

Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Comparison of Clinical Characteristics Between Enrolled Patients in 2 Cohorts

Variables	Nanjing cohort (n=4,948)	Huai'an cohort (n=1,586)	P value
Age (yr)	40.0 (32.0, 51.0)	45.0 (34.0, 54.0)	<.001
Male (%)	2,991 (60.4)	1,042 (65.7)	<.001
PLT ($\times 10^3/\mu\text{L}$)	189.5 (152.0, 226.0)	157.0 (104.3, 205.0)	<.001
Not available	0	34	
ALT (U/L)	30.8 (20.1, 54.8)	83.0 (41.0, 222.0)	<.001
Not available	0	17	
AST (U/L)	25.7 (20.5, 37.5)	56.0 (32.0, 127.0)	<.001
Not available	0	22	
HBsAg (Log_{10} IU/ml)	3.2 (2.4, 3.8)	3.4 (2.9, 3.9)	<.001
Group			<.001
<3	1,936 (41.1)	458 (28.9)	
3 to <4	1,798 (38.2)	803 (50.6)	
≥ 4	976 (20.7)	325 (20.5)	
Not available	238	0	
Anti-HBs positive (%)	184 (3.7)	93 (5.9)	<.001
Not available	0	0	
HBeAg positive (%)	1,425 (28.8)	813 (51.3)	<.001
Not available	0	0	
HBV DNA (Log_{10} IU/ml)	2.9 (2.7, 5.5)	5.6 (3.5, 7.0)	<.001
Group			<.001

<3	2,265 (51.0)	292 (20.0)	
3 to <5	959 (21.6)	312 (21.3)	
5 to <7	457 (10.3)	482 (33.0)	
≥7	762 (17.2)	376 (25.7)	
Not available	505	124	
APRI	0.3 (0.3, 0.6)	1.1 (0.5, 2.8)	<.001
APRI ≥1.5 (%)	484 (9.8)	621 (40.4)	<.001
APRI ≥2.0 (%)	351 (7.1)	505 (32.9)	<.001
Not available	0	50	
FIB-4	1.0 (0.7, 1.7)	2.0 (1.1, 4.4)	<.001
FIB-4 ≥3.25 (%)	453 (9.2)	510 (33.2)	<.001
FIB-4 ≥6.5 (%)	173 (3.5)	240 (15.6)	<.001
Not available	0	50	
Cirrhosis by ultrasound	338 (10.3)	217 (25.0)	<.001
Not available	1664	718	
Liver stiffness (kPa)	6.4 (5.3, 8.1)	-	
Liver stiffness ≥8.0 (%)	192 (26.8)	-	
Liver stiffness ≥11.0 (%)	66 (9.2)	-	
Not available	4,232	1,586	

ALT, alanine aminotransferase; anti-HBs, hepatitis B core antibody; APRI, aspartate aminotransferase to platelet ratio index; AST, aspartate aminotransferase; FIB-4, fibrosis index based on the four factors; HBeAg, hepatitis B e antibody; HBsAg, hepatitis B surface antigen; HBV, Hepatitis B virus; PLT, platelet.

eTable 2. Comparison of Clinical Characteristics Between Enrolled and Excluded Patients in Each Cohort

Variables	Nanjing cohort				Huai'an cohort		
	Enrolled patients (n=4,948)	Excluded patients (n=8,106)	P value		Enrolled patients (n=1,586)	Excluded patients (n=1,886)	P value
Age (yr)	40.0 (32.0, 51.0)	42.0 (33.0, 53.0)	<.001		45.0 (34.0, 54.0)	52.0 (43.0, 59.3)	<.001
Male (%)	2,991 (60.4)	5,660 (69.8)	<.001		1,042 (65.7)	1,423 (75.5)	<.001
PLT ($\times 10^3/\mu\text{L}$)	189.5 (152.0, 226.0)	180.0 (134.0, 221.0)	<.001		157.0 (104.3, 205.0)	149.0 (95.0, 207.3)	.16
Not available	0	2,816			34	152	
ALT (U/L)	30.8 (20.1, 54.8)	31.1 (20.3, 54.4)	.85		83.0 (41.0, 222.0)	43.0 (26.0, 104.0)	<.001
Not available	0	669			17	94	
AST (U/L)	25.7 (20.5, 37.5)	26.5 (20.9, 38.4)	.005		56.0 (32.0, 127.0)	38.0 (25.0, 78.0)	<.001
Not available	0	708			22	97	
HBsAg (Log_{10} IU/ml)	3.2 (2.4, 3.8)	3.2 (2.4, 3.7)	.002		3.4 (2.9, 3.9)	3.1 (2.3, 3.6)	<.001
Group			<.001				<.001
<3	1,936 (41.1)	2,910 (41.9)			458 (28.9)	725 (44.6)	
3 to <4	1,798 (38.2)	2,916 (42.0)			803 (50.6)	710 (43.7)	
≥ 4	976 (20.7)	1,117 (16.1)			325 (20.5)	190 (11.7)	
Not available	238	1,163			0	261	
anti-HBs positive (%)	184 (3.7)	218 (3.0)	.02		93 (5.9)	107 (6.4)	.53
Not available	0	739			0	213	
HBeAg positive (%)	1,425 (28.8)	2,580 (35.4)	<.001		813 (51.3)	666 (39.8)	<.001
Not available	0	822			0	213	

HBV DNA (Log₁₀ IU/ml)	2.9 (2.7, 5.5)	2.7 (2.7, 3.9)	<.001		5.6 (3.5, 7.0)	2.7 (2.7, 5.6)	<.001
Group			<.001				<.001
<3	2,265 (51.0)	4,552 (64.2)			292 (20.0)	817 (53.9)	
3 to <5	959 (21.6)	1,219 (17.2)			312 (21.3)	251 (16.6)	
5 to <7	457 (10.3)	615 (8.7)			482 (33.0)	276 (18.2)	
≥7	762 (17.2)	709 (10.0)			376 (25.7)	171 (11.3)	
Not available	505	1,011			124	371	
APRI	0.3 (0.3, 0.6)	0.4 (0.3, 0.7)	<.001		1.1 (0.5, 2.8)	0.8 (0.4, 1.9)	<.001
APRI ≥1.5 (%)	484 (9.8)	569 (11.1)	.03		621 (40.4)	531 (31.8)	<.001
APRI ≥2.0 (%)	351 (7.1)	386 (7.5)	.38		505 (32.9)	408 (24.4)	<.001
Not available	0	2,993			50	214	
FIB-4	1.0 (0.7, 1.7)	1.2 (0.8, 2.2)	<.001		2.0 (1.1, 4.4)	2.2 (1.2, 4.9)	.006
FIB-4 ≥3.25 (%)	453 (9.2)	764 (14.9)	<.001		510 (33.2)	593 (35.5)	.18
FIB-4 ≥6.5 (%)	173 (3.5)	291 (5.7)	<.001		240 (15.6)	293 (17.5)	.15
Not available	0	2,993			50	214	
Cirrhosis by ultrasound	338 (10.3)	437 (17.2)	<.001		217 (25.0)	388 (55.6)	<.001
Not available	1,664	5,564			718	1,188	
Liver stiffness (kPa)	6.4 (5.3, 8.1)	7.0 (5.8, 9.1)	<.001		-	-	
Liver stiffness ≥8.0 (%)	192 (26.8)	214 (35.8)	<.001		-	-	
Liver stiffness ≥11.0 (%)	66 (9.2)	90 (15.1)	.001		-	-	
Not available	4,232	7,508			1,586	1,886	

ALT, alanine aminotransferase; anti-HBs, hepatitis B core antibody; APRI, aspartate aminotransferase to platelet ratio index; AST, aspartate aminotransferase; FIB-4, fibrosis index based on the four factors; HBeAg, hepatitis B e antibody; HBsAg, hepatitis B surface antigen; HBV, Hepatitis B virus; PLT, platelet.

eTable 3. Analysis of Clinical Parameters Associated With Severe Liver Fibrosis by HBeAg Status

Variables	HBeAg positive				HBeAg negative			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Sex								
Female	Reference				Reference			
Male	1.321 (1.096, 1.592)	0.004	1.397 (1.096,1.779)	.007	1.389 (1.178, 1.638)	<0.001	1.165 (0.950, 1.428)	.14
ALT (U/L)	1.010 (1.009, 1.011)	<0.001	1.010 (1.009, 1.012)	<.001	1.014 (1.012, 1.015)	<0.001	1.010 (1.008, 1.012)	<.001
HBsAg (Log₁₀ IU/ml)	0.468 (0.416, 0.527)	<0.001	0.381 (0.327, 0.445)	<.001	0.989 (0.923, 1.058)	0.743		
HBsAg/anti-HBs coexistence								
No	Reference				Reference			
Yes	1.584 (1.096, 2.289)	0.014	1.891 (1.126, 3.174)	.02	2.198 (1.551, 3.114)	<0.001	2.279 (1.525, 3.407)	<.001
HBV DNA (Log₁₀ IU/ml)	0.997 (0.948, 1.049)	0.921			1.827 (1.720, 1.942)	<0.001	1.387 (1.289, 1.492)	<.001

ALT, alanine aminotransferase; HBeAg, hepatitis B e antibody; HBsAg, hepatitis B surface antigen; HBV, Hepatitis B virus; OR, odds ratio; PLT, platelet.

eTable 4. Analysis of Clinical Parameters Associated With Cirrhosis by HBeAg Status

Variables	HBeAg positive				HBeAg negative			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Sex								
Female	Reference				Reference			
Male	1.541 (1.266, 1.877)	<0.001	1.095 (0.845, 1.418)	.49	1.365 (1.143, 1.631)	0.001	1.110 (0.889, 1.386)	.36
ALT (U/L)	1.007 (1.007, 1.008)	<0.001	1.008 (1.007, 1.009)	<.001	1.011 (1.010, 1.013)	<0.001	1.008 (1.007, 1.009)	<.001
HBsAg (Log₁₀ IU/ml)	0.448 (0.397, 0.506)	<0.001	0.393 (0.328, 0.471)	<.001	1.043 (0.967, 1.125)	0.272		
HBsAg/anti-HBs coexistence								
No	Reference				Reference			
Yes	1.857 (1.282, 2.689)	0.001	1.450 (0.867, 2.425)	.16	1.719 (1.168, 2.530)	0.006	1.656 (1.048, 2.617)	.03
HBV DNA (Log₁₀ IU/ml)	0.940 (0.893, 0.990)	0.018	0.961 (0.889, 1.038)	.31	1.902 (1.784, 2.027)	<0.001	1.469 (1.363, 1.585)	<.001

ALT, alanine aminotransferase; HBeAg, hepatitis B e antibody; HBsAg, hepatitis B surface antigen; HBV, Hepatitis B virus; OR, odds ratio; PLT, platelet.

eTable 5. Comparison of Clinical Characteristics Between Patients With and Without Anti-HBs in Patients Who Underwent Liver Biopsy

Variables	Patients without anti-HBs (n=290)	Patients with anti-HBs (n=13)	P value
Age (yr)	42.0 (35.0, 51.0)	41.0 (31.5, 53.0)	.77
Male (%)	183 (63.1)	10 (76.9)	.31
PLT ($\times 10^3/\mu\text{L}$)	179.0 (146.0, 218.5)	180.0 (122.0, 217.0)	.66
ALT (U/L)	37.0 (23.7, 55.0)	40.0 (21.5, 196.5)	.59
AST (U/L)	27.0 (21.7, 37.4)	33.1 (21.6, 117.5)	.20
HBsAg (Log_{10} IU/ml)	3.5 (2.9, 4.1)	3.3 (3.0, 3.8)	.61
HBeAg positive status (%)	101 (34.8)	5 (38.5)	.79
HBV DNA (Log_{10} IU/ml)	3.7 (2.7, 6.7)	3.7 (2.8, 6.4)	.89
Fibrosis stage			.03
S0	56 (19.3)	2 (15.4)	
S1	141 (48.6)	3 (23.1)	
S2	65 (22.4)	5 (38.5)	
S3	19 (6.6)	1 (7.7)	
S4	9 (3.1)	2 (15.4)	
Severe fibrosis (S ≥ 2 , %)	93 (32.1)	8 (61.5)	.03
Advanced fibrosis (S ≥ 3 , %)	28 (9.7)	3 (23.1)	.12
Cirrhosis (S4, %)	9 (3.1)	2 (15.4)	.02

ALT, alanine aminotransferase; anti-HBs, hepatitis B core antibody; AST, aspartate aminotransferase; HBeAg, hepatitis B e antibody; HBsAg, hepatitis B surface antigen; HBV, Hepatitis B virus; PLT, platelet.

eFigure. Flowchart of Patient Selection in Each Cohort

