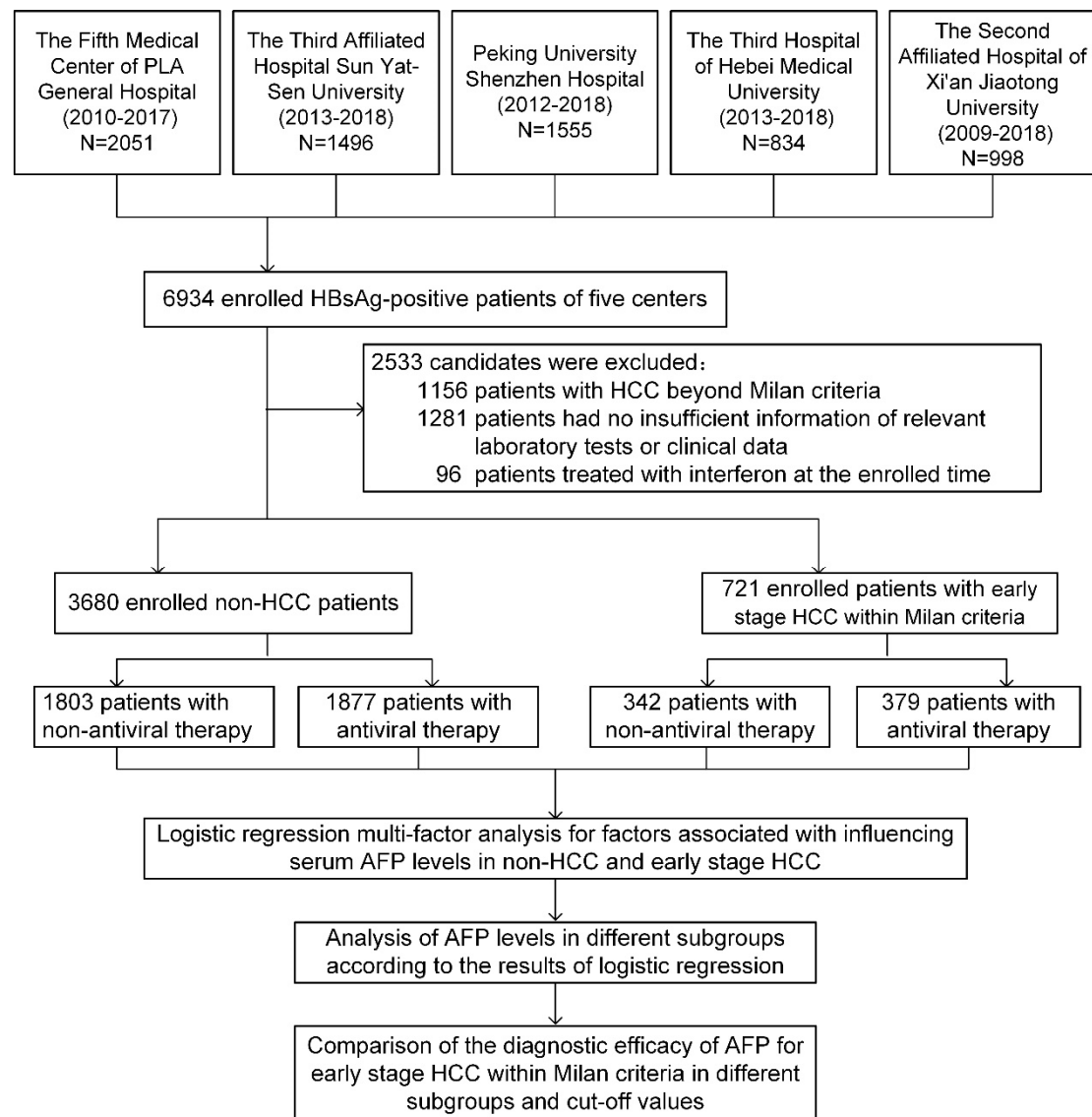
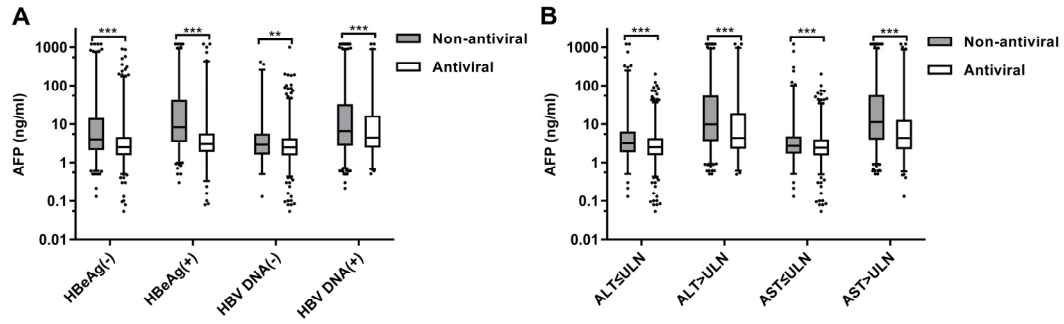


Supplementary Materials

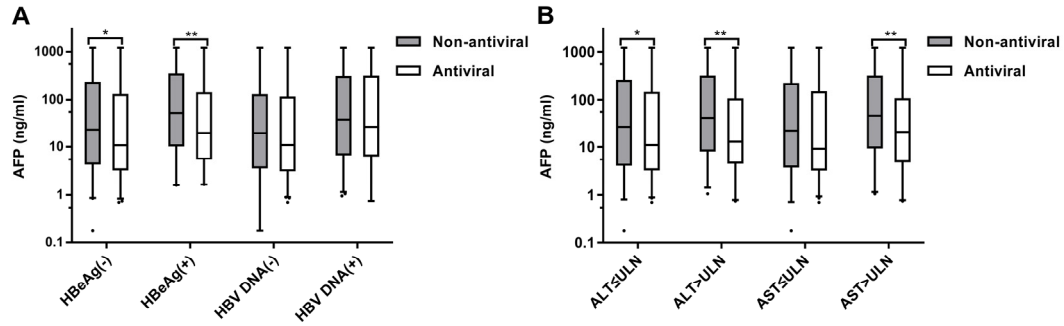
Supplementary Figures



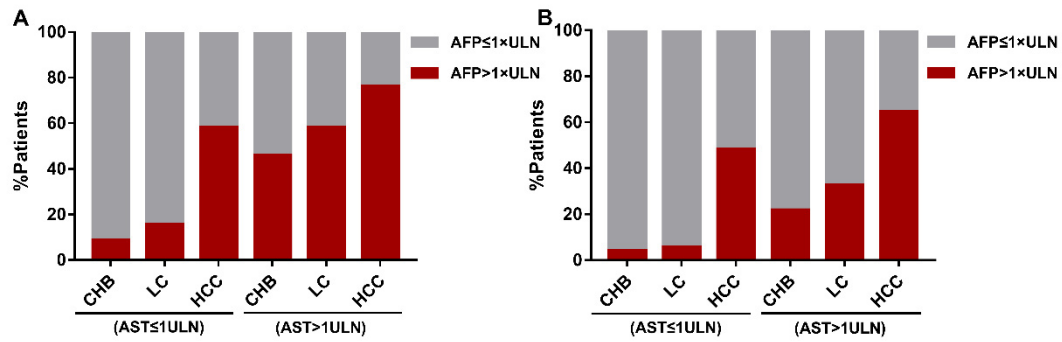
Supplementary Figure S1. The distribution and analysis process of patients enrolled in this study.



Supplementary Figure S2. Comparisons of serum AFP levels between non-HCC patients with and without antiviral treatment in different subgroups. (A) Subgroups of HBeAg(-), HBeAg(+), HBV DNA (-) and HBV DNA(+); (B) Subgroups of ALT \leq 1 \times ULN, ALT > 1 \times ULN, AST \leq 1 \times ULN and AST > 1 \times ULN. ** P < 0.01, * P < 0.001.**



Supplementary Figure S3. Comparisons of serum AFP levels between early stage HCC patients with and without antiviral treatment in different subgroups. (A) Subgroups of HBeAg (-), HBeAg (+), HBV DNA (-) and HBV DNA (+); (B) Subgroups of ALT \leq 1 \times ULN, ALT > 1 \times ULN, AST \leq 1 \times ULN and AST > 1 \times ULN. * P < 0.05, ** P < 0.01.



Supplementary Figure S4. Proportions of abnormal AFP levels between $AST \leq 1 \times ULN$ and $AST > 1 \times ULN$ for patients with chronic hepatitis B (CHB), liver cirrhosis (LC) and early stage HCC in (A) the non-antiviral therapy group, (B) the antiviral therapy group.

Supplementary Table S1 The normal ranges for AFP, ALT, AST, TBIL, Albumin and Platelet by each clinical center.

Variables	Center A	Center B	Center C	Center D	Center E
AFP(ng/mL)	0~10	0~8.1	0~13.4	0~9	0~7.02
ALT(U/L)					
Male	5~40	3~35	9~50	9~50	9~50
Female	5~35	3~35	7~40	7~40	7~40
AST(U/L)					
Male	8~40	15~40	15~40	15~40	15~40
Female	8~40	13~35	13~35	13~35	13~35
TBIL(μ mol/L)	3.4~20.5	4~23.9	6.1~25.9	3~20	5~20
Albumin (g/L)	35~55	36~51	40~55	40~55	35~55
Platelet(10^9 /L)	85~303	100~350	125~350	125~350	100~300

Center A: The Fifth Medical Center of Chinese PLA General Hospital; Center B: The Third Affiliated Hospital of Sun Yat-Sen University; Center C: Peking University Shenzhen Hospital; Center D: The Third Hospital of Hebei Medical University; Center E: The Second Affiliated Hospital of Xi'an Jiaotong University; AFP, alpha-fetoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin.

Supplementary Table S2. Performance characteristics of serum AFP discriminating early stage HCC in different subgroups.

Variables	AUC (95%CI)	Cut-off	Se (%)	Sp (%)	LR+	LR-	P-value
Whole cohort	0.737 (0.716, 0.758)	8.30	62.69	74.37	2.45	0.50	-
Antiviral Therapy							< 0.001
+	0.783 (0.756, 0.811)	6.33	61.74	84.02	3.86	0.46	-
-	0.701 (0.669, 0.733)	16.07	59.65	70.22	2.00	0.57	-
HBeAg							0.397
-	0.754 (0.729, 0.779)	6.90	61.40	78.37	2.84	0.49	-
+	0.734 (0.697, 0.771)	7.38	75.96	61.45	1.97	0.39	-
HBV DNA							< 0.001
-	0.788 (0.759, 0.816)	7.04	56.88	89.60	5.47	0.48	-
+	0.707 (0.677, 0.738)	7.99	72.59	57.29	1.70	0.48	-
ALT							< 0.001
≤ 1×ULN	0.797 (0.772, 0.823)	7.73	59.96	88.83	5.37	0.45	-
> 1×ULN	0.649 (0.612, 0.686)	8.60	69.69	51.85	1.45	0.58	-
AST							< 0.001
≤ 1×ULN	0.811 (0.786, 0.837)	6.90	59.27	90.78	6.42	0.45	-
> 1×ULN	0.664 (0.628, 0.699)	10.14	70.07	55.18	1.56	0.54	-

AUC, area under the ROC curve; CI, confidence interval; Se, sensitivity; Sp, specificity; LR+, positive likelihood ratio; LR-, negative likelihood ratio; HBeAg, hepatitis B e antigen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.