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Hepatocellular carcinoma in Korea: an analysis of the 2016-2018 Korean Nationwide Cancer Registry

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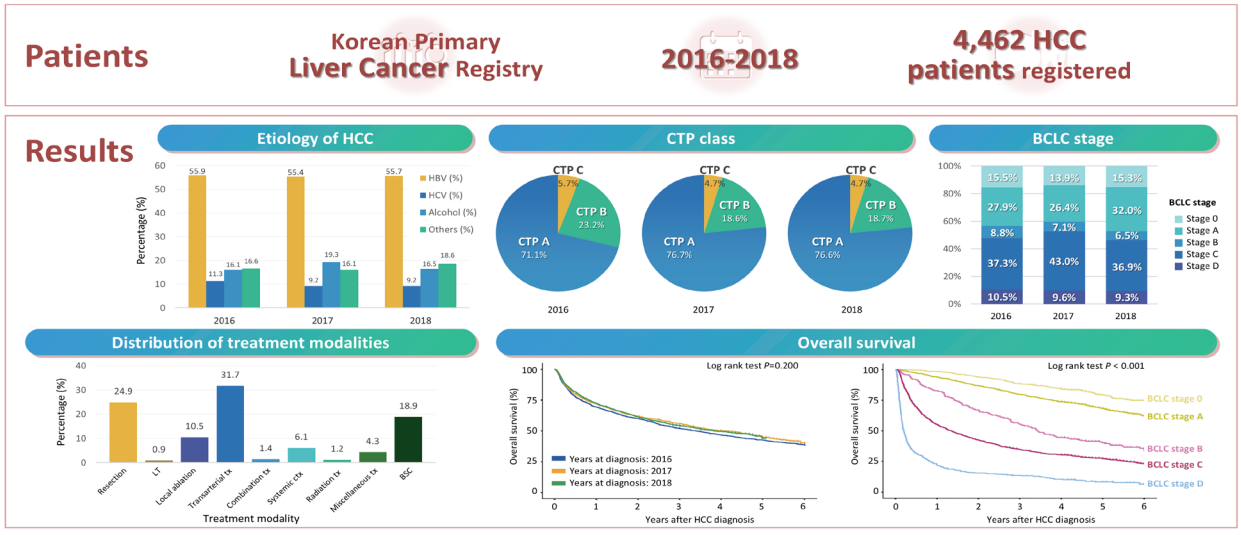

Conclusion

- The median overall survival was 3.72 years, with 5-year overall survival rates of 44.3%.
- The most common initial treatments were transarterial therapy (31.7%), followed by surgical resection (24.9%).
- During the study period (2016-2018), there was a shift toward BCLC stage 0-A and CTP liver function class A.

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Hepatocellular carcinoma in Korea: an analysis of the 2016-2018 Korean Nationwide Cancer Registry

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Backgrounds/Aims: Hepatocellular carcinoma (HCC) is the sixth most common cancer and second leading cause of cancer-related deaths in South Korea. This study evaluated the characteristics of Korean patients newly diagnosed with HCC in 2016-2018.

Methods: Data from the Korean Primary Liver Cancer Registry (KPLCR), a representative database of patients newly diagnosed with HCC in South Korea, were analyzed. This study investigated 4,462 patients with HCC registered in the KPLCR in 2016-2018.

Results: The median patient age was 63 years (interquartile range, 55-72). 79.7% of patients were male. Hepatitis B infection was the most common underlying liver disease (54.5%). The Barcelona Clinic Liver Cancer (BCLC) staging system classified patients as follows: stage 0 (14.9%), A (28.8%), B (7.5%), C (39.0%), and D (9.8%). The median overall survival was 3.72 years (95% confidence interval, 3.47-4.14), with 1-, 3-, and 5-year overall survival rates of 71.3%, 54.1%, and 44.3%, respectively. In 2016-2018, there was a significant shift toward BCLC stage 0-A and Child-Turcotte-Pugh liver function class A ($P<0.05$), although survival rates did not differ by diagnosis year. In the treatment group (n=4,389), the most common initial treatments were transarterial therapy (31.7%), surgical resection (24.9%), best supportive care (18.9%), and local ablation therapy (10.5%).

Conclusions: Between 2016 and 2018, HCC tended to be diagnosed at earlier stages, with better liver function in later years. However, since approximately half of the patients remained diagnosed at an advanced stage, more rigorous and optimized HCC screening strategies should be implemented. **(J Liver Cancer 2025;25:109-122)**

Keywords: Epidemiology; Carcinoma, hepatocellular; Hepatitis B; Korea; Survival

INTRODUCTION

Hepatocellular carcinoma (HCC), accounting for more than 80% of liver cancers, represents a major global health burden as the sixth most commonly diagnosed cancer and third most common cause of cancer-related deaths worldwide, with over 900,000 new cases and 830,000 deaths reported in 2020.[1,2] HCC ranks among the top five causes of cancer-related deaths in 90 countries, with a predicted increase in incidence and mortality of over 50% in the next two decades.[3] The emerging epidemiological data indicate a significant shift in causal factors from virus-related to non-viral liver diseases, which has important implications for primary and secondary prevention strategies, including HCC surveillance and treatment approaches.[4]

In South Korea, HCC is the sixth most common cancer and ranks as the second most common cause of cancer-related deaths.[5] The Korean Primary Liver Cancer Registry (KPLCR) serves as a representative database, randomly sampling approximately 15% of newly diagnosed primary liver cancer cases from the Korea Central Cancer Registry (KCCR), which captures more than 95% of all cancer cases in South Korea. This systematic sampling strategy, which stratifies by regions and hospitals of diagnosis, effectively minimizes voluntary reporting bias while adhering to privacy regulations.[6] Since 2008, the KPLCR has published detailed reports on liver cancer data, offering valuable longitudinal insights into the disease characteristics in South Korea, which has substantially influenced clinical practice and healthcare policy development.[7-9]

In the present study, we aimed to examine HCC patterns in South Korea using data from the KPLCR during 2016-2018, analyzing patient characteristics, therapeutic approaches, and clinical outcomes. Furthermore, we sought to evaluate temporal changes in disease etiology, tumor staging at diagnosis, treatment strategies, and patient survival.

METHODS

Patient population

Initially, 4,478 patients were registered in the KPLCR between

January 1, 2016 and December 31, 2018. As detailed in our previous reports.[7-9] HCC diagnosis was established through either histological confirmation or imaging criteria using dynamic computed tomography (CT) and/or magnetic resonance imaging (MRI) (nodules >1 cm with arterial hypervascularity and portal-/delayed-phase washout). After 16 patients histologically diagnosed with other malignancies were excluded, 4,462 patients were included in the study. From this group, we selected 4,389 participants for the designated treatment group after excluding patients for the following reasons: 1) delayed initial treatment beyond 120 days after diagnosis, which could lead to stage migration (n=44), and 2) missing data on diagnosis or treatment initiation dates (n=29). A flow diagram of the study population is shown in Supplementary Fig. 1.

The Institutional Review Board (IRB) of Hanyang University Guri Hospital waived the need for IRB approval and written informed consent (IRB No. 2024-02-010) because the KPLCR data were collected anonymously as part of the KCCR in accordance with the Cancer Control Act.

Data collection and definitions

Patient information was extracted from the medical records of the hospitals where HCC was diagnosed. Well-trained KCCR data recorders at each hospital collected data using a standardized case record form, which was subsequently validated by statisticians affiliated with the KCCR and KPLCR. The collected data included baseline characteristics (demographic information, laboratory parameters, and tumor variables) and treatment-related factors (treatment modalities and overall survival [OS]). All tumor characteristics were assessed using diagnostic imaging techniques such as dynamic CT or MRI. Disease staging was performed using the modified Union for International Cancer Control (mUICC) staging system and the most updated Barcelona Clinic Liver Cancer (BCLC) staging system.[10,11] OS was calculated from the date of HCC diagnosis until death from any cause. Mortality data were obtained from death certificates provided by the Korean Ministry of Government Administration and Home Affairs, with patients identified through their unique 13-digit resident registration numbers. The data cutoff date was December 31, 2022. The median duration of the follow-up period was 3.62 years (interquartile range [IQR], 0.74-5.25).

Statistical analysis

Data are presented as numbers (percentage) for categorical variables and medians (IQR) for continuous variables. Differences between groups were compared using Student's *t*-test (or Mann-Whitney *U* test) for continuous variables and the chi-squared test (or Fisher's exact test) for categorical variables. OS was analyzed using the Kaplan-Meier method, and survival differences were evaluated using the log-rank test. The annual OS rate was calculated from the date of HCC diagnosis (index date) using Kaplan-Meier survival probabilities. The annual OS rate represents the proportion of patients surviving at the end of each consecutive year following diagnosis.

All statistical analyses were performed using R version 4.4.1 (R Foundation, Vienna, Austria; http://www.r-project.org), and two-sided $P<0.05$ were considered statistically significant.

RESULTS

Baseline characteristics

The baseline characteristics of the study population are summarized in Table 1. The median age of the study participants was 63 years (IQR, 55-72), and males represented 79.7% of the population. Hepatitis B virus (HBV) infection was the predominant cause of chronic liver disease (55.7%), followed by alcohol abuse (17.3%), hepatitis C virus infection (9.9%), and other causes (17.1%). According to the Child-Turcotte-Pugh (CTP) classification, 74.8%, 20.1%, and 5.0% of the patients were categorized as classes A, B, and C, respectively.

In terms of tumor factors, single tumors were observed in 63.4% of patients, with a median maximal tumor diameter of 3.3 cm (IQR, 2.2-6.9). Baseline imaging revealed portal vein invasion in 22.4% of patients and hepatic vein invasion in 5.1%. Lymph node and distant metastases were present in 5.8% and 9.4% of patients, respectively. The median serum alpha-fetoprotein level was 20.5 ng/mL (IQR, 4.6-423.0). Based on the mUICC staging system, 16.8%, 38.0%, 24.9%, 10.8%, and 9.4% of patients were in stages I, II, III, IV-A, and IV-B, respectively. According to the BCLC staging system, stage C was the most prevalent (39.0%), followed by stages A (28.8%), 0 (14.9%), D (9.8%), and B (7.5%). Age at diagnosis and the etiology of chronic liver disease were significantly different across the BCLC stages ($P=0.002$ and $P=0.001$, respectively) (Fig. 1A, B).

When comparing baseline parameters across years at diagnosis from 2016 to 2018, the proportion of 'others' among etiology of chronic liver disease showed an increasing trend (16.6%, 16.0%, and 18.6% for 2016, 2017, and 2018, respectively). Similarly, the proportion of CTP class A patients demonstrated a

Table 1. Baseline characteristics of the study population

Variable	Total	2016	2017	2018	*P*-value
Year					
Number of patients	4,462	1,500	1,491	1,471	-
Demographic variable					
Age (years)	63 (55-72)	63 (55-72)	63 (56-73)	63 (55-72)	0.247
Male	3,554 (79.7)	1,184 (78.9)	1,196 (80.2)	1,174 (79.8)	0.673
Diabetes	1,362 (30.7)	459 (30.9)	435 (29.4)	468 (32.0)	0.309
Hypertension	1,786 (40.3)	596 (40.2)	584 (39.4)	606 (41.5)	0.503
BMI (kg/m^2)	24.0 (21.8-26.2)	23.9 (21.9-26.0)	24.0 (21.8-26.4)	24.0 (21.8-26.2)	0.733
Smoking habitus	2,026 (45.9)	653 (44.9)	684 (46.2)	679 (46.5)	0.631
Etiology					0.042
HBV*	2,485 (55.7)	839 (55.9)	826 (55.4)	820 (55.7)	
HCV	442 (9.9)	170 (11.3)	137 (9.2)	135 (9.2)	
Alcohol	772 (17.3)	242 (16.1)	288 (19.3)	242 (16.5)	
Others	763 (17.1)	249 (16.6)	240 (16.1)	274 (18.6)	
Liver cirrhosis	3,131 (71.0)	1,083 (72.7)	1,034 (70.1)	1,014 (70.1)	0.199
ECOG PS					0.028
PS 0	2,142 (66.8)	737 (67.3)	650 (63.5)	755 (69.5)	
PS 1	761 (23.7)	253 (23.1)	266 (26.0)	242 (22.3)	
PS 2	170 (5.3)	60 (5.5)	66 (6.4)	44 (4.0)	
PS 3	85 (2.7)	23 (2.1)	31 (3.0)	31 (2.9)	
PS 4	48 (1.5)	22 (2.0)	11 (1.1)	15 (1.4)	
Ascites					0.011
None	3,341 (75.3)	1,089 (73.2)	1,146 (77.1)	1,106 (75.6)	
Mild	680 (15.3)	230 (15.5)	212 (14.3)	238 (16.3)	
Moderate to severe	414 (9.3)	168 (11.3)	128 (8.6)	118 (8.1)	
Encephalopathy					0.211
None	4,354 (97.6)	1,468 (97.9)	1,451 (97.4)	1,435 (97.6)	
Grade 1-2	80 (1.8)	25 (1.7)	25 (1.7)	30 (2.0)	
Grade 3-4	26 (0.6)	7 (0.5)	14 (0.9)	5 (0.3)	
Laboratory variable					
Total bilirubin (mg/dL)	0.9 (0.6-1.4)	0.9 (0.6-1.5)	0.9 (0.6-1.3)	0.9 (0.6-1.4)	0.089
Albumin (g/dL)	3.9 (3.4-4.3)	3.8 (3.3-4.2)	3.9 (3.4-4.3)	4.0 (3.5-4.4)	<0.001
ALT (IU/L)	32 (21-54)	33 (21-55)	32 (21-54)	31 (21-52)	0.771
Platelet count (10^9/L)	153 (107-208)	145 (101-206)	155 (108-210)	157 (111-211)	0.015
INR	1.1 (1.0-1.2)	1.1 (1.0-1.2)	1.1 (1.0-1.2)	1.1 (1.0-1.2)	<0.001
Creatinine (mg/dL)	0.8 (0.7-1.0)	0.8 (0.7-1.0)	0.9 (0.7-1.0)	0.8 (0.7-1.0)	0.588
Sodium (mmol/L)	139.0 (136.2-141.0)	139.0 (136.0-141.0)	139.0 (137.0-141.0)	139.0 (137.0-141.0)	0.036
CTP class					0.003
CTP A	3,210 (74.8)	1,021 (71.1)	1,105 (76.8)	1,084 (76.6)	
CTP B	864 (20.1)	333 (23.2)	267 (18.6)	264 (18.7)	
CTP C	216 (5.0)	82 (5.7)	67 (4.7)	67 (4.7)	
MELD score	8 (7-11)	8 (7-11)	8 (7-11)	8 (7-10)	<0.001
MELD-Na score	10 (8-13)	10 (8-14)	10 (8-13)	10 (8-13)	<0.001

Table 1. Continued

Variable	Total	2016	2017	2018	*P*-value
Tumor variable					
AFP (ng/mL)	20.5 (4.6-423.0)	27.6 (5.0-527.0)	21.1 (4.5-382.5)	16.1 (4.5-340.4)	0.017
PIVKA-II (mAU/mL)	107.3 (27.0-2,355.0)	102.0 (26.1-2,551.5)	100.3 (26.0-2,194.8)	117.0 (29.0-2,270.0)	0.464
Tumor number					0.607
1	2,811 (63.4)	930 (62.5)	950 (64.0)	931 (63.8)	
2	620 (14.0)	214 (14.4)	215 (14.5)	191 (13.1)	
3	174 (3.9)	52 (3.5)	57 (3.8)	65 (4.5)	
4	53 (1.2)	15 (1.0)	17 (1.1)	21 (1.4)	
≥5	773 (17.4)	276 (18.6)	245 (16.5)	252 (17.3)	
Maximal tumor diameter (cm)	3.3 (2.0-6.9)	3.3 (2.0-6.8)	3.2 (2.0-7.0)	3.4 (2.0-6.8)	0.899
Portal vein invasion	994 (22.4)	330 (22.2)	349 (23.5)	315 (21.6)	0.444
Hepatic vein invasion	226 (5.1)	76 (5.1)	67 (4.5)	83 (5.7)	0.351
Bile duct invasion	130 (2.9)	45 (3.0)	44 (3.0)	41 (2.8)	0.933
Lymph node metastasis	258 (5.8)	99 (6.7)	85 (5.7)	74 (5.1)	0.173
Distant metastasis	418 (9.4)	163 (11.0)	129 (8.7)	126 (8.6)	0.044
Modified UICC stage					0.137
Stage I	749 (16.9)	238 (16.1)	254 (17.1)	257 (17.6)	
Stage II	1,679 (38.0)	567 (38.3)	554 (37.3)	558 (38.3)	
Stage III	1,102 (24.9)	377 (25.5)	378 (25.5)	347 (23.8)	
Stage IV-A	477 (10.8)	137 (9.3)	169 (11.4)	171 (11.7)	
Stage IV-B	414 (9.4)	160 (10.8)	129 (8.7)	125 (8.6)	
BCLC stage					0.019
BCLC 0	479 (14.9)	172 (15.5)	141 (13.9)	166 (15.3)	
BCLC A	925 (28.8)	309 (27.9)	268 (26.4)	348 (32.0)	
BCLC B	240 (7.5)	97 (8.8)	72 (7.1)	71 (6.5)	
BCLC C	1,250 (39.0)	413 (37.3)	436 (43.0)	401 (36.9)	
BCLC D	314 (9.8)	116 (10.5)	97 (9.6)	101 (9.3)	

Values were presented as number (%) for categorical variables and as median (interquartile range) for continuous variables. Data were missing for the following variables: diabetes (n=30), hypertension (n=34), BMI (n=293), smoking habitus (n=44), liver cirrhosis (n=50), ECOG PS (n=1,256), ascites (n=27), encephalopathy (n=2), total bilirubin (n=103), albumin (n=105), ALT (n=95), platelet count (n=119), INR (n=155), creatinine (n=112), sodium (n=214), CTP class (n=172), MELD score (n=244), MELD-Na score (n=244), AFP (n=333), PIVKA-II (n=913), tumor number (n=32), tumor size (n=238)†, portal vein invasion (n=33), hepatic vein invasion (n=35), bile duct invasion (n=35), lymph node metastasis (n=33), distant metastasis (n=34), modified UICC stage (n=41), and BCLC stage (n=1,254).

BMI, body mass index; HBV, hepatitis B virus; HCV, hepatitis C virus; ECOG PS, Eastern Cooperative Oncology Group performance status; ALT, alanine aminotransferase; INR, international normalized ratio; CTP, Child-Turcotte-Pugh; MELD, model for end-stage liver disease; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence or antagonist-II; UICC, Union for International Cancer Control; BCLC, Barcelona Clinic Liver Cancer.

*Patients co-infected with HBV and HCV (n=51) were also included; †Among the 238 cases with incomplete tumor size data, 203 were identified to have a tumor size exceeding 10 cm.

progressive increase over the study period (71.1% in 2016, 76.8% in 2017, and 76.6% in 2018; *P*=0.003). In terms of BCLC staging classification, the proportion of early-stage disease, comprising BCLC stages 0 and A, showed temporal variation, accounting for 43.4%, 40.3%, and 47.3% in 2016, 2017, and 2018, respectively, with a notable increase in 2018 (*P*=0.019) (Fig. 1C).

Initial treatment modality

Table 2 shows the initial treatment modalities of the 4,389 patients in the treatment group. Among the initial treatment modalities, surgical interventions, including surgical resection (n=1,095, 24.9%) and liver transplantation (LT) (n=40, 0.9%), were performed in 25.8% of patients. Local ablation therapy was

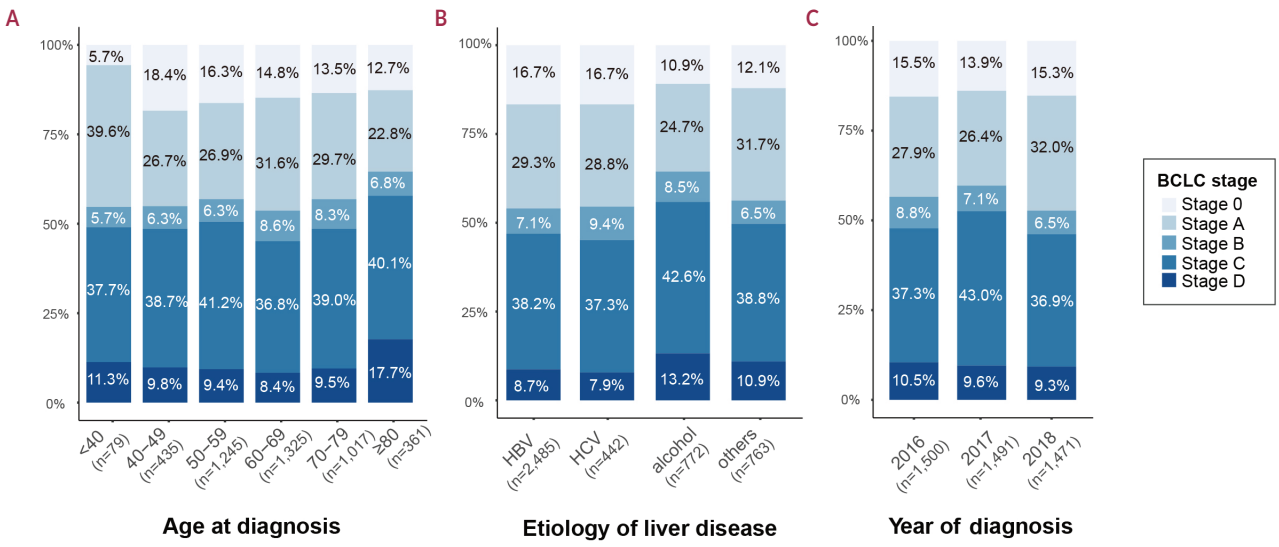

Figure 1. Distribution of BCLC stage according to age (A), etiology (B), and year of diagnosis (C) in the KPLCR cohort in 2016-2018 (n=4,462). BCLC, Barcelona Clinic Liver Cancer; HCV, hepatitis C virus; HBV, hepatitis B virus; KPLCR, Korean Primary Liver Cancer Registry.

Table 2. Distribution of initial treatment modalities by year of diagnosis in the treatment group (n=4,389)

Treatment modality	Total (n=4,389)	2016 (n=1,473)	2017 (n=1,469)	2018 (n=1,447)
Surgical resection	1,095 (24.9)	346 (23.5)	358 (24.4)	391 (27.0)
Liver transplantation	40 (0.9)	10 (0.7)	14 (1.0)	16 (1.1)
Local ablation therapy	460 (10.5)	154 (10.5)	169 (11.5)	137 (9.5)
Radiofrequency ablation	435	147	160	128
Percutaneous ethanol injection	7	2	3	2
Others	18	5	6	7
Transarterial therapy	1,393 (31.7)	468 (31.8)	471 (32.1)	454 (31.4)
Conventional TACE	1,208	435	419	354
TACE with drug-eluting beads	124	2	30	74
Radioembolization	37	7	14	16
Hepatic arterial infusion chemotherapy	24	6	8	10
Combination therapy*	60 (1.4)	21 (1.4)	20 (1.4)	19 (1.3)
Systemic chemotherapy	267 (6.1)	82 (5.6)	85 (5.8)	99 (6.8)
Sorafenib	242	76	77	89
Other systemic agents	25	6	8	10
Radiation therapy	53 (1.2)	12 (0.8)	21 (1.4)	20 (1.4)
Miscellaneous therapy†	190 (4.3)	64 (4.3)	63 (4.3)	63 (4.4)
Best supportive care	831 (18.9)	316 (21.5)	268 (18.2)	247 (17.1)

Values are presented as number (%).
TACE, transarterial chemoembolization.
*Combination therapy was defined as a combined treatment with local ablation therapy and transarterial therapy; †Miscellaneous therapies were defined as unclassifiable treatment modalities, including transarterial therapy combined with radiation therapy (n=99), transarterial therapy combined with chemotherapy (n=43), and chemotherapy combined with radiation therapy (n=48).

used in 10.5% (n=460) of the cases. The most frequently employed initial treatment was transarterial therapy (n=1,393, 31.7%), with conventional transarterial chemoembolization (TACE) being the predominant treatment (n=1,208). Sorafenib was the main agent used in 6.1% (n=267) of the patients who received systemic chemotherapy (n=242). The best supportive care was

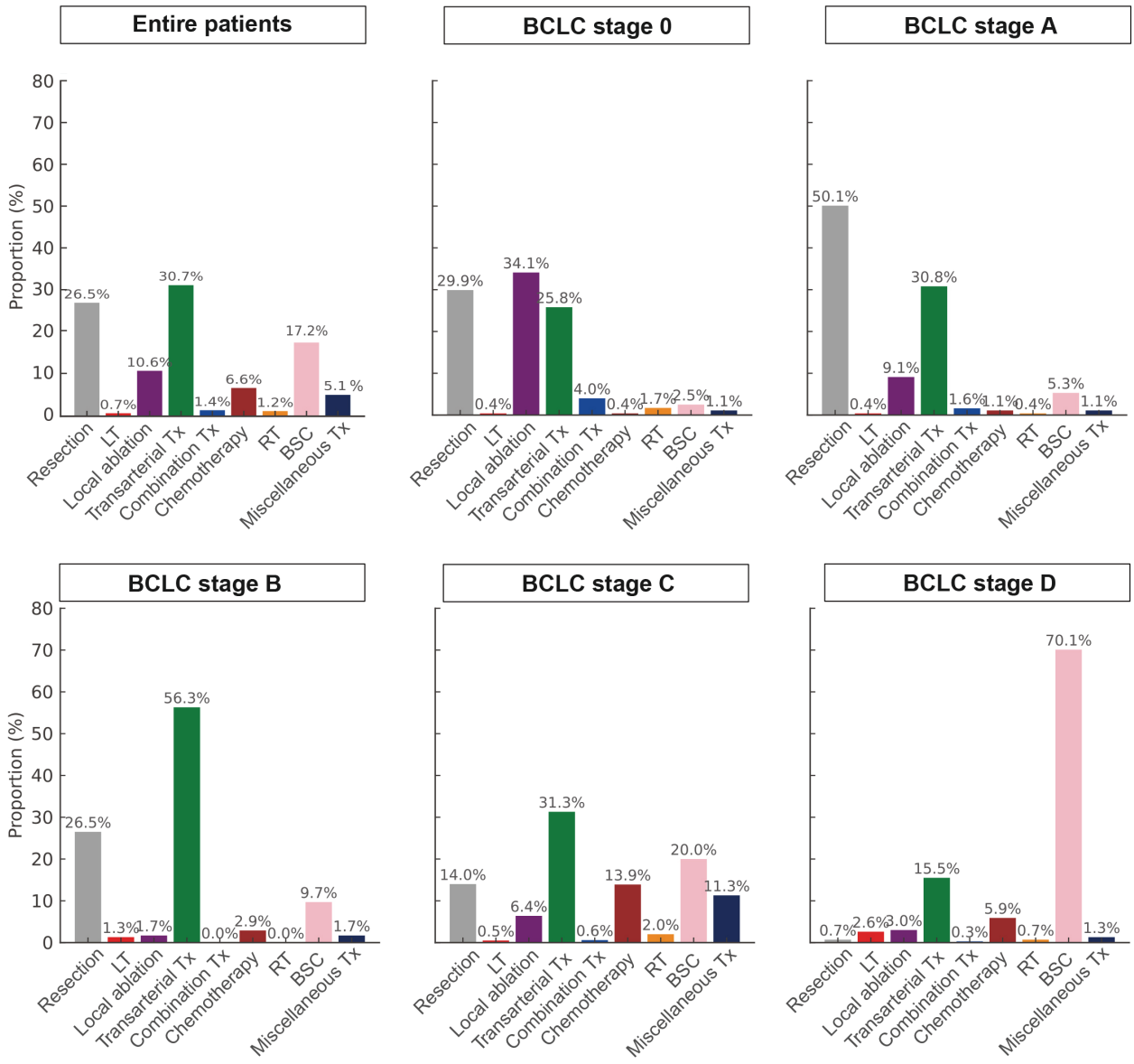

Figure 2. Initial treatment modalities according to BCLC stage in the treatment group of the KPLCR cohort in 2016-2018 (n=3,174). BCLC, Barcelona Clinic Liver Cancer; LT, liver transplantation; Tx, treatment; RT, radiation therapy; BSC, best supportive care; KPLCR, Korean Primary Liver Cancer Registry.

provided to 18.9% (n=831) of the patients.

Initial treatment patterns varied across years at diagnosis from 2016 to 2018. The proportion of patients undergoing surgical resection gradually increased (23.5%, 24.4%, and 27.0% in 2016, 2017, and 2018, respectively). Similarly, the use of TACE with drug-eluting beads increased substantially from 2 cases in 2016 to 74 cases in 2018. Conversely, the proportion of patients receiving the best supportive care showed a declining trend, decreasing from 21.5% in 2016 to 17.1% in 2018.

Treatment distribution according to BCLC stage

Treatment modalities were analyzed according to the BCLC stage in 3,174 patients with available BCLC staging data from the treatment group (Fig. 2). For BCLC stage 0, curative treatments were administered to 64.4% of patients, including surgical resection (29.9%), LT (0.4%), and local ablation therapy (34.1%), while transarterial treatment was performed in 25.8% of the cases. In BCLC stage A, 59.6% of patients received standard treatments, including surgical resection (50.1%), LT (0.4%), and local ablation therapy (9.1%). Among patients with BCLC

Table 3. Overall survival rates of the study population according to baseline characteristics and initial treatment modalities

Variable	Patients	Median OS (years)	Year 1	Year 2	Year 3	Year 4	Year 5
All patients	4,462 (100.0)	3.72 (3.47-4.14)	71.3 (70.0-72.6)	61.2 (59.8-62.7)	54.2 (52.7-55.6)	48.9 (47.5-50.4)	44.4 (42.9-45.9)
Year of diagnosis (n=4,462)							
2016	1,500 (33.6)	3.41 (2.90- 3.89)	69.5 (67.2-71.8)	60.0 (57.6-62.5)	52.1 (49.6-54.7)	46.7 (44.3-49.3)	42.7 (40.3-45.3)
2017	1,491 (33.4)	4.16 (3.51- 4.67)	71.8 (69.6-74.2)	62.2 (59.8-64.7)	56.0 (53.5-58.6)	50.4 (47.8-53.0)	45.2 (42.7-47.8)
2018	1,471 (33.0)	3.84 (3.38-4.70)	72.6 (70.4-74.9)	61.5 (59.0-64.0)	54.5 (52.0-57.1)	49.7 (47.2-52.3)	44.2 (40.6-48.0)
Age at diagnosis, years (n=4,462)							
<40	79 (1.8)	NR	69.6 (60.2-80.5)	62.0 (52.2-73.7)	59.5 (49.6-71.4)	57.0 (47.0-69.0)	55.5 (45.5-67.7)
40-49	435 (9.7)	5.10 (3.74-NR)	70.3 (66.2-74.8)	63.0 (58.6-67.7)	58.2 (53.7-63.0)	54.5 (50.0-59.4)	50.3 (45.8-55.3)
50-59	1,245 (27.9)	4.68 (3.92-5.22)	70.5 (68.0-73.1)	61.1 (58.5-63.9)	56.4 (53.7-59.2)	52.4 (49.7-55.3)	48.1 (45.4-51.0)
60-69	1,325 (29.7)	5.02 (4.44-5.57)	76.2 (74.0-78.6)	67.2 (64.7-69.7)	59.4 (56.8-62.1)	54.4 (51.8-57.2)	50.0 (47.4-52.9)
70-79	1,017 (22.8)	3.03 (2.72-3.37)	71.1 (68.4-73.9)	59.6 (56.6-62.7)	50.3 (47.4-53.5)	43.0 (40.0-46.1)	37.3 (34.4-40.5)
≥80	361 (8.1)	1.47 (1.16-1.80)	57.9 (53.0-63.2)	41.8 (37.0-47.2)	32.1 (27.7-37.3)	24.9 (20.8-29.8)	21.2 (17.3-26.0)
Sex (n=4,462)							
Male	3,554 (79.7)	3.46 (3.21-3.81)	70.5 (69.0-72.0)	60.1 (58.5-61.8)	52.8 (51.2-54.5)	47.6 (46.0-49.3)	43.0 (41.4-44.7)
Female	908 (20.3)	4.88 (4.31-6.16)	74.6 (71.8-77.4)	65.4 (62.4-68.6)	59.5 (56.4-62.8)	54.1 (50.9-57.4)	49.8 (46.6-53.2)
Etiology (n=4,462)							
HBV	2,485 (55.7)	5.00 (4.48-5.68)	71.3 (69.5-73.1)	62.7 (60.8-64.6)	57.3 (55.4-59.3)	53.7 (51.8-55.7)	50.0 (48.0-52.0)
HCV	442 (9.9)	3.49 (2.98-4.28)	77.8 (74.1-81.8)	63.6 (59.2-68.2)	54.3 (49.8-59.1)	46.6 (42.2-51.5)	39.8 (35.4-44.8)
Alcohol	772 (17.3)	2.84 (2.45-3.31)	70.1 (66.9-73.4)	58.3 (54.9-61.9)	48.7 (45.3-52.4)	41.4 (38.0-45.0)	37.0 (33.7-40.7)
Others	763 (17.1)	2.83 (2.53-3.32)	68.8 (65.6-72.2)	57.9 (54.5-61.5)	49.4 (46.0-53.1)	42.2 (38.8-45.9)	36.2 (32.9-39.9)
CTP class (n=4,290)							
CTP A	3,210 (74.8)	6.00 (5.62-6.26)	82.3 (81.0-83.6)	72.3 (70.8-73.9)	65.2 (63.6-66.9)	59.7 (58.0-61.4)	54.9 (53.1-56.7)
CTP B	864 (20.1)	0.68 (0.57-0.90)	44.6 (41.4-48.0)	33.6 (30.6-36.9)	25.9 (23.2-29.0)	21.1 (18.5-24.0)	17.1 (14.7-19.9)
CTP C	216 (5.0)	0.17 (0.14-0.22)	20.8 (16.1-27.0)	15.3 (11.2-20.9)	13.9 (10.0-19.4)	12.0 (8.4-17.3)	10.4 (7.0-15.5)
AFP, ng/mL (n=4,130)							
<20.0	2,048 (49.6%)	6.25 (5.91-NR)	86.6 (85.1-88.1)	77.5 (75.8-79.4)	70.0 (68.0-72.0)	63.8 (61.8-65.9)	58.0 (55.8-60.2)
20.0-199.9	853 (20.7%)	4.11 (3.46-4.98)	75.5 (72.7-78.4)	63.9 (60.7-67.2)	55.8 (52.6-59.2)	50.5 (47.4-54.0)	46.3 (43.1-49.9)
≥200.0	1,229 (29.8%)	0.76 (0.65-0.89)	45.2 (42.5-48.1)	34.2 (31.6-36.9)	29.0 (26.5-31.6)	25.5 (23.2-28.1)	23.2 (20.9-25.7)
Modified UICC stage (n=4,421)							
Stage I	749 (16.9)	NR	94.8 (93.2-96.4)	89.7 (87.6-91.9)	84.0 (81.4-86.6)	78.6 (75.7-81.6)	73.4 (70.3-76.8)
Stage II	1,679 (38.0)	6.67 (6.24-NR)	89.2 (87.7-90.7)	80.0 (78.2-82.0)	72.5 (70.4-74.7)	66.4 (64.2-68.7)	60.8 (58.4-63.2)
Stage III	1,102 (24.9)	2.23 (2.02-2.56)	68.1 (65.4-70.9)	53.0 (50.1-56.0)	43.5 (40.6-46.5)	37.4 (34.6-40.4)	32.4 (29.7-35.4)

Table 3. Continued

Variable	Patients	Median OS (years)	Year 1	Year 2	Year 3	Year 4	Year 5
Stage IV-A	477 (10.8)	0.43 (0.39-0.52)	28.3 (24.5-32.6)	17.4 (14.3-21.2)	13.0 (10.3-16.4)	8.6 (6.4-11.5)	6.4 (4.5-9.1)
Stage IV-B	414 (9.4)	0.27 (0.23-0.31)	15.0 (11.9-18.8)	6.8 (4.7-9.7)	3.4 (2.0-5.7)	3.1 (1.8-5.4)	2.8 (1.6-5.0)
BCLC stage (n=3,208)							
BCLC 0	479 (14.9)	NR	98.5 (97.5-99.6)	93.9 (91.8-96.1)	88.5 (85.7-91.4)	84.3 (81.2-87.7)	79.4 (75.7-83.2)
BCLC A	925 (28.8)	NR	93.9 (92.4-95.5)	86.9 (84.8-89.1)	79.8 (77.2-82.4)	73.7 (70.9-76.6)	68.3 (65.3-71.5)
BCLC B	240 (7.5)	3.43 (2.97-4.39)	82.9 (78.3-87.8)	67.1 (61.4-73.3)	55.4 (49.5-62.1)	44.6 (38.7-51.3)	40.2 (34.4-47.0)
BCLC C	1,250 (39.0)	1.35 (1.17-1.58)	55.3 (52.6-58.1)	42.6 (39.9-45.4)	35.0 (32.4-37.7)	30.4 (28.0-33.1)	27.4 (25.0-30.0)
BCLC D	314 (9.8)	0.21 (0.17-0.26)	22.6 (18.4-27.7)	15.6 (12.1-20.2)	13.7 (10.4-18.1)	10.8 (7.9-14.9)	8.9 (6.2-12.8)
Initial treatment modality (n=4,389)							
Surgical resection	1,095 (24.9)	NR	94.6 (93.3-96.0)	90.0 (88.2-91.8)	85.0 (82.9-87.2)	81.7 (79.5-84.1)	78.5 (76.0-81.0)
Liver transplantation	40 (0.9)	NR	95.0 (88.5-100.0)	90.0 (81.2-99.8)	87.5 (77.8-98.4)	82.5 (71.5-95.2)	78.9 (66.8-93.3)
Local ablation therapy	460 (10.5)	NR	96.3 (94.6-98.0)	89.3 (86.6-92.2)	84.6 (81.3-87.9)	80.2 (76.7-83.9)	74.0 (70.0-78.2)
Transarterial therapy	1,393 (31.7)	3.49 (3.24-3.74)	82.1 (80.1-84.1)	66.7 (64.3-69.2)	54.7 (52.1-57.4)	45.6 (43.1-48.3)	38.6 (36.1-41.3)
Combination therapy*	60 (1.4)	NR	96.7 (92.2-100.0)	86.7 (78.5-95.7)	83.3 (74.4-93.3)	76.7 (66.7-88.2)	70.5 (59.4-83.5)
Systemic chemotherapy	267 (6.1)	0.41 (0.38-0.50)	20.2 (15.9-25.7)	8.6 (5.8-12.7)	6.7 (4.3-10.5)	5.2 (3.1-8.7)	5.2 (3.1-8.7)
Radiation therapy	53 (1.2)	1.38 (0.16-0.25)	56.6 (44.7-71.7)	43.4 (31.9-59.0)	35.8 (25.0-51.4)	32.1 (21.7-47.5)	29.6 (19.4-45.2)
Miscellaneous therapy†	190 (4.3)	1.17 (0.88-1.40)	53.2 (46.5-60.7)	32.1 (26.1-39.5)	22.6 (17.4-29.4)	17.4 (12.7-23.7)	13.8 (9.6-19.8)
Best supportive care	831 (18.9)	0.27 (0.24-0.31)	25.6 (22.8-28.8)	19.3 (16.8-22.1)	15.2 (12.9-17.8)	12.4 (10.3-14.9)	10.3 (8.4-12.6)

Values are presented as number (%) or median (95% CI).

OS, overall survival; NR, not reached; HBV, hepatitis B virus; HCV, hepatitis C virus; CTP, Child-Turcotte-Pugh; AFP, alpha-fetoprotein; UICC, Union for International Cancer Control; BCLC, Barcelona Clinic Liver Cancer; CI, confidence interval.

*Combination therapy was defined as a combined treatment with local ablation therapy and transarterial therapy; †Miscellaneous therapies were defined as unclassifiable treatment modalities, including transarterial therapy combined with radiation therapy (n=99), transarterial therapy combined with chemotherapy (n=43), and chemotherapy combined with radiation therapy (n=48).

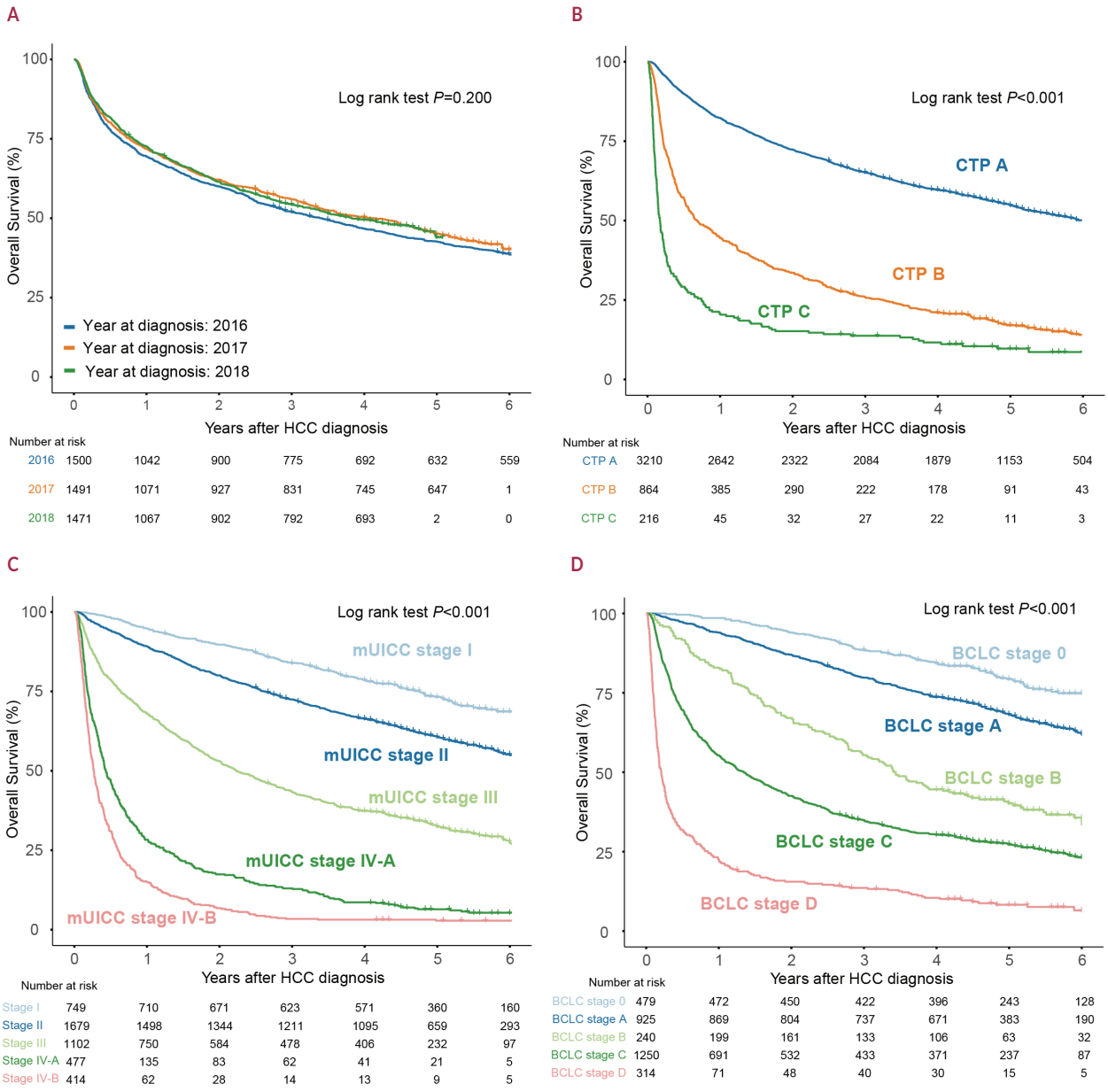

Figure 3. Kaplan-Meier curves for overall survival according to (A) year of diagnosis, (B) Child-Turcotte-Pugh (CTP) class, (C) modified Union for International Cancer Control (mUICC) stage, and (D) BCLC stage in the KPLCR cohort in 2016-2018. HCC, hepatocellular carcinoma; BCLC, Barcelona Clinic Liver Cancer; KPLCR, Korean Primary Liver Cancer Registry.

stage B, 56.3% received transarterial treatment in accordance with the BCLC guidelines, whereas surgical resection was performed in 26.5% of cases. For patients with BCLC stage C, systemic treatment was administered in only 13.9% of cases despite being the BCLC-recommended therapy, while transarterial treatment was more commonly utilized as initial therapy (31.3%). In BCLC stage D, 70.1% of patients received the best supportive care, consistent with the guideline recommendations. Overall adherence to the BCLC stage-suggested treatment was 43.2%.

Overall survival

Table 3 presents the median and annual OS rates for the entire study population stratified by baseline characteristics. The median OS was 3.72 years (95% confidence interval [CI], 3.44-4.14), with 1-, 3-, and 5-year OS rates of 71.3%, 54.1%, and 44.3%, respectively. When survival was compared according to the year of diagnosis, no significant differences were observed (log-rank *P*=0.200) (Fig. 3A). The survival curves demonstrated signifi-

Table 4. Overall survival according to treatment recommended by BCLC stage (n=3,174)

Treatment modality	Value	Median OS (years)	5 Year OS (%)
BCLC stage 0/A (n=1,391)			
Surgical resection	601 (43.2)	NR	84.0 (81.1-87.1)
Liver transplantation	6 (0.4)	NR	80.0 (51.6-100.0)
Local ablation therapy	245 (17.6)	NR	83.4 (78.7-88.3)
Treatments beyond BCLC recommendations	539 (38.8)	5.68 (5.09-6.40)	54.6 (50.4-59.1)
BCLC stage B (n=238)			
Transarterial therapy	134 (56.3)	3.08 (2.46-3.47)	31.7 (24.7-40.8)
Treatments beyond BCLC recommendations	104 (43.7)	5.20 (3.58-NR)	50.9 (42.0-61.8)
BCLC stage C (n=1,241)			
Systemic chemotherapy	173 (13.9)	0.41 (0.34-0.48)	2.3 (0.9-6.1)
Treatments beyond BCLC recommendations	1,068 (86.1)	1.80 (1.52-2.11)	31.1 (28.4-34.1)
BCLC stage D (n=304)			
Best supportive care	213 (70.1)	0.14 (0.13-0.17)	4.1 (2.1-7.9)
Treatments beyond BCLC recommendations	91 (29.9)	0.79 (0.46-1.26)	16.8 (10.5-27.0)

Values are presented as number (%) or median (95% CI).
OS, overall survival; BCLC, Barcelona Clinic Liver Cancer; NR, not reached; CI, confidence interval.

cant differences according to the CTP class, mUICC stage, and BCLC stage (all log-rank tests, P<0.001) (Fig. 3B-D). Post hoc analyses of log-rank tests for multiple comparisons revealed significant survival differences between all CTP classes and HCC stages (all pairwise log-rank comparisons, P<0.001). The overall OS rate of the 2016-2018 cohort was significantly higher than that of the 2008-2010, 2011-2013, and 2014-2015 cohorts (log-rank tests, all P<0.001), as shown in Supplementary Fig. 2.

Among the 3,174 patients with available BCLC stage and treatment information, analysis of 5-year OS in those who received recommended treatment for their respective BCLC stage (Table 4) revealed survival rates of 83.8% (95% CI, 81.3-86.4) for BCLC stage 0/A, 31.7% (24.7-40.8) for stage B, 2.3% (0.9-6.1) for stage C, and 4.1% (2.1-7.9) for stage D. Notably, BCLC stage 0/A patients who received guideline-recommended treatment showed significantly better survival outcomes (P<0.001). In contrast, patients with BCLC stages B-D who received guideline-recommended treatment had significantly worse survival outcomes than those who received alternative therapies (all P<0.05).

DISCUSSION

In this comprehensive analysis of the KPLCR database from 2016 to 2018, we observed several notable findings regarding the HCC characteristics and treatment patterns in South Korea. The median OS of 3.72 years and 5-year survival rate of 44.3% in our 2016-2018 cohort demonstrate improved outcomes compared to those before 2016, likely attributable to the high proportion of early-stage diagnoses and the substantial proportion of patients with preserved liver function.[7-9]

Our findings demonstrate notable temporal changes in HCC characteristics over the study period in South Korea. The increasing proportion of non-viral etiologies (from 33.7% in 2016 to 35.1% in 2018) aligns with global trends and reflects the changing landscape of HCC risk factors.[2,12,13] Indeed, metabolic dysfunction-associated steatotic liver disease (MASLD) is the fastest growing cause of HCC in many parts of the world, including the USA and parts of Europe, with projected dramatic increases by 2030 (82%, 117%, and 122% from 2016 in China, France, and the USA, respectively).[13,14] Although MASLD was not included as a distinct etiologic variable in our 2016-2018 registry, the proportion of MASLD-related HCC is expected to increase progressively in South Korea.[15] While the proportion of alcohol-related HCC showed a modest increase from 13.5% in the previous KPLCR report (2012-2014)[8] to 17.3% in our 2016-2018 cohort, the proportion of HBV-related HCC demonstrated a substantial decline from 72.0% in 2008-2011 to 55.7%.[9] This decline likely reflects the successful implementation of nationwide HBV vaccination programs reducing vertical transmission rates and effective antiviral treatment strategies.[16,17] Furthermore, advances in antiviral treatment for chronic viral hepatitis have led to improved liver function status in our cohort, as evidenced by the increasing proportion of CTP class A patients from 71.1% to 76.6%.[18,19] These changing patterns in HCC eti-

ology and underlying liver function may have important implications for surveillance strategies and treatment approaches.

Regarding the tumor stage at diagnosis, early-stage disease (BCLC stage 0-A) accounted for 43.7% of the cases in our 2016-2018 cohort, showing an increasing trend from 43.4% in 2016 to 47.3% in 2018. While this represents an improvement from 40.8% in the 2012-2014 cohort,[8] it still indicates that, at least until 2018, more than half of patients with HCC are diagnosed at advanced stages. When analyzing BCLC stage distribution by age and etiology, we found that patients aged ≥80 years and those with non-viral etiologies, particularly alcohol-related HCC, were more likely to be diagnosed at advanced stages. This finding aligns with previous studies reporting lower surveillance rates and more advanced tumor stages at diagnosis in elderly patients and those with alcohol-related liver disease.[20,21] In particular, a large Italian cohort study demonstrated significantly lower surveillance rates in alcohol-related HCC than in viral-related HCC (38% vs. 69%),[22] which may be attributed to multiple psychosocial factors including poor disease awareness, inadequate motivation, concomitant depression and anxiety, poor social support, and inadequate screening for alcohol use disorder among care providers.[23-25] Furthermore, technical limitations such as reduced visualization with ultrasonography in alcohol-related cirrhosis may additionally compromise surveillance efficacy.[26] Collectively, these findings demonstrate that specific patient populations, especially patients with alcohol-related liver disease, are at higher risk for late HCC diagnosis, emphasizing the urgent need for tailored surveillance strategies based on individual risk factors.

The increasing proportion of very early and early stages in BCLC and preserved liver function at initial diagnosis during 2016-2018 was accompanied by an increase in the proportion of patients receiving curative treatments (36.3%), continuing the upward trend observed in previous cohorts.[7-9] Notably, the gradual increase in surgical resection rates from 23.5% to 27.0% during 2016-2018 reflects an expanding role of curative-intent treatments. Although this trend did not translate into significant OS improvements during the study period, the long-term impact of increased curative-intent treatments, including surgical resection, remains to be determined. Extended follow-up through longitudinal studies will help elucidate their effects on survival outcomes. While transarterial therapy remained the most commonly used treatment modality during this period (31.7%), the substantial increase in drug-eluting bead TACE use represents a notable shift in practice patterns. During 2016-2018, systemic therapy options were largely limited to sorafenib, resulting in low utilization of systemic therapy in BCLC stage C patients. However, with the subsequent introduction of new first-line options, including lenvatinib and atezolizumab plus bevacizumab,[27,28] future analyses of post-2018 KPLCR data may reveal changes in BCLC guideline adherence and corresponding survival outcomes.

Our analysis demonstrated that patients with BCLC stage 0-A had superior survival outcomes when treated according to the BCLC guideline-recommended therapies. However, patients with BCLC stages B and C who received treatment beyond the guideline recommendations had better survival rates than those who strictly adhered to the guidelines. This discrepancy may be attributed to various factors including baseline liver function, tumor biology, treatment response, and subsequent therapies. These findings suggest that a more individualized treatment approach is beneficial for selecting patients with intermediate- to advanced-stage HCC. In line with this observation, the 2022 Korean Liver Cancer Association guidelines advocate broader treatment options for carefully selected cases.[29]

This study has several limitations that should be considered when interpreting the results. First, as a registry-based study, there were substantial missing data for clinical variables, particularly performance status, which is crucial for BCLC staging and treatment decisions.[11] Second, the relatively short follow-up period may not fully capture long-term outcomes, especially for early-stage patients. Moreover, patients enrolled in later periods had shorter follow-up durations, potentially affecting the 5-year OS estimates compared with those with longer observation periods. Future updates on the survival outcomes will provide more comprehensive long-term analyses. Nevertheless, our findings provide valuable insights into the real-world HCC management patterns and outcomes in South Korea.

In conclusion, this analysis of the KPLCR database reveals key trends in HCC management in South Korea between 2016 and 2018: increasing non-viral etiologies, improved liver function status at diagnosis, higher early-stage disease proportions, and evolving treatment patterns. Despite encouraging increases in early-stage diagnoses and favorable survival outcomes, the fact that more than half of the HCC cases were diagnosed at advanced stages through 2018 underscores the need for improved surveillance strategies. These findings provide valuable insights into the changing landscape of HCC in South Korea, and future comparisons with post-2018 KPLCR data will be essential for understanding ongoing trends in real-world practice.

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Conflicts of Interest
Young Chang is an editorial board member of *Journal of Liver Cancer*, and was not involved in the review process of this article. Otherwise, the authors have no conflicts of interest to disclose.

Ethics Statement
The Institutional Review Board (IRB) of Hanyang University Guri Hospital decided to waive the need for IRB approval and written informed consent (IRB No. 2024-02-010) because the KPLCR data were collected anonymously as part of the KCCR in accordance with the Cancer Control Act.

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Supplementary Material
Supplementary data can be found with this article online https://doi.org/10.17998/jlc.2025.02.20.

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