2023 APPLE
The 13th Asia-Pacific Primary Liver Cancer Expert Meeting
Novel Insights into the Evolution of Liver Cancer Management
July 6-8, 2023 | Grand InterContinental Seoul Parnas, Seoul, Korea

The efficacy of biliary drainage in HCC with bile duct invasion: a multicenter retrospective cohort study

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Background

- **Bile duct invasion (BDI)** is rarely observed in advanced hepatocellular carcinoma (HCC), which can lead to **hyperbilirubinemia**.
- Nevertheless, it remains uncertain whether **pre-treatment biliary drainage** is effective for HCC patients with BDI and obstructive jaundice.
- This research aims to investigate the **impact of biliary drainage** on the prognostic outcomes of these patients.

Method

- We retrospectively enrolled **a total of 200 HCC patients with BDI** from multicenter cohorts.
- Patients without obstructive jaundice (total bilirubin level < 3 mg/dL; n = 99) or those who did not undergo HCC treatment (n = 37) were excluded from the further analysis.
- Finally, **64 patients with obstructive jaundice** (43 with drainage and 21 without drainage) were included, and **propensity score matching (PSM)** was conducted.
- The modalities of biliary drainage were percutaneous transhepatic biliary drainage or endoscopic retrograde cholangiopancreatography.

- Baseline demographics and clinical characteristics in **treated HCC** patients with **bile duct invasion (Total bilirubin ≥ 3 mg/dL)**

→ **Propensity score matching (PSM)** was conducted for further analysis.

Table. Baseline demographics and clinical characteristics intreated HCC patients with bile duct invasion (Total bilirubin ≥ 3 mg/dL)

Characteristic	Before PSM				After PSM			
	Overall, N = 64[1]	Biliary drainage		*P* value[2]	Overall, N = 42[1]	Biliary drainage		*P* value[2]
		No, N = 21[1]	Yes, N = 43[1]			No, N = 21[1]	Yes, N = 21[1]	
Sex (Male)	51 (80)	14 (67%)	37 (86%)	0.099	13 (69%)	14 (67%)	15 (71%)	0.739
Age ≥ 60	28	9 (43%)	19 (44%)	0.920	16 (38%)	9 (43%)	7 (33%)	0.525
Previous treatment history	23 (36%)	9 (43%)	14 (33%)	0.420	18 (43%)	9 (43%)	9 (43%)	1.000
Etiology								
HBV	50 (78%)	18 (86%)	32 (74%)	0.356	37 (88%)	18 (86%)	19 (90%)	1.000
HCV	2 (3.1%)	0 (0%)	2 (4.7%)	> 0.999	0 (0%)	0 (0%)	0 (0%)	
Alcohol	15 (23%)	7 (33%)	8 (19%)	0.220	12 (29%)	7 (33%)	5 (24%)	0.495
Others	5 (7.8%)	0 (0%)	5 (12%)	0.163	1 (2.4%)	0 (0%)	1 (4.8%)	1.000
ALBI grade 1	45 (70%)	13 (62%)	32 (74%)	0.304	28 (67%)	13 (62%)	15 (71%)	0.513
Child-Pugh score ≥ 8	28 (44%)	12 (57%)	16 (37%)	0.131	21 (50%)	12 (57%)	9 (43%)	0.355
AFP ≥ 400 ng/mL	37 (58%)	16 (76%)	21 (49%)	0.037	28 (67%)	13 (62%)	15 (71%)	0.190
PIVKA-II ≥ 1000 mAU/mL	35 (55%)	12 (57%)	23 (53%)	0.783	25 (60%)	12 (57%)	13 (62%)	0.753
Tumor type								
Infiltrative	26 (41%)	12 (57%)	14 (33%)	0.083	23 (44%)	12 (57%)	11 (52%)	1.000
Massive	27 (42%)	8 (38%)	19 (44%)		17 (40%)	8 (38%)	9 (43%)	
Nodular	11 (17%)	1 (4.8%)	10 (23%)		2 (4.8%)	1 (4.8%)	1 (4.8%)	
Maximum tumor size ≥ 5cm	44 (69%)	16 (76%)	28 (65%)	0.369	31 (74%)	16 (76%)	15 (71%)	0.726
Multiple tumors	30 (47%)	11 (52%)	19 (44%)	0.537	21 (50%)	11 (52%)	10 (48%)	0.758
PVTT	52 (81%)	18 (86%)	34 (79%)	0.736	38 (90%)	18 (86%)	20 (95%)	0.606
BCLC stage								
B	9 (14%)	2 (9.5%)	7 (16%)	0.706	3 (7.1%)	2 (9.5%)	1 (4.8%)	1.000
C	55 (86%)	19 (90%)	36 (84%)		39 (93%)	19 (90%)	20 (95%)	
Time from BDI diagnosis to HCC treatment (days)	24.9 ± 32.0	12 ± 22.4	31.4 ± 34.3	< 0.001	21.3 ± 29.4	12.0 ± 22.4	30.5 ± 33.0	0.001
Decreased TB within 7 days after HCC treatment	44 (66%)	11 (52%)	31 (72%)	0.119	27 (64%)	11 (52%)	16 (76%)	0.107
Decreased TB within 30 days after HCC treatment	51 (80%)	14 (67%)	37 (86%)	0.099	32 (76%)	14 (67%)	18 (86%)	0.147

[1]n (%), [2]Pearson's Chi-squared test.

HCC: hepatocellular carcinoma, PSM: propensity score matching, HBV: hepatitis B virus, HCV: hepatitis C virus, ALBI: albumin-bilirubin, AFP: alpha-fetoprotein, PIVKA: protein induced by vitamin K antagonist, PVTT: portal vein tumor thrombosis, BCLC: Barcelona Clinic Liver Cancer, BDI: bile duct invasion, TB: total bilirubin

The first response evaluation of HCC treatment

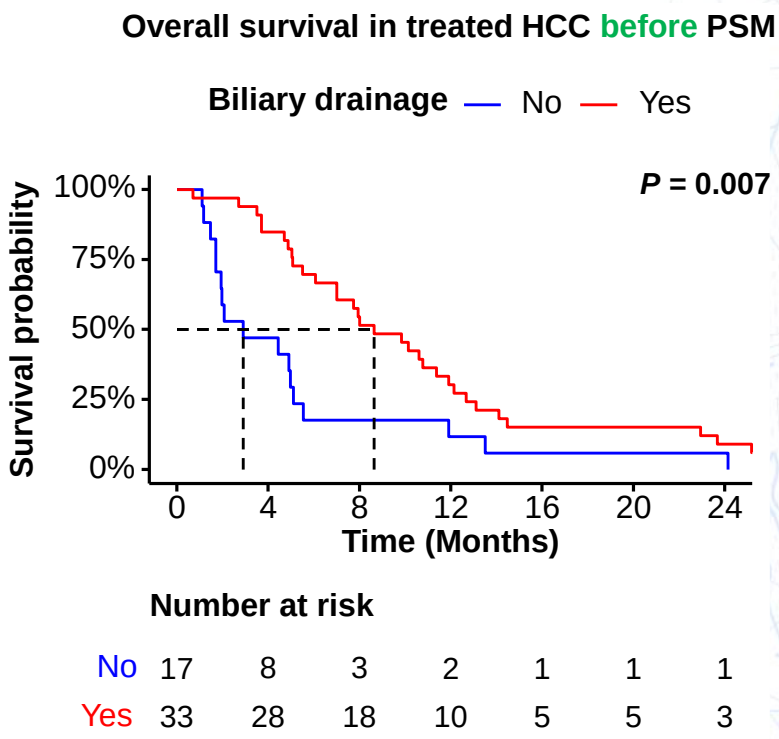
Table. The first response evaluation of HCC treatment

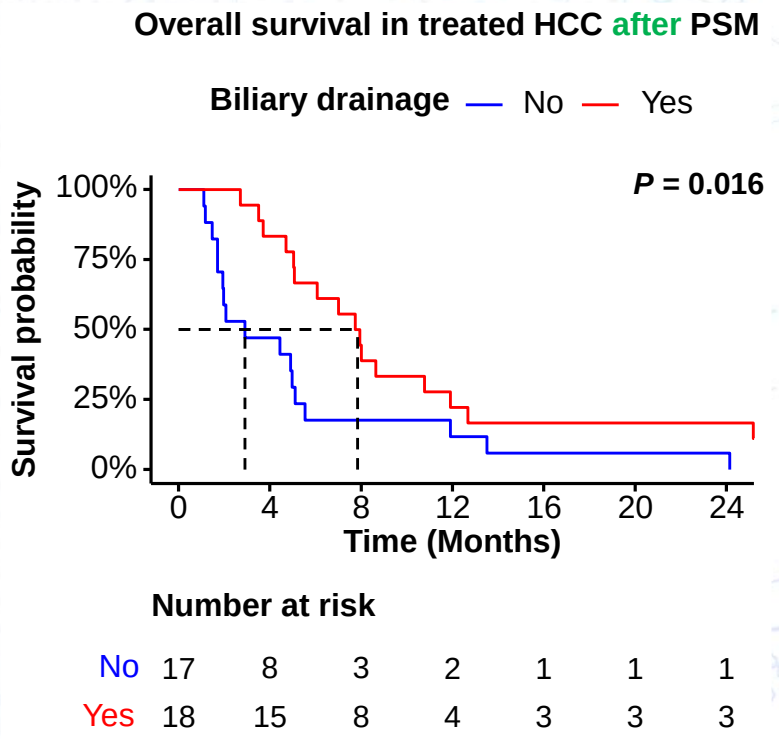
HCC patients with hyperbilirubinemia (TB ≥ 3 mg/dL)					Treated HCC patients with hyperbilirubinemia (TB ≥ 3 mg/dL)				
Response	Overall[1]	Biliary drainage		*P* value[2]	Response	Overall[1]	Biliary drainage		*P* value[2]
		No[1]	Yes[1]				Yes[1]	No[1]	
CR, PR, SD	38	7	31	0.009	CR, PR, SD	38	7	31	0.005
PD	17	9	7		PD	16	9	7	
Unknown	46	14	32		Unknown	10	5	5	

[1]n, [2]Pearson's Chi-squared test.

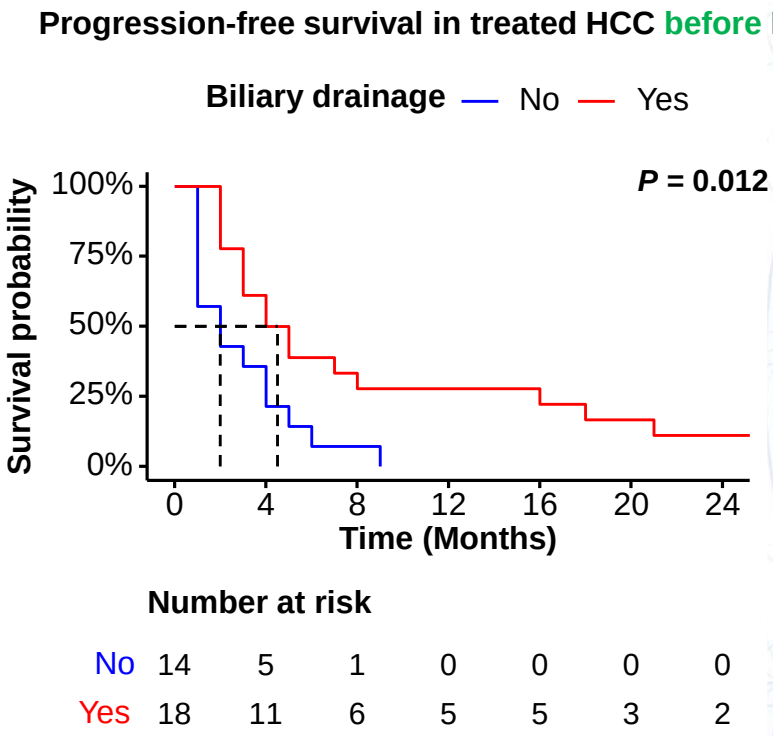
HCC: hepatocellular carcinoma, TB: total bilirubin, CR: complete response, PR: partial response, SD: stable disease, PD: progression disease

Overall survival before and after PSM





Progression-free survival before and after PSM



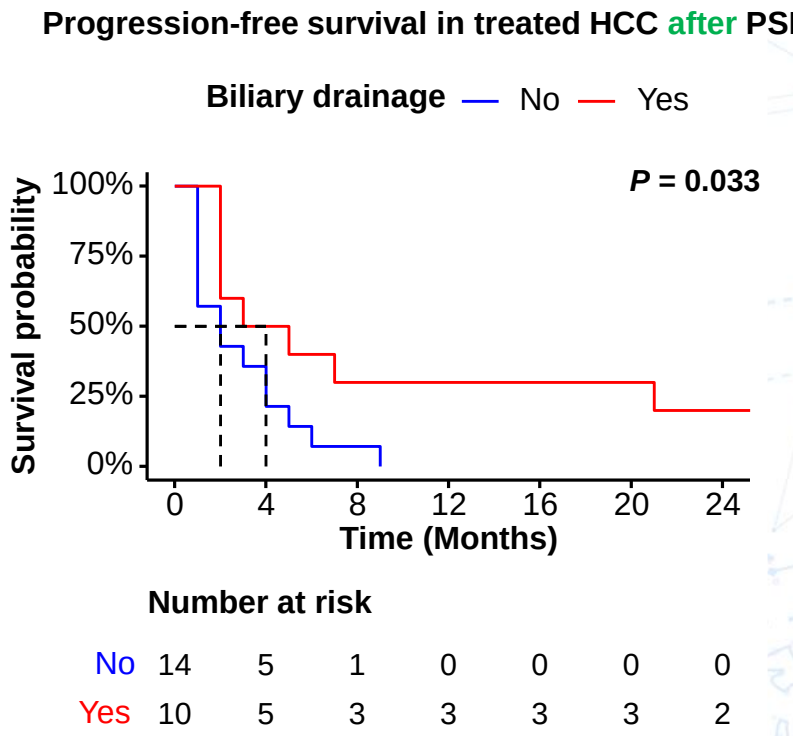


Table. Univariate and multivariate analyses of the factors for OS and PFS before PSM

Characteristic	OS				PFS			
	Univariate		Multivariate		Univariate		Multivariate	
	HR [95% CI]	*P* value	HR [95% CI]	*P* value	HR [95% CI]	*P* value	HR [95% CI]	*P* value
Sex (Male)	1.12 [0.56, 2.27]	0.746			1.30 [0.57, 2.99]	0.535		
Age ≥ 60	1.25 [0.69, 2.26]	0.460			0.97 [0.45, 2.11]	0.942		
Previous treatment history	1.24 [0.91, 1.93]	0.384			1.92 [1.28, 3.48]	0.049	1.96 [0.98, 4.07]	0.166
Etiology								
HBV	1.08 [0.53, 2.17]	0.834			1.69 [0.65, 4.45]	0.284		
Alcohol	0.99 [0.50, 1.97]	0.975			1.12 [0.48, 2.63]	0.794		
ALBI grade 1	0.51 [0.34, 0.88]	0.050	0.55 [0.29, 1.05]	0.068	0.84 [0.43, 1.28]	0.316		
Child-Pugh score ≥ 8	1.01 [0.57, 1.77]	0.980			0.80 [0.39, 1.65]	0.550		
AFP ≥ 400 ng/mL	1.51 [0.83, 2.74]	0.177			2.18 [1.25, 4.58]	0.042	2.28 [1.35, 4.97]	0.067
PIVKA-II ≥ 1000 mAU/mL	0.83 [0.46, 1.50]	0.536			1.13 [0.55, 2.35]	0.736		
Tumor type								
Massive	1.34 [0.73, 2.47]	0.348			1.25 [0.57, 2.75]	0.571		
Nodular	0.94 [0.39, 2.23]	0.880			1.03 [0.35, 2.99]	0.694		
Maximum tumor size ≥ 5cm	1.13 [0.59, 2.17]	0.717			1.38 [0.61, 3.11]	0.434		
Multiple tumors	1.27 [0.71, 2.25]	0.418			0.94 [0.46, 1.92]	0.870		
PVTT	1.2 [0.60, 2.38]	0.605			1.21 [0.49, 2.98]	0.676		
BCLC stage C	1.17 [0.54, 2.54]	0.696			1.04 [0.36, 3.03]	0.939		
Biliary drainage	0.44 [0.24, 0.80]	0.007	0.44 [0.23, 0.84]	0.013	0.37 [0.17, 0.81]	0.012	0.43 [0.18, 1.02]	0.056
Time from BDI diagnosis to HCC treatment (days)	1.00 [0.99, 1.01]	0.758			1.00 [0.99, 1.01]	0.860		
Decreased TB within 7 days after HCC treatment	0.61 [0.34, 1.11]	0.103			0.76 [0.35, 1.66]	0.485		
Decreased TB within 30 days after HCC treatment	0.45 [0.22, 0.92]	0.030	0.59 [0.28, 1.25]	0.172	0.28 [0.10, 0.79]	0.016	0.53 [0.15, 1.90]	0.327

Conclusion

- **Biliary drainage** is an independent **favorable prognostic factor for HCC patients with BDI** and obstructive jaundice.
- Therefore, this study suggests that **biliary drainage should be contemplated in the treatment of advanced HCC patients with BDI** for better survival outcomes.