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Research Article

Clinical outcomes of sorafenib treatment in Child-Pugh B hepatocellular carcinoma patients: a retrospective single-center study

Child-Pugh B hepatoselüler karsinom hastalarında sorafenib tedavisinin klinik sonuçları ve prognostik faktörleri: retrospektif tek merkezli bir çalışma

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Abstract

Aim: Hepatocellular carcinoma (HCC) is a leading cause of liver-related mortality, particularly in patients with cirrhosis. sorafenib is the one of primary systemic therapies for advanced HCC. This study evaluates the clinical outcomes and prognostic factors of sorafenib treatment in this patient group.

Material and Methods: This retrospective, single-center study included 28 Child-Pugh B HCC patients treated with sorafenib. Patient characteristics, OS, and PFS were analyzed. Kaplan-Meier survival analysis and Cox regression were performed to identify prognostic factors, including TACE, TARE, and tumor size.

Results: Among 28 patients, 85.7% were male, and 89.3% had cirrhosis. Most (64.3%) underwent biopsy, and extrahepatic disease was rare (3.6%). HCC lesions were >5 cm in 67.9% of patients. Sorafenib resulted in SD (57.1%), PR (10.7%), and PD (32.1%). Median OS and PFS were 8.1 and 5.9 months, respectively. Cox regression analysis did not identify significant prognostic factors, as TACE, TARE, and tumor size showed no meaningful impact on survival. The median OS and PFS were 8.1 and 5.9 months, respectively. Most patients (57.1%) SD, while 32.1% had PD.

Conclusions: Sorafenib stabilized disease in most patients (57.1%), but 32.1% experienced progression, highlighting the need for improved patient selection and combination therapies. Compared to SHARP and Asia-Pacific trials, our study's outcomes differed due to the exclusive inclusion of Child-Pugh B score 7 patients. These findings underscore the importance of refining treatment strategies and identifying predictive biomarkers to optimize outcomes.

Keywords: hepatocellular carcinoma, sorafenib, child-B

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Öz

Amaç: Hepatoselüler karsinom (HCC), özellikle sirozu olan hastalarda karaciğerle ilişkili ölümlerin önde gelen nedenlerinden biridir. Sorafenib, ileri evre HCC için birincil sistemik tedavilerden biridir. Bu çalışma, Sorafenib tedavisinin klinik sonuçlarını ve prognostik faktörlerini değerlendirmektedir.

Gereç ve Yöntemler: Bu retrospektif, tek merkezli çalışma, Sorafenib ile tedavi edilen 28 Child-Pugh B HCC hastasını içermektedir. Hasta özellikleri, genel sağkalım (OS) ve progresyonsuz sağkalım (PFS) analiz edilmiştir. Kaplan-Meier sağkalım analizi ve Cox regresyon analizi, transarteryel kemoembolizasyon (TACE), transarteryel radyoembolizasyon (TARE) ve tümör boyutu gibi prognostik faktörleri belirlemek için kullanılmıştır.

Bulgular: Çalışmadaki 28 hastanın %85,7'si erkek ve %89,3'ü sirozluydu. Çoğu (%64,3) biyopsi yapılmıştı ve ekstrahepatik hastalık nadirdi (%3,6). Hastaların %67,9'unda HCC lezyonları >5 cm idi. Sorafenib tedavisi ile hastaların %57,1'inde stabil hastalık (SD), %10,7'sinde kısmi yanıt (PR) ve %32,1'inde progresif hastalık (PD) gözlendi. Ortanca OS ve PFS sırasıyla 8,1 ve 5,9 ay olarak hesaplandı. Cox regresyon analizi, TACE, TARE ve tümör boyutunun sağkalım üzerinde anlamlı bir etkisi olmadığını gösterdi.

Sonuçlar: Sorafenib, hastaların çoğunda (%57,1) hastalığın stabil kalmasını sağladı, ancak %32,1'inde progresyon gözlendi. Bu durum, hasta seçiminin iyileştirilmesi ve kombine tedavi yaklaşımlarının değerlendirilmesi gerektiğini vurgulamaktadır. SHARP ve Asya-Pasifik çalışmalarına kıyasla, çalışmamızda yalnızca Child-Pugh B hastalarının dahil edilmesi nedeniyle farklı sonuçlar elde edilmiştir. Bu bulgular, tedavi stratejilerinin optimize edilmesi ve prognostik biyobelirteçlerin belirlenmesinin önemini ortaya koymaktadır.

Anahtar Kelimeler: hepatosellür kanser, sorafenib, child-B

Introduction

Hepatocellular carcinoma (HCC) is a primary liver malignant tumor that typically develops in the setting of chronic liver disease, particularly in patients with cirrhosis or chronic hepatitis B virus infection. Approximately 75% of primary liver tumors are HCC, with cholangiocarcinoma comprising most of the remaining cases [1]. Recent advances in imaging have increased the early detection rate of HCC. Curative therapies, such as hepatic resection, liver transplantation, and radiofrequency ablation, are possible in early-stage HCC and thus improve patient survival rates [2,3]. Otherwise, trans-arterial chemoembolization is an important locoregional treatment for patients with unresectable HCC [4]. Sorafenib is a multitargeted, orally active small molecule tyrosine kinase inhibitors (TKI) that inhibits Raf kinase and the vascular endothelial growth factor receptor (VEGFR) intracellular kinase pathway [5]. It was the first systemic agent to show an overall survival (OS) benefit for advanced HCC in a placebo-controlled trial [6].

The efficacy of sorafenib has been extensively studied, with pivotal trials such as the SHARP and Asia-Pacific studies establishing its role in improving OS and progression-free survival (PFS) in patients with advanced HCC. However, real world studies indicate significant variability in patient response, particularly among different liver function subgroups. The GIDEON study and other prospective analyses suggest that treatment outcomes may be influenced by factors such as Child-Pugh classification, prior locoregional therapies, and baseline tumor burden.

In this study, we aimed to evaluate the clinical outcomes of sorafenib treatment in a cohort of patients with advanced HCC, focusing on survival metrics and potential prognostic factors. Unlike previous large-scale studies, our analysis exclusively included patients classified as Child-Pugh B, allowing for a more detailed assessment of treatment response in this specific patient population. Additionally, we sought to determine the impact of trans-arterial chemoembolization (TACE) and trans-arterial radioembolization (TARE) and HCC lesion size on survival outcomes in this cohort.

Material and Methods

This study was conducted retrospectively on 28 patients who were diagnosed with HCC and used sorafenib between 2017 and 2023 at Gülhane Training and Research Hospital.

Patient demographic and clinical characteristics were extracted from medical records, including gender, cirrhosis status, biopsy status, and presence of extrahepatic disease. Tumor characteristics such as lesion size and metastatic involvement were also recorded. The primary endpoints were OS and PFS,

assessed using Kaplan-Meier survival analysis. Ethical approval for this study was obtained from the Gülhane Training and Research Hospital Ethics Committee, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Due to the retrospective nature of the study, the Ethics Committee of Gülhane Training and Research Hospital (2024/506) waived the obligation to obtain informed consent.

Stastistical Analysis

Cox-regression analysis was utilized to identify potential prognostic factors influencing survival outcomes. The independent variables examined included the administration of TACE and TARE procedures (performed vs. not performed) and HCC lesion size. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated to determine statistical significance. OS was defined as the time from diagnosis to death from any cause, whereas PFS was defined as the time from the initiation of sorafenib treatment to disease progression.

All statistical analyses were performed using the IBM SPSS Statistics 27.0 software package. Continuous variables were described as medians (interquartile range (IQR)) and categorical variables as percentages. The Chi-square test was used to compare categorical variables, while the Mann-Whitney U test or Student's T-test was used to compare continuous variables. Survival curves and rates were estimated using the Kaplan-Meier method. The log-rank test was used to compare the survival outcomes between the groups. All reported p values were two-sided, and p values < 0.05 were regarded as statistically significant.

Results

An analysis of patient characteristics in this study, which included 28 patients, revealed that most of the study cohort was male (85.7%) and had underlying cirrhosis (89.3%). Additionally, a substantial proportion of patients (64.3%) had undergone a biopsy, while extrahepatic disease was observed in only a small fraction (3.6%).

None of the patients exhibited lung or bone involvement. Regarding HCC lesion size, 67.9% of patients had lesions larger than 5 cm. The analysis of responses to sorafenib indicates that most patients (57.1%) exhibited stable disease (SD), suggesting that sorafenib effectively maintains disease stability in a significant proportion of cases. A smaller percentage (10.7%) achieved a partial response (PR), while no patients achieved a complete response (CR). Progressive disease (PD) was observed in 32.1% of patients, highlighting the variability in treatment outcomes (Table 1).

Table 1. Baseline characteristics

Variable	Category	Count (n)	Percentage (%)
Gender	Male	24	85.7
	Female	4	14.3
Biopsy status	No	10	35.7
	Yes	18	64.3
Cirrhosis status	No	3	10.3
	Yes	25	89.3
Extrahepatic disease	No	27	96.4
	Yes	1	3.6
HCC lesion size	<5 cm	9	32.1
	>5 cm	19	67.9
TAKE rtatus	No	22	78.6
	Yes	6	21.4
TARE rtatus	No	23	82.1
	Yes	5	17.9
Best response to sorafenib	CR	0	0
	PR	3	10.7
	SD	16	57.1
	PD	9	32.1

The Kaplan-Meier survival analysis estimated a median OS was calculated as 8.1 months (95% CI: 6.274-10.059) (Figure 1). The median PFS time was 5.9 months (95% CI: 4.463–7.403) (Figure 2).

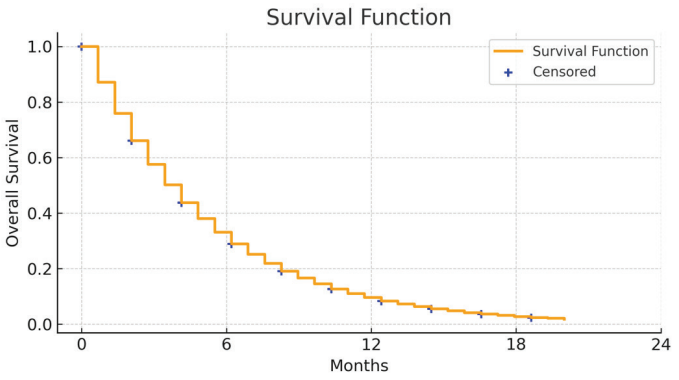

Figure 1. The median OS was calculated as 8.1 months (95% CI: 6.274-10.059)

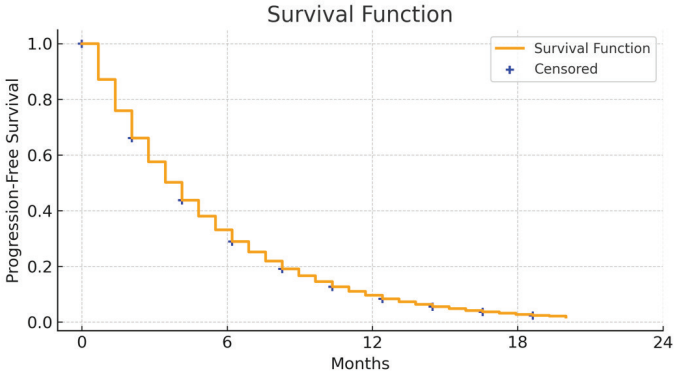

Figure 2. The median PFS time was 5.9 months (95% CI: 4.463–7.403).

A Cox-regression analysis was performed to evaluate the prognostic factors influencing patient outcomes. The variables included in the model were the presence of TACE (performed vs. not performed), TARE (performed vs. not performed), and HCC lesion size. None of the variables showed statistically significant associations with patient survival ($p > 0.05$ for all). Specifically, the HR for TACE (performed vs. not performed) was 1.39 (95% CI: 0.433–4.500, $p = 0.576$), indicating no significant impact on prognosis. Similarly, TARE (performed vs. not performed) had a HR of 0.78 (95% CI: 0.251–2.479, $p = 0.684$), suggesting no meaningful effect on survival. HCC lesion size also did not demonstrate a significant association with patient outcomes (95% CI: 0.351–2.198, $p = 0.781$).

Discussion

The findings of this study indicate that sorafenib treatment resulted in a SD response in most patients (57.1%), suggesting a role in disease stabilization rather than inducing tumor regression. This aligns with previous studies demonstrating that sorafenib provides a clinical benefit primarily by delaying disease progression rather than achieving high response rates [6,7].

Despite the observed disease stabilization, a significant proportion of patients (32.1%) exhibited PD, highlighting the need for improved patient selection criteria or combination therapies to enhance treatment effectiveness. The lack of CR and low PR rates (10.7%) emphasize the limited tumor shrinkage potential of sorafenib, reinforcing its role as a disease-modifying rather than curative agent in HCC management.

In the SHARP study, 95% of the patients were classified as Child-Pugh A, while the remaining 5% were Child-Pugh B. Based on the study findings, the median PFS and OS were measured as 5.5 months and 10.7 months, respectively [6]. In another study, the sorafenib Asia-Pacific trial, in which 97% of the patients were classified as Child-Pugh A, the median PFS and OS were reported as 6.5 months and 2.8 months, respectively [7]. The differences observed in our study may be attributed to the smaller patient cohort and the fact that all patients included were classified as Child-Pugh B, which could have influenced the treatment outcomes. T. Pressiani et al. conducted a prospective study on patients receiving sorafenib, in which the PFS and OS in the Child-Pugh B subgroup were determined to be 2.1 months and 3.8 months, respectively [8]. In an order prospective study conducted by M. Nakomo et al., which included a total of 365 patients, of whom 100 were classified as Child-Pugh B, the median PFS and OS were reported as 3.6 and 10.3 months, respectively [9]. In our study Kaplan-Meier survival analysis revealed a median OS of 8.1 and a median PFS of 5.9 months.

An analysis based on the results of the GIDEON study reported that in patients receiving sorafenib, those who underwent TACE had a median OS of 19 months and a median PFS of 8.4 months, whereas in patients who did not undergo TACE, the median OS and PFS were 9.8 months and 5.9 months, respectively [10]. In our study, the Cox-regression analysis did not identify significant prognostic factors among the examined variables (TACE and TARE procedures, HCC lesion size), suggesting that these clinical parameters may not serve as strong independent predictors of survival in patients treated with sorafenib. Unlike the GIDEON analysis, our study exclusively included patients classified as Child-Pugh B, which may have contributed to this difference in findings. The STAH trial, which randomized 339 patients with advanced HCC to receive sorafenib with or without concurrent TACE, demonstrated that the addition of TACE did not improve overall survival compared with sorafenib alone but was associated with a significant deterioration in liver function [11]. SORAMIC trial, which included 424 patients not eligible for TACE (90% classified as Child-Pugh A), showed that the addition of radioembolization to sorafenib did not lead to a significant survival benefit (median OS of 12.1 vs. 11.4 months) and was linked to increased rates of grade 3 or 4 adverse events [12] .These findings further emphasize the need for careful patient selection when considering combination approaches with sorafenib.

Overall, while sorafenib remains a standard treatment for advanced HCC, its limited efficacy highlights the importance of ongoing clinical investigations to identify novel therapeutic strategies that can improve patient prognosis and treatment response rates.

The analysis of responses to sorafenib indicates that most patients (57.1%) exhibited SD, suggesting that sorafenib effectively maintains disease stability in a significant proportion of cases. A smaller percentage (10.7%) achieved a PR, while no patients achieved a CR. PD was observed in 32.1% of patients, highlighting the variability in treatment outcomes. These findings underscore the need for further investigation into optimizing treatment efficacy and identifying predictive biomarkers for better patient stratification.

In conclusion, this study demonstrated that in the treatment of Child-Pugh B score 7 HCC patients, sorafenib primarily provides clinical benefit by delaying disease progression rather than achieving high response rates.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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Ethics approval

This study was approved by Gülhane Training and Research Hospital Ethics Committee with protocol number 2024/506

Authors' contribution

ÖFK: writing, original draft, methodology, investigation, data curation, conception, literature review, analisis, AT: writing, original draft, methodology, data curation, EKT: investigation, data curation, HA: investigation, data curation, supervision, NK: methodology, editing, critical review

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