
Title

Quantitative assessment of liver fibrosis (qFibrosis) reveals precise outcomes in Ishak “stable” patients on anti-HBV therapy

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Supplementary Table 1. Description of 15 collagen features selected for establishing qFibrosis.

Number	Feature	Description
1	Total CPA	Total collagen percentage area
2	StrLength	String Length
3	StrWidth	String Width
4	StrSolidity	String Solidity
5	StrPerimeter	String Perimeter
6	PortalAGG	Portal aggregated collagen percentage
7	PortalDIS	Portal distributed collagen percentage
8	NoStrP	Number of Strings (Portal)
9	NoXlinkP	Number of Crosslinks (Portal)
10	NoThickStrS	Number of Thick Strings (Septal)
11	StrLengthS	String length (Septal)
12	NoXlinkS	Number of Crosslinks (Septal)
13	Fibrillar	Fibrillar Collagen Percentage
14	NoStrF	Number of Strings (Fibrillar)
15	NoXlinkF	Number of Crosslinks (Fibrillar)

Supplementary Table 2. ROC analysis of Δ qFibrosis for fibrosis regression

Changes of qFibrosis (post-pretreatment)	Sensitivity %	Specificity %	PPV %	NPV %
For prediction of fibrosis regression				
-0.1	88	46	55	84
-0.2	88	47	55	85
-0.3	81	50	54	78
-0.4	75	53	54	78
-0.5	71	57	55	73
-0.6	62	61	54	69
-0.7	58	65	55	67
-0.8	52	69	55	66
-0.9	46	75	58	65
-1.0	43	76	58	65

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

Supplementary Table 3 Characters associated with fibrosis regression and progression at baseline and after treatment.

	Regression by Ishak or qFibrosis	Stable by qFibrosis	Progression by Ishak or qFibrosis	<i>P</i> value
Baseline				
N (%)	109 (67.3)	29 (17.9)	24 (14.8)	-
Age, year	36 ± 11	36 ± 8	39 ± 9	0.444
Gender (male), n (%)	83 (76.1)	23 (79.3)	20 (83.3)	0.814
PLT, ×10 ⁹ /L	164.0 (123.3, 199.5)	180.0 (132.8, 229.8)	159.0 (129.8, 208.5)	0.515
ALT, U/L	87.0 (46.5, 155.8)	85.4 (37.6, 200.3)	61.5 (35.3, 98.2)	0.295
AST, U/L	53.5 (40.0, 95.0)	54.7 (32.6, 107.0)	38.5 (27.8, 55.5)	0.045
ALB, g/L	42.5 (40.0, 45.6)	43.8 (40.7, 46.8)	45.1 (40.6, 46.9)	0.097
HBV DNA, Log IU/mL	6.8 (5.7, 7.9)	6.9 (5.9, 7.7)	6.0 (4.4, 7.9)	0.300
LSM, Kpa	12.0 (8.1, 17.3)	7.5 (6.7, 11.3)	8.6 (6.8, 12.5)	0.002
qFibrosis	3.3 (2.6, 4.3)	2.6 (2.0, 3.3)	2.0 (1.7, 3.3)	<0.001
Necroinflammation score, n (%)				0.001
0-3, n=15	6 (5.5)	3 (10.3)	6 (25.0)	
4-6, n=68	41 (37.6)	15 (51.7)	12 (50.0)	
7-9, n=52	37 (33.9)	11 (37.9)	4 (16.7)	
≥10, n=27	25 (22.9)	0	2 (8.3)	
Ishak score, n (%)				0.001
1, n=5	2 (1.8)	0	3 (12.5)	
2, n=35	18 (16.5)	10 (34.5)	7 (29.2)	
3, n=54	31 (28.4)	15 (51.7)	8 (33.3)	
4, n=43	35 (32.1)	3 (10.3)	5(20.8)	

5, n=21	20 (18.3)	0	1 (4.2)	
6, n=4	3 (2.8)	1 (3.4)	0	
Post-treatment				
ALT, U/L	24.0 (17.0, 33.0)	28.0 (20.0, 39.0)	32.5 (16.0, 42.4)	0.230
AST, U/L	21.9 (18.0, 29.0)	27.0 (20.5, 30.5)	25.2 (21.5, 35.9)	0.048
ALB, g/L	45.6 (43.2, 48.1)	45.0 (43.0, 47.5)	44.6 (42.4, 46.3)	0.120
HBV DNA, Log IU/mL	0 (0, 1.3)	0 (0, 1.3)	0 (0, 0)	0.871
LSM, Kpa	6.3 (5.2, 8.3)	6.5 (5.3, 9.0)	6.9 (6.1, 9.6)	0.227
qFibrosis	2.3 (1.9, 2.9)	2.5 (1.9, 3.4)	2.7 (2.4, 4.0)	0.013
Necroinflammation score, n (%)				0.447
0-3, n=68	49 (45.0)	12 (41.4)	7 (29.2)	
4-6, n=91	58 (53.2)	17 (58.6)	16 (66.7)	
7-9, n=3	2 (1.8)	0	1 (4.2)	
≥10, n=0	0	0	0	
Ishak score, n (%)				0.084
0, n=3	3 (2.8)	0	0	
1, n=12	12 (11.0)	0	0	
2, n=47	29 (26.6)	10 (34.5)	8 (33.3)	
3, n=59	36 (33.0)	15 (51.7)	8 (33.3)	
4, n=23	16 (14.7)	3 (10.3)	4 (16.7)	
5, n=17	13 (11.9)	0	4 (16.7)	
6, n=1	0	1 (3.4)	0	

Figure Legend

Supplementary Figure 1. Liver biopsy samples of CHB patients by SHG/TPEF morphometry at Ishak fibrosis stages 0-6.

CHB, chronic hepatitis B; SHG/TPEF, second harmonic generation/two photon excitation fluorescence.

Supplementary Figure 2. Dynamic changes of liver stiffness measurements in groups of (A) Fibrosis regression (≥ 1 -point decrease by Ishak fibrosis score), (B) stable by Ishak score, (C) fibrosis progression (≥ 1 -point increase by Ishak score) and the subclassified groups (D) *Regression by qFibrosis*, (E) *Stable by qFibrosis*”, (F) *Progression by qFibrosis*.

Supplementary Figure 3. Association between qFibrosis and liver stiffness pre- and post-treatment.





