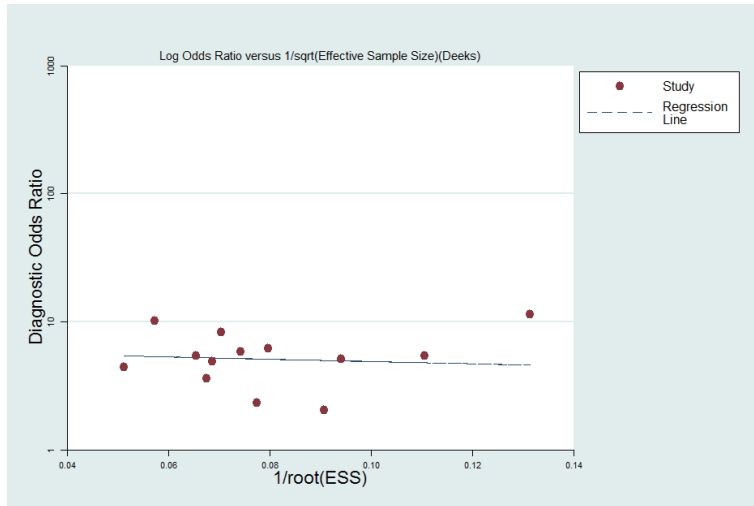
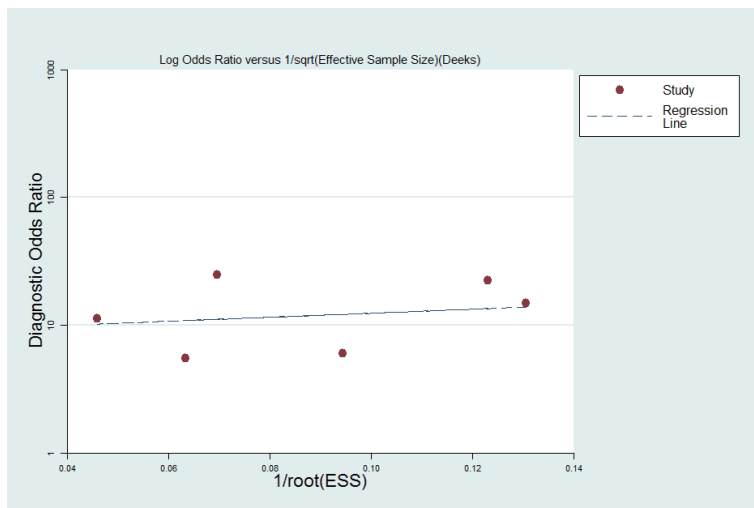


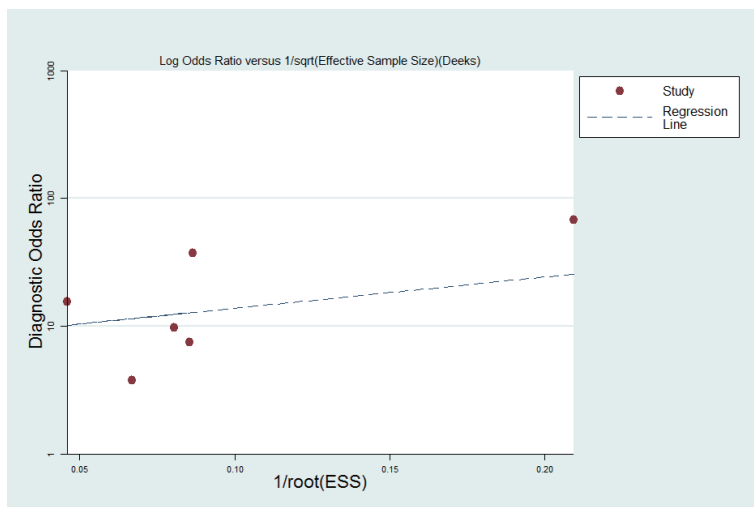
A



B



C



Supplemental Digital Content

Supplemental Table 1. Summary sensitivity and specificity for RPR at various diagnostic thresholds for prediction of significant fibrosis.

Cut-off values	No. of Studies (Patients)	Sensitivity (95% CI)	Specificity (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC
0.0625-0.075	5 (1187)	0.66 (0.63-0.69)	0.75 (0.70-0.80)	2.21 (1.71-2.85)	0.54 (0.44-0.69)	4.33 (3.00-6.23)	0.721
0.0804-0.081	4 (1021)	0.55 (0.51-0.60)	0.70 (0.66-0.74)	2.06 (1.63-2.60)	0.56 (0.42-0.74)	4.19 (2.76-6.36)	0.726
0.09	2 (541)	0.66 (0.58-0.74)	0.68 (0.64-0.73)	2.50 (1.18-5.31)	0.46 (0.37-0.59)	5.37 (2.36-12.21)	-
0.10	1 (58)	0.46	0.92	-	-	-	0.736
Unclear	1 (310)	0.63	0.86	-	-	-	0.825

AUC, area under the curve; CI: confidence interval; DOR, diagnostic odds ratio; NLR, negative likelihood ratio; No., number; PLR, positive likelihood ratio.

Supplemental Digital Content

Supplemental Table 2. Results of meta-regression analysis

Variations	Coeff.	Std. Err.	P -value	RDOR [95%CI]
Significant fibrosis				
Aetiology (CHB vs. Others)	-0.17	0.40	0.67	0.84 (0.35;2.03)
Region (China vs. Others)	0.28	0.31	0.38	1.33 (0.67;2.64)
Age (> Mean vs. < Mean)	0.25	0.29	0.40	1.29 (0.68;2.46)
Male% (> Mean vs. < Mean)	-0.13	0.28	0.65	0.88 (0.47;1.63)
Sample sizes (> Mean vs. < Mean)	-0.03	0.30	0.93	0.97 (0.50;1.90)
Scoring system	-0.06	0.12	0.64	0.94 (0.72;1.23)
Length of LB (≥ 10 mm vs. unclear)	0.73	0.28	0.02	2.08 (1.12;3.85)
ALT (> Mean vs. < Mean)	0.18	0.32	0.58	1.20 (0.59;2.43)
AST (> Mean vs. < Mean)	0.17	0.33	0.62	1.18 (0.56;2.50)
RDW (> Mean vs. < Mean)	0.26	0.31	0.42	1.30 (0.65;2.61)
PLT (> Mean vs. < Mean)	-0.08	0.33	0.81	0.92 (0.45;1.91)
Advanced fibrosis				
Aetiology (CHB vs. Others)	-1.30	0.99	0.28	0.27 (0.01;6.29)
Region (China vs. Others)	-0.84	0.35	0.10	0.43 (0.14;1.31)
Age (> Mean vs. < Mean)	0.54	0.69	0.48	1.72 (0.19;15.25)
Male% (> Mean vs. < Mean)	-0.54	0.69	0.48	0.58 (0.07;5.14)
Sample sizes (> Mean vs. < Mean)	-1.01	0.48	0.13	0.36 (0.08;1.67)
Scoring system	0.31	0.23	0.28	1.36 (0.66;2.79)
Length of LB (≥ 10 mm vs. unclear)	0.54	0.69	0.49	1.72 (0.19;15.25)
ALT (> Mean vs. < Mean)	0.81	0.43	0.16	2.24 (0.57;8.82)
AST (> Mean vs. < Mean)	0.81	0.43	0.16	2.24 (0.57;8.82)
RDW (> Mean vs. < Mean)	0.54	0.69	0.49	1.72 (0.19;15.25)
PLT (> Mean vs. < Mean)	0.84	0.35	0.10	2.32 (0.76;7.05)
Cirrhosis				
Aetiology (CHB vs. Others)	-0.51	1.10	0.67	0.60 (0.02;19.63)
Region (China vs. Others)	-1.78	1.06	0.19	0.17 (0.01;4.89)
Age (> Mean vs. < Mean)	1.78	1.06	0.19	5.94 (0.20;172.75)
Male% (> Mean vs. < Mean)	-1.78	1.06	0.19	0.17 (0.01;4.89)
Sample sizes (> Mean vs. < Mean)	-0.17	0.97	0.87	0.84 (0.04;18.66)
Scoring system	-0.24	1.42	0.87	0.78 (0.01;71.26)
Length of LB (>10mm vs. unclear)	1.29	0.59	0.12	3.61 (0.56;23.34)
RDW (> Mean vs. < Mean)	1.01	0.74	0.26	2.76 (0.26;29.04)
PLT (> Mean vs. < Mean)	0.17	0.97	0.87	1.19 (0.05;26.45)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CHB, chronic hepatitis B; CI, confidence interval; Coeff. coefficient; LB, liver biopsy; PLT, platelet; RDOR relative diagnostic odds ratio; RDW, red cell distribution width; SE, standard error; vs. Versus.

Supplemental Digital Content

Supplemental Table 3. Data of diagnostic accuracy of RPR, FIB-4 and APRI for the prediction of liver fibrosis in the same individuals of each stage.

Study	RPR				FIB-4				APRI			
	AUC	Cut-off	Sen (%)	Spe (%)	AUC	Cut-off	Sen (%)	Spe (%)	AUC	Cut-off	Sen (%)	Spe (%)
Significant fibrosis												
Chen 2018	0.64	0.081	39.2	90.0	0.72	0.997	57.5	83.3	0.72	0.669	57.5	78.3
Koksal 2016	0.68	0.07	56.0	21.0	0.68	1.45	51.0	86.0	0.73	0.50	67.0	69.0
Lee 2016	0.75	0.0625	72.3	67.7	0.78	1.025	75.4	73.8	0.72	0.415	80.8	49.2
Li 2018	0.74	0.10	45.5	91.7	0.71	1.45	59.1	80.6	0.70	0.50	31.8	86.1
Wang 2016	0.80	0.09	63.5	82.5	0.71	2.29	54.1	83.9	0.69	0.52	77.0	49.6
Wu 2017	0.64	0.09	70.7	60.4	0.68	1.45	58.5	70.2	0.72	0.52	80.8	52.8
Zhu-1 2017	0.71	0.0804	63.0	72.0	0.71	1.1951	69.0	66.0	0.66	0.4315	84.0	46.0
Zhu-2 2017	0.68	0.0804	53.0	67.0	0.65	1.1951	62.0	56.0	0.61	0.4315	71.0	43.0
Zhu-3 2017	0.78	0.0804	82.0	58.0	0.78	1.1951	74.0	61.0	0.75	0.4315	90.0	47.0
Advanced fibrosis												
Huang 2017	0.72	0.075	75.7	64.5	0.76	1.098	80.5	62.6	0.71	0.657	66.4	71.0
Koksal 2016	0.90	0.07	93.0	67.0	0.87	1.45	83.0	74.0	0.79	0.50	92.0	54.0
Lee 2016	0.80	0.0675	81.8	71.3	0.81	1.085	88.3	63.4	0.64	0.525	72.7	48.5
Wu 2017	0.71	0.098	73.1	67.5	0.73	1.15	95.7	53.1	0.80	0.69	86.4	66.9
Cirrhosis												
Chen 2018	0.79	0.0797	75.0	76.3	0.81	1.324	70.8	78.8	0.70	0.509	91.7	41.4
Huang 2017	0.74	0.096	60.2	78.6	0.76	1.341	83.1	60.7	0.69	0.78	65.1	67.6
Lee 2016	0.81	0.0685	66.0	67.6	0.80	1.415	80.6	67.9	0.68	0.795	58.5	67.9

APRI, Aspartate aminotransferase-platelet index; AUC, area under the curve; FIB-4, fibrosis index based on the four factors; RPR, red cell volume distribution width to platelet ratio; Sen, sensitivity; Spe, specificity.