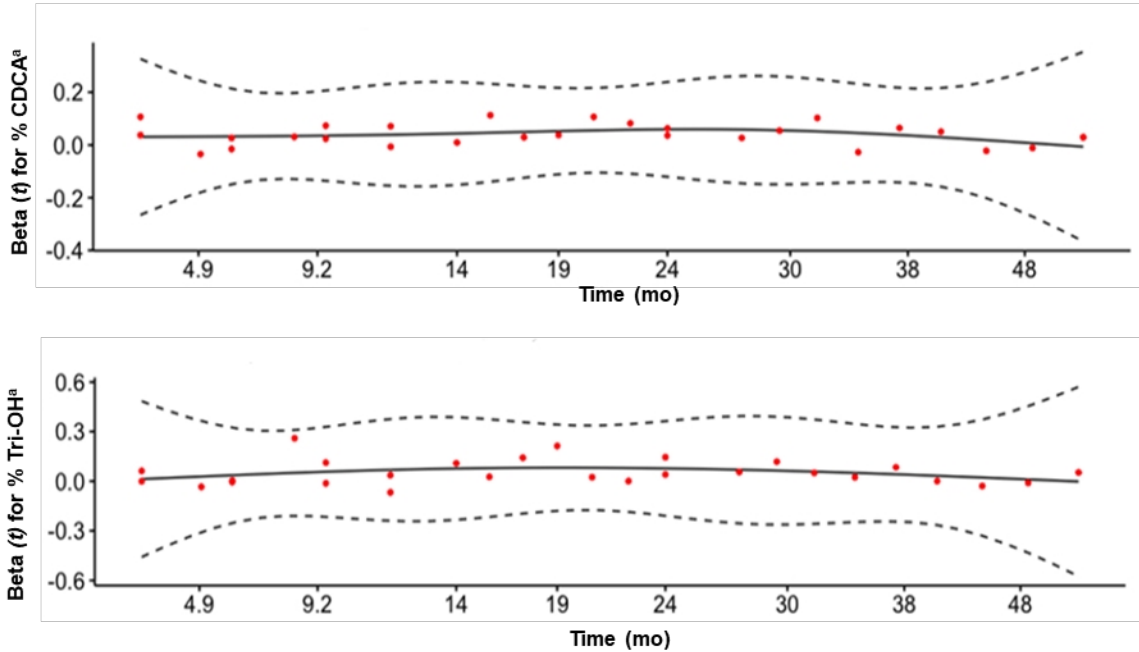
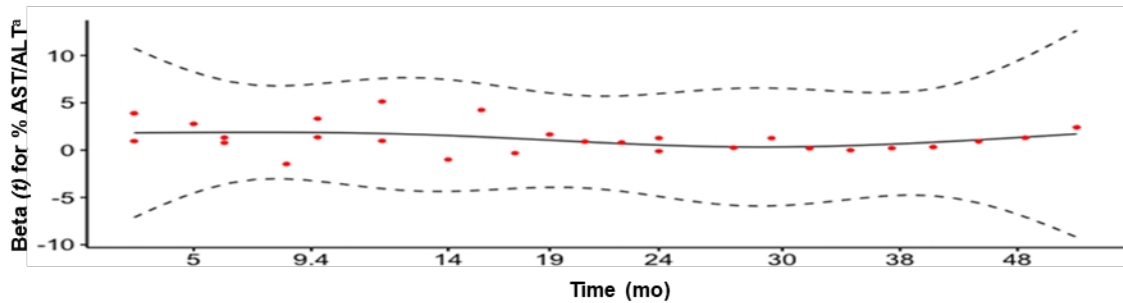


A BAS model



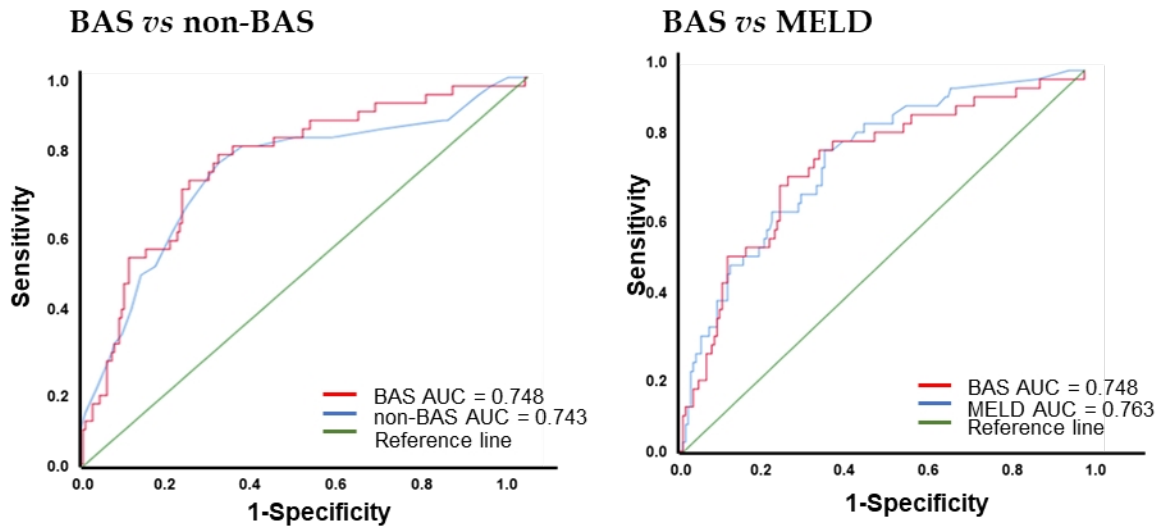
B non-BAS model



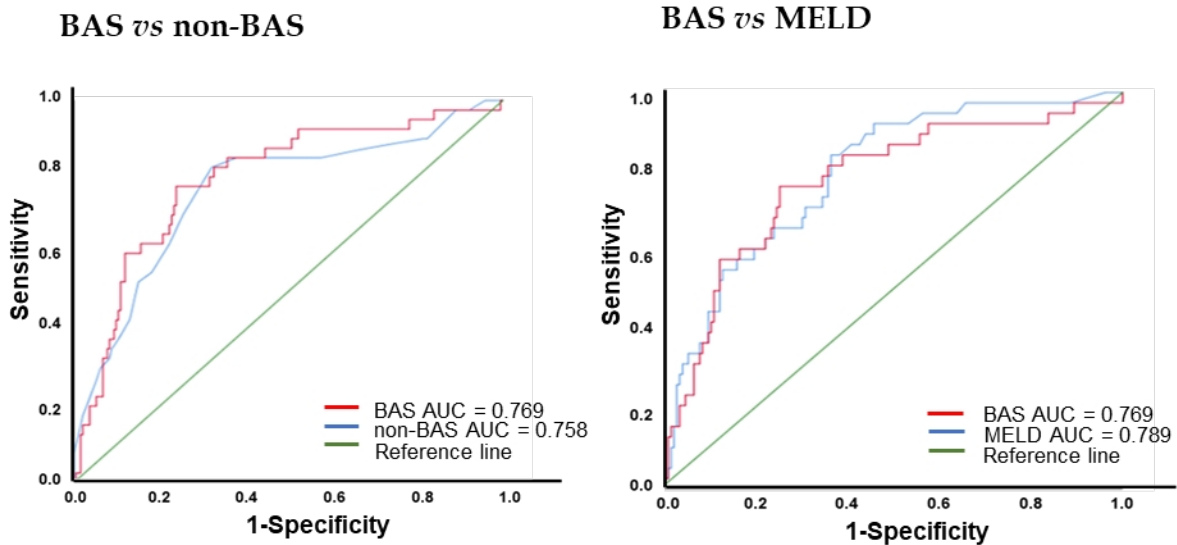
Variable Schoenfeld test ^aP values = 0.85, 0.97, 0.19 for %CDCA, %Tri-OH, and AST/ALT, respectively

Supplementary Figure 1 Schoenfeld residual plots for death prediction by the bile acid score and non-bile acid score models. The solid line is a smoothing spline fit to the plot, with the dashed lines representing a ± 2 -standard-error band around the fit. A: The global Schoenfeld test ^aP value = 0.974 for bile acids score (BAS); B: The global Schoenfeld test ^aP value = 0.199 for non-BAS. BAS: Bile acids score.

A 5-year death and/or liver transplant prediction

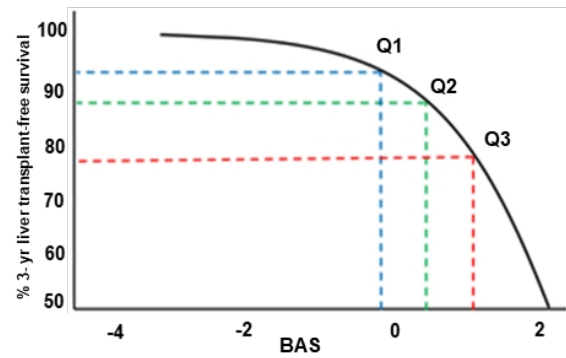
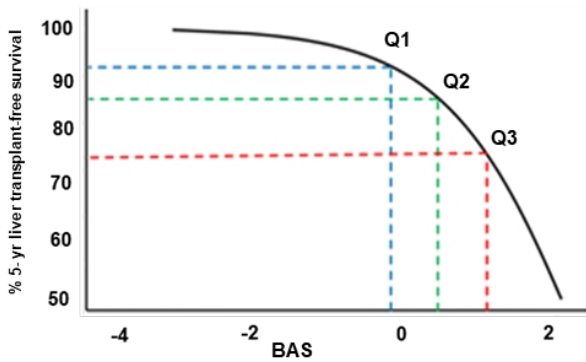


B 3-year death and/or liver transplant prediction

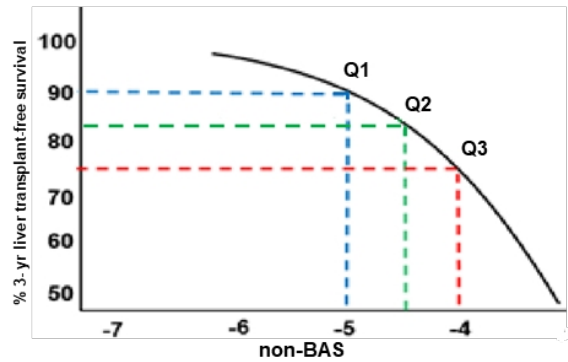
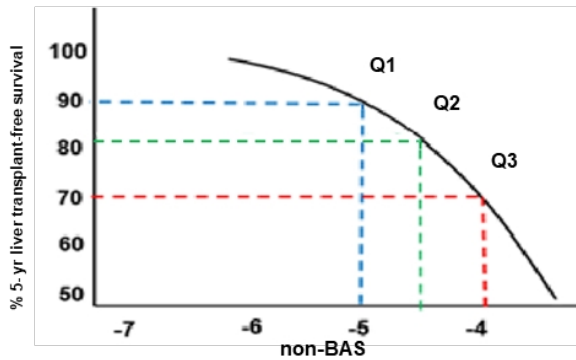


Supplementary Figure 2 Receiver operating characteristics curves of bile acids score, non-bile acids score, and model for end stage liver diseases for death and/or liver transplant prediction. A: The area under the receiver operating characteristics (ROC) curves (AUC) for bile acids score (BAS), non-BAS, and model for end stage liver diseases (MELD) for 5-year death and/or liver transplant prediction; B: The AUC for BAS, non-BAS, and MELD for 3-year death and/or liver transplant prediction. BAS: Bile acids score; MELD: Model for end stage liver diseases.

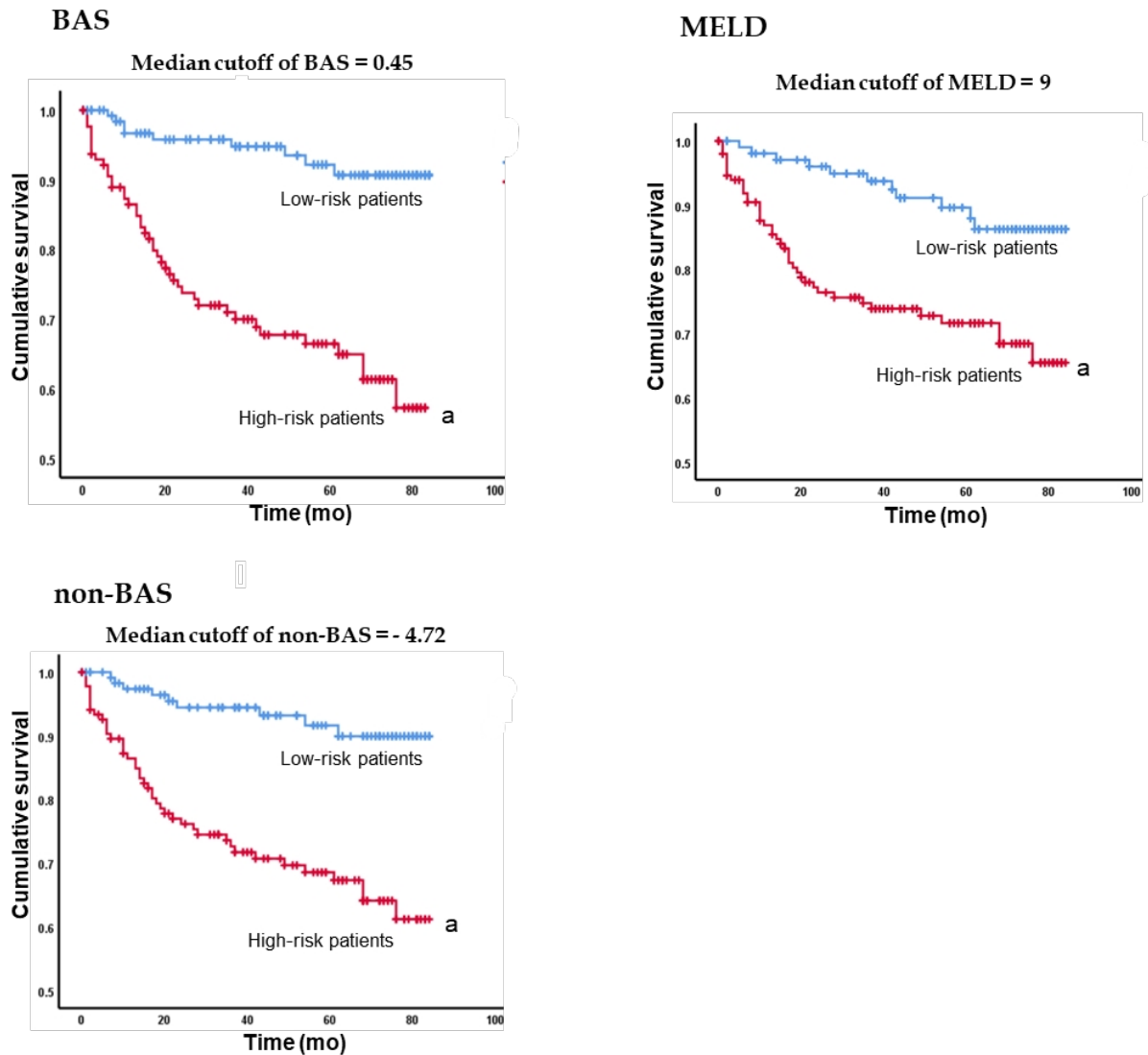
A BAS



B non-BAS



Supplementary Figure 3 Estimated 5- and 3-year liver transplant-free survival [S (t)] from the bile-acids score and non-bile-acids score models. A: The relationship between estimated 5- and 3- year liver transplant-free survival probability [S (t)] as a function of bile acids score (BAS); B: The relationship between estimated 5- and 3- year liver transplant-free survival probability [S (t)] as a function of non-BAS. Q1, Q2, and Q3 are 25th, 50th, and 75th percentiles of the population, respectively. BAS: Bile acids score.



Supplementary Figure 4 Kaplan-Meier liver transplant-free survival plots for high vs low bile acids score, non-bile acids score, and model for end stage liver diseases models. The median cutoff values of the bile acids score (BAS), non-BAS, and model for end stage liver diseases (MELD) were used to define high vs low risk of death and/or liver transplant. A: BAS; B: Non-BAS; C: MELD. ^a*P* values < 0.05 from the Log rank and Breslow tests. BAS: Bile acids score; MELD: Model for end stage liver diseases.

Supplementary Table 1 Univariate Cox regression analyses for death prediction by bile acids indices

BA indices (%)	(μM)/BA	B-value coefficient)	(regression	P value	Hazard ratio: Exp (B)		
					1 unit change	10% change	20% change
Total BA		-0.001		0.683	1.00	0.99	0.99
Total LCA		-0.063		0.331	0.94	0.98	0.96
Total UDCA		-0.005		0.477	1.00	0.99	0.98
Total CDCA		0.002		0.617	1.00	1.01	1.01
Total DCA		-0.047		0.266	0.95	0.97	0.94
Total HDCA		-13.76		0.424	0.00	0.98	0.97
Total MDCA		-5.021		0.347	0.01	0.98	0.95
Total CA		-0.005		0.783	1.00	1.00	1.00
Total MCA		-0.006		0.793	0.99	1.00	1.00
Total HCA		0.061		0.631	1.06	1.00	1.00
%LCA		-0.101		0.016	0.90	0.92	0.84
%UDCA		-0.027		0.070	0.97	0.94	0.89
%CDCA		0.031		0.000	1.03	1.12	1.26
%DCA		-0.092		0.001	0.91	0.87	0.76
%HDCA		-11.28		0.170	0.00	0.97	0.93
%MDCA		-0.325		0.599	0.72	0.99	0.98
%CA		0.067		0.003	1.07	1.04	1.09
%MCA		0.020		0.322	1.02	1.01	1.02
%HCA		0.454		0.015	1.57	1.02	1.04
Total unamidated		0.007		0.804	1.01	1.00	1.00
Total G-amidated		-0.001		0.667	1.00	0.99	0.99
Total T-amidated		-0.002		0.799	1.00	1.00	1.00
%Amidation		0.012		0.577	1.01	1.11	1.24
%G-amidation		-0.025		0.032	0.98	0.82	0.68

%T-amidation	0.039	0.001	1.04	1.04	1.09
Total unsulfated	-0.001	0.968	1.00	1.00	1.00
Total sulfated	-0.001	0.659	1.00	0.99	0.99
%Sulfation	-0.023	0.081	0.98	0.82	0.68
Total Mono-OH	-0.063	0.331	0.94	0.98	0.96
Total Di-OH	-0.001	0.703	1.00	0.99	0.99
Total Tri-OH	-0.004	0.766	1.00	1.00	0.99
%Mono-OH	-0.101	0.016	0.90	0.92	0.84
%Di-OH	-0.004	0.761	1.00	0.97	0.94
%Tri-OH	0.034	0.011	1.03	1.04	1.09
Total 12 α -OH	-0.012	0.465	0.99	0.99	0.98
Total non-12 α -OH	-0.001	0.762	1.00	0.99	0.99
12 α -OH/non12 α - OH	-2.837	0.020	0.06	0.91	0.83
CA/CDCA	-0.099	0.828	0.91	1.00	1.00
%12 α -OH	-0.043	0.019	0.96	0.91	0.83
%non-12 α -OH	0.043	0.019	1.04	1.40	1.95
Total primary	0.001	0.769	1.00	1.00	1.01
Total secondary	-0.006	0.397	0.99	0.98	0.96
Primary/secondar y	0.037	0.016	1.04	1.01	1.02
%Primary	0.041	0.000	1.04	1.23	1.51
%Secondary	-0.041	0.000	0.96	0.82	0.67
HI	-0.092	0.912	0.91	1.00	1.00

BA: Bile acids.

Supplementary Table 2 Univariate Cox regression analyses for death prediction by non-bile acids parameters and demographics

Demographics and non-BA parameters	B-value (regression coefficient)	P value	Hazard ratio: Exp (B)		
			1 unit change	10% change	20% change
Gender	1.251	0.007	3.492	-	-
Age (yr)	0.029	0.093	1.029	1.162	1.350
BMI	-0.025	0.390	0.975	0.926	0.857
Race	¹	0.950	¹	¹	¹
Creatinine (mg/dL)	0.030	0.737	1.03	1.00	1.01
Albumin (g/dL)	-1.189	0.000	0.30	0.65	0.43
INR	0.781	0.013	2.19	1.10	1.20
Prottime (s)	0.073	0.002	1.08	1.09	1.19
AST (U/L)	0.002	0.443	1.00	1.01	1.02
ALT (U/L)	-0.003	0.437	1.00	0.98	0.97
Bilirubin (mg/dL)	0.096	0.035	1.10	1.02	1.03
AST/ALT	1.236	0.000	3.44	1.16	1.36
MELD	0.104	0.000	1.11	1.11	1.24
APRI	0.267	0.000	1.31	1.03	1.06

¹Race is a categorical variable, which has five race groups. There are five values for the regression coefficient and hazard ratio, one for each race group, which are not shown, because race was not statistically significant in univariate Cox regression analysis. BMI: Body mass index; INR: International normalized ratio; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; MELD: Model for end stage liver diseases; APRI: Aspartate aminotransferase/platelet ratio index.

Supplementary Table 3 Developing other survival models for death prediction

Other models	Cox (<i>P</i> value)	Bootstrapping (<i>P</i> value)
Mixed BA and non-BA		
%CDCA	0.006	0.004
% G-amidation	0.015	0.018
AST/ALT	0.031	0.072
MELD variables with coefficients from our data set		
Creatinine	0.677	NA
INR	0.150	NA
Bilirubin	0.614	NA
Serum Na	0.058	NA
Original MELD modified with BA variables		
%CDCA	0.008	NA
%Tri-OH	0.129	NA
MELD	0.271	NA
Original MELD modified with non-BA variables		
AST/ALT	0.016	NA
MELD	0.253	NA
Original MELD modified with BA and non-BA variables		
%CDCA	0.017	NA
% G-amidation	0.029	NA
AST/ALT	0.040	NA
MELD	0.963	NA

NA: Not applicable. Bootstrapping was not performed because *P* values of model parameters were not significant (*P* value > 0.05). BA: Bile acids; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; MELD: Model for end stage liver diseases.

Supplementary Table 4 Bootstrapping validation for death prediction by bile acids score and non-bile acids score models

Variables	Regression coefficient	Bias	Standard error	<i>P</i> value	95%CI	
					Lower	Upper
BAS						
%CDCA	0.039	0.001	0.009	0.001	0.023	0.059
%Tri-OH	0.052	0.001	0.019	0.002	0.016	0.089
non-BAS						
AST/ALT	1.236	0.026	0.342	0.001	0.606	1.992

BAS: Bile acids score; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase.

Supplementary Table 5 Multivariate Cox regression analysis for death and/or liver transplant prediction

BAS¹						
BA indices (%)	B-value (regression coefficient)	Standard error	<i>P</i> value	Hazard ratio: Exp (B)		
				1 unit change	10% change	20% change
%Primary	0.021	0.007	0.003	1.021	1.107	1.226
%DCA	-0.049	0.020	0.013	0.952	0.926	0.857
non-BAS²						
Non-BA parameters (g/dL)	B-value (regression coefficient)	Standard error	<i>P</i> value	Hazard ratio: Exp (B)		
				1 unit change	10% change	20% change
Albumin	-1.277	0.222	0.000	0.279	0.627	0.393

¹Using the regression coefficients from this table, the bile acids score (BAS) equation is: $BAS = 0.021 \times \%Primary - 0.049 \times \%DCA$; ²Using the regression coefficients from this table, the non-BAS equation is: $non-BAS = -1.277 \times Albumin \left(\frac{g}{dL}\right)$. BAS: Bile acids score.

Supplementary Table 6 Receiver operating characteristics analysis of bile acids score, non-bile acids score, and model for end stage liver diseases for death and/or liver transplant prediction

Models	AUC (5-yr)	AUC (3-yr)	(Cutoff value; sensitivity, specificity)
BAS	0.748	0.769	(0.76; 71, 72)
non-BAS	0.743	0.758	(-4.41; 78, 70)
MELD	0.763	0.789	(10; 70, 66)

BAS: Bile acids score; AUC: Area under the curve; MELD: Model for end stage liver diseases.

Supplementary Table 7 Kaplan-Meier analysis for liver transplant-free survival

Cutoff	Total <i>n</i>	<i>n</i> of events	Estimated mean (mo)	Standard error	95%CI
BAS					
Median cutoff of 0.45					
Low risk < 0.45	128	9	79.22	1.56	76.16-82.28
High risk > 0.45	129	43	59.75	2.93	54.01-65.49
non-BAS					
Median cutoff of -4.72					
Low risk < -4.72	120	9	78.79	1.69	75.49-82.09
High risk > -4.72	137	43	61.97	2.83	56.42-67.52
MELD					
Median cutoff of 9					
Low risk < 9	105	11	77.67	1.84	74.05-81.28
High risk > 9	152	42	63.98	2.69	58.71-69.24

BAS: Bile acids score; MELD: Model for end stage liver diseases.