS One*. 2012;7(4):e35781. doi:10.1371/journal.pone.0035781
19. Pullikuth AK, Routh ED, Zimmerman KD, et al. Bulk and single-cell profiling of breast tumors identifies TREM-1 as a dominant immune suppressive marker associated with poor outcomes. *Front Oncol*. 2021;11:734959. doi:10.3389/fonc.2021.734959