Table S1. The comparison of baseline characteristics of the training set and the

validation set

Parameter	Training Set	Validation Set	P-value
Number of Patients	3 966	1 700	-
Age, yr, median (IQR)	47.00 (16.00)	47.00 (16.00)	0.309
Male Sex, n (%)	3 150 (79.43)	1 366 (80.35)	0.426
Nucleoside Analog Therapy, n (%)	928 (23.40)	388 (22.82)	0.638
HBV-related HCC, n (%)	1 712 (43.17)	733 (43.12)	0.973
AFP, ng/mL, median (IQR)	28.69 (227.45)	25.11 (205.36)	0.131
PIVKA-II, mAU/mL, median (IQR)	48.00 (250.75)	47.00 (209.75)	0.622
ALT, IU/L, median (IQR)	51.00 (126.00)	51.50 (132.00)	0.891
AST, IU/L, median (IQR)	59.00 (106.25)	58.00 (114.00)	0.655
INR, median (IQR)	1.14 (0.34)	1.14 (0.32)	0.791
ALB, g/L, median (IQR)	37.80 (11.50)	37.90 (11.30)	0.891
GGT, IU/L, median (IQR)	71.00 (106.00)	71.00 (110.75)	0.960
ALP, IU/L, median (IQR)	109.00 (67.00)	111.00 (64.00)	0.261
PLT, 10^9/L, median (IQR)	114.00 (96.25)	109.00 (90.00)	0.027
TBIL, μmol/L, median (IQR)	21.90 (78.73)	21.80 (72.50)	0.830

| HBV-DNA, IU/mL, median (IQR) | 5.61×10^3 (1.98×10^5) | 4.87×10^3 (2.16×10^5) | 0.434 |

Abbreviations: AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence or antagonist-II; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; ALB, albumin; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; PLT, platelet; TBIL, total bilirubin; IQR, interquartile range.

Table S2. The comparison of baseline characteristics of NA-treated patients and

untreated patients in the training set

Parameter	NA-treated patients	Untreated patients	P-value
CHB			
Number of Patients	306	713	-
Age, yr, median (IQR)	41.00 (18.25)	39.00 (19.00)	0.194
Male Sex, n (%)	203 (66.34)	505 (70.83)	0.154
ALT, IU/L, median (IQR)	117.50 (423.75)	193.00 (459.50)	0.010
AST, IU/L, median (IQR)	80.00 (202.00)	121.00 (272.00)	0.006
INR, median (IQR)	1.10 (0.26)	1.11 (0.28)	0.353
ALB, g/L, median (IQR)	38.65 (9.75)	38.10 (9.15)	0.844
GGT, IU/L, median (IQR)	72.00 (128.50)	89.00 (132.50)	0.032
ALP, IU/L, median (IQR)	105.50 (76.50)	111.00 (68.00)	0.126
PLT, 10^9/L, median (IQR)	146.50 (90.75)	155.00 (88.00)	0.191
TBIL, μmol/L, median (IQR)	25.05 (160.05)	38.90 (176.10)	0.022
HBV-DNA, IU/mL, median (IQR)	$2.14*10^3$ $(9.38*10^4)$	$2.25*10^4$ $(1.36*10^6)$	0.009
HBV-related Cirrhosis			
Number of Patients	358	877	-
Age, yr, median (IQR)	47.00 (15.25)	47.00 (14.00)	0.711

|			
Male Sex, n (%)	285 (79.61)	702 (80.05)	0.862
ALT, IU/L, median (IQR)	56.00 (130.50)	70.00 (206.00)	0.012
AST, IU/L, median (IQR)	77.00 (109.00)	96.00 (167.00)	<0.001
INR, median (IQR)	1.3750 (0.54)	1.46 (0.62)	0.019
ALB, g/L, median (IQR)	30.65 (13.52)	30.05 (12.95)	0.529
GGT, IU/L, median (IQR)	63.50 (82.00)	65.00 (84.00)	0.613
ALP, IU/L, median (IQR)	120.50 (72.25)	128.00 (68.50)	0.054
PLT, 10^9/L, median (IQR)	70.50 (69.00)	76.00 (71.00)	0.161
TBIL, μmol/L, median (IQR)	48.60 (180.35)	85.90 (249.90)	0.002
HBV-DNA, IU/mL, median (IQR)	$7.92*10^3$ $(6.94*10^4)$	$8.06*10^3$ $(3.64*10^5)$	0.936
HBV-related HCC			
Number of Patients	264	1 448	-
Age, yr, median (IQR)	50.00 (15.00)	51.00 (16.00)	0.246
Male Sex, n (%)	227 (85.98)	1 228 (84.81)	0.622
ALT, IU/L, median (IQR)	42.50 (39.00)	38.00 (34.00)	0.004
AST, IU/L, median (IQR)	46.50 (44.00)	41.00 (36.75)	0.027
INR, median (IQR)	1.09 (0.17)	1.08 (0.14)	0.093
ALB, g/L, median (IQR)	39.95 (8.75)	41.35 (6.98)	<0.001
GGT, IU/L, median (IQR)	78.50 (109.75)	67.00 (106.75)	0.423
ALP, IU/L, median (IQR)	102.00 (58.75)	97.00 (57.00)	0.206

PLT, 10^9/L, median (IQR)	109.00 (89.75)	122.00 (97.00)	0.008
TBIL, μmol/L, median (IQR)	17.80 (14.18)	14.80 (9.98)	<0.001
HBV-DNA, IU/mL, median (IQR)	$9.56*10^2$ $(2.54*10^4)$	$2.03*10^3$ $(7.39*10^4)$	0.259
Maximum Tumor Diameter ≥3cm, n (%)	150 (56.82)	844 (58.29)	0.656
BCLC Staging: 0/A, n (%)	171 (64.77)	873 (60.29)	0.170

Abbreviations: CHB, chronic hepatitis B; HCC, hepatocellular carcinoma; HBV, Hepatitis B virus; NA, nucleoside analog; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; ALB, albumin; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; PLT, platelet; TBIL, total bilirubin; IQR, interquartile range; BCLC, Barcelona Clinic Liver Cancer stage.

Table S3. The comparison of baseline characteristics of NA-treated patients in the

training set and in the validation set

Parameter	Training Set	Validation Set	P-value
Number of Patients	928	388	-
Age, yr, median (IQR)	46.00 (16.00)	45.00 (17.25)	0.918
Male Sex, n (%)	715 (77.05)	304 (78.35)	0.604
HBV-related HCC, n (%)	264 (28.45)	107 (27.58)	0.748
AFP, ng/mL, median (IQR)	14.79 (81.44)	13.64 (72.19)	0.504
PIVKA-II, mAU/mL, median (IQR)	34.00 (51.00)	35.00 (38.25)	0.930
ALT, IU/L, median (IQR)	56.00 (137.50)	55.50 (174.75)	0.290
AST, IU/L, median (IQR)	62.00 (109.25)	60.00 (121.75)	0.197
INR, median (IQR)	1.18 (0.36)	1.18 (0.37)	0.166
ALB, g/L, median (IQR)	36.40 (12.33)	35.95 (11.65)	0.689
GGT, IU/L, median (IQR)	70.00 (104.00)	66.00 (99.25)	0.126
ALP, IU/L, median (IQR)	110.00 (72.25)	112.00 (65.00)	0.788
PLT, 10^9/L, median (IQR)	105.00 (96.00)	93.50 (90.00)	0.005
TBIL, µmol/L, median (IQR)	25.00 (106.30)	27.70 (104.18)	0.957
HBV-DNA, IU/mL, median (IQR)	$5.93*10^2$ ($4.64*10^4$)	$5.49*10^2$ ($1.49*10^4$)	0.552

Abbreviations: HCC, hepatocellular carcinoma; HBV, Hepatitis B virus; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence or antagonist-II; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; ALB, albumin; GGT, gamma-glutamyl transferase; ALP, alkaline phosphatase; PLT, platelet; TBIL, total bilirubin; IQR, interquartile range.
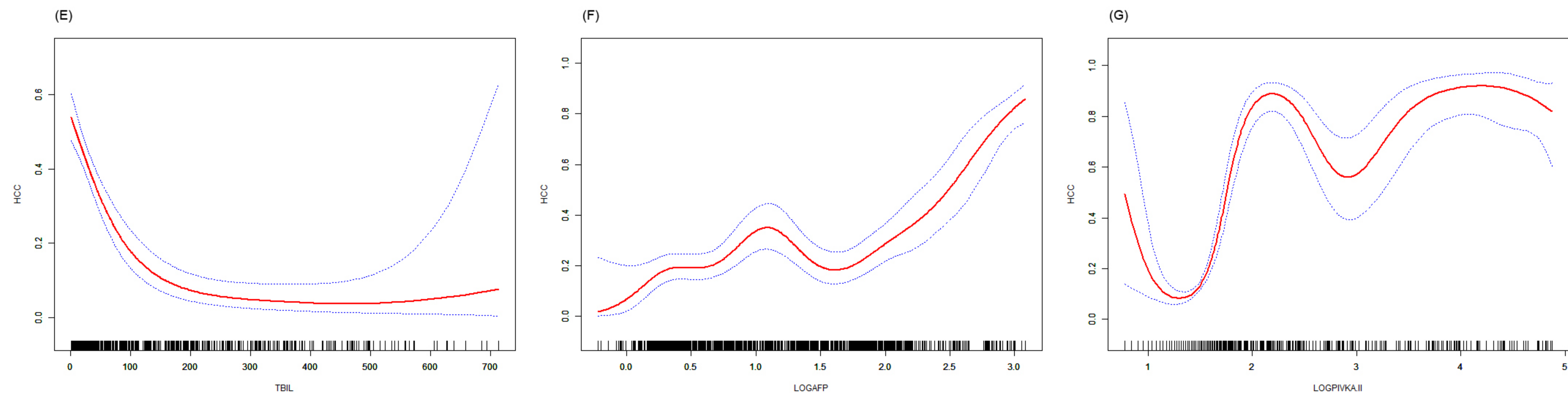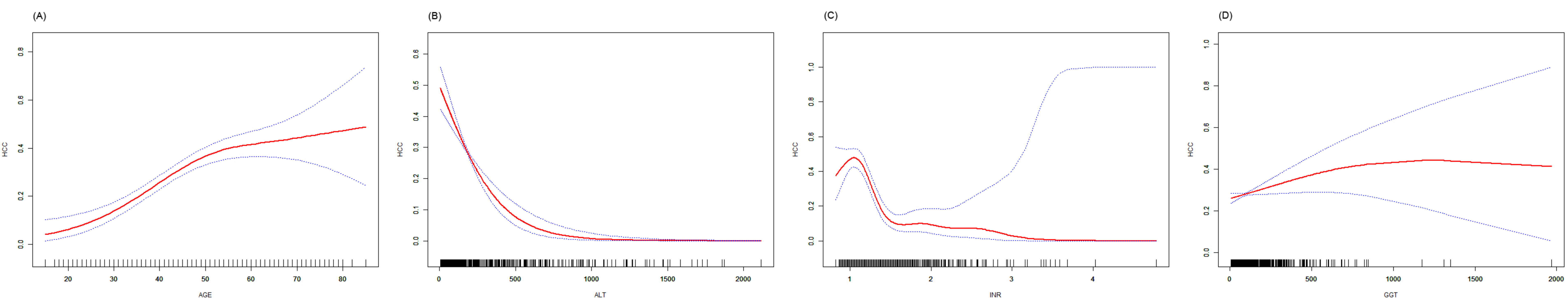
Supplementary Figure Caption

Figure S1. Calibration curves for independent predictors of HBV-related HCC in NA-treated patients of the training set.

A: Age calibration curve. B: ALT calibration curve. C: INR calibration curve. D: GGT calibration curve. E: TBIL calibration curve. F: LogAFP calibration curve. G: LogPIVKA-II calibration curve.