

## Supplementary Information

**Table S1** Patient demographics and clinicopathological characteristics

Variable	Total (n=340)	HBOL cohort (n=95)	HMOL cohort (n=245)
Gender n (%)			
Female	92	56 (58.95%)	36 (14.69%)
Male	248	39 (41.05%)	209 (85.31%)
Age (years), mean $\pm$ SD	340	47.21 $\pm$ 14.29	55.07 $\pm$ 10.85
Tumor size (cm), n (%)			
$\leq$ 5	169	61 (64.21%)	108 (44.08)
$>$ 5	171	34 (35.79%)	137 (55.92)
Tumor number n (%)			
Single	251	50 (52.63%)	201 (82.04%)
Multiple	89	45 (47.37%)	44 (17.96%)
Hepatitis B Virus n (%)			
Negative	199	86 (90.53%)	113 (46.12%)
Positive	141	9 (9.47%)	132 (53.88%)
Hepatitis C Virus n (%)			
Negative	338	95 (100.00%)	243 (99.18%)
Positive	2	0 (0.00%)	2 (0.82%)
BCLC staging n (%)			
A	159	-	159 (64.90%)
B	34	-	34 (13.88%)
C	51	-	51 (20.82%)
D	1	-	1 (0.41%)
Tumor classification n (%)			
Hepatic hemangiomas	35	35 (36.84%)	-
FNH	14	14 (14.74%)	-
HCA	5	5 (5.26%)	-
Hepatic cyst	27	27 (28.42%)	-
Multiple HBOL	14	14 (14.74)	-
HCC	210	-	210 (85.71%)
ICC	29	-	29 (11.84%)
cHCC-CCA	2	-	2 (0.82%)
Unclear HMOL	4	-	4 (1.63%)

**Abbreviations:** HBOL, hepatic benign occupying lesions; HMOL, hepatic malignant occupying lesions; BCLC, Barcelona Clinic Liver Cancer; FNH, focal nodular hyperplasia; HCA, hepatocellular adenoma; HCC, hepatocellular cholangiocarcinoma; ICC, intrahepatic cholangiocarcinoma; cHCC-CCA, combined hepatocellular-cholangiocarcinoma.

**Table S2** Comparison of variables between training and validation sets

Variable	Training set (n = 237)	Validation set (n = 103)	P
Group n (%)			0.748
HBOL	65 (27.43%)	30 (29.13%)	
HMOL	172 (72.57%)	73 (70.87%)	
Gender n (%)			0.973
Female	64 (27.00%)	28 (27.18%)	
Male	173 (73.00%)	75 (72.82%)	
Age (years)	54.00 (46.00 - 62.00)	53.00 (45.50 - 62.50)	0.446
PLT ( $\times 10^9/L$ )	218.00 (173.00 - 267.00)	227.00 (172.00 - 282.50)	0.582
PT (s)	12.20 (11.60 - 13.20)	12.40 (11.55 - 13.35)	0.692
TT (s)	17.90 (17.10 - 19.10)	18.20 (17.10 - 19.10)	0.627
FIB (g/L)	2.97 (2.44 - 3.64)	2.90 (2.31 - 3.98)	0.916
D-Dimer (mg/L)	0.38 (0.14 - 2.11)	0.35 (0.15 - 1.08)	0.582
Log <sub>10</sub> (DCP) (ng/mL)	1.33 (0.70 - 2.24)	1.37 (0.68 - 2.13)	0.99
TBIL ( $\mu\text{mol/L}$ )	13.30 (10.10 - 18.30)	12.10 (10.15 - 16.80)	0.281
DBIL ( $\mu\text{mol/L}$ )	4.80 (3.30 - 6.90)	4.40 (3.45 - 6.10)	0.606
SF ( $\mu\text{g/L}$ )	331.00 (171.00 - 572.00)	322.00 (168.00 - 535.00)	0.686
ALT (U/L)	29.00 (18.00 - 44.00)	28.00 (16.00 - 43.00)	0.42
AST (U/L)	34.00 (26.00 - 46.00)	31.00 (25.00 - 52.00)	0.755
ALP (U/L)	82.00 (65.00 - 121.00)	85.00 (64.00 - 123.00)	0.612
LDH (U/L)	176.00 (155.00 - 208.00)	181.00 (161.50 - 228.00)	0.123
$\gamma$ -GGT (U/L)	54.00 (30.00 - 119.00)	51.00 (28.00 - 124.50)	0.893
AFU (U/L)	23.00 (17.00 - 28.00)	22.00 (17.00 - 30.50)	0.81
5'-NT (U/L)	8.00 (6.10 - 12.60)	8.50 (6.25 - 12.30)	0.512
TBA ( $\mu\text{mol/L}$ )	7.40 (4.20 - 14.40)	7.30 (3.80 - 16.95)	0.703
TK1 (pmol/L)	0.91 (0.34 - 1.61)	0.93 (0.39 - 1.62)	0.618
HSP90 $\alpha$ (ng/mL)	46.40 (33.80 - 72.20)	47.90 (34.88 - 74.65)	0.575
C4 (g/L)	0.21 (0.17 - 0.29)	0.21 (0.15 - 0.33)	0.924
CEA (ng/mL)	2.24 (1.49 - 3.62)	2.21 (1.30 - 3.41)	0.471
CA125 (U/mL)	11.60 (8.10 - 20.20)	12.50 (8.70 - 20.30)	0.257
CA153 (U/mL)	11.70 (7.80 - 17.40)	11.50 (6.85 - 15.50)	0.199
CA199 (U/mL)	8.10 (3.80 - 19.30)	9.40 (3.60 - 21.20)	0.664
Log <sub>10</sub> (AFP) (ng/mL)	0.56 (0.36 - 0.76)	0.54 (0.41 - 0.87)	0.309
AFP-L3 (ng/mL)	0.17 (0.10 - 0.28)	0.17 (0.11 - 0.39)	0.407
HBsAg (IU/mL)	36.95 (0.00 - 564.35)	0.05 (0.00 - 534.39)	0.163
HBeAg (PEIU/mL)	0.32 (0.05 - 0.40)	0.32 (0.05 - 0.41)	0.629

**Abbreviations:** HBOL, hepatic benign occupying lesions; HMOL, hepatic malignance occupying lesions; PLT, blood platelet; PT prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen; DCP, des-gamma-carboxy prothrombin ; TBIL, total bilirubin; DBIL, direct bilirubin; SF, serum ferritin; ALT, alanine aminotransferase; AST, aspartate transaminase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase;  $\gamma$ -GGT, gamma-glutamyltransferase; AFU, alpha-L-fucosidase; 5'-NT, 5'-nucleotidase; TBA, total bile acid; TK1, thymidine kinase 1; HSP90 $\alpha$ , heat-shock protein 90

alpha; C4, complement protein 4; CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CA153, carbohydrate antigen 153; CA199, carbohydrate antigen 199; AFP, alpha-fetoprotein; lens culinaris agglutinin-reactive fraction of AFP; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e antigen.

**Table S3** LASSO results of training set

<b>Variable</b>	<b>Lambda.1SE</b>
(Intercept)	-2.2413915
Gender	0.7893091
Age	0.00529061
PLT	0
PT	0
TT	0
FIB	0
D-Dimer	0
log <sub>10</sub> (DCP)	0.46909374
TBIL	0
DBIL	0
SF	0.00110221
ALT	0
AST	0
ALP	0
LDH	0
γ-GGT	0
AFU	0
5-NT	0
TBA	0
TK1	0
HSP90α	0
C4	0
CEA	0
CA125	0
CA153	0
CA199	0
log <sub>10</sub> (AFP)	0.69516552
AFP-L3	0
HBsAg	0.00065917
HBeAg	0

**Abbreviations:** LASSO, least absolute shrinkage and selection operator; SE, standard error; PLT, blood platelet; PT prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen; DCP, des-gamma-carboxy prothrombin ; TBIL, total bilirubin; DBIL, direct bilirubin; SF, serum ferritin; ALT, alanine aminotransferase; AST, aspartate transaminase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; γ-GGT, gamma-glutamyltransferase; AFU, alpha-L-fucosidase; 5'-NT, 5'-nucleotidase; TBA, total bile acid; TK1, thymidine kinase 1; HSP90α, heat-shock protein 90 alpha; C4, complement protein 4; CEA, carcinoembryonic antigen; CA125, carbohydrate antigen 125; CA153, carbohydrate antigen 153; CA199, carbohydrate antigen 199; AFP, alpha-fetoprotein; lens culinaris agglutinin-reactive fraction of AFP; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e antigen.

**Table S4** ROC results of single index and logistic regression model

Model	Training set						Validation set					
	AUC (95%CI)	Sensitivity	Specificity	Accuracy	Optimal cutoff	Youden Index	AUC (95%CI)	Sensitivity	Specificity	Accuracy	Optimal cutoff	Youden Index
Gender=Male	0.727 (0.662 - 0.793)	0.85465	0.6	0.78481	-	0.45465	0.708 (0.609 -0.807)	0.84932	0.56667	0.76699	-	0.41598
Age	0.641 (0.556-0.726)	0.87791	0.4	0.74684	42.5	0.27791	0.68 (0.563 - 0.798)	0.67123	0.63333	0.66019	50.5	0.30457
Log <sub>10</sub> (DCP)	0.799 (0.741 - 0.857)	0.65698	0.83077	0.70464	1.2082	0.48775	0.834 (0.759 - 0.909)	0.72603	0.9	0.7767	1.216	0.62603
SF	0.801 (0.734 - 0.868)	0.83721	0.66154	0.78903	207.5	0.49875	0.717 (0.591 -0.843)	0.78082	0.7	0.75728	228	0.48082
Log <sub>10</sub> (AFP)	0.741 (0.676-0.805)	0.61047	0.78462	0.65823	0.56169	0.39508	0.646 (0.526-0.766)	0.64384	0.66667	0.65049	0.52178	0.3105
HBsAg	0.758 (0.689 -0.827)	0.70349	0.81538	0.73418	0.055	0.51887	0.795 (0.705-0.885)	0.67123	0.9	0.73786	0.035	0.57123
GADSAH	0.905 (0.861 - 0.950)	0.86628	0.8	0.8481	0.62436	0.66628	0.88 (0.799 - 0.962)	0.82192	0.86667	0.83495	0.96197	0.68858

**Abbreviations:** ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; GADSAH: gender, age, log<sub>10</sub>(DCP), SF, log<sub>10</sub>(AFP)

and HBsAg; DCP, des-gamma-carboxy prothrombin; SF, serum ferritin; AFP, alpha-fetoprotein; HBsAg, hepatitis B surface antigen.