Research Article

HEPATOLOGY FORUM

Features and survival in hepatocellular carcinoma

doi: 10.14744/hf.2021.2021.0031

Baseline characteristics associated with survival in patients with hepatocellular carcinoma

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Abstract

Background and Aim: Hepatocellular carcinoma (HCC) is one of the most common and most lethal cancers worldwide. The objective of this study was to investigate the relationship between basal parameters and survival characteristics in patients with HCC.

Materials and Methods: The records of 1447 HCC patients of a tertiary center during the period 2000-2017 were screened retrospectively. The demographic details; basal clinical, laboratory, and radiological characteristics; treatments; and survival time were recorded and prognostic scores were calculated.

Results: A total of 788 patients with HCC (male/female: 623/165; mean age: 60.5±10.9 years) were included in the study. The median length of survival was 26.3 months (95% confidence interval [CI], 22.3-30.4 months). The 5-year survival rate was 28.1%. The number and diameter of the tumors; platelet count; platelet-to-lymphocyte ratio; level of aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase; portal and hepatic vein involvement; and an alpha-fetoprotein level of <9.6 ng/mL were found to be independently related to survival.

Conclusion: The positive predictive value of the prognostic index derived from independent survival-related parameters for 5- and 10-year survival or overall survival was approximately 86%. Integration of this prognostic index to the criteria used in making treatment decisions for patients with HCC should be considered.

Keywords: Alpha-fetoproteins; hepatocellular carcinoma; survival rate.

Introduction

Hepatocellular carcinoma (HCC) represents 85% to 90% of primary liver cancers.[1] HCC is the fifth most common cancer worldwide and third among cancer-related causes of death. Worldwide, 250,000 to 1 million people die from HCC annually. The etiological distribution of HCC varies according to geographical region.[2] In the Far East, the most common cause of HCC is hepatitis B virus (HBV) infection, and >90% of cases develop with a background of cirrhosis, whereas in Western countries, alcohol is a common cause and a high percentage of HCC cases are non-cirrhotic. The growing incidence of fatty liver disease worldwide is associated with an anticipated increase in HCC.[3] Various scoring systems have been developed based on the basal characteristics of the tumors and the liver. However, there is as yet no ideal staging system that meets all needs.

Although there are publications regarding HCC etiology and characteristics in Turkey,[4-7] there is only 1 known study that includes follow-up and survival analysis of a limited number of patients.[8]

This study was designed to investigate the relationship between survival and the basal clinical features, laboratory findings, and tumor characteristics of patients with HCC.

Materials and Methods

This study was approved by the Ege University Clinical Research Ethics Committee on September 1, 2018 (no: 18-1/27).

Records of patients with HCC treated during the period 2000-2017 in the hepatology database of the gastroenterology department and Hepato-Pancreato-Biliary Council files were retrospectively screened. Patients <18 years of age, those who had insufficient basal or follow-up data, and those without a definite diagnosis of HCC were excluded. Patients with only minor data missing were included in the binary analysis.

The patient demographic data and details of etiology, comorbid illnesses, presence of cirrhosis, decompensation characteristics of patients with cirrhosis, hemogram and biochemical parameters, diameter and number of tumors at diagnosis, radiological and histopathological features (if available), portal venous invasion, hepatic venous invasion, presence of distant metastasis, treatments administered, and survival information were recorded from the electronic files. Based on these data, the Child-Pugh (CP) score, Model For End-stage Liver Disease (MELD) score, Barcelona Clinic Liver Cancer (BCLC) stage, Cancer of the Liver Italian Program (CLIP) score, Okuda stage, and albumin-bilirubin (ALBI) value were calculated. The diagnosis of cirrhosis was based on clinical, radiological, and laboratory findings, as well as the histopathological data available for a few patients. The diagnosis of fatty liver was based on ultrasonographic findings. According to international guidelines, the diagnosis of non-alcoholic steatohepatitis

How to cite this article: Aslanov S, Gulsen Unal N, Senkaya A, Celik F, Buyruk AM, Uysal A, et al. Baseline characteristics associated with survival in patients with hepatocellular carcinoma. Hepatology Forum 2022; 3(1):3–10.

Received: August 18, 2021; **Accepted:** September 14, 2021; **Available online:** December 05, 2021

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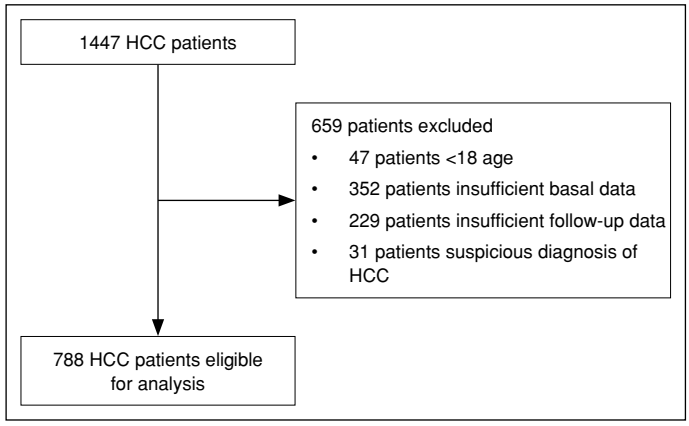

Figure 1. Flow diagram of the study.
HCC: Hepatocellular carcinoma.

(NASH) was based only on liver biopsy findings. Diffuse HCC was defined as a tumor >10 cm in diameter.

For the survival analysis, patient identity numbers were used to search the Death Notification System of the National Ministry of Health (https://obs.saglik.gov.tr) to ascertain which of the study patients had died and the date of death was recorded.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics for Windows Version 22.0 (IBM Corp., Armonk, NY, USA) and MedCalc Statistical Software version 19.2 (MedCalc Software bv, Ostend, Belgium). Intergroup differences of categorical data were investigated using a chi-squared test. All of the continuous variables were dichotomized according to the cutoff values obtained in receiver operating characteristic (ROC) analysis based on overall survival. These were included in Kaplan-Meier analysis, and the relationship of these parameters to survival time was examined using a log-rank test. Each measurable parameter that demonstrated a relationship to survival time was included in regression analysis using both the raw values and a dichotomized form. Among the dichotomized variables, only alpha-fetoprotein (AFP) was found to be more significant than the raw value for the prediction of survival time and was therefore included in the multiple regression analysis in this form. All of the other measurable parameters were included in the multiple regression analysis in the raw form. The staging system results, MELD score, and CP score were excluded in the multivariate analysis because they consist of basal parameters. A value of $p<0.05$ was accepted as statistically significant.

Results

The analysis was performed using the data of 788 of 1447 patients with HCC. A total of 659 patients were excluded: 47 patients aged <18 years, 352 with insufficient basal data, 229 with insufficient follow-up data, and 31 with an indefinite diagnosis of HCC (Fig. 1).

The distribution of etiologies as well as demographic and clinical data of the patients at the time of diagnosis are shown in Table 1. Of 588 (74.6%) patients with cirrhosis, 312 (53%) had signs of decompensation. Most commonly, this was ascites, which was observed in 284 (36%) patients. In all, 172 (34.1%) had diabetes and 46 (8.7%) patients had a fatty liver.

Table 1. Clinical features of patients at HCC diagnosis

	n	%
Gender (male)	623	79.1
Age at diagnosis (years)	60.5±10. 9	
Diagnosis in follow-up period	458[a]	60.3
Diabetes mellitus	172[b]	34.1
Fatty liver	46[c]	8.7
Liver biopsy	99	12.6
Cirrhosis	588	74.6
Decompensated cirrhosis findings		
Ascites	284	36.0
Hepatic encephalopathy	57	7.2
Bleeding esophageal varices	67	8.5
Child-Pugh[d]		
A	273	46.4
B	192	32.7
C	108	18.4
Portal vein involvement	164	20.8
Hepatic vein involvement	33	4.2
Lymph node metastasis	9	1.1
Distant metastasis	34	4.3
Number of tumors[e]		
1	464	60.3
2-3	145	18.8
4-5	17	2.2
>5 or infiltrated	144	18.7
Tumor size[f]		
<3 cm	157	21.0
3-<5 cm	140	18.7
5-<10 cm	188	25.1
≥10 cm or diffuse	263	35.2
Etiological distribution		
Hepatitis B	404	51.3
Hepatitis C	148	18.8
Alcohol	37	4.7
Hepatitis delta	23	2.9
Cryptogenic cirrhosis	49	6.2
Hepatitis B+alcohol	18	2.3
Hepatitis B+hepatitis C	14	1.8
NASH	9	1.1
Other[g]	17	2.2
No data	69	8.7

a: Calculated using 760 patients with available data; b: Calculated using 505 patients with available data; c: Calculated using 526 patients with available data; d: Calculated using 573 cirrhotic patients with available data; e: Calculated using 770 patients with available data; f: Calculated using 748 patients with available data; g: Other: HCV+alcohol (n=6), Budd-Chiari syndrome (n=2), HBV+autoimmune hepatitis (n=1), HCV+autoimmune hepatitis (n=1), Wilson disease (n=1), primary biliary cholangitis (n=2), autoimmune hepatitis (n=2), hepatitis B+C+delta (n=1), primary biliary cholangitis +autoimmune hepatitis (n=1). HBV: Hepatitis B virus; HCC: Hepatocellular carcinoma; HCV: Hepatitis C virus; NASH: Non-alcoholic steatohepatitis.

Table 2. Laboratory features of patients at HCC diagnosis

	Median	95% CI of median
Neutrophils (x/mm³)	3490	3200-3614
Lymphocytes(x/mm³)	1310	1270-1400
Platelets (x/mm³)	120000	114000-130000
NLR	2.54	2.38-2.69
PLR	93.37	89.9-100
AST (U/L)	58	53-62
ALT (U/L)	41	37-44
ALP (U/L)	173	157-183
GGT (U/L)	76	67-85
Total protein (g/dL)	7.3	7.3-7.4
Albumin (g/dL)	3.50	3.5-3.6
Urea (mg/dL)	34	33-36
Creatinine (mg/dL)	1.0	1-1
Total bilirubin (mg/dL)	1.25	1.13-1.33
INR	1.2	1.2-1.2
Total cholesterol (mg/dL)	154	148-158
Triglyceride (mg/dL)	87	83-91
Na (mEq/L)	139	139-140
AFP (µg/L)	23	18-32
LogAFP	1.36	1.25-1.5
MELD	10.00	10-11

AFP: Alpha-fetoprotein; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl transpeptidase; HCC: Hepatocellular carcinoma; INR: International normalized ratio; MELD: Model for End-stage Liver Disease; Na: Sodium; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.

Table 2 shows the laboratory values measured at diagnosis. Although the values are generally consistent with the expected values in cases of cirrhosis, the median parameter values related to liver function, such as albumin, creatinine, total bilirubin, and the international normalized ratio remained within the normal range.

Table 3 provides details of the tumor stage recorded at diagnosis. The BCLC classification data indicated that 404 (51.3%) patients were in stage B, C, or D, signifying that the HCC of approximately half of the study patients was beyond standard curative treatment limits. Of the 700 patients with treatment data, 175 (25%) underwent curative treatment.

Survival Time and Associated Factors

The median length of survival of all of the patients was 26.3 months (95% confidence interval [CI]: 22.3-30.4) (Fig. 2). The median 5-year survival rate was 28.1±0.21%. The survival time of patients diagnosed with HCC during follow-up was longer than that of those who were referred with HCC (median: 35.8 vs. 13.6 months; p<0.0001). The median tumor diameter was 4.7 cm (95% CI: 4.3-5.1) in the former group and 7.9 cm (95% CI: 7.2-8.5) (p<0.0001) in the latter group. The number of tumors was 2.5 (95% CI: 2.2-2.8) and 3.8 (95% CI:3.4-4.3) (p<0.0001), respectively.

The basal parameters related to survival time are shown in Table 4a. Tumor characteristics and poor prognostic variables were strongly related to survival.

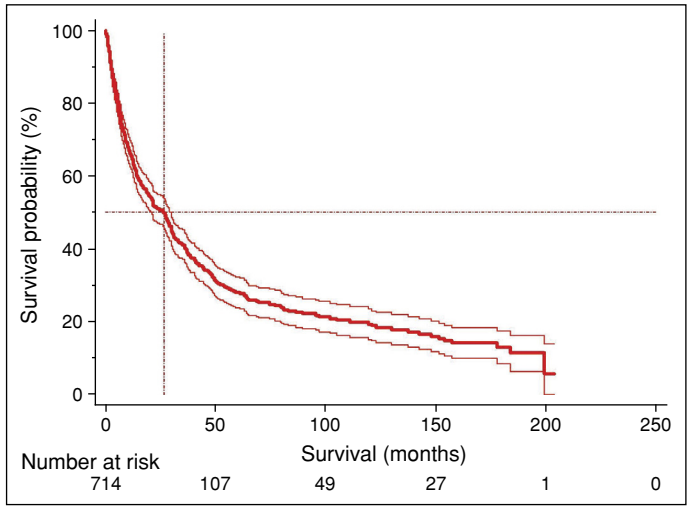

Figure 2. Survival time of all of the study patients (median: 26.3 months).

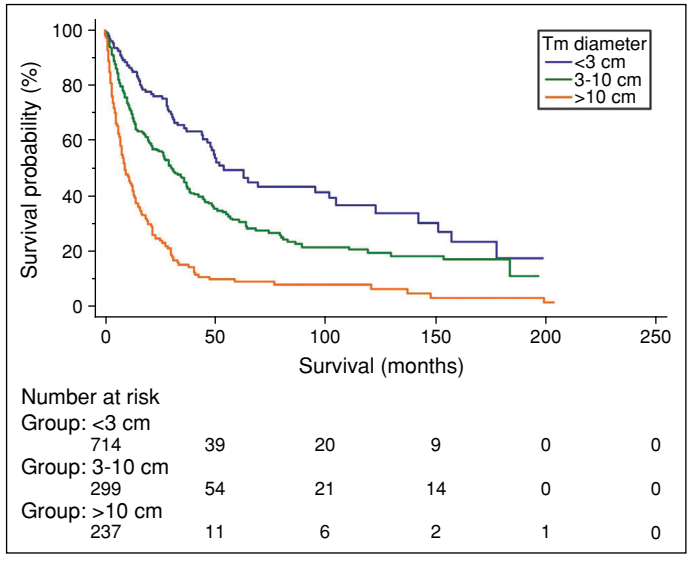

Figure 3. Survival time according to tumor size (3-<10 cm was considered a single group) Log-rank test p<0. 0001.

The etiology also had an effect on survival time. Among the 4 most common causes of HCC, the survival time of those with alcohol-related HCC was significantly less than that of the other leading etiologies (Table 5a, b). The length of survival of patients with hepatitis delta-related HCC was longer than that of HBV- or hepatitis C (HCV)-related HCC patients.

The number of tumors and tumor size was closely related to survival time. No significant change in lifespan was observed in cases of ≤3 tumors; the median survival time was 58.0±4.2 months in patients with 1 tumor and 68.4±7.8 months in those with 2-3 tumors. However, when there were >3 tumors, the survival time was significantly reduced. A greater number of tumors is associated with a poor prognosis; however, it is perhaps notable that other poor prognostic indicators were present in patients with more tumors (Table 6). The relationship between the total tumor diameter and survival time is shown in Figure 3. Because the overall survival time of patients with tumor diameters 3-10 cm was similar, tumor size was categorized as <3 cm, 3-10 cm, and ≥10 cm.

Table 3. Relationship between staging systems and survival time

Scoring systems	Subgroups	n	%	Survival (months)	95% CI		p
					Lower limit	Upper limit	
BCLC	0	89	11.3	51.9	19.4	84.5	
	A	295	37.4	36.7	28.3	45.1	
	B	139	17.6	21.5	15.8	27.1	<0.0001
	C	145	18.4	8.5	5.4	11.7	
	D	120	15.2	7.8	3.5	30.4	
CLIP[a]	0	159	24.1	45.5	35.1	55.8	
	1	176	26.7	31.6	24.5	38.8	
	2	150	22.8	18.5	12.7	24.3	
	3	90	13.7	8.3	6.0	10.6	<0.0001
	4	58	8.8	5.1	2.7	7.5	
	5	24	3.6	2.5	1.3	3.8	
	6	2	0.3	0.9	0.9	1.9	
Okuda[b]	1	293	39.3	36.7	28.9	44.5	
	2	383	51.4	16.6	11.9	21.3	<0.0001
	3	69	9.3	3.9	1.2	6.7	
ALBI[c]	1	204	27.2	36.2	28.9	43.6	
	2	392	52.2	22.8	16.6	29.1	0.003
	3	155	20.6	8.8	3.2	14.3	

a: 129 patients could not be evaluated; b: 43 patients could not be evaluated; c: 37 patients could not be evaluated; ALBI: Albumin-bilirubin; BCLC: Barcelona Clinic Liver Cancer; CI: Confidence interval; CLIP: Cancer of the Liver Italian Program.

Relationship Between Staging Systems and Survival Time

In all staging systems, as the stage progresses, the survival time is dramatically shortened. Staging scores were observed to be associated with survival (Table 3).

The CLIP score was found to be the best predictive score for survival in multivariate analysis (p<0.0001) and had a linear relationship to survival. Stages B and C were the most distinctive in the BCLC staging system based on survival time, but the difference was not statistically significant.

Multiple Regression Analysis

The basal parameters that demonstrated an independent relationship to survival time are presented in Table 4b. A prognostic index using these 10 parameters was calculated by multiplying the B values by the values of corresponding parameters, and summing the results. When the calculated prognostic index was included in ROC analysis with a cutoff of >1.1628, the sensitivity and specificity in predicting overall survival was 66.1% and 78.6%, respectively (area under the curve [AUC]: 0.768). The sensitivity, specificity, positive predictive value (PPV), and AUC values of the same cutoff value to predict a 5- and 10-year cumulative survival time were 66.4%, 78.8%, 82.9%, and 0.772, and 68.5%, 76.9%, 86.2%, and 0.777, respectively. The PPV of the prognostic index was high, that is, it demonstrated a high level of accuracy. The value of this index to predict survival was superior to other known prognostic indices.

Discussion

HCC was associated with HBV in more than half of the patients in this study. HCV infection is the second most common risk factor for HCC. This finding is more similar to those observed in Asian countries, rather than Western countries.[9] Although the overall prevalence of HBV is gradually decreasing,[10] many are diagnosed at an advanced stage of liver disease since >80% of patients are unaware of the disease.[11] Among the most prevalent etiologies, alcohol-related HCC patients had the lowest survival time, which may be due to more advanced liver disease and late diagnosis.[12] Hepatitis delta-related HCC patients had the longest survival, which was associated with the higher transplantation rate in these patients.

Cirrhosis was observed in 74.6% of the study patients. Since the diagnosis of cirrhosis was based on clinical and laboratory data, the actual prevalence might have been higher. Given that 53% of the cirrhosis cases were described as decompensated and that more than half of the patients had a BCLC classification beyond stage A, it appears that the disease is often recognized at an advanced stage. Only 25% of the patients were eligible for curative treatment. Clearly, greater public awareness of hepatitis is needed.

The number and size of tumors were the primary prognostic parameters in our study, as in previous research.[13,14] The Milan criteria and the BCLC specify ≤3 tumors for the application of curative treatment.[15] Survival of our study patients declined sharply in cases of >3 tumors. ROC analysis indicated that the best categorization of tumor size was <3 cm, 3-10 cm, and >10 cm. In this case, the Milan criteria cutoff of 5 cm does not seem to be a wholly appropriate threshold value. It may be that a larger size could be acceptable in patients with good prognostic criteria.

The prognostic value of the different scoring systems were also evaluated. The CLIP scoring system showed the best and most linear relationship to lifespan. The BCLC scoring system was created with the primary aim of directing treatment and it is not technically a prognostic

Table 4. Parameter relationship to survival time

A. Univariate analysis

	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
Number of tumors	0.080	0.013	38.032	1	<0.0001	1.083	1.056	1.111
Tumor diameter	0.102	0.009	130.999	1	<0.0001	1.107	1.088	1.127
Total tumor diameter	0.097	0.010	96.001	1	<0.0001	1.102	1.081	1.124
Identification during follow-up	0.582	0.099	34.576	1	<0.0001	1.790	1.474	2.173
Portal vein involvement	-0.708	0.112	40.069	1	<0.0001	0.493	0.396	0.613
Hepatic vein involvement	-0.599	0.235	6.480	1	0.011	0.549	0.346	0.871
Distant metastasis	-0.791	0.207	14.603	1	<0.0001	0.453	0.302	0.680
Presence of ascites	-0.332	0.100	11.036	1	0.001	0.717	0.590	0.873
Neutrophil count	0.110	0.027	16.739	1	<0.0001	1.116	1.059	1.176
Platelet count	0.003	0.000	45.486	1	<0.0001	1.003	1.002	1.004
NLR	0.049	0.008	35.916	1	<0.0001	1.050	1.034	1.067
PLR	0.003	0.001	23.428	1	<0.0001	1.003	1.002	1.004
AST	0.002	0.000	55.203	1	<0.0001	1.002	1.002	1.003
ALT	0.001	0.000	7.220	1	0.007	1.001	1.000	1.002
ALP	0.002	0.000	61.481	1	<0.0001	1.002	1.001	1.002
GGT	0.001	0.000	36.237	1	<0.0001	1.001	1.001	1.002
Na	-0.043	0.013	11.483	1	0.001	0.958	0.934	0.982
Albumin	-0.206	0.068	9.129	1	0.003	0.814	0.712	0.930
Urea	0.005	0.002	5.508	1	0.019	1.005	1.001	1.009
Total bilirubin	0.042	0.011	14.079	1	<0.0001	1.043	1.020	1.066
AFP <9.6 ng/mL	-0.652	0.108	36.545	1	<0.0001	0.521	0.422	0.644

B. Multivariate analysis

Covariate	b	SE	Wald	P	Exp (B)	95% CI for Exp (B)
Number of tumors	0.05673	0.01906	8.8628	0.0029	1.0584	1.0196 to 1.0987
Tumor diameter	0.09595	0.01388	47.7518	<0.0001	1.1007	1.0712 to 1.1311
Platelet count	-0.00192	0.000954	4.0548	0.044	0.9981	0.9962 to 0.9999
PLR	0.002783	0.000919	9.1623	0.0025	1.0028	1.0010 to 1.0046
AST	0.006726	0.001103	37.1713	<0.0001	1.0067	1.0046 to 1.0089
ALT	-0.00528	0.002048	6.6576	0.0099	0.9947	0.9907 to 0.9987
GGT	0.001502	0.000487	9.5107	0.002	1.0015	1.0005 to 1.0025
Portal vein involvement	0.6732	0.1676	16.1299	0.0001	1.9604	1.4115 to 2.7229
Hepatic vein involvement	-0.761	0.3279	5.3867	0.0203	0.4672	0.2457 to 0.8884
AFP <9.6 ng/mL	-0.4873	0.1403	12.0702	0.0005	0.6143	0.4666 to 0.8086

-Backward likelihood ratio analysis. Chi-squared=154.171; p<0.0001. AFP: Alpha-fetoprotein; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; CI: Confidence interval; GGT: Gamma-glutamyl transpeptidase; Na: Sodium; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.

tool. The CLIP score is more comprehensive, as it includes the Child-Pugh grade, AFP value, and tumor size as numerical values.

Among the 10 independent parameters we used in multivariate analysis, tumor size and number, AFP level, and vascular invasion are well known prognostic parameters. However, platelet count, platelet-to-lymphocyte ratio (PLR), and the levels of gamma-glutamyl transferase (GGT), aspartate transaminase (AST), and alanine transaminase (ALT) have not been yet been used in any score. Transaminase elevation increases HCC risk,[16-18] but there are few studies that have examined its relationship to HCC prognosis.[19,20] The greater the damage to liver cells, the greater the enzyme elevation. More cell turnover and inflammation occurs, which increases the risk of cancer[16-18] and recurrence.[20] Some research has indicated that an inflammatory environment appears to be related to HCC prognosis.[21,22] It may be that the instability of transaminase levels prevented the use of these parameters in prognostic scores.

The negative relationship between platelet count and survival is probably related to the acute phase reactant properties of platelets in aggressive and spreading cancers. In recent years, the neutrophil-to-lymphocyte ratio and the PLR have been associated with prognosis in many cancers, and it has been suggested that these ratios can be used as a

Table 5. Survival comparisons

A. Survival time in cases of hepatitis B, hepatitis C, hepatitis delta, and alcoholic liver diseases (months)

Etiology	Mean[a]				Median			
	Estimate	SE	95% CI		Estimate	SE	95% CI	
			Lower bound	Upper bound			Lower bound	Upper bound
HBV	57.9	4.7	48.7	67.1	27	3.3	20.5	33.5
HCV	67.4	7.5	52.7	82.1	42.5	8.1	26.5	58.4
Alcohol	40.4	11.3	18.2	62.5	12.5	5.4	1.9	23.0
Delta	79.6	18.4	43.6	115.6	68.3	30.4	8.7	127.9
Overall	59.9	3.8	52.5	67.3	29.8	2.6	24.7	34.8

B. Survival time comparisons in binary groups (p values)

Etiology	HBV	HCV	Alcohol	Delta
HBV		0.106	0.029	0.158
HCV	0.106	0.002	0.495	
Alcohol	0.029	0.002	0.033	
Delta	0.158	0.495	0.033	

a: Estimation is limited to the greatest survival time if it is censored; In general comparison: Chi-squared=10.899; p=0. 012. CI: Confidence interval; HCV: Hepatitis C virus; HBV: Hepatitis B virus.

Table 6. Factors associated with the number of tumors at the time of diagnosis

Variables	A (n=461)	B (n=145)	C (n=160)	p	Post hoc test
Gender (% male)	76.1	80	86.3	0.017	
Follow-up duration before HCC (median-weeks)	199.5	137	34	0.008	A-C
Diagnosis in follow-up period (%)	64.6	67.6	41.3	<0.0001	
Portal vein involvement (%)	17.6	18.8	35.7	<0.0001	
Hepatic vein involvement (%)	3.1	3.5	8.5	0.026	
Ascites (%)	31.4	41.7	47.1	0.001	
Inactive HBV (%)	59.9	43.6	31.8	0.002	
Log HBV DNA (IU/mL)	2	2.87	3.63	0.002	A-C
Neutrophils (x/mm^3)	3732	3451	4709	<0.0001	A-C,B-C
Platelets (x/mm^3)	121000	92000	175500	<0.0001	A-B,A-C,B-C
Neutrophil-lymphocyte ratio	3.28	3.14	5.2	0.028	A-C
Platelet-lymphocyte ratio	94.2	73.5	113.57	<0.0001	A-B,B-C
AST (U/L)	45	49.5	65	<0.0001	A-C
ALT (U/L)	32.5	33	44	0.003	A-C
ALP (U/L)	118	107	146	<0.0001	A-C,B-C
GGT (U/L)	67.5	63	103	<0.0001	A-C,B-C
Albumin (g/dL)	3.8	3.7	3.5	<0.0001	A-C,A-B
INR	1.1	1.1	1.2	0.01	A-B
Total bilirubin (mg/dL)	1	1.13	1.3	<0.0001	A-B,A-C
Log AFP (ng/mL)	1.15	1.47	1.65	<0.0001	A-C,B-C
MELD	9	10	10	0.001	A-B,A-C
Child-Pugh	5	5	6	<0.0001	

A: Number of tumors: 1; B: Number of tumors: 2 or 3; C: Number of tumors: >3 or infiltrated or multifocal. Post hoc analysis: Comparison of binary groups pairwise analyzed after Kruskal-Wallis analysis. Letters with hyphens between them indicate groups with a significant difference between them. n: The data of 22 patients was not available; the distribution reflects 766 patients. AFP: Alpha-fetoprotein; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGT: Gamma-glutamyl transpeptidase; INR: International normalized ratio; MELD: Model for End-stage Liver Disease; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio.

marker.[23,24] In this study, both parameters were associated with length of survival, however, the PLR was more prominent in the multiple regression analysis. A good prognosis was associated with an AFP of <9.6 ng/mL. In many prognostic systems, the AFP level is excluded. However, it is gradually becoming better understood that this value is important to prognosis, and it is anticipated that AFP may be included in the BCLC in the future. AFP may play a role in the better correlation of the CLIP score to survival time.

The prognostic index derived from multivariate analysis demonstrated a better association with survival than the BCLC, CLIP, Okuda, or ALBI measures in our population. However, it must of course, be validated in other HCC populations to be generally accepted.

Study Limitations

As in other retrospective observational studies, difficulty obtaining sufficient data and verification were obstacles. Since this is a single-center study, the results cannot be generalized before validation in other populations.

A major drawback of HCC prognostic studies is that treatment can affect prognosis. To our knowledge, the published studies of HCC survival time have all included post-treatment survival in the overall survival analysis. If the treatment time data are eliminated, it is impossible to predict the actual long-term lifespan of patients, and survival data are often obtained using the outcome of late-stage patients who cannot be cured, which also does not reflect the whole truth. It is more realistic to calculate an expected lifespan by including the outcomes of treatment. It is clear that patients who can undergo curative treatment have a better prognosis.

Conclusion

The number and diameter of tumors, blood platelet count, PLR, AST, ALT, GGT, portal vein involvement, hepatic vein involvement, and an AFP level of <9.6 ng/mL were independently associated with the length of survival of patients with HCC. The positive predictive value of the prognostic index derived from these parameters for 5- and 10-year survival or overall survival was approximately 86%. We should consider integrating this prognostic index into the criteria we use for the treatment decision of patients with HCC.

Ethics Committee Approval: The Ege University Clinical Research Ethics Committee granted approval for this study (date: 01.09.2018, number: 18-1/27).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – SA, USA, AZK, FG; Design – SA, NGU, USA, AOO; Supervision – USA, FG, AZK; Fundings – AOO, GE, AZK; Materials – SA, AU, FC, MA; Data Collection and/or Processing – AMB, IT, MA, AS, AU, FC; Analysis and/or Interpretation – AOO, AS, NGU, FC, AU, AMB; Literature Search – AS, IT, MA, AMB, GE; Writing – SA, NGU, USA, FG; Critical Reviews – AOO, USA, FG, GE, IT.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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