

Research Article

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Compliance with hepatocellular carcinoma screening and the effectiveness of screening in cirrhotic patients

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Abstract

Current guidelines recommend that patients with cirrhosis be screened for the development of HCC every 6 months. The aim of our study was to determine whether HCC screening is performed with appropriate methods and at appropriate intervals in cirrhotic patients, and to evaluate the outcomes of the screening. This research is a retrospective cohort study. The study included patients aged 18 and over, diagnosed with Child-Pugh class A or B cirrhosis, who applied to our clinic between 2010 and 2020. Patients were divided into two groups: those who underwent guideline-recommended surveillance (imaging with ultrasound, CT, or MRI and/or measurement of AFP every 4-8 months) and those who did not undergo recommended surveillance (insufficient screening or no screening). These groups were compared in terms of HCC development, curative treatment, and survival. A total of 641 cirrhotic patients were included in the study. Only 146 (22.7%) patients underwent guideline-recommended HCC screening. During the follow-up period, a total of 89 patients were diagnosed with HCC (42 patients (28.8%) in the surveillance group and 47 patients (9.5%) in the nonsurveillance group, $p < 0.001$). In the surveillance group, the rate of early-stage HCC detection (83.3% vs. 40.4%), curative treatment rate (78.4% vs. 33.3%), and median survival time (74 vs. 21.7 months) were higher compared to the nonsurveillance group ($p < 0.001$). HCC screening rates in cirrhotic patients are quite low. Guideline-recommended HCC screening in these patients results in earlier diagnosis and increases both the likelihood of receiving curative treatment and overall survival.

Keywords: surveillance, screening, hepatocellular carcinoma, cirrhosis

1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary malignant tumor originating from hepatocytes. According to the World Health Organization's 2020 data, HCC ranks sixth in terms of incidence among all cancers and third among cancer-related causes of death (1). Prognosis for patients with advanced-stage HCC is generally poor, and treatment responses are limited. Clinical signs and symptoms related to the tumor often do not manifest until the early stages, making early diagnosis of HCC challenging in at-risk patients. Curative treatments for HCC, such as surgical resection, local ablation, and liver transplantation, can only be performed in early-stage cases. Hence, as in many other solid cancers, early diagnosis is crucial in HCC.

The majority of HCC patients have an underlying risk factor. Liver cirrhosis, viral hepatitis, and consumption of aflatoxin-contaminated foods are the most significant risk factors for HCC development. However, regardless of the cause, liver cirrhosis is recognized as the most significant risk

factor for HCC (2). Approximately 90% of cases of HCC develop on a background of cirrhosis, with an annual HCC incidence rate of 1-8% reported in cirrhotic patients.² For this reason, many guidelines, including those from the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD), recommend screening for HCC in patients at risk for early diagnosis (3-5). However, there is no complete consensus among guidelines regarding the optimal screening protocol for HCC. Additionally, there is no clear consensus on the most appropriate method for diagnosis in these patients. Therefore, new studies are needed to assess the effectiveness of diagnostic methods and screening programs for HCC. The aim of our study was to determine whether HCC screening was performed in cirrhotic patients using appropriate methods and intervals and to evaluate the outcomes of the screening.

2. Materials and Methods

2.1. Patient selection and study design

A total of 1196 patients, including 752 males and 444 females,

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were screened between January 2010 and January 2020, who had presented to the Gastroenterology Clinic of Karadeniz Technical University Medical Faculty or were being followed up for liver cirrhosis in the gastroenterology department. Patients aged 18 and above with a diagnosis of cirrhosis were included in the study. Patients with malignancies other than HCC, those with Child-Pugh class C cirrhosis, those diagnosed with HCC at admission, and patients with missing medical records were excluded from the study. The patient selection flowchart is shown in Fig. 1. Patients were initially defined based on the International Classification of Diseases, Ninth Revision (ICD-9) codes for confirmed cirrhosis (456.0, 456.1, 456.20, 456.21, 567.2, 567.23, 571.2, 571.5, and 572.2). The diagnosis of cirrhosis was established based on typical cirrhosis findings in imaging methods (nodular appearance, heterogeneous echogenicity, decreased vascularity, caudate lobe hypertrophy, etc.), consistent laboratory findings (elevated serum bilirubin and INR, decreased serum albumin and platelets), and clinical signs related to cirrhosis (ascites, splenomegaly, esophageal varices, spider angiomas, palmar erythema, gynecomastia, hepatic encephalopathy, etc.). Demographic data of patients, date of cirrhosis and HCC diagnosis, number of lesions, largest lesion size, comorbidities, cirrhosis complications, and administered treatment methods were retrospectively retrieved from patient files and recorded.

The study was approved by the Karadeniz Technical University Health Application and Research Center Ethics Committee dated 14.12.2020 and numbered 48814514-501.07.01-E.14680.

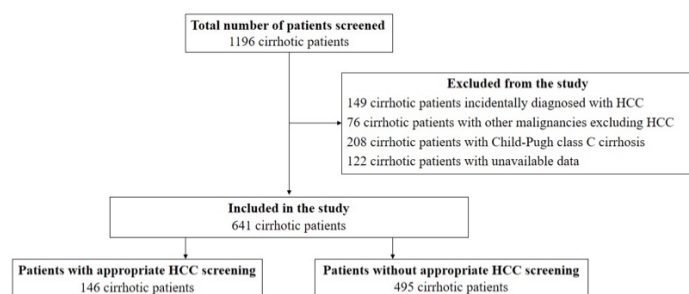


Fig. 1. The patient selection flowchart

2.2. HCC surveillance, detection, staging, and outcomes

All included patients were divided into two groups based on the follow-up interval: the surveillance group and the nonsurveillance group. Patients with an HCC diagnosis were categorized as the surveillance group if abdominal ultrasound, MRI, or CT had been performed for liver imaging within 4-8 months prior to diagnosis. Patients in the nonsurveillance group included those who had undergone liver imaging using any of the aforementioned methods within 8-24 months, or those who had not undergone any imaging at all. These groups were compared in terms of HCC development, curative treatment, and survival.

The diagnosis of HCC was made based on typical radiological findings according to the American Association for the Study of Liver Diseases (AASLD) criteria (4,5). In suspected cases, tumor biopsy was performed using imaging methods. Tumor characteristics, such as maximum diameter, number, and the presence of vascular invasion or distant metastasis, were determined. HCC staging was done using the Barcelona Clinic Liver Cancer (BCLC) system, and early HCC was defined as BCLC 0-A (6). HCC treatment was categorized as liver transplantation, surgical resection, local ablative treatment, transarterial chemoembolization (TACE) or transarterial radioembolization (TARE), systemic chemotherapy, or best supportive care. If HCC treatment included liver transplantation, surgical resection, or local ablative treatment, it was considered curative. Furthermore, using the Central Population Administration System - NVI (MERNİS), we defined overall mortality as any cause of death monitored until March 31, 2022.

2.3. Statistical Analysis

Categorical data were presented as counts (n) and percentages (%), while numerical data were presented as mean, standard deviation, median, and quartile values. The Mann-Whitney U test was used for the analysis of numerical data. The Chi-square or Fisher's exact test was employed for comparing categorical data. Survival rates of HCC patients were calculated using the Kaplan-Meier survival analysis. Differences in survival times were assessed using the Log-Rank test for treatment type, follow-up status, and HCC stage. A p-value less than 0.05 was considered statistically significant.

3. Results

3.1. Demographic and clinical characteristics according to follow-up status of all patients

Among the 641 patients in our study, 146 (22.7%) underwent HCC screening according to guidelines using any of the methods: USG, CT, or MRI (surveillance group), while it was found that 495 (77.3%) patients were not screened for HCC according to guidelines (non surveillance group). Among the 146 patients in the surveillance group, HCC developed in 42 (28.8%), and among the 495 patients in the nonsurveillance group, HCC developed in 47 (9.5%). The rate of HCC development was statistically higher in the surveillance group compared to the nonsurveillance group (28.8% vs. 9.5%, $p < 0.001$). In Table 1, the relationship between patients with and without follow-up with multiple variables such as gender and etiology was evaluated and no significant difference was found (there is no difference in etiology and gender between follow-up/non-follow-up). Demographic characteristics, clinical findings, and laboratory results of the cirrhotic patients included in the study according to their follow-up status are shown in Table 1. Table 2 shows the etiology distribution of HCC, and no significant difference was observed between etiologic groups in terms of follow-up benefit ($p = 0.944$).

Table 1. Demographic characteristics according to patient follow-up status

Variable	Follow-Up Group	Non-Follow-Up Group	p-value
Total patients, n (%)	146 (22,7)	495 (77,3)	
Age, mean $\pm$ SD	61,38 $\pm$ (54-71)	60,24 $\pm$ (52-69)	0,178
Age group, n (%)			0,226
40 years and below	10 (6,8)	33 (6,7)	
41-55 years	44 (30,1)	112 (22,6)	
56-70 years	63 (43,2)	222 (44,8)	
71 years and over	29 (19,9)	128 (25,9)	
Gender, n (%)			0,05
Male	93 (63,7)	270 (54,5)	
Female	53 (36,3)	225 (45,5)	
Comorbid diseases, n (%)			
HT	63 (43,2)	223 (45,1)	0,546 †
DM	62 (42,5)	205 (41,4)	0,548 †
CKD	23 (15,8)	69 (13,9)	0,745 †
HF	18 (12,3)	71 (14,3)	0,204 †
HL	23 (15,8)	79 (16)	0,349 †
Etiology of Cirrhosis, n (%)			
Hepatitis B	42 (29)	102 (20,6)	
Hepatitis C	28 (19,3)	82 (16,6)	
Alcohol consumption	10 (6,9)	28 (5,7)	
NASH	9 (6,2)	49 (9,9)	
Biliary	8 (5,5)	28 (5,7)	
Cryptogenic	15 (10,3)	77 (15,6)	
Cardiac causes	6 (4,1)	16 (3,2)	
Vascular causes	4 (2,8)	10 (2)	
Metabolic causes	4 (2,8)	6 (1,2)	
Other	1 (0,7)	15 (3)	
Unknown	19 (12,4)	82 (16,6)	
Cirrhosis Complications, n (%)			
Variceal bleeding	23 (15,8)	74 (14,9)	0,467 ‡
Ascites	54 (37)	208 (42)	0,277 ‡
Peritonitis	13 (8,9)	25 (5,1)	0,083 ‡
Hepatic encephalopathy	30 (20,5)	73 (14,7)	0,149 ‡
Hepatorenal syndrome	0 (0)	7 (1,4)	
AFP, n (%)			0,492
10 ng/ml and below	116 (87,2)	361 (88)	
11-400 ng/ml	15 (11,3)	47 (11,5)	
400 ng/ml and above	2(1,5)	2 (0,5)	
Child-Pugh Score, n (%)			0,934
A	77 (52,7)	263 (53,1)	
B	69 (47,3)	232 (46,9)	
Fib-4, median (IQR)	4,44 (3,16-6,82)	4,74 (2,84-7,39)	0,389
APRI, median (IQR)	1,21 (0,62-2,09)	1,2 (0,7-2,2)	0,437
MELD-Na, median (IQR)	11 (9-15)	11 (9-15)	0,190
HCC status, n (%)			<0,001
HCC developed	42 (28,8)	47 (9,5)	
HCC not developed	104 (71,2)	448 (90,5)	

HT: Hypertension, DM: Diabetes mellitus, CKD: Chronic kidney disease, HF: Heart failure, HL: Hyperlipidemia, HCC: Hepatocellular Carcinoma, FIB-4: The Fibrosis-4, APRI: AST to platelet ratio index, MELD: Model for end stage liver disease † Comparison between patients with and without the respective comorbidities ‡ Comparison between patients with and without the respective complications *p-value less than 0.05 was considered statistically significant

3.2. Demographic and clinical characteristics of patients diagnosed with HCC

Among the 641 patients in our study, 89 (13.9%) developed HCC during their follow-up. Among the patients diagnosed with HCC, 42 (47.2%) were in the surveillance group and 47

(52.8%) were in the nonsurveillance group. In the surveillance group, the rate of detecting early-stage (BCLC stage 0/A) HCC was higher compared to the nonsurveillance group (83.3% vs. 40.4%), the rate of detecting uni-nodular HCC lesions was higher (18.5% vs. 3.6%), and the rate of receiving curative

treatment was also higher (78.4% vs. 33.3%) ($p<0.001$). The mortality rate was lower in the surveillance group (38.1%) compared to the nonsurveillance group (72.3%) ($p<0.001$).

The demographic characteristics, laboratory findings, clinical features, and treatment outcomes of patients who developed HCC according to their follow-up status are

presented in Table 2.

When Kaplan-Meier survival analysis was conducted based on the follow-up status of patients who developed HCC, the median survival of patients in the surveillance group was 74 months, while it was 21.7 months (95% CI, 12.7-30.7) in the nonsurveillance group ($p<0.001$) (Fig. 2).

Table 2. Demographic and clinical characteristics, laboratory findings, and treatment outcomes of patients who developed HCC according to follow-up status

Variable	All HCC Patients	Follow-up Group	Non-Follow-Up Group	p-value
Number of Patients n (%)	89 (100%)	42 (47,2%)	47(52,8%)	
Age, mean $\pm$ SD	67,27 $\pm$ 10,09	68,48 $\pm$ 9,22	66,19 $\pm$ 10,8	0,418
Gender, n (%)				0,084
Male	62 (69,7)	33 (78,6)	29 (61,7)	
Female	27 (30,3)	9 (21,4)	18 (38,3)	
Etiology, n (%)				
Hepatitis B	41 (46,1)	18 (42,9)	23 (48,9)	
Hepatitis C	25 (28,1)	13 (31)	12 (25,5)	
Alcohol	5 (5,6)	3 (7,1)	2 (4,3)	
NASH	6 (6,7)	1 (2,4)	5 (10,6)	
Biliary	1 (1,1)	0	1 (2,1)	
Metabolic	1 (1,1)	0	1 (2,1)	
Cryptogenic	10 (11,2)	7 (16,6)	3 (6,4)	
Etiology Group, n (%)				0,944
Viral	66 (74,2)	31, (73,8)	35, (74,5)	
Nonviral	23 (25,8)	11, (26,2)	12, (25,5)	
HCC Diagnosis MELD-Na, n (%)				0,222
10 (%) and below	29 (34,9)	18 (43,9)	11 (26,2)	
11-18 (%)	48 (57,8)	20 (48,8)	28 (66,7)	
19 (%) and above	6 (7,2)	3 (7,3)	3 (7,1)	
MELD-Na Score, Median (IQR)	12(10-15)	11,5 (9-13)	12 (10-16)	0,058
AFP, median (IQR)	14,39(5,14-243,7)	12,12 (5,46-141,6)	38,87(5,14-258)	0,322
Largest Nodule Diameter, (%)				0,068
<2 cm	10 (11,2)	6 (14,3)	4 (8,5)	
2-3 cm	30 (33,7)	16 (38,1)	14 (29,8)	
>3 cm	49 (55,1)	20 (47,6)	29 (61,7)	
HCC Count				<0,001
Uninodular	45 (51,6)	27(18,5)	18 (3,6)	
Multinodular	44 (49,4)	15 (10,3)	29 (5,9)	
BCLC Stage, n (%)				<0,001
0/A	54 (60,7)	35 (83,3)	19 (40,4)	
B/C/D	35 (39,3)	7 (16,7)	28 (59,6)	
Diagnosis Method, n (%)				0,279
USG	9 (10,1)	2 (4,8)	7 (14,9)	
CT	41 (46,1)	20 (47,6)	21 (44,7)	
MR	39 (43,8)	20 (47,6)	19 (40,4)	
Treatment Method, n (%)				<0,001
Curative*	44 (53,7)	29 (78,4)	15 (33,3)	
Noncurative**	38 (46,3)	8 (21,6)	30 (66,7)	
Death Status n (%)				<0,001
Deceased	50 (56,2)	16 (38,1)	34 (72,3)	
Surviving	39 (43,8)	26 (61,9)	13 (27,7)	

HCC: Hepatocellular Carcinoma, MELD-Na: Model for End-Stage Liver Disease-Sodium, BCLC: Barcelona Clinic Liver Cancer, USG: Ultrasonography, CT: Computed Tomography, MR: Magnetic Resonance, AFP: Alpha feto protein,

*Curative treatment: liver transplantation, resection, RF, TACE (Transcatheter arterial chemoembolization);

** Noncurative treatment: systemic chemotherapy and best palliative treatment

p-value less than 0.05 is considered statistically significant.

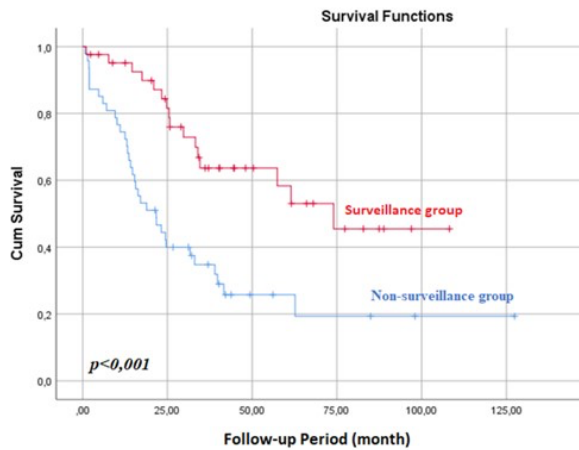


Fig.2. Survival analysis of patients diagnosed with hcc according to follow-up status

4. Discussion

Patients with cirrhosis are the highest-risk group for developing HCC, and the development of HCC in these patients is a significant cause of both mortality and morbidity (3,8). Therefore, guidelines such as AASLD and EASL recommend HCC screening every six months for cirrhotic patients with the aim of early detection and improved patient outcomes (3-5). However, despite guideline recommendations, low rates of HCC screening have been reported in these patients. In our study, the rate of cirrhotic patients undergoing HCC screening in accordance with guidelines was only 22.7%. Similar to our findings, several meta-analyses conducted between 2012 and 2021 reported HCC screening rates ranging from 18.4% to 24% (7-9). Our findings were also consistent with low adherence rates to HCC surveillance guidelines in various high-risk cohorts as reported in the literature (10-15). The markedly low HCC screening rates observed in cirrhotic patients can be attributed to several factors, including poor physician knowledge of screening guidelines, screening costs, and additional issues that may arise during contrast imaging, such as renal insufficiency, in these patients with accompanying comorbidities. Additionally, non-compliance of patients with physician recommendations could also have influenced adherence rates. To enhance screening rates in patients at risk, informing physicians about the recognition of chronic liver diseases, using nurse-patient reminder systems (such as phone calls, SMS, emails), and increasing patient-physician communication regarding HCC mortality could be beneficial. Furthermore, it is evident that there is a scarcity of studies assessing the effectiveness of HCC screening, highlighting the need for more research in this area.

In our study, the rates of HCC detection were statistically significantly higher in patients who underwent guideline-recommended HCC screening compared to those who did not (28.8% vs. 9.5%, $p < 0.001$) (Table 1). Similar to our study, other cohort studies in cirrhotic populations have reported higher rates of HCC diagnosis in screened patients (11,13). These studies have demonstrated that early-stage, unimodular,

or small-sized HCC lesion detection is associated with more frequent application of curative treatments and improved survival rates (10,13,16-19). Consequently, in light of our study's findings, we emphasize the need to include more cirrhotic patients who meet the criteria recommended by guidelines in screening programs.

HCC surveillance in cirrhotic patients is associated with a multitude of parameters prone to failure, including access to healthcare services in clinical practice, comorbid conditions, and cirrhosis-related complications. However, the absence of screening in these patients can lead to late-stage tumor detection (20). In our study, the rates of early-stage HCC (BCLC stage 0/A) detection were significantly higher in patients who underwent guideline-recommended HCC screening compared to those who did not (83.3% vs. 40.4%, $p < 0.001$) (Table 2). Similar to our study, it has been demonstrated in cirrhotic patients that guideline-adherent HCC screening is associated with early-stage tumor detection (21-24). However, Singal et al.'s prospective study in 2021 involving 614 cirrhotic patients found that although a proportionally higher number of early-stage HCC lesions were detected in the surveillance group compared to the nonsurveillance group, no statistically significant difference was observed (62.5% vs. 50%, $p = 0.69$) (25). Since only 26 of the 614 patients in this study developed HCC lesions during follow-up, the lack of statistically significant results may be explained by the small number of patients who developed HCC. Patients with very early and early stages of BCLC may be offered more effective survival-enhancing treatments than patients with intermediate and advanced stages (26). Therefore, it is an undeniable fact that including patients in the risk groups recommended by the guidelines in screening programs and detecting more early stage HCC will increase the number of patients reaching curative treatments.

As in all cancers, the goal for HCC patients should be to evaluate curative treatment options. Curative treatments depend on the stage of HCC disease and liver reserve. In early-stage HCC patients with preserved liver reserve, surgical resection and/or local ablative therapies are typically applied, whereas patients with a cirrhotic background should be evaluated for transplantation (3,15). Liver transplantation is one of the most frequent indications, especially in cases of HCC arising on a cirrhotic background. Liver transplantation for HCC treatment not only offers a curative approach for the tumor but also addresses the impaired liver function.²⁶ In our study, the rate of receiving curative treatment was significantly higher in the surveillance group compared to the nonsurveillance group (78.4% vs. 33.3%, $p < 0.001$) (Table 2). Similar findings are supported by multicenter studies conducted in cirrhotic patients (16,21). In a retrospective study conducted by Singal et al. in 2017 involving 374 patients with HCC on a cirrhotic background, those diagnosed through surveillance had a higher rate of receiving curative treatment compared to nonsurveillance patients (30.6% vs. 13.0%,

$p=0.02$) (28). Unlike our study, this study included patients receiving incidental/symptomatic treatment and Child-Pugh class C patients. The inclusion of Child-Pugh class C patients in their study might explain the lower rate of curative treatments compared to our study (78.4%). It is evident that many early-stage HCC patients in the non surveillance group were deprived of curative treatments. Given the retrospective nature of our data collection, we were unable to determine the reasons for inadequate treatment utilization. A multicenter prospective study involving a larger number of patients is needed to identify limitations in treatment access. In light of these studies, interventions that facilitate access to curative treatment can improve the effectiveness of the HCC screening process.

In our study, the mortality rate in the surveillance group was lower (38.1%) compared to the nonsurveillance group (72.3%) ($p<0.001$). Survival analysis based on patients' surveillance status revealed that median survival of patients with surveillance was higher than that of patients without surveillance. Similarly, a meta-analysis conducted by Signal et al. in 2022, which included 59 studies and 145,396 patients, demonstrated an association between HCC surveillance and increased overall survival (18). In various cohorts of patients diagnosed with HCC between 2015 and 2018, as in our study, retrospective studies showed that patients who underwent guideline-adherent HCC screening had significantly longer median survival compared to those who did not undergo screening (17,26,29). Yang et al.'s retrospective study in 2020 involving 401 patients with HCC on a cirrhotic background found a proportionally higher median survival in the monitored group; however, unlike our study, no statistically significant difference was observed (14.5 months vs. 12 months, $p=0.375$) (2). In this study, the higher number of patients with severe liver disease in the monitored group compared to our study might have led to lower median survival rates in this cohort, and the impact of screening on survival might not have been significant. Similarly, Mancebo et al.'s prospective study in 2017 involving 770 cirrhotic patients found a proportionally higher median survival in the monitored patients; however, no statistically significant difference was observed (24.7 months vs. 14.2 months, $p=0.16$) (23). This could be explained by the limited number of non-monitored patients who developed HCC in this study. The aim of screening is to detect early-stage HCC and increase access to curative treatments that can improve survival. Although our study showed a higher median survival in the surveillance group compared to the non surveillance group, longer follow-up periods, larger prospective studies evaluating contrast agent-related complications, and the psychological effects of screening on patients are needed to confirm the benefits of HCC surveillance in current cohorts.

Our study is a substantial investigation encompassing a significant number of cirrhotic patients with an extended follow-up duration, emphasizing the significance of HCC

surveillance in this patient group. However, there are certain limitations associated with our study primarily due to its retrospective nature. The foremost limitation is that our study is not a randomized controlled trial (RCT). Nevertheless, considering the results of a study where patients were surveyed about participating in an RCT (31) for HCC surveillance (99.5% declined randomization, and 88% opted for non-randomized surveillance), we observe that conducting randomized controlled trials may not be currently feasible. Additionally, being a single-center study, the generalizability of our findings may be limited. The data for our study were obtained from electronic records and patient files, leading to potential missing data as outcomes of excluded patients were not evaluated. Furthermore, it's possible that some patients continued their follow-up or received treatment at another facility after exiting our study. Another limiting factor is that deaths were due to non-HCC complications.

In conclusion, our study has revealed that HCC surveillance in cirrhotic patients falls short of the desired levels. Nonetheless, patients who underwent HCC surveillance exhibited higher rates of early-stage HCC detection, greater likelihood of receiving curative treatment, and higher median survival rates. To enhance HCC surveillance in cirrhotic patients, clinicians must understand the significance of adherence to screening and continue exploring options to enhance screening rates through system-based approaches and awareness campaigns. Furthermore, considering the substantial impact of adhering to the recommended time frame on overall survival, initiating patient-physician educational programs to achieve a 6-month screening policy in line with guidelines and improve compliance could be beneficial.

Conflict of interest

There is no conflict of interest in our study.

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None to declare.

Authors' contributions

Concept: Ü.Y.K., S.F., A.M.C., Design: Ü.Y.K., S.F., A.M.C., Data Collection or Processing: Ü.Y.K., S.F., C.K.S., S.N.K., M.E., A.M.C., Analysis or Interpretation: Ü.Y.K., S.F., C.K.S., S.N.K., M.E., A.M.C., Literature Search: Ü.Y.K., S.F., Writing: Ü.Y.K., S.F.

Ethical Statement

The study was approved by the Karadeniz Technical University Health Application and Research Center Ethics Committee dated 14.12.2020 and numbered 48814514-501.07.01-E.14680.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide

- for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209–49.
2. Yang JD, Roberts LR. Hepatocellular carcinoma: a global view. *Nat Rev Gastroenterol Hepatol*. 2010;7(8):448.
3. Galle PR, Forner A, Llovet JM, et al. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol*. 2018;69(1):182–236.
4. Singal, Amit G. et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. *Hepatology* 2023;78(6):p 1922-1965.
5. Taddei, Tamar H. Critical Update: AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. *Hepatology*. 2025;10.1097/HEP.0000000000001269.
6. Tellapuri S, Sutphin PD, Beg MS, Singal AG, Kalva SP. Staging systems of hepatocellular carcinoma: A review. *Indian Journal of Gastroenterology*. 2018;37(6):481–91.
7. Singal AG, Yopp A, S. Skinner C, Packer M, Lee WM, Tiro JA. Utilization of Hepatocellular Carcinoma Surveillance Among American Patients: A Systematic Review. *J Gen Intern Med*. 2012;27(7):861.
8. Tzartzeva K, Obi J, Rich NE, Parikh ND, Marrero JA, Yopp A. Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients with Cirrhosis: A Meta-analysis. *Gastroenterology*. 2018;154(6):1706.
9. Wolf E, Rich NE, Marrero JA, Parikh ND, Singal AG. Use of Hepatocellular Carcinoma Surveillance in Patients With Cirrhosis: A Systematic Review and Meta-Analysis. *Hepatology*. 2021;73(2):713–25.
10. Wong CR, Garcia RT, Trinh HN, et al. Adherence to Screening for Hepatocellular Carcinoma Among Patients with Cirrhosis or Chronic Hepatitis B in a Community Setting. *Dig Dis Sci*. 2009;54(12):2712–21.
11. Wang C, Chen V, Vu V, Trinh H, Nguyen MH. Poor adherence and low persistency rates for hepatocellular carcinoma surveillance in patients with chronic hepatitis B. *Medicine*. 2016;95(35):e4744.
12. Yao FY, Ferrell L, Bass NM, et al. Liver transplantation for hepatocellular carcinoma: Expansion of the tumor size limits does not adversely impact survival. *Hepatology*. 2001;33(6):1394–403.
13. Tran SA, Le A, Zhao C, et al. Rate of hepatocellular carcinoma surveillance remains low for a large, real-life cohort of patients with hepatitis C cirrhosis. *BMJ Open Gastroenterol*. 2018;5(1):192.
14. Mittal S, Kanwal F, Ying J, et al. Effectiveness of surveillance for hepatocellular carcinoma in clinical practice: A United States cohort. *J Hepatol*. 2016;65(6):1148–54.
15. Mazzaferro V, Regalia E, Doci R, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med*. 1996;334(11):693–700.
16. Kim HY, Nam JY, Lee JH, et al. Intensity of surveillance for hepatocellular carcinoma determines survival in patients at risk in a hepatitis B-endemic area. *Aliment Pharmacol Ther*. 2018;47(11):1490–501.
17. Hong TP, Gow PJ, Fink M, et al. Surveillance improves survival of patients with hepatocellular carcinoma: a prospective population-based study. *Medical Journal of Australia*. 2018;209(8):348–54.
18. Singal AG, Zhang E, Narasimman M, et al. HCC surveillance improves early detection, curative treatment receipt, and survival in patients with cirrhosis: A meta-analysis. *J Hepatol*. 2022;77(1):128–39.
19. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol*. 2004;130(7):417–22.
20. Singal AG, Marrero JA, Yopp A. Screening Process Failures for Hepatocellular Carcinoma. *J Natl Compr Canc Netw*. 2014;12(3):375.
21. Costentin CE, Layese R, Bourcier V, et al. Compliance with Hepatocellular Carcinoma Surveillance Guidelines Associated with Increased Lead-Time Adjusted Survival of Patients with Compensated Viral Cirrhosis: A Multi-Center Cohort Study. *Gastroenterology*. 2018;155(2):431–442.e10.
22. Choi DT, Kum HC, Park S, et al. Hepatocellular Carcinoma Screening is Associated with Increased Survival of Patients with Cirrhosis. *Clin Gastroenterol Hepatol*. 2019;17(5):976.
23. Mancebo A, González-Diéguez MI, Navascués CA, et al. Adherence to a Semiannual Surveillance Program for Hepatocellular Carcinoma in Patients with Liver Cirrhosis. *J Clin Gastroenterol*. 2017;51(6):557–63.
24. Van Meer S, De Man RA, Coenraad MJ, et al. Surveillance for hepatocellular carcinoma is associated with increased survival: Results from a large cohort in the Netherlands. *J Hepatol*. 2015;63(5):1156–63.
25. Singal AG, Patibandla S, Obi J, et al. Benefits and Harms of Hepatocellular Carcinoma Surveillance in a Prospective Cohort of Patients with Cirrhosis. *Clinical Gastroenterology and Hepatology*. 2021;19(9):1925-1932.e1.
26. Huang Y, Wallace MC, Adams LA, et al. Rate of Nonsurveillance and Advanced Hepatocellular Carcinoma at Diagnosis in Chronic Liver Disease. *J Clin Gastroenterol*. 2018;52(6):551–6.
27. Mohamed E Akoad, Elizabeth A Pomfret. Surgical resection and liver transplantation for hepatocellular carcinoma. *Clin Liver Dis* 2015;19(2):381-99.
28. Singal AG, Mittal S, Yerokun OA, et al. Hepatocellular Carcinoma Screening Associated with Early Tumor Detection and Improved Survival Among Patients with Cirrhosis in the US. *Am J Med*. 2017;130(9):1099-1106.e1.
29. Thein HH, Campitelli MA, Yeung LT, Zaheen A, Yoshida EM, Earle CC. Improved Survival in Patients with Viral Hepatitis-Induced Hepatocellular Carcinoma Undergoing Recommended Abdominal Ultrasound Surveillance in Ontario: A Population-Based Retrospective Cohort Study. *PLoS One*. 2015;10(9).
30. Lang S, Martin A, Kasper P, et al. Hepatocellular carcinoma surveillance with liver imaging is not associated with improved survival. *Scand J Gastroenterol*. 2020;55(2):222–7.
31. Poustchi H, Farrell GC, Strasser SI, Lee AU, McCaughan GW, George J. Feasibility of conducting a randomized control trial for liver cancer screening: Is a randomized controlled trial for liver cancer screening feasible or still needed? *Hepatology*. 2011;54(6):1998–2004.