

Supplementary Materials

Table S1 Baseline characteristics of the included participants.

Characteristics	Total (<i>n</i> = 504)	HEV-LF onset during follow-up		<i>P</i> value
		No (<i>n</i> = 445)	Yes (<i>n</i> = 59)	
Hospitalization (day), <i>M</i>(IQR)	20 (13, 27)	19 (13, 26)	25 (17, 33)	< 0.001
Sex, <i>n</i> (%)				0.035
Male	355 (70.44)	306 (68.76)	49 (83.05)	
Female	149 (29.56)	139 (31.24)	10 (16.95)	
Age, <i>M</i>(IQR)	55 (48, 65)	55 (48, 65)	55 (48, 65)	0.947
Alcohol drinker, <i>n</i> (%)	115 (22.82)	102 (22.92)	13 (22.03)	>0.900
Type 2 diabetes, <i>n</i> (%)	86 (17.06)	73 (16.4)	13 (22.03)	0.370
Laboratory, <i>M</i>(IQR)				
NEU (109/L)	3.09 (2.26, 3.95)	3.07 (2.23, 3.92)	3.41 (2.46, 4.54)	0.087
MONO (109/L)	0.51 (0.40, 0.70)	0.50 (0.40, 0.68)	0.62 (0.45, 0.94)	0.004
LYM (109/L)	1.42 (1.03, 1.95)	1.45 (1.07, 1.95)	1.30 (0.92, 1.76)	0.072
SIRI	1.09 (0.65, 1.96)	1.02 (0.64, 1.87)	1.65 (1.10, 3.08)	< 0.001
PT (second)	13.01 (11.9, 14.40)	12.90 (11.7, 14.00)	17.00 (14.35, 19.45)	< 0.001
INR	1.00 (0.94, 1.15)	0.99 (0.93, 1.10)	1.40 (1.19, 1.60)	< 0.001
AST (U/L)	222.50 (71.75, 750.00)	189.00 (64.00, 623.00)	934.00 (259.00, 1553.50)	< 0.001
ALT (U/L)	596.35 (147.10, 1447.38)	536.60 (139.00, 1260.00)	1655.30 (595.50, 2509.00)	< 0.001
TBIL (μmol/L)	68.30 (20.20, 148.80)	54.80 (19.60, 134.40)	149.70 (78.85, 200.25)	< 0.001
DBIL (μmol/L)	46.17 (8.80, 110.43)	38.70 (7.80, 98.00)	109.40 (56.30, 164.45)	< 0.001
CLDs, <i>n</i> (%)	282 (55.95)	246 (55.28)	36 (61.02)	0.487
CHB, <i>n</i> (%)	95 (18.85)	79 (17.75)	16 (27.12)	0.121
CHC, <i>n</i> (%)	6 (1.19)	5 (1.12)	1 (1.69)	0.528
Other CLDs, <i>n</i> (%)	182 (36.11)	162 (36.4)	20 (33.90)	0.816
Cirrhosis, <i>n</i> (%)	58 (11.51)	47 (10.56)	11 (18.64)	0.107

Abbreviations: HEV-LF, hepatitis E virus-related liver failure; NEU, neutrophil; LYM, lymphocyte; MONO, monocyte; SIRI, systemic inflammation response index; PT, prothrombin time; INR, international normalized ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TBIL, total bilirubin; DBIL, direct bilirubin; CLDs, chronic liver diseases; CHB, chronic hepatitis B; CHC, chronic hepatitis C.

Table S2. Statistical description of the fibrosis markers among the included participants ($n = 504$).

Fibrosis markers	Unit	<i>M</i> (IQR)	Tertile1	Tertile2	Tertile3
LN	ng/mL	33.19 (20.70, 73.60)	<23.66	23.66-56.96	>56.96
HA	ng/mL	153.00 (78.42, 266.00)	<99.95	99.95-221.70	>221.70
IV-C	ng/mL	48.90 (29.78, 88.63)	<35.69	35.69-74.40	>74.40
PIIINP	ng/mL	56.90 (25.08, 184.65)	<31.88	31.88-120.75	>120.75
FIB-4	—	3.61 (1.57, 7.57)	<2.20	2.20-5.76	>5.76
APRI	—	3.91 (1.17, 12.34)	<1.76	1.76-8.66	>8.66

Abbreviations: LN, laminin; HA, hyaluronic acid; IV-C, type IV collagen; PIIINP, N-terminal propeptide of type III collagen; FIB-4, fibrosis-4 score; APRI, aspartate aminotransferase to platelet ratio index.

Table S3 Apparent and bootstrap mean AUROC of the fibrosis profiles ($n=504$)

	Apparent AUROC (95% CI)	Bootstrap mean AUC (95% CI) ^a
7-day HEV-LF		
LN	74.94 (66.16-83.71)	75.09 (66.20-83.99)
HA	73.01 (65.72-80.30)	73.17 (65.81-80.53)
IV-C	73.37 (65.51-81.23)	73.62 (65.69-81.55)
PIIINP	67.74 (59.02-76.46)	68.04 (59.22-76.85)
FIB-4	73.85 (66.15-81.55)	73.93 (66.11-81.75)
APRI	75.30 (67.36-83.24)	75.21 (67.04-83.38)
TOP-3 markers	84.98 (78.55-91.41)	85.03 (78.60-91.46)
14-day HEV-LF		
LN	69.25 (60.84-77.65)	69.28 (60.90-77.66)
HA	67.71 (60.40-75.02)	67.78 (60.29-75.28)
IV-C	69.10 (61.73-76.47)	69.24 (61.90-76.58)
PIIINP	63.39 (55.02-71.76)	63.59 (59.22-76.85)
FIB-4	70.82 (63.04-78.60)	70.96 (62.94-78.98)
APRI	71.32 (63.19-79.45)	71.30 (62.90-79.71)
TOP-3 markers	80.11 (73.49-86.73)	80.10 (73.34-86.88)

Notes: ^a 1000 bootstrap iterations were used to reduce the optimism bias.

Abbreviations: AUROC, area under the receiver-operating-characteristic curve; LN, laminin; HA, hyaluronic acid; IV-C, type IV collagen; PIIINP, N-terminal propeptide of type III collagen; FIB-4, fibrosis-4 score; APRI, aspartate aminotransferase to platelet ratio index.

Table S4 Bootstrap mean AUROC of the top three marker combination in subgroups.

Subgroups	<i>n</i>	bootstrap mean 7d-AUROC (95% CI) ^a	bootstrap mean 14d-AUROC (95% CI) ^a
No CLD	222	92.57 (86.99-98.15)	86.11 (77.60-94.62)
CHB or CHC	100	89.85 (76.67-100.00)	84.31 (70.84-97.78)
Other CLDs	182	73.47 (59.72-87.23)	71.77 (58.81-84.74)

Notes: ^a 1000 bootstrap iterations were used to reduce the optimism bias.

Abbreviations: AUROC, area under the receiver-operating-characteristic curve; CLD, chronic liver disease; CHB, chronic hepatitis B; CHC, chronic hepatitis C.

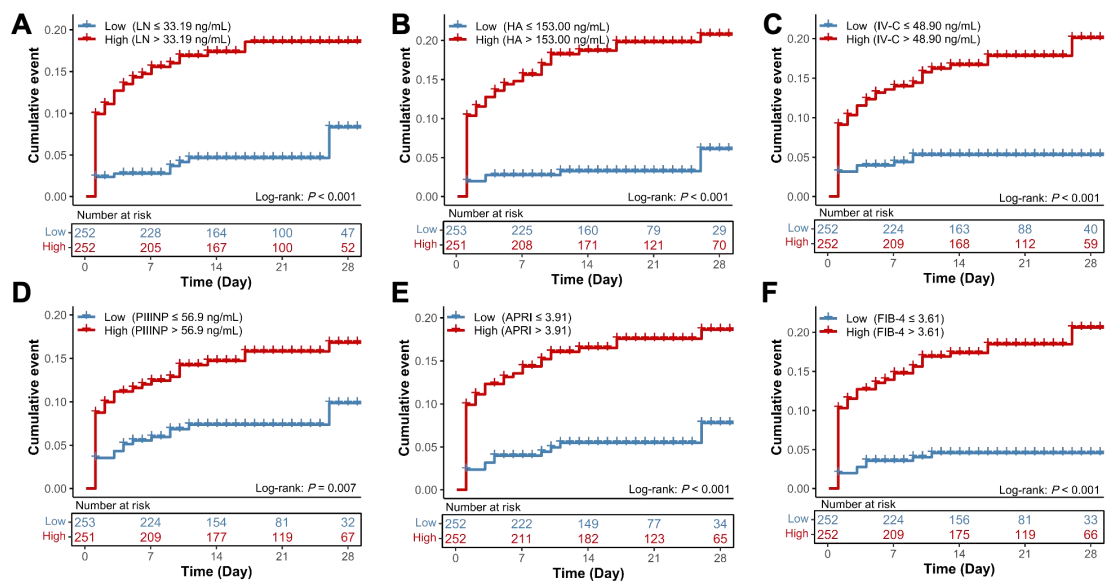


Fig.S1 The Kaplan-Meier cumulative event curves ($n = 504$).

Abbreviations: LN, laminin; HA, hyaluronic acid; IV-C, type IV collagen; PIIINP, N-terminal propeptide of type III collagen; FIB-4, fibrosis-4 score; APRI, aspartate aminotransferase to platelet ratio index.