Supplementary Figure 1 Flowchart of the patient population. HCC: Hepatocellular carcinoma; AFP: Alpha-fetoprotein.

Supplementary Table 1 Baseline characteristics of patients in the training set and validation set

Variables	Training set (n = 311)	Validation set (n = 311)	P value
Demographic variables			
Age, years	56.8 ± 13.8	56.2 ± 13.3	0.627
Male gender	169 (54.3)	175 (56.3)	0.628
Chronic liver disease	169 (54.3)	186 (59.8)	0.168
Etiology of liver disease			0.260
Hepatitis B virus	92 (29.6)	119 (38.3)	
Hepatitis C virus	14 (4.5)	12 (3.9)	
Alcoholic liver disease	39 (12.5)	33 (10.6)	
Others	24 (7.7)	22 (7.1)	
Liver cirrhosis	102 (32.8)	106 (34.1)	0.734
Hepatocellular carcinoma	80 (25.7)	80 (25.7)	1.000
Laboratory variables			
Total bilirubin, mg/dL	1.4 ± 2.8	1.5 ± 2.6	0.659
Albumin, g/dL	4.2 ± 2.3	4.1 ± 0.6	0.484
Prothrombin time, INR	1.4 ± 2.8	1.5 ± 2.6	0.659
Alanine aminotransferase, IU/L	4.2 ± 2.3	4.1 ± 0.6	0.484
AFP level, ng/mL	1021.4 ± 7406.9	6255.8 ± 82843.9	0.268

AFP-L3 fraction, %	6.7 ± 16.5	6.7 ± 17.0	0.981
AFP-L3 level, ng/mL	1688.1 ± 11031.6	1538.7 ± 10087.0	0.860
PIVKA-II level, mAU/mL	634.9 ± 5546.3	1031.2 ± 11166.4	0.575
ALPs score	2750.3 ± 21481.1	4226.4 ± 42566.3	0.585

Variables are expressed as mean ± standard deviation or n (%). AFP: Alpha-fetoprotein; AFP-L3: *Lens culinaris* agglutinin- reactive fraction of AFP; PIVKA-II: Protein induced by vitamin K absence or antagonist-II; ALPs, AFP, AFP-L3 fraction, and PIVKA-II

**Supplementary Table 2 Baseline characteristics of patients with very early an
d early stage hepatocellular carcinoma (*n* = 85)**

Variables	
Demographic variables	
Age, years	65.0 ± 10.8
Male gender	58 (68.2)
Chronic liver disease	84 (98.8)
Etiology of liver disease	
Hepatitis B virus	48 (56.5)
Hepatitis C virus	13 (15.3)
Alcoholic liver disease	18 (21.2)
Others	6 (7.0)
Liver cirrhosis	60 (70.6)
Laboratory variables	
Total bilirubin, mg/dL	1.2 ± 0.9
Albumin, g/dL	3.8 ± 0.7
Prothrombin time, INR	1.1 ± 0.2
Alanine aminotransferase, IU/L	42.8 ± 43.2
AFP level, ng/mL	45.4 ± 113.1
AFP-L3 fraction, %	11.3 ± 18.1
AFP-L3 level, ng/mL	12.3 ± 44.8
PIVKA-II level, mAU/mL	1581.7 ± 10928.0
ALPs score	81.0 ± 2193.6

Variables are expressed as mean ± standard deviation or *n* (%). HCC: Hepatoc
ellular carcinoma; AFP: Alpha-fetoprotein; AFP-L3: *Lens culinaris* agglutinin-reac
tive fraction of AFP; PIVKA-II: protein induced by vitamin K absence or antag
onist-II; ALPs, AFP, AFP-L3 fraction, and PIVKA-II