

**Simple new clinical score to predict hepatocellular carcinoma after sustained viral
response with direct-acting antivirals**

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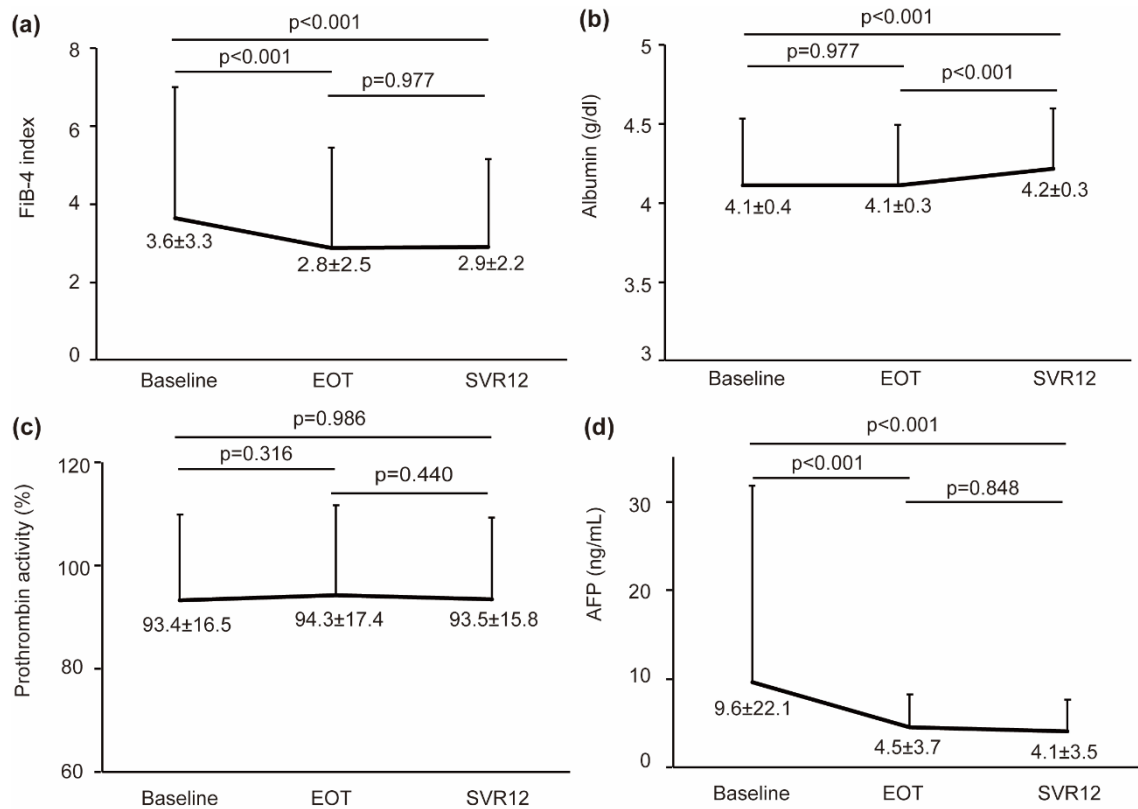


Figure S1.

FIB-4 index (a), serum albumin level (g/dL) (b), prothrombin activity (%) (c), and AFP (ng/ml) (d) values at baseline, EOT, and SVR12. The FIB-4 index is significantly lower at EOT and SVR12 than at baseline (a). P values were calculated with RM ANOVA with Bonferroni's multiple comparisons.

Table S1. Factors at treatment start including baseline factors associated with the occurrence of HCC after DAA treatment in the training set

	HCC occurrence		Univariate analysis		Multivariate analysis	
	Yes	No	Hazard ratio	p-value	Hazard ratio	p-value
			(95% CI)		(95% CI)	
Age (y)	68.9 ± 8.2	65.4 ± 10.3	1.03 (1.00-1.06)	0.029		
Male (n, %)	31, 67.3	416, 43.7	2.75 (1.48-5.10)	0.001	2.08 (1.06-40.4)	0.031
Body mass index (kg/m ²)	24.1 ± 3.1	23.2 ± 3.8	1.06 (0.98-1.14)	0.106		
Diabetes mellitus (n, %)	16, 34.7	154, 16.2	2.73 (1.49-5.02)	0.001	2.51 (1.27-4.95)	0.008
Alcohol (n, %)	5, 16.6	125, 16.7	1.17 (0.63-2.18)	0.60		
White blood cell count (/μL)	4399 ± 1640	5108 ± 1630	0.99 (0.99-0.99)	0.009	0.99 (0.99-0.99)	0.001
Platelet count (×10 ⁴ /μL)	12.0 ± 5.7	16.6 ± 6.5	0.87 (0.83-0.92)	<0.001		
ALT (U/L)	51.5 ± 22.3	50.9 ± 46.5	1.00 (0.99-1.00)	0.89		
AST (U/L)	56.2 ± 29.2	48.4 ± 34.0	1.00 (0.99-1.01)	0.09		
Total bilirubin (mg/dL)	0.8 ± 0.3	0.8 ± 0.6	1.04 (0.69-1.57)	0.83		

Albumin level (g/dL)	3.9 ± 0.3	4.1 ± 0.4	0.35 (0.19-0.65)	<0.001		
Prothrombin activity (%)	83.0 ± 15.6	93.7 ± 16.9	0.97 (0.96-0.98)	<0.001	0.97 (0.96-0.99)	0.002
AFP level (ng/mL)	16.4 ± 17.9	9.9 ± 25.6	1.00 (0.99-1.01)	0.15		
FIB-4 index	4.8 ± 4.4	2.7 ± 2.0	1.04 (1.02-1.07)	<0.001	-	-

Data are expressed as means ± standard deviation.

HCC, hepatocellular carcinoma; DAA, direct-acting antiviral; CI, confidence interval; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, α -fetoprotein; FIB-4, fibrosis-4; SVR, sustained virological response

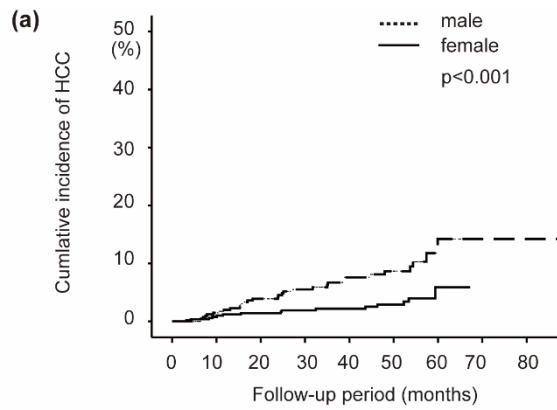
Table S2. Factors at the end of treatment associated with the occurrence of HCC after DAA treatment in the training set

	HCC occurrence		Univariate analysis		Multivariate analysis	
	Yes	No	Hazard ratio	p-value	Hazard ratio	p-value
			(95% CI)		(95% CI)	
Age (y)	68.9 ± 8.2	65.4 ± 10.3	1.03 (1.00-1.06)	0.029		
Male (n, %)	31, 67.3	416, 43.7	2.75 (1.48-5.10)	0.001	4.84 (1.83-12.8)	0.001
Body mass index (kg/m ²)	24.1 ± 3.1	23.2 ± 3.8	1.06 (0.98-1.14)	0.106		
Diabetes mellitus (n, %)	16, 34.7	154, 16.2	2.73 (1.49-5.02)	0.001	-	-
Alcohol (n, %)	5, 16.6	125, 16.7	1.17 (0.63-2.18)	0.60		
White blood cell count (/μL)	4746 ± 1891	5249 ± 1753	1.00 (0.99-1.00)	0.11		
Platelet count (×10 ⁴ /μL)	13.3 ± 6.4	17.3 ± 7.0	0.90 (0.85-0.95)	<0.001		
ALT (U/L)	29.5 ± 35.3	20.0 ± 13.9	1.01 (1.00-1.01)	0.002		
AST (U/L)	33.5 ± 27.3	24.5 ± 11.3	1.01 (1.00-1.02)	<0.001		
Total bilirubin (mg/dL)	0.8 ± 0.4	0.8 ± 0.4	1.21 (0.70-2.08)	0.48		
Albumin level (g/dL)	4.0 ± 0.3	4.1 ± 0.3	0.41 (0.19-0.89)	0.024	-	-

Prothrombin activity (%)	84.4 ± 19.0	95.3 ± 17.0	0.97 (0.95-0.98)	<0.001	-	-
AFP level (ng/mL)	7.4 ± 5.5	4.2 ± 3.2	1.11 (1.06-1.17)	<0.001	1.13 (1.06-1.19)	<0.001
FIB-4 index	4.6 ± 4.5	2.7 ± 2.7	1.07 (1.03-1.11)	<0.001	1.09 (1.01-1.18)	0.028

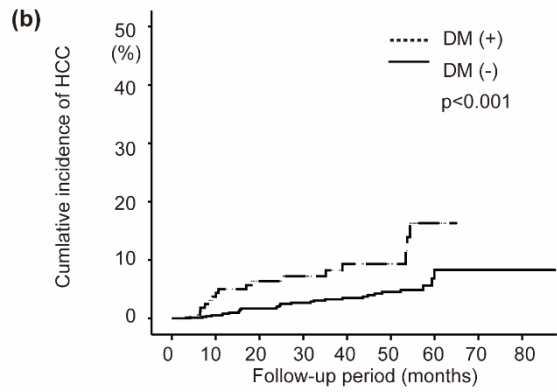
Data are expressed as means ± standard deviation.

HCC, hepatocellular carcinoma; DAA, direct-acting antiviral; CI, confidence interval; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AFP, α -fetoprotein; FIB-4, fibrosis-4; SVR, sustained virological response



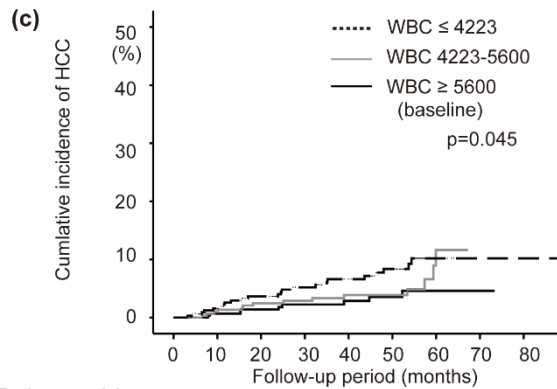
Patients at risk

male	447	324	202	33	1
female	549	435	309	39	0



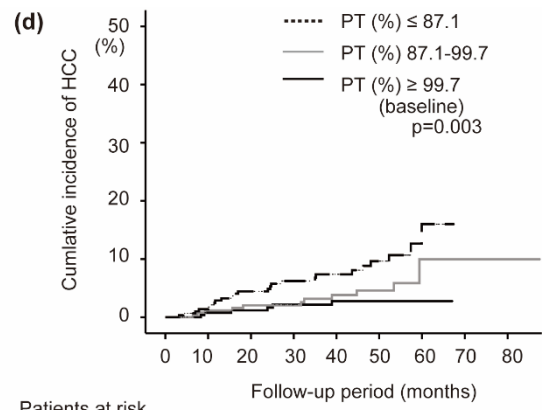
Patients at risk

DM (+)	170	128	80	11	0
DM (-)	825	630	431	61	1



Patients at risk

WBC ≤ 4223	332	262	180	23	1
WBC 4223-5600	336	248	175	31	0
WBC ≥ 5600 (baseline)	328	249	156	18	0

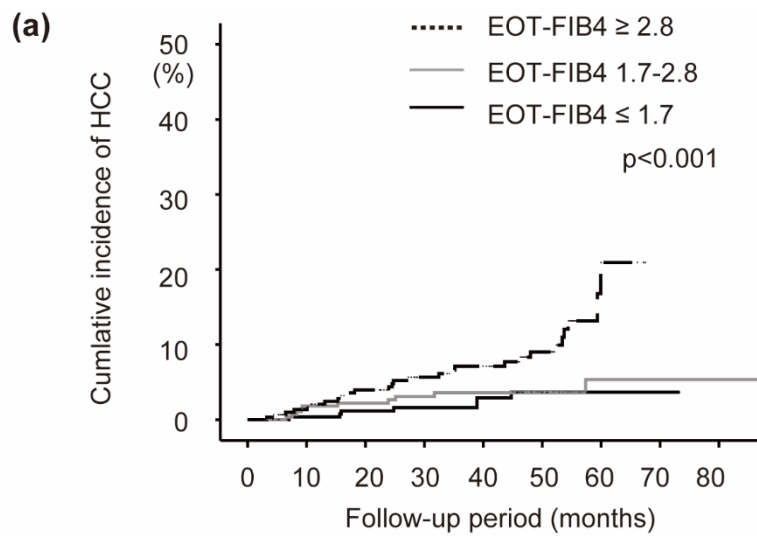


Patients at risk

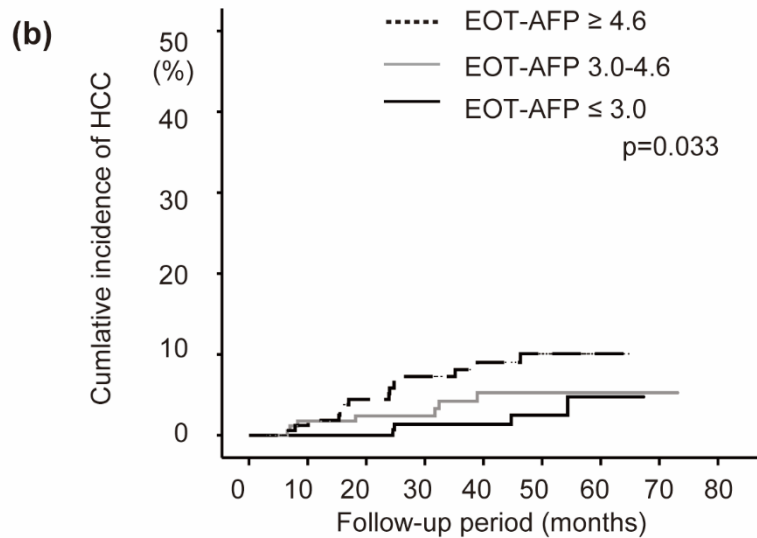
PT (%) ≤ 87.1	301	230	148	23	0
PT (%) 87.1-99.7	283	222	141	21	1
PT (%) ≥ 99.7 (baseline)	299	218	154	19	0

Figure S2.

Comparison of cumulative HCC occurrence rate in the training set. The cumulative occurrence of HCC is significantly stratified by sex ($p < 0.001$) (a), DM ($p < 0.001$) (b), white blood cell counts ($/\mu\text{L}$) ($p=0.045$) (c), and prothrombin activity (%) ($p = 0.003$) (d) with the log-rank test.



Patients at risk					
EOT-FIB4 ≥ 2.8	312	245	172	18	0
EOT-FIB4 1.7-2.8	307	236	161	26	1
EOT-FIB4 ≤ 11.7	293	234	149	23	0



Patients at risk				
EOT-AFP ≥ 4.6	183	137	98	11
EOT-AFP 3.0-4.6	188	145	88	13
EOT-AFP ≤ 3.0	185	152	106	11

Figure S3.

Comparison of cumulative HCC occurrence rate in the training set. There was a significant difference among the patients by FIB-4 index at EOT ($p < 0.001$) (a), AFP level (ng/mL) at EOT ($p = 0.033$) (b) with the log-rank test.