ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Effect of Treatment Cost and Methods on Survival in Hepatocellular Carcinoma

Hepatosellüler Karsinomda Tedavi Maliyeti ve Tedavi Yöntemlerinin Sağkalım Üzerine Etkisi

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ABSTRACT

Aim: *Survival data for patients with hepatocellular carcinoma (HCC) is heterogeneous. We aimed to analyze the survival and cost of treatment in cirrhotic patients with HCC.*

Materials and methods: *From May 1998 to March 2015, 157 patients with HCC diagnosed and treated in a single center were assessed retrospectively. Etiology, biopsy findings, Child-Pugh-Turcotte (CPT) scores, Barcelona Clinical Liver Cancer (BCLC) stages, treatment response, cost, and prognostic factors were recorded. Deaths due to complications of cirrhosis or other diseases were excluded.*

Results: *157 patients (82.8% male) with a mean age of 62.2±11.4 years at diagnosis were included. Etiology was HBV (56%), HCV (26.1%), cryptogenic (11.5%), and others (6.4%). Median lesion diameter was 4 (0.5–28) cm. 1, 2, and ≥3 lesions were present in 46.5%, 19.1%, and 34.2% of patients, respectively. Treatments were as follows: palliative (n: 53), transarterial chemoembolization-TACE (n: 53), radiofrequency ablation-RF (n: 14), radioembolization (n: 3), alcohol (n: 5), and chemotherapy (n: 14). Resection (n: 9) and transplantation (n: 6) were amenable in few patients. Before treatment, 114 (72.6%) patients were in the CPT A/B group, but 93 (59.3%) of all patients were initially staged as BCLC-C/D. Overall survival was 11.6±0.9 months, with 32% probability of surviving one year. Kaplan-Meier analysis revealed that pre-treatment CPT score, BCLC stage, TACE, and resection significantly affect survival. Cox regression defined BCLC stage (stage B: HR=9.58, 95% CI=1.03–88.98, p=0.047; stage C: HR=13.41, 95% CI=1.37–130.85, p=0.026, stage D: HR=24.72, 95% CI=2.33–262.46, p=0.008) and TACE (HR=2.36, 95% CI=1.18–4.71, p=0.015) as independent predictors of survival.*

Conclusion: *Treatment modalities were not significantly different in terms of cost (p=0, 656). Hepatocellular carcinoma was usually diagnosed late, and treatment modalities were similar in cost. Barcelona clinical liver cancer stage and TACE were predictive of survival.*

Keywords: *hepatocellular carcinoma; cirrhosis; treatment methods; survival; cost-effectiveness*

ÖZET

Amaç: *Hepatosellüler karsinom (HSK) tanısı alan hastaların sağkalım verileri farklılık göstermektedir. Çalışmamızın amacı, HSK tanısı alan sirotik hastaların tedavi ile ilişkili olarak maliyet ve sağkalım verilerini incelemektir.*

Materyal ve metot: *Mayıs 1998 ve Mart 2015 tarihleri arasında tek merkezde tedavi gören, 157 hastanın bilgileri tarandı. Etiyoloji, biyopsi sonucu, Child-Pugh-Turcotte (CPT) skoru, Barcelona Clinic Liver Cancer (BCLC) evrelemesi, tedavi cevabı, maliyet ve prognostik faktörleri kaydedildi. Siroz komplikasyonları ve diğer hastalalıklara bağlı vefat edenler çalışmadan çıkarıldı.*

Bulgular: *157 hastanın (%82,8 erkek) tanı anındaki ortalama yaşı 62,2±1,4 yıl idi. Etiyolojide HBV (%56), HCV (%26,1), kriptojenik (%11,7) ve diğer patolojiler (%19,1) mevcuttu. Ortanca kitle boyutu 4 (0,5–28) cm idi. Kitle sayılarına göre %46,5 tek kitle, %19,1'inde iki adet kitle ve %34,2 hastada ise ≥3 kitle saptandı. Uygulanan tedaviler, palyatif (n: 53), transarteriyel kemoembolizasyon-TAKE (n: 53), radyofrekans ablasyon-RF (n: 14), radyoembolizasyon (n: 3), alkol (n: 5) ve kemoterapi (n: 14) idi. Rezeksiyon (n: 9) ve transplantasyon (n: 6) sadece birkaç hastaya uygulanmıştı. Tedavi öncesi, 114 hasta (%72,6) CPT A/B idi. Fakat başlangıçta tüm hastaların %59,3'ünde (n: 93) BCLC evrelemesi B/C idi. Ortalama sağkalım 11,6±0,9 ay ve bir senelik sağkalım olasılığı %32 olarak saptandı. Kaplan-Meier analizi ile incelendiğinde tedavi öncesi CPT skoru, BCLC evresi (evre B: HR=9,58, %95 G.A.=1,03–88,98, p=0,047; evre C: HR=13,41, %95 G.A.=1,37–130,85, p=0,026, evre D: HR=24,72, %95 G.A.=2,33–262,46, p=0,008), TAKE yapılması (HR=2,36, %95 G.A.=1,18–4,71, p=0,015) ve rezeksiyon yapılmasının sağkalımla anlamlı olarak ilişkili olduğu bulundu. Cox regresyon analizine göre BCLC evrelemesinin, sağkalım üzerinde bağımsız risk faktörü olduğu saptandı. Tedavi modaliteleri arasında maliyet açısından anlamlı fark saptanmadı. (p=0,656)*

Sonuç: *Hepatosellüler karsinom tanı anında, öncelikle rezeksiyon ve transplantasyon uygunluğu değerlendirilmeli, küçük kitlelerin varlığında ise RF düşünülmelidir. Hepatosellüler karsinom için erken dönemde uygulanan küratif tedavilerin maliyet açısından daha etkin olduğunu, BCLC evresi ve TAKE uygulamasının ise sağkalım açısından önemli olduğunu gözlemledik.*

Anahtar kelimeler: *hepatosellüler karsinom; siroz; tedavi metodları; sağkalım; maliyet*

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Introduction

Hepatocellular carcinoma (HCC) is a tumor originating in the liver[1]. Globally, it ranks sixth among all malignancies and fourth in cancer-related deaths[2–4]. The average survival time is 6 to 20 months. This type of carcinoma is mainly observed in males between 50 and 70[5,6]. The most prominent risk factor known in the etiology is cirrhosis[7]. While alcohol consumption is the most common cause of cirrhosis-related HCC in Europe, hepatitis B (HBV) and hepatitis C virus (HCV)-associated chronic hepatitis are the leading causes in Türkiye[8]. Türkiye is in the intermediate incidence group in terms of HCC[9]. It is also established that non-alcoholic steatohepatitis (NASH) and diabetes mellitus play a role in the development of HCC[10].

Etiologic factors, clinical status of the patient, stage of the disease, and comorbidities should be assessed in the treatment of HCC, which is usually diagnosed at an advanced stage despite known risk factors. Treatment options include surgical resection, transplantation, transarterial radioembolization (TARE), percutaneous radiofrequency ablation (RFA), transarterial chemoembolization (TACE), transarterial embolization (TAE), and sorafenib. Treatments may vary depending on how advanced the disease is at the time of diagnosis, liver reserve, and comorbidities. The present study aimed to analyze the effects of different treatment options on survival and the cost of treatment in patients who were followed and treated for HCC.

Materials and Methods

This cross-sectional retrospective study was conducted in the Gastroenterology Clinic of Başkent University Adana Dr. Turgut Noyan Training and Research Hospital. The study was approved by the Başkent University Research Board (KA14/177). Three hundred potential HCC patients with International Classification of Diseases (ICD) code C22.0 who were seen in the Training and Research Hospital between June 1998 and January 2015 were analyzed. Data on the patients were obtained from the hospital data bank. Missing information and data updates were completed in consultation with patients or their relatives. Seventy-seven patients with inconsistent/uncertain pathology findings and incorrect ICD coding were excluded.

Patient Selection

From a total of 223 patients, those with a second malignancy other than HCC, fibrolamellar variant, suspicious pathology results, other primary or secondary tumors of the liver, and those with severe immunosuppressive agents were excluded. Additionally, patients with incomplete documentation, patients without regular follow-ups, and patients who died due to cirrhosis complications after HCC diagnosis were also excluded from the study (Fig. 1). After applying exclusion criteria, 157 patients diagnosed with HCC were included in the study.

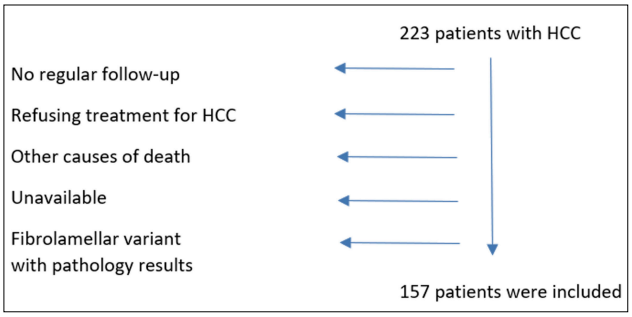

Figure 1. *Algorithm for patient selection.*

Diagnosis of Hepatocellular Carcinoma

The current guidelines of the American Association for the Study of Liver Disease (AASLD) were used to diagnose HCC[8,11,12]. The diagnosis was made by assessing serum AFP levels and radiologic imaging features (large and/or arterial hypervascularity)[11].

- For patients seen between 1998 and 2010, the AASLD 2005 guidelines (at least 1 criterion) were followed:
  - Specific radiologic sign with two different imaging modalities such as MRI, CT, or USG,
  - Alpha-fetoprotein (AFP) >200 ng/mL and specific radiologic signs by MRI or CT,
  - Pathological criterion.
- For patients seen between 2010 and 2015, the AASLD 2010 guidelines (at least 1 criterion) were utilized:
  - Specific radiologic signs by MRI or CT,
  - Pathological criterion.

Disease Burden and Prognostic Assessment

Etiology, duration of chronic liver disease, time from the diagnosis of chronic liver disease to the diagnosis of HCC, number of masses (1,2, or ≥3 (multiple)), pathology results, and treatment modalities were analyzed. Disease severity was graded based on the Child-Pugh Turcotte (CPT) and Barcelona Clinic Liver Cancer (BCLC) staging systems. The treatments (curative, palliative, or symptomatic), pre-and post-treatment CPT

and BCLC stages, AFP values, and mass sizes were recorded. All patients were subjected to survival analysis.

Cost Analysis

Treatments were divided into surgical, systemic, and local treatments. Palliative treatments were excluded from the cost analysis as they included symptomatic treatments. Total price values in terms of patient and institutional payments were calculated in Turkish Lira (TRY). The average US dollar exchange rate between 1998 and 2015 was TRY 2.03 (https: //www. tcmb. gov. tr/). Local ablative treatments were calculated proportionally to the number of applications, and systemic chemotherapy was calculated proportionally to the number of courses. Surgical procedures with a total (package) price are calculated based on this price.

Statistical Analysis

Statistical analysis was performed with the IBM Statistical Package for Social Sciences (SPSS) program version 17.0 package program. Nonparametric values were expressed as numbers and percentages, while parametric values were expressed as mean and standard deviation. Chi-square and Fisher Exact tests were employed to compare parametric data. The Mann-Whitney U test was utilized for non-normally distributed data. Survival evaluations were performed using Kaplan-Meier analysis. Cox Regression Analysis was used to analyze the factors affecting mortality based on the survival analysis results. The dependent variable in the regression analysis designed to assess risk factors on life expectancy was set at overall survival. The statistical significance level for all tests was set at p=0.05.

Results

Among the 157 patients in the study, 17.19% were women, and the mean age for all patients at diagnosis was 62.2±11.4 years. The etiology was HBV 57.3%, HCV 26.1%, NASH 3.8%, alcohol 4.4%, and cryptogenic 11.4%. The median mass size was 4.0 cm (0.5–28.0). Child-Pugh Turcotte and BCLC stages pre- and post-treatment were found to be statistically and significantly different (for both; p<0.001). Diagnostic methods, biopsy results, mass sizes, CPT – BCLC scores, and treatment modalities are summarized in Table 1.

In the pre-treatment assessment, the number of masses did not affect the CPT score at the time of diagnosis (p=0.279). Recurrence of HCC was detected in 21.7% of all patients. However, no data on the recurrence status of 39.6% of the patients could be found in the records. A total of 91.1% of the patients were found to be deceased at the time of the study, according to telephone calls and/or hospital records. The mean survival time was 11.6±0.9 months. The 12-month survival probability of patients was 32%. Factors affecting survival in HCC patients are summarized in Table 2.

Low pre-treatment CPT stage, low BCLC stage, and TACI were associated with a positive effect on survival (p<0.001 for all). Mass resection was also positively affected survival (p=0.008) (Fig. 2). Furthermore, an increase in CPT stage from A to C and BCLC stage from 0 to D were associated with a negative effect on survival. However, disease etiology, RFA, alcohol injection, or chemotherapy did not significantly affect survival (p>0.05).

Table 1. *Diagnostic methods, pathology results, mass sizes, and disease staging*

		n (%)
Diagnostic method	Radiology and AFP	34 (21.7)
	Biopsy	123 (78.3)
Pathology result	Differentiated	26 (16.6)
	Less differentiated	4 (2.5)
	Clear	3 (1.9)
	Other / mix	33 (21)
	Malignant epithelial	17 (10.8)
	Medium differentiation	6 (3.8)
	Good differentiation	17 (10.8)
	Indiscriminate[∞]	17 (10.8)
Number of audiences	1	73 (46.5)
	2	30 (19.1)
	3	16 (10.2)
	>3	38 (24.2)
Pre-treatment HSK staging	CPT stage A	62 (39.5)
	CPT stage B	52 (33.1)
	CPT stage C	43 (27.4)
	BCLC stage 0	1 (0.5)
	BCLC stage A	16 (10.2)
	BCLC stage B	47 (29.9)
	BCLC stage C	40 (25.5)
	BCLC stage D	53 (33.8)
Post-treatment HCC staging	CPT stage A	6 (3.8)
	CPT stage B	21 (13.4)
	CPT stage C	130 (82.8)
	BCLC stage 0	-
	BCLC stage A	-
	BCLC stage B	4 (2.5)
	BCLC stage C	13 (7.6)
	BCLC stage D	140 (89.8)
Treatment methods	Palliative treatment	53 (33.8)
	Trans arterial radioembolization	3 (1.9)
	Trans arterial chemoembolization	53 (33.8)
	Percutaneous radiofrequency ablation	14 (8.9)
	Alcohol injection	5 (3.2)
	Resection	9 (5.7)
	Chemotherapy	47 (29.9)
	Transplantation	6 (3.8)

[∞]There was no differentiation in the pathology report.
BCLC: Barcelona Clinic Liver Cancer; **CPT:** Child-Pugh Turcotte.

Table 2. *Survival factors and risk*

		Alive; n: 14; n (%)	Exitus; n: 143; n (%)	p
Gender (F)		4 (14.8)	23 (85.2)	0.264
Age at the time of diagnosis of HCC*		65 (16–72)	63 (27–93)	0.695
Time elapsed between the diagnosis of chronic liver disease and HCC (months)*		22 (1–141.0)	18 (0–182)	0.424
Etiology	HBV	10 (71.4)	81 (55.9)	0.080
	HCV	4 (28.6)	37(25.9)	0.760
	NASH	0 (0.0)	6 (4.2)	1.000
	Cryptogenic	1 (7.1)	17 (11.9)	1.000
	Alcohol	1 (7.1)	6 (4.2)	0.487
Mass Size (cm)		3 (1–13)	4 (0.5–28)	0.221
Number of mass	1	7 (50)	66 (46.2)	0.413
	2	4 (28.6)	26 (18.2)	
	3	2 (14.3)	14 (9.8)	
	Multiple	1 (7.1)	37 (25.9)	
Pre-treatment AFP (ng/mL) *		6.5 (1.0–1560)	318 (3–1162686)	0.0001
Post-treatment AFP (ng/mL) *		13.4 (4.0–6315)	703 (2.2–1050724)	0.056
Treatment initiation time (months)*		1.5 (0–160)	1 (0–12)	0.550
Treatments	Palliative	2(14.3)	51 (35.7)	0.142
	Radioembolization	-	3 (2.1)	1.000
	TACE	5 (35.7)	48 (33.6)	1.000
	FRG	1 (7.1)	13 (9.1)	1.000
	Alcohol injection	1 (7.1)	4 (2.8)	0.377
	Resection	1 (7.1)	8 (5.6)	0.579
	Chemotherapy	2 (14.3)	45 (31.5)	0.232
	Transplantation	2 (14.3)	4 (2.8)	0.090
Total cost (TL)*		923.1 (542.1–84086.5)	1022 (0–84000.7)	0.656
Length of stay (days)*		6.0 (2–15)	5.5 (0–26)	0.857

* average (min-max).
AFP: Alpha feto-protein; **HCC:** Hepatocellular carcinoma; **TACE:** Transarterial chemoembolization; **RF:** Radiofrequency ablation; **NASH:** Non-alcoholic steatohepatitis; **HBV:** Hepatitis B virus; **HCV:** Hepatitis C virus.

Age, baseline CPT and BCLC stages, and receipt of TACE, RFA, alcohol injection, resection, and chemotherapy were included in the regression model, analyzing the effect of treatment modalities and scoring systems on survival. Age, initial CPT stage, RFA, alcohol injection, resection, and chemotherapy alone were not found to be risk factors for survival ($p>0.05$). Pre-treatment BCLC stage and TAC were detected as independent survival risk factors. Barcelona clinic liver cancer stage 0 and CPT stage A did not affect exitus (Table 3).

The average HCC treatment for one patient was TRY 7722.50±1946.50 (approximately 3600 USD). Regardless of etiology, diagnosis mode, and size, the number of masses did not make a statistically significant difference in cost. However, it was demonstrated that as the pre-treatment CPT and BCLC stages increased, the cost spent also increased ($p=0.003$) (Table 4).

Discussion

After applying exclusion criteria, 157 HCC patients were included in this retrospective cross-sectional study. The hepatitis B virus was detected to be the primary etiologic agent, and cases were more common in the male gender. In patients diagnosed with HCC, having an early BCLC stage at the time of diagnosis and being able to perform TACE may increase survival. It was also found that patients with high CPT and BCLC stage at the time of HCC diagnosis had higher treatment costs.

HCC is closely associated with advanced liver injury and cirrhosis due to different underlying causes[13]. The most common etiologic agents are hepatitis viruses. Hepatitis B and HCV cause 60% and 33% of cases in developing countries and 23% and 20% in developed countries, respectively[12,14]. In a multicenter study involving 963 patients with chronic liver disease in Türkiye, the primary etiology for 57.6% of patients was HBV; for 16.5%, it was HCV; and for 14.2%, it was chronic alcohol use (more than ten years)[15]. The median age at diagnosis of HCC is 50–60 years in Asia and Western Europe, and it is more common in men regardless of region[16,17]. Although the mean age at diagnosis in the present study was similar to that in European countries, the interval between liver disease and tumor diagnosis was shorter. This may be due to a later detection of the disease and/or etiologic factors. It is recognized that the median survival in HCC is between 6 and 20 months[18–21]. The mean survival of the patients in this current study correlated with the literature.

When CPT and BCLC stages, which are essential in the follow-up and treatment of HCC, were evaluated,

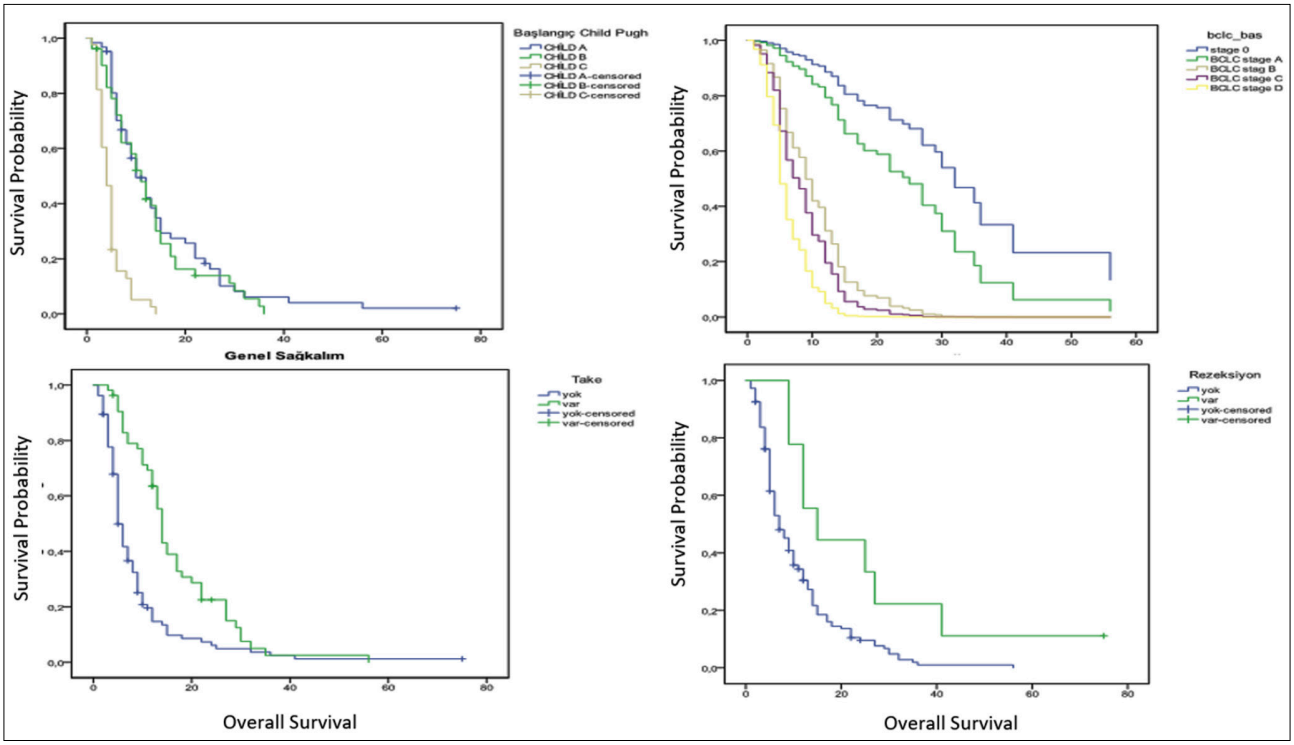

Figure 2. *Effect of scoring methods and treatments on survival.*

Table 3. *The effect of treatment methods and scoring systems on life expectancy*

	B	Standard Error	Forest	Degree of freedom	p	Hazard Risk	95% Confidence Interval
Age at the time of diagnosis of HCC	-0.01	0.009	0.33	1	0.562	0.99	0.98/1.01
CPT Stage A*	-	-	1.96	2	0.376	-	-
CPT Stage B	-0.11	0.227	0.25	1	0.616	0.89	0.57/1.39
CPT Stage C	0.35	0.359	0.93	1	0.334	1.41	0.70/2.86
TACE	0.86	0.352	5.96	1	0.015	2.36	1.18/4.71
FRG	0.32	0.340	0.86	1	0.354	1.37	0.70/2.67
Alcohol injection	0.23	0.539	0.19	1	0.663	1.26	0.44/3.64
Resection	0.54	0.468	1.32	1	0.250	1.71	0.68/4.28
Chemotherapy	0.03	0.269	0.01	1	0.903	1.03	0.61/1.75
BCLC Stage 0 *	-	-	27.69	4	0.000	-	-
BCLC Stage A	0.64	1.151	0.31	1	0.576	1.903	0.20/18.17
BCLC Stage B	2.26	1.137	3.95	1	0.047	9.58	1.03/88.98
BCLC Stage C	2.60	1.162	4.99	1	0.026	13.41	1.37/130.85
BCLC Stage D	3.21	1.205	7.08	1	0.008	24.72	2.33/262.46

*Referenced (dependent) variable.
BCLC: Barcelona Clinic Liver Cancer; **CPT:** Child-Pugh Turcotte.

it was observed that more than half of the patients in the present study were in CPT stage A. However, when tumor size, performance, and liver reserve were assessed, most of the patients were found to be in an advanced BCLC stage. The presence of HCC in the setting of advanced chronic liver disease with a high tumoral burden reduces treatment options. Tumor resection can be a curative treatment option in BCLC Stage 0 patients and BCLC Stage A patients with a single tumoral lesion, preserved liver reserve, and no portal hypertension. Liver transplantation can provide a cure for HCC patients with portal hypertension within the Milan criteria[22,23].

The present study revealed that resection and transplantation could be applied to very few patients because most had advanced liver disease and/or extensive tumors. Transarterial chemoembolization and ablative therapies have come to the forefront in patients on the liver transplant list in whom RF or surgical treatment options are not suitable as bridging therapy[24]. We observed that the TACE treatment option was

Table 4. *Cost analysis according to disease characteristics (TL)*

		n	Average	At least	At the most	p
CPT	Stage A	52	1326.2	85.8	84086.5	0.003
Before treatment	Stage B	40	923.1	103.2	84000.7	
	Stage C	10	4966.4	-	84000.7	
BCLC	Stage 0	1	542.1	542.1	542.1	0.003
Before treatment	Stage A	11	703.1	95.8	84086.5	
	Stage B	47	1002.6	542.1	9400.3	
	Stage C	35	1041.3	85.8	84000.7	
	Stage D	8	4314.3	-	84000.7	
Number of mass	1	47	1002.6	-	84000.7	0.404
	2	24	1021.9	-	84086.5	
	3	12	601.2	103.2	8628.6	
	Multiple	19	3389.8	-	10980.4	
Therapy	Resection	9	1348.4	703.1	9400.3	0.454
	Chemotherapy	47	8086.5	85.8	84086.5	0.668
	Transplantation	6	84000.7	84000.7	84086.5	<0.001
	Local ablative treatment	29	1002.6	501.3	9400.3	0.069

BCLC: Barcelona Clinic Liver Cancer; **CPT:** Child-Pugh Turcotte.

frequently used among the groups of patients included in this study, including a large number of patients for whom surgery or liver transplantation were not valid options. Several studies have compared the efficacy of TACE with resection in patients with BCLC stage B HCC. Among 171 patients with BCLC stage B and CPT stage A in a study where both methods were compared, it was revealed that the mean survival was longer in those who underwent TACE ($p<0.01$) with no significant difference in mortality rates at follow-up[25]. Another study demonstrated that the post-procedure complication rate and length of hospitalization were higher for patients with BCLC stage B HCC than those undergoing hepatic resection. According to survival rates, surgical resection was more beneficial in BCLC stage B patients with masses 1–3.

In contrast, surgical resection and TACE were similar in patients with masses >3[26]. Moreover, studies show that for cirrhotic patients with intermediate-stage HCC who can undergo mass resection, resection provides a survival advantage over TACE[27,28]. The current study revealed that TACE prolonged survival, which could be since patients at all stages were included. It can be concluded that success rates may be high at the research hospital because the TACE treatment has been used for many patients over a significant period, creating experienced treatment practitioners. RF, another ablative method and one of the curative treatments, was less preferred because most patients within the current study were in an advanced BCLC stage at the time of diagnosis. The high frequency of palliative treatment is also due to the advanced BCLC stage.

Tumor size, microvascular invasion, multifocality, and poor differentiation are key to detecting disease recurrence. In particular, poor differentiation, micro and/or macrovascular invasion, and the presence of satellitic nodules increase the recurrence rate of HCC up to 70% at 5 years[29,30]. The present research found a high recurrence rate due to the large tumor diameter at the time of diagnosis, the high number of masses, and the frequent occurrence of poor differentiation. Inadequate liver reserve at the time of diagnosis, and therefore inability to utilize curative treatments, and the growth of micronodules also increase the frequency of recurrence.

The serum AFP level in HCC patients is generally thought to be proportional to the growth activity of the tumor[18]. Therefore, a return to elevated AFP levels after treatment is interpreted as tumor growth and can be used as a survival predictor. In a study of 1579 patients with HCC, the association of AFP alone with survival was found to have a sensitivity of 52.9% and specificity of 93.3%[19]. In parallel with the literature, it was observed that in this current study, survival was low in patients with high AFP levels, which included most patients with advanced HCC. A high pre-treatment AFP value may indicate increased mortality. Another reason for the high mortality rates may be that the majority of patients were in advanced BCLC stages. However, most patients were initially diagnosed as CPT stage A. Hepatocellular carcinoma is a malignancy that often develops in the setting of chronic liver injury, and cirrhosis has a high biological variability. Its diagnosis may be delayed even during follow-up.

Considering the treatment methods selected by assessing various factors such as the number of tumoral

masses, liver reserve, stage of the disease, and supportive interventions, it is seen that HCC treatment can lead to significant health expenditures. The application of curative treatments is practical regarding both prognosis and cost[20,21,31]. This research determined that liver transplantation was more cost-effective than other treatment options. This research also demonstrated that high CPT and BCLC stages may increase healthcare expenditures. The belief is that financial spending may be higher than the general average because the patient profile had advanced stage HCC, and local ablative treatments were preferred as first-line treatment.

Conclusion

For HCC patients who are mostly diagnosed at advanced stages, with low initial BCLC stages, the possibility of curative treatment and the application of TACE as a treatment option seems to increase survival and reduce health expenditures.

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