

Supplementary Materials

This appendix is intended to provide readers with additional information about the present study. Supplement to: Jonel Trebicka, Wenyi Gu, Victor de Lédinghen, Christophe Aubé, Aleksander Krag, Christian P. Strassburg et al.

Two-Dimensional Shear Wave Elastography Predicts Survival in Advanced Chronic Liver Disease

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Supplementary Methods

Two-dimension shear wave elastography (2D-SWE) procedure

Up to five measurements were repeated to avoid bias. A mean value of the total number of all measurements was calculated and documented. All L-SWE measurements were performed by experienced physicians. The participants were required to fast for at least two hours prior to measurement. L-SWE were carried out through the right intercostal space of the supine position during a breath-hold, with the right arm straightened, and at least 10mm below the liver capsule. The Q-box was used over the selected region of interest (ROI) to obtain the stiffness value. The diameter of the Q box was set to >15 mm. Valid L-SWE was defined as LSM with an interquartile range (IQR) / median (M) value below 30%^{1,2}. The Aixplorer US system (SuperSonic Imagine S.A., Aix-en-Provence, France) with a convex broadband probe (SC6-1) was used.

Transient elastography (TE) procedure

One-dimension TE was measured using the Fibroscan® (Echosens, Paris, France). TE measurements were performed at baseline as per EASL-ALEH clinical practice guideline^{3,4}. In the derivation study, TE values with a success rate of at least 80% and with a ratio of IQR / M < 0.3 were considered valid and used for statistical analysis.

Point shear wave elastography (p-SWE) procedure

The protocol for pSWE of the liver utilizing the Elast PQ module on the Philips system was previously described^{5,6}. Briefly, patients were fasted at least 5 hours and were placed in a supine position. The transducer was positioned in an intercostal space on the medio-axillary line. The rectangular ROI for pSWE was placed 1-1.5cm underneath the liver capsule, centrally situated targeted by B-mode ultrasound imaging. At least 5 measurements, were performed per patient in mid-inspiratory position.

Definition of ascites

Ascites was defined according to the 2020 EASL guideline⁷. Mild ascites was detected by ultrasound. Moderate ascites was defined by moderate symmetrical distension of abdomen. Large or gross ascites was detected by clinically marked abdominal distension.

Definition of non-invasive scores⁸⁻¹⁰

FIB-4 score = [Age (years) × AST Level (U/L)] / [Platelet Count (10⁹/L) × ALT (U/L)^(1/2)]

APRI score = [AST Level (IU/L) / AST (Upper Limit of Normal) (IU/L)] / Platelet Count (10⁹/L) × 100

ALBI score = [log₁₀ Bilirubin (mmol/l) × 0.66] + [albumin(g/l) × -0.085]

Supplementary table 1. Numbers of inclusion, demographic data and coefficient variation of each participated center with 2D-SWE or p-SWE

Participated center	Screening n (%)	Valid inclusion n (%)	Male n (%)	Age M (IQR)	L-SWE CV%
<u>CHU du Haut-Lévêque</u>	<u>349 (16.2)</u>	<u>333 (18.2)</u>	<u>215 (64.6)</u>	<u>55.1 (45.0 - 64.5)</u>	<u>123.3%</u>
<u>Centre Hospitalier Universitaire d'Angers</u>	<u>336 (15.6)</u>	<u>267 (14.6)</u>	<u>181 (67.8)</u>	<u>55.0 (47.0 – 61.0)</u>	<u>89.1%</u>
<u>University of Bonn</u>	<u>274 (12.8)</u>	<u>237 (13)</u>	<u>130 (54.9)</u>	<u>57.0 (50.5 - 63.9)</u>	<u>74.3%</u>
<u>University of Southern Denmark & Odense University Hospital</u>	<u>267 (12.4)</u>	<u>209 (11.4)</u>	<u>112 (53.8)</u>	<u>57.0 (48.0 – 66.0)</u>	<u>58.5%</u>
<u>Hôpital Beaujon Université Paris VII</u>	<u>193 (9.0)</u>	<u>184 (10.1)</u>	<u>136 (73.9)</u>	<u>56.3 (50.7 - 61.6)</u>	<u>57.7%</u>
<u>Hôpital Edouard Herriot</u>	<u>148 (6.9)</u>	<u>131 (7.2)</u>	<u>82 (62.6)</u>	<u>56.0 (47.0 – 62.0)</u>	<u>74.4%</u>
<u>J. W. Goethe University Hospital</u>	<u>122 (5.7)</u>	<u>117 (6.4)</u>	<u>60 (51.3)</u>	<u>52.0 (40 - 59)</u>	<u>76.5%</u>
<u>Hôpital Cochin</u>	<u>121 (5.6)</u>	<u>82 (4.5)</u>	<u>64 (78)</u>	<u>63.0 (58 - 68)</u>	<u>41.8%</u>
<u>University Hospital Dubrava</u>	<u>82 (3.8)</u>	<u>62 (3.4)</u>	<u>47 (75.8)</u>	<u>48 (34.8 - 54.3)</u>	<u>78.8%</u>
<u>Third Affiliated Hospital Sun-Yat Sen University</u>	<u>68 (3.2)</u>	<u>53 (2.9)</u>	<u>40 (75.5)</u>	<u>37.0 (26.5 - 46)</u>	<u>72.2%</u>
<u>University Hospital Antwerp</u>	<u>58 (2.7)</u>	<u>53 (2.9)</u>	<u>29 (54.7)</u>	<u>45.0 (33.0 - 55.5)</u>	<u>68.5%</u>
<u>Prague SSI</u>	<u>34 (1.6)</u>	<u>33 (1.8)</u>	<u>13 (39.4)</u>	<u>54 (37.5 - 62)</u>	<u>67.8%</u>
<u>Institute for Clinical and Experimental Medicine (IKEM)</u>	<u>32 (1.5)</u>	<u>31 (1.7)</u>	<u>12 (38.7)</u>	<u>54 (38 - 62)</u>	<u>68.0%</u>
<u>“Victor Babes” University of Medicine and Pharmacy</u>	<u>28 (1.3)</u>	<u>26 (1.4)</u>	<u>15 (57.7)</u>	<u>50 (34.5 - 56)</u>	<u>45.7%</u>
<u>Universitätsspital Bern</u>					
<u>Universitätsklinik für Viszerale Chirurgie und Medizin</u>	<u>26 (1.2)</u>	<u>9 (0.5)</u>	<u>4 (44.4)</u>	<u>50 (34.5 - 56)</u>	<u>61.5%</u>
<u>Zhongshan Hospital Shanghai Fudan University</u>	<u>10 (0.5)</u>	<u>0 (0)</u>	<u>0 (0)</u>	<u>/</u>	<u>/</u>
<u>Vienna</u>	<u>211</u>	<u>119</u>	<u>81 (68.1)</u>	<u>55 (46.0 – 66.0)</u>	<u>93.5%</u>
Total	2359	1946	1221 (62.8)	55 (45.9 – 62.9)	90.9%

Abbreviation: CV, coefficient of variation; M, median; IQR, interquartile range.

Supplementary table 2. Intraclass correlation coefficient of intercenters and interobservers reliability.

<u>Intraclass Correlation Coefficient</u>		<u>Intraclass Correlation_b</u>	<u>95% Confidence Interval</u>		<u>F Test with True Value 0</u>			
			<u>Lower Bound</u>	<u>Upper Bound</u>	<u>Value</u>	<u>df1</u>	<u>df2</u>	<u>Sig</u>
<u>Centers</u>								
<u>ANG</u>	<u>Average Measures</u>	<u>.921^c</u>	<u>0.905</u>	<u>0.935</u>	<u>12.677</u>	<u>328</u>	<u>656</u>	<u>0.000</u>
<u>BER</u>	<u>Average Measures</u>	<u>.972^c</u>	<u>0.940</u>	<u>0.988</u>	<u>36.007</u>	<u>18</u>	<u>36</u>	<u>0.000</u>
<u>BJN</u>	<u>Average Measures</u>	<u>.951^c</u>	<u>0.937</u>	<u>0.962</u>	<u>20.363</u>	<u>176</u>	<u>352</u>	<u>0.000</u>
<u>BON</u>	<u>Average Measures</u>	<u>.849^c</u>	<u>0.810</u>	<u>0.881</u>	<u>6.623</u>	<u>206</u>	<u>412</u>	<u>0.000</u>
<u>COC</u>	<u>Average Measures</u>	<u>.985^c</u>	<u>0.978</u>	<u>0.991</u>	<u>68.352</u>	<u>60</u>	<u>120</u>	<u>0.000</u>
<u>HEH</u>	<u>Average Measures</u>	<u>.977^c</u>	<u>0.970</u>	<u>0.983</u>	<u>44.205</u>	<u>128</u>	<u>256</u>	<u>0.000</u>
<u>IKM</u>	<u>Average Measures</u>	<u>.980^c</u>	<u>0.964</u>	<u>0.990</u>	<u>51.097</u>	<u>30</u>	<u>60</u>	<u>0.000</u>
<u>ODE</u>	<u>Average Measures</u>	<u>.963^c</u>	<u>0.955</u>	<u>0.970</u>	<u>27.280</u>	<u>258</u>	<u>516</u>	<u>0.000</u>
<u>SSI</u>	<u>Average Measures</u>	<u>.982^c</u>	<u>0.968</u>	<u>0.990</u>	<u>54.886</u>	<u>32</u>	<u>64</u>	<u>0.000</u>
<u>TIM</u>	<u>Average Measures</u>	<u>.994^c</u>	<u>0.982</u>	<u>0.999</u>	<u>176.008</u>	<u>8</u>	<u>16</u>	<u>0.000</u>
<u>UZA</u>	<u>Average Measures</u>	<u>.740^c</u>	<u>0.579</u>	<u>0.847</u>	<u>3.852</u>	<u>46</u>	<u>92</u>	<u>0.000</u>
<u>ZHE</u>	<u>Average Measures</u>	<u>.994^c</u>	<u>0.991</u>	<u>0.997</u>	<u>174.214</u>	<u>51</u>	<u>102</u>	<u>0.000</u>
<u>Operators</u>								
<u>AB</u>	<u>Average Measures</u>	<u>.951^c</u>	<u>0.473</u>	<u>0.999</u>	<u>20.213</u>	<u>2</u>	<u>4</u>	<u>0.008</u>
<u>AH</u>	<u>Average Measures</u>	<u>.710^c</u>	<u>-10.151</u>	<u>1.000</u>	<u>3.453</u>	<u>1</u>	<u>2</u>	<u>0.204</u>
<u>CM</u>	<u>Average Measures</u>	<u>.986^c</u>	<u>0.964</u>	<u>0.995</u>	<u>69.953</u>	<u>12</u>	<u>24</u>	<u>0.000</u>
<u>FTT</u>	<u>Average Measures</u>	<u>.999^c</u>	<u>0.995</u>	<u>1.000</u>	<u>915.274</u>	<u>5</u>	<u>10</u>	<u>0.000</u>
<u>HG</u>	<u>Average Measures</u>	<u>.967^c</u>	<u>0.947</u>	<u>0.980</u>	<u>30.197</u>	<u>49</u>	<u>98</u>	<u>0.000</u>
<u>MP</u>	<u>Average Measures</u>	<u>.997^c</u>	<u>0.985</u>	<u>1.000</u>	<u>331.462</u>	<u>4</u>	<u>8</u>	<u>0.000</u>
<u>RS</u>	<u>Average Measures</u>	<u>.996^c</u>	<u>0.991</u>	<u>0.998</u>	<u>251.181</u>	<u>15</u>	<u>30</u>	<u>0.000</u>

Supplementary table 3. Parameters that related to the outcome and put into regression analysis

Parameters
Male sex
2D-SWE at baseline (kPa)
Age (year)
CRP
Bilirubin (mg/dl)
Platelets (G/l)
White blood cell count ($\times 10^9/L$)
INR
Serum creatinine (mg/dl)
Albumin (g/l)
Alanine transaminase (U/L)
Variceal bleeding episode
Hepatic encephalopathy
Ascites grade
Bacterial infections episode
spontaneous bacterial peritonitis episode
Abstinence from alcohol drinking
Alkaline phosphatase (U/L)
aspartate transaminase (U/L)

Supplementary table 4. Valid and missing value in cohort of patients with 2D-SWE and additional cohort of p-SWE

Parameters	Cohort with 2D-SWE		Additional cohort with p-SWE	
	Valid	Missing / Lost to follow-up	Valid	Missing / Lost to follow-up
2D-SWE	1827	0	119	0
TE	754	1073	119	0
Cause of chronic liver disease	1546	281	119	0
Age	1826	1	119	0
Gender	1826	1	119	0
Height (m)	1392	435	119	0
Weight (kg)	1518	309	118	1
BMI (kg/m ²)	1467	360	118	1
ALT (U/L)	1782	45	117	2
AST (U/L)	1723	104	118	1
Alkaline phosphatase (U/L)	1691	136	118	1
Bilirubin (mg/dl)	1766	61	118	1
Creatinine (mg/dl)	1758	69	117	2
CRP	960	867	115	4
WBC (×10 ⁹ /L)	1331	496	118	1
Albumin (g/l)	1702	125	118	1
Platelets (G/l)	1796	31	118	1
INR	1729	98	118	1
MELD score	1667	160	117	2
Child-Pugh score	1640	187	117	2
Child-Pugh class	1640	187	117	2
28-day follow-up	1827	0	119	0
90-day follow-up	1783	44	113	6
1-year follow up	1618	209	84	35
2-year follow-up	1293	534	46	73

Supplementary table 5. Portal and systemic hemodynamic results of compensated and decompensated patients included

<u>Parameter</u>	<u>Compensated</u>	<u>Decompensated</u>	<u>P* value</u>	<u>All</u>	<u>R**</u>	<u>Correlation P</u>
<u>Heart rate (bpm)</u> <u>n = 194</u>	<u>68 (60 - 77.8)</u>	<u>72 (64 - 82)</u>	<u>0.023</u>	<u>70 (61 - 80)</u>	<u>0.118</u>	<u>0.101</u>
<u>MAP (mmHg)</u> <u>n = 193</u>	<u>92 (80 - 99)</u>	<u>88.3 (78 - 96.2)</u>	<u>0.198</u>	<u>90 (78.3 - 98)</u>	<u>-0.162</u>	<u>0.024</u>
<u>HVPG (mmHg)</u> <u>n = 140</u>	<u>17 (11 - 20)</u>	<u>20 (16 - 22)</u>	<u>0.001</u>	<u>18 (14 - 21)</u>	<u>0.256</u>	<u>0.002</u>
<u>EF by TTE</u> <u>n = 81</u>	<u>62.2 (58.6 - 68.4)</u>	<u>66.1 (60.6 - 70.2)</u>	<u>0.170</u>	<u>64.6 (59.6 - 69)</u>	<u>0.241</u>	<u>0.030</u>
<u>MELD score</u> <u>n = 194</u>	<u>9 (7.3 - 13)</u>	<u>12 (9 - 16)</u>	<u><0.001</u>	<u>11 (9 - 14)</u>	<u>0.258</u>	<u><0.001</u>

*p values are compared between compensated and decompensated groups using Mann-Whitney U test;

** R, Pearson correlation was calculated between the parameter and L-SWE;

Abbreviations: MAP, mean arterial pressure; EF, ejection fraction; SV, stroke volume; TTE, transthoracic echocardiography; PHPG, portal hepatic pressure gradient; HVPG, hepatic venous pressure gradient.

Supplementary Table 6. Univariate and multivariate Cox regression analysis in compensated and all patients for 2-year mortality and all-time of follow-up

Parameters	Univariate				Multivariate			
	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits		Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
All time of follow-up in all included patients in derivation cohort								
Gender	0.0253	1.485	1.050	2.100
2D-SWE	<0.0001	1.026	1.021	1.031	<0.0001	1.020	1.010	1.030
Age	<0.0001	1.050	1.035	1.066	0.0075	1.041	1.011	1.073
CRP	<0.0001	1.014	1.007	1.021	0.0024	1.017	1.006	1.028
Albumin	<0.0001	0.976	0.965	0.988	0.0051	0.964	0.940	0.989
All time of follow-up in compensated patients of derivation cohort								
Gender
2D-SWE	<0.0001	1.025	1.018	1.033	0.0001	1.019	1.009	1.029
Age	0.0001	1.045	1.022	1.069	0.0194	1.035	1.006	1.065
CRP	0.0073	1.015	1.004	1.026	0.0056	1.015	1.004	1.027
Bilirubin	0.0283	1.098	1.01	1.194	0.0500	1.102	1.000	1.214
Platelets	0.0118	0.996	0.992	0.999
WBC	0.0184	1.107	1.017	1.204
2-year outcome in all included patients in derivation cohort								
Gender
2D-SWE	<0.0001	1.028	1.022	1.034	0.0009	1.019	1.008	1.030
Age	<0.0001	1.054	1.034	1.073	0.0010	1.062	1.025	1.101
CRP	0.0002	1.014	1.007	1.022	0.0400	1.015	1.001	1.029
Albumin	<0.0001	0.971	0.958	0.983	0.0022	0.957	0.930	0.984
2-year outcome in compensated patients of derivation cohort								
Gender
2D-SWE	<.0001	1.027	1.019	1.035	<.0001	1.019	1.01	1.028
Age	<.0001	1.07	1.042	1.099	<.0001	1.063	1.034	1.093
Bilirubin	0.0016	1.125	1.046	1.209	0.0016	1.142	1.052	1.241
Platelets	0.0003	0.993	0.989	0.997	0.0478	0.996	0.992	1.000
Albumin	0.0318	0.98	0.962	0.998
Variceal bleeding	0.0023	2.587	1.404	4.769
<u>2-year outcome in decompensated patients of derivation cohort</u>								
<u>Gender</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>
<u>Age</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>
<u>Bacterial infection</u>	<u>0.0046</u>	<u>1.58</u>	<u>1.151</u>	<u>2.17</u>	<u>0.0009</u>	<u>1.744</u>	<u>1.254</u>	<u>2.425</u>
<u>2D-SWE</u>	<u>0.0201</u>	<u>1.019</u>	<u>1.003</u>	<u>1.035</u>	<u>0.0272</u>	<u>1.023</u>	<u>1.003</u>	<u>1.043</u>
<u>INR</u>	<u>0.0002</u>	<u>1.049</u>	<u>1.022</u>	<u>1.076</u>	<u><.0001</u>	<u>1.073</u>	<u>1.039</u>	<u>1.109</u>
<u>Bilirubin</u>	<u>0.0091</u>	<u>1.065</u>	<u>1.016</u>	<u>1.117</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>
<u>Albumin</u>	<u>0.0232</u>	<u>0.97</u>	<u>0.944</u>	<u>0.996</u>	<u>---</u>	<u>---</u>	<u>---</u>	<u>---</u>

Supplementary Table 7. Univariate and multivariate Cox regression analysis in decompensated patients for 28-day and 2-year mortality after adjusted for age and MELD score

<u>Parameters</u>	<u>Univariate</u>				<u>Multivariate</u>			
	<u>Pr > ChiSq</u>	<u>Hazard Ratio</u>	<u>95% Hazard Ratio Confidence Limits</u>		<u>Pr > ChiSq</u>	<u>Hazard Ratio</u>	<u>95% Hazard Ratio Confidence Limits</u>	
<u>28-day</u>								
<u>2D-SWE</u>	<u>0.015</u>	<u>1.048</u>	<u>1.009</u>	<u>1.089</u>	<u>0.0159</u>	<u>1.075</u>	<u>1.014</u>	<u>1.139</u>
<u>MELD</u>	<u><.0001</u>	<u>1.119</u>	<u>1.066</u>	<u>1.176</u>	<u>0.0002</u>	<u>1.158</u>	<u>1.073</u>	<u>1.251</u>
<u>Age</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>
<u>Platelet count</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>
<u>2-year</u>								
<u>2D-SWE</u>	<u>0.0201</u>	<u>1.019</u>	<u>1.003</u>	<u>1.035</u>	<u>0.0203</u>	<u>1.019</u>	<u>1.003</u>	<u>1.035</u>
<u>MELD</u>	<u>0.0004</u>	<u>1.043</u>	<u>1.019</u>	<u>1.068</u>	<u>0.0003</u>	<u>1.047</u>	<u>1.021</u>	<u>1.073</u>
<u>Age</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>
<u>Platelets</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>	<u>..</u>

Supplementary Table 8. Best cut-off value of SWE and related sensitivity, specificity for mortality

Time	SWE (kPa)				MELD score				
	AUC and 95%CI	Best cut-off	Sensitivity	Specificity	AUC and 95%CI	Best cut-off	Sensitivity	Specificity	
28 days	0.864 (0.800-0.928)	25.15	100.0%	76.3%	0.902 (0.821-0.983)	10	100.0%	70.4%	
90 days	0.788 (0.723-0.853)	16.35	94.7%	63.3%	0.898 (0.852-0.944)	10	94.7%	70.8%	
6 months	0.799 (0.750-0.847)	16.35	96.3%	63.6%	0.889 (0.849-0.929)	10	96.3%	71.1%	
1 year	0.782 (0.734-0.831)	16.35	89.4%	64.1%	0.800 (0.732-0.869)	10	83.0%	71.6%	
2 years	0.796 (0.759-0.833)	16.09	88.1%	74.9%	0.788 (0.744-0.832)	10	75.3%	72.9%	

Supplementary Table 9. Best cut-off value of SWE and related sensitivity, specificity, positive predictive value and negative predictive value with different MELD scores

Time	MELD < 10				MELD ≥ 10				
	AUC and 95%CI	Best cut-off	Sensitivity	Specificity	AUC and 95%CI	Best cut-off	Sensitivity	Specificity	
28 days					0.719 (0.577-0.860)	25.15	100.0	49.3	
90 days	0.822 (0.800-0.844)	21.03	100.0	82.2	0.599 (0.484-0.714)	16.35	94.4	30.6	
6 months	0.822 (0.800-0.844)	21.03	100.0	82.0	0.608 (0.520-0.695)	19.69	88.5	39.2	
1 year	0.764 (0.590-0.938)	21.02	75.0	82.5	0.606 (0.529-0.683)	15.39	94.9	29.2	
2 years	0.794 (0.704-0.884)	19.87	70.8	81.5	0.625 (0.565-0.685)	15.39	94.5	31.1	

Supplementary table 10. Best cut-off for MELD score and L-SWE of 2-year out-come in compensated patients and decompensated patients, and related sensitivity, specificity, positive predictive value, and negative predictive value.

Best cut-off of 10 for MELD Score	Value	95% CI
Compensated		
Sensitivity	61.54%	47.02% to 74.70%
Specificity	84.96%	82.59% to 87.13%
Positive Likelihood Ratio	4.09	3.15 to 5.31
Negative Likelihood Ratio	0.45	0.32 to 0.64
Positive Predictive Value	17.68%	14.20% to 21.80%
Negative Predictive Value	97.68%	96.76% to 98.35%
Accuracy	83.80%	81.42% to 85.98%
Decompensated		
Sensitivity	90.91%	78.33% to 97.47%
Specificity	32.94%	23.13% to 43.98%
Positive Likelihood Ratio	1.36	1.14 to 1.62
Negative Likelihood Ratio	0.28	0.10 to 0.74
Positive Predictive Value	41.24%	37.05% to 45.55%
Negative Predictive Value	87.50%	72.38% to 94.92%
Accuracy	52.71%	43.74% to 61.56%
Best cut-off of 20 kPa for L-SWE		
Compensated		
Sensitivity	68.52%	54.45% to 80.48%
Specificity	81.63%	79.22% to 83.87%
Positive Likelihood Ratio	3.73	2.99 to 4.64
Negative Likelihood Ratio	0.39	0.26 to 0.57
Positive Predictive Value	15.42%	12.77% to 18.50%
Negative Predictive Value	98.15%	97.28% to 98.75%
Accuracy	81.02%	78.64% to 83.24%
Decompensated		
Sensitivity	89.13%	76.43% to 96.38%
Specificity	29.55%	20.29% to 40.22%
Positive Likelihood Ratio	1.27	1.07 to 1.50
Negative Likelihood Ratio	0.37	0.15 to 0.89
Positive Predictive Value	39.81%	35.84% to 43.91%
Negative Predictive Value	83.87%	68.15% to 92.67%
Accuracy	50.00%	41.25% to 58.75%

Supplementary table 11. Univariate and multivariate competing risk (death as competing risk) analysis of SWE with outcome of development of decompensations in 2 years

Variables	Univariate		Multivariate	
	P value	sHR & 95.0% CI	P value	sHR & 95.0% CI
SWE at baseline	<0.001	1.026 (1.020 - 1.031)	<0.001	1.020 (1.014 – 1.026)
MELD score	<0.001	1.074 (1.052 – 1.096)	0.028	1.036 (1.004 – 1.069)
Child-Pugh score	<0.001	1.545 (1.417 – 1.684)	0.001	1.272 (1.110 – 1.456)
Age	<0.001	1.030 (1.014 – 1.046)	0.050	1.018 (1.000 – 1.035)

Abbreviations: MELD, model for end-stage liver disease; SWE, shear wave elastography; sHR, sub-Hazard ratio; CI, confidential interval.

Supplementary table 12. Baseline characteristics of cohort with 2D-SWE and the additional cohort with p-SWE

	Characteristics	2D-SWE cohort (n = 1827)		p-SWE cohort (n = 119)		
At baseline	Age	55.0 (45.9 - 62.7)		55 (46 - 66)		
	Male	1140 (62.4)		81 (68.1)		
	BMI (kg/m ²)	26.5 (23.2 - 30.6)		25.2 (21.8 - 29.2)		
	Scores					
	MELD score	8 (6 - 10)		10 (8 - 14)		
	Child Pugh score	5 (5 - 6)		6 (5 - 8)		
	Child Pugh class (A/B/C)	1334 / 206 / 44 (84.2 / 13.0 / 2.8)		74 / 29 / 14 (62.2 / 24.4 / 11.8)		
	SWE at baseline (kPa)	11.8 (7.4 - 24.5)		17 (9.7 - 26.8)		
	TE at baseline (kPa)	8.3 (5.7 - 14.0)		23 (14.4 - 39.7)		
	Etiology: Alcohol / NAFLD / HCV / HBV / Other or multiple causes	414 / 389 / 267 / 166 / 310 (26.8 / 25.2 / 17.3 / 10.7 / 20.0)		33 / 25 / 31 / 5 / 25 (27.7 / 21.0 / 26.1 / 4.2 / 21.0)		
	Laboratory test					
	Albumin (g/L)	40.0 (33.8 - 43.0)		38.9 (34.8 - 42.6)		
	Alkaline phosphatase (U/L)	90.0 (67.0 - 128.0)		89.5 (66.3 - 120.0)		
	ALT (U/L)	44.9 (28.0 - 77.0)		32 (22 - 51.5)		
	AST (U/L)	43.0 (30.0 - 69.0)		41 (30 - 58.8)		
	Bilirubin (mg/dl)	0.8 (0.5 - 1.3)		0.9 (0.6 - 1.6)		
	Creatinine (mg/dl)	0.8 (0.7 - 1.0)		0.8 (0.6 - 1.1)		
	INR	1.1 (1.0 - 1.2)		1.2 (1.1 - 1.4)		
	Platelets (G/l)	179.0 (122.0 - 242.0)		120.5 (86 - 168.3)		
	WBC (×10 ⁹ /L)	6.2 (5.0 - 7.9)		5.4 (3.8 - 6.6)		
	CRP	2.9 (1.1 - 7.0)		0.4 (0.1 - 0.8)		
	Clinical complications					
	Absent from alcohol drinking	1394 (76.3)		105 (88.2)		
	HCV SVR before SWE	81 (16.8)		21 (17.6)		
	Ascites (absent / mild / tense)	1574 / 134 / 107 (86.7 / 7.4 / 5.9)		81 / 29 / 8 (68.1 / 24.4 / 6.7)		
	Hepatic encephalopathy (Grade 0 / 1 / 2 / 3)	1262 / 172 / 44 / 6 (85.0 / 11.6 / 3.0 / 0.4)		77 / 25 / 15 / 1 (64.7 / 21.0 / 12.6 / 0.8)		
	Previous variceal bleeding	113 (6.9)		13 (10.9)		
	Previous bacterial infection	99 (6.0)		10 (8.4)		
	Previous hepatorenal syndrome	51 (3.1)		6 (5.0)		
	Follow-up	Had decompensation episodes	2-year	Till end of follow-up	2-year	Till end of follow-up
Ascites		73 (4.0)	132 (7.2)	6 (5.0)	8 (6.7)	
Bacterial infection		71 (3.9)	159 (8.7)	26 (21.8)	28 (23.5)	
Hepatic encephalopathy		48 (2.6)	93 (5.1)	19 (16.0)	27 (22.7)	
Hepatorenal syndrome		25 (1.4)	44 (2.4)	8 (6.7)	9 (7.6)	
Variceal bleeding		21 (1.1)	36 (2.0)	4 (3.4)	4 (3.4)	

Supplementary table 13. Baseline characteristics of compensated patients and randomly selected into 2/3 of derivation group and 1/3 of internal validation group

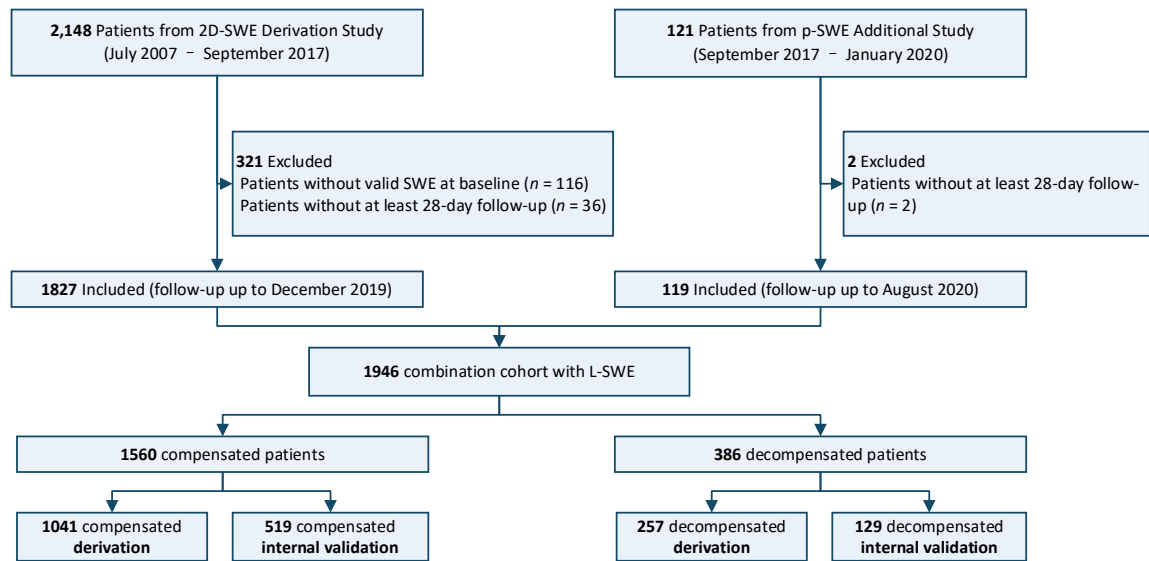
<u>Baseline characteristics</u>	<u>Derivation in compensated (n=1041)</u>	<u>Internal validation in compensated (n=519)</u>	<u>p value</u>
<u>Age</u>	<u>54 (44 - 61.8)</u>	<u>55.1 (44.3 - 64)</u>	<u>0.019</u>
<u>Male gender</u>	<u>637 (61.2)</u>	<u>325 (62.6)</u>	<u>0.600</u>
<u>BMI (kg/m²)</u>	<u>26.5 (23.1 - 31)</u>	<u>26.9 (23.5 - 30.7)</u>	<u>0.937</u>
<u>SWE (kPa)</u>	<u>8.8 (5.8 - 15.5)</u>	<u>10.3 (7 - 17.4)</u>	<u>0.185</u>
<u>TE (kPa)</u>	<u>8.9 (5.9 - 15.6)</u>	<u>9.5 (6.9 - 17.2)</u>	<u>0.509</u>
<u>Etiology</u>			<u>0.501</u>
<u>NAFLD</u>	<u>248 (23.8)</u>	<u>127 (24.5)</u>	
<u>Alcohol</u>	<u>214 (20.6)</u>	<u>113 (21.8)</u>	
<u>HCV</u>	<u>156 (15)</u>	<u>62 (11.9)</u>	
<u>HBV</u>	<u>99 (9.5)</u>	<u>48 (9.2)</u>	
<u>Other causes</u>	<u>195 (18.7)</u>	<u>95 (18.4)</u>	
<u>Multiple causes</u>	<u>8 (0.8)</u>	<u>2 (0.4)</u>	
<u>Scores for chronic liver diseases</u>			
<u>MELD score</u>	<u>7 (6 - 9)</u>	<u>7 (6 - 9)</u>	<u>0.698</u>
<u>Child-pugh score</u>	<u>5 (5 - 5)</u>	<u>5 (5 - 5)</u>	<u>0.346</u>
<u>Child-pugh class</u>			<u>0.717</u>
<u>A</u>	<u>871 (83.7)</u>	<u>434 (83.6)</u>	
<u>B</u>	<u>57 (5.5)</u>	<u>26 (5.0)</u>	
<u>Laboratory data</u>			
<u>Albumin (g/l)</u>	<u>41 (37 - 44)</u>	<u>41 (37 - 43.2)</u>	<u>0.785</u>
<u>Bilirubin (mg/dl)</u>	<u>0.7 (0.5 - 1.1)</u>	<u>0.7 (0.5 - 1.1)</u>	<u>0.296</u>
<u>Creatinine (mg/dl)</u>	<u>0.8 (0.7 - 1)</u>	<u>0.8 (0.7 - 1)</u>	<u>0.421</u>
<u>INR</u>	<u>1.0 (1.0 - 1.1)</u>	<u>1.0 (1.0 - 1.2)</u>	<u>0.367</u>
<u>Platelets (G/l)</u>	<u>193 (141 - 249.8)</u>	<u>190.5 (139.3 - 251)</u>	<u>0.736</u>
<u>WBC (×10⁹/l)</u>	<u>6.2 (5.1 - 7.8)</u>	<u>6.2 (4.9 - 7.9)</u>	<u>0.686</u>
<u>usCRP</u>	<u>2.2 (0.9 - 5.1)</u>	<u>2.4 (0.9 - 6.6)</u>	<u>0.292</u>
<u>Hemodynamic data</u>			
<u>Pulse (bpm)</u>	<u>68 (60 - 80)</u>	<u>65 (60 - 76)</u>	<u>0.588</u>
<u>MAP (mmHg)</u>	<u>79.8 (70 - 92.7)</u>	<u>89.3 (78.3 - 96.0)</u>	<u>0.118</u>
<u>Scores for fibrosis or cirrhosis</u>			
<u>ALBI</u>	<u>-2.8 (-3 - -2.2)</u>	<u>-2.7 (-3 - -2.2)</u>	<u>0.690</u>
<u>FIB-4</u>	<u>1.6 (1 - 2.8)</u>	<u>1.8 (1.1 - 3.2)</u>	<u>0.019</u>
<u>APRI</u>	<u>0.5 (0.3 - 0.9)</u>	<u>0.5 (0.3 - 1)</u>	<u>0.164</u>

Supplementary table 14. Baseline characteristics of decompensated patients and randomly selected into 2/3 of derivation group and 1/3 of internal validation group

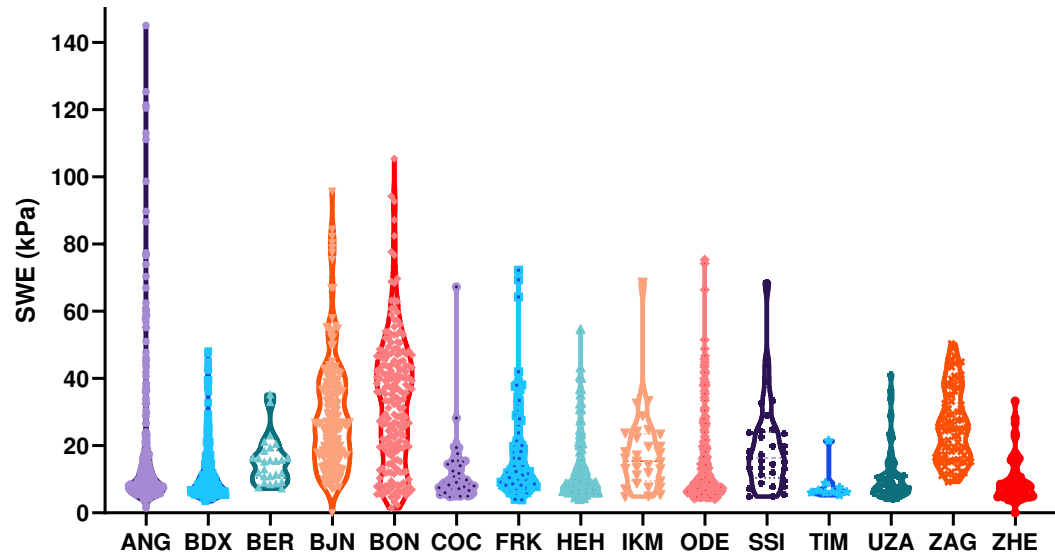
Baseline characteristics	Derivation in decompensated (n=257)	Internal validation in decompensated (n=129)	p value
Male	178 (69.3)	81 (62.8)	0.202
Age	57.2 (50.4 - 64)	58.3 (52.4 - 65)	0.119
BMI (kgm²)	25.3 (22.5 - 29.1)	26.5 (23 - 30.4)	0.195
Mean value of SWE	28.7 (19.1 - 40.5)	30.2 (19.2 - 43.9)	0.292
Median value of TE	36.1 (26.6 - 46.9)	61.6 (31.2 - 75)	0.021
Etiology			0.517
Alcohol	78 (30.4)	42 (32.6)	
HCV	55 (21.4)	25 (19.4)	
NAFLD	23 (8.9)	16 (12.4)	
HBV	17 (6.6)	7 (5.4)	
Other causes	25 (9.7)	9 (7)	
Multiple causes	0 (0.0)	1 (0.8)	
Scores for chronic liver diseases			
MELD	13 (9 - 17)	12.5 (9.8 - 17)	0.662
Child-pugh	8 (6 - 9)	8 (6 - 9)	0.785
Child-pugh class			0.897
A	69 (26.8)	36 (27.9)	
B	100 (38.9)	52 (40.3)	
C	40 (15.6)	18 (14)	
Laboratory data			
Albumin (g/l)	31.5 (26 - 37)	32.5 (25.2 - 37)	0.913
Bilirubin (mg/dl)	1.6 (1 - 3.1)	1.5 (0.9 - 3.2)	0.248
Creatinine (mg/dl)	0.8 (0.7 - 1.1)	0.8 (0.7 - 1.2)	0.614
INR	1.4 (1.2 - 1.6)	1.3 (1.2 - 1.5)	0.337
Platelets (G/l)	98 (70 - 144)	102 (72.5 - 145.5)	0.836
WBC (×10 ⁹ /l)	6.1 (4.2 - 8.1)	5.7 (4.1 - 7.3)	0.477
usCRP	10.3 (5.8 - 30.7)	9.5 (4 - 27.6)	0.298
Hemodynamic data			
Pulse (bpm)	72 (64 - 79)	64 (62 - 78)	0.256
MAP (mmHg)	82.3 (73.3 - 90.3)	81.7 (75 - 90.8)	0.732
Scores for fibrosis or cirrhosis			
ALBI	-1.6 (-2.2 - -1.1)	-1.6 (-2.3 - -0.9)	0.738
FIB-4	5.1 (3.1 - 8.5)	5.3 (3.2 - 8.8)	0.882
APRI	1.4 (0.7 - 2.4)	1.2 (0.8 - 2.4)	0.838

Supplementary table 15. Multivariate analysis of TE and MELD score of 2-year mortality.

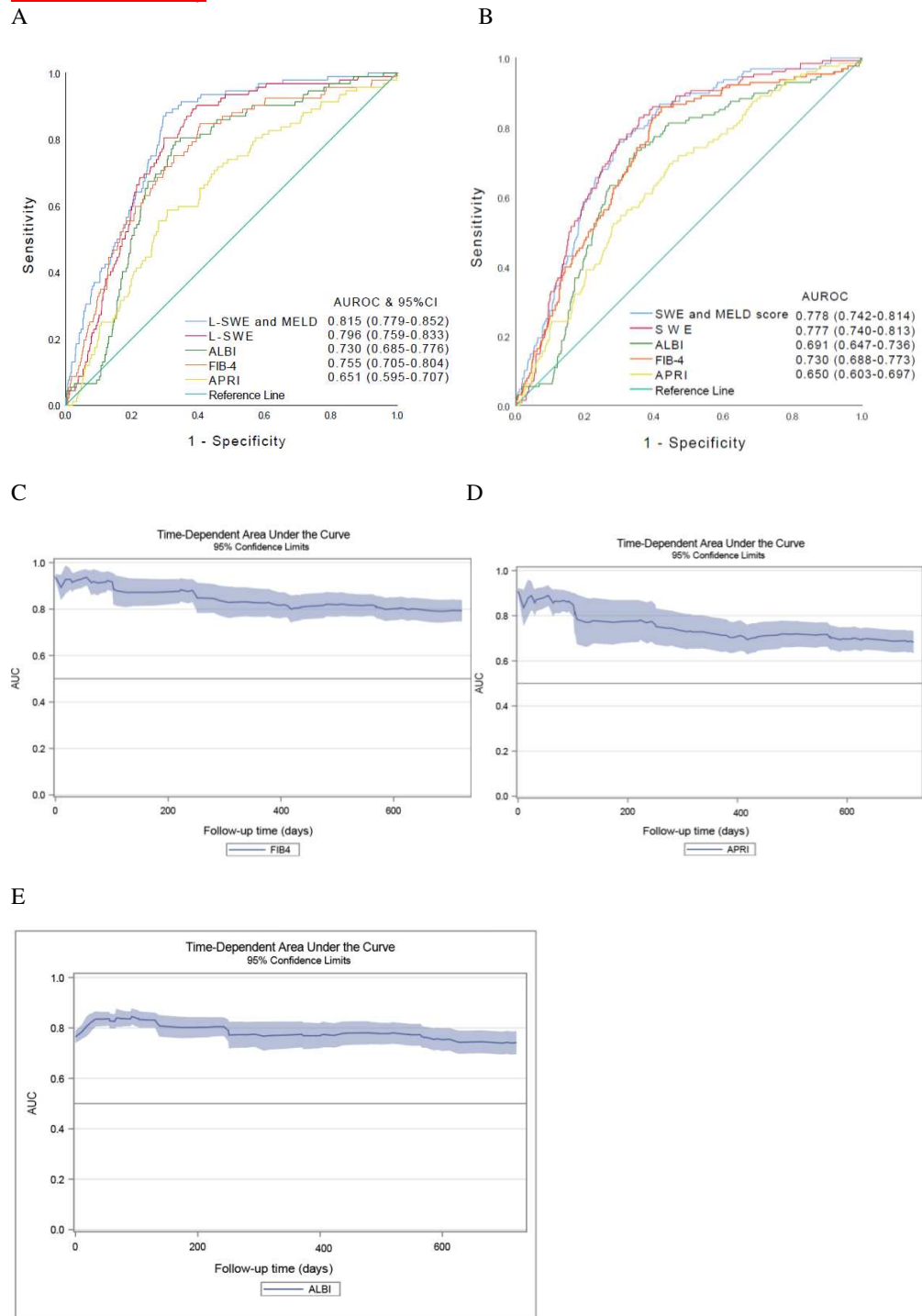
Parameter	Chi-Square	Pr > ChiSq	Hazard Ratio	95% Hazard Ratio Confidence Limits	
TE (kPa)	16.8366	<.0001	1.038	1.02	1.056
MELD	10.2248	0.0014	1.198	1.073	1.339

Supplementary figure 1. Flow chart of the 2D-SWE and additional p-SWE cohort

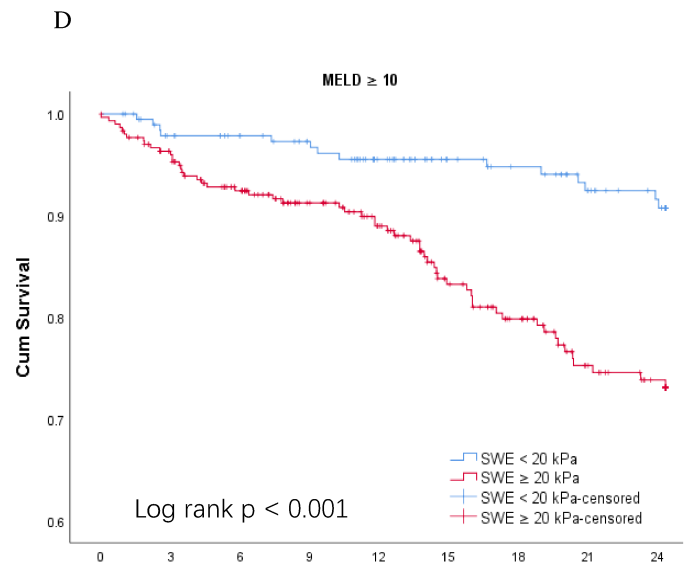
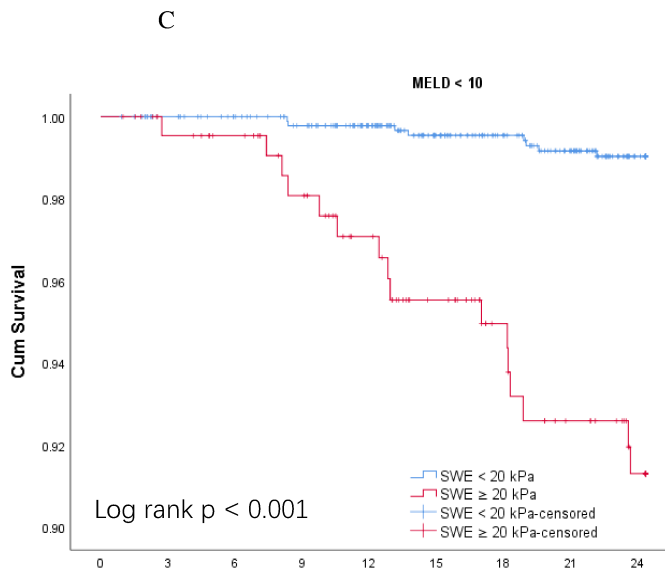
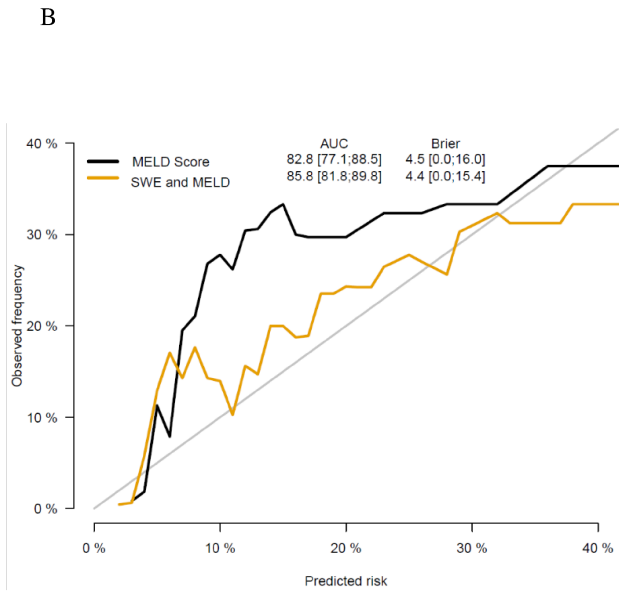
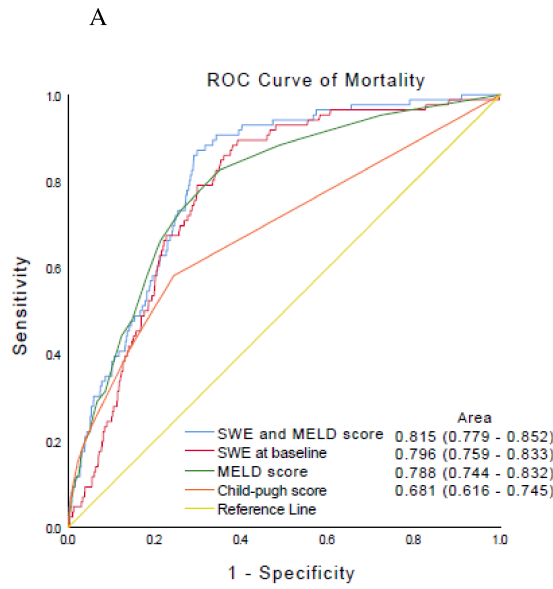
Supplementary figure 2. Violin plot of L-SWE measurements of each participated center.



Supplementary Figure 3. ROC curve of combination of SWE and MELD, SWE, ALBI score, FIB-4 score and APRI score. Panel A. ROC curve of mortality; Panel B. ROC curve of decompensations. Panel C, D and E. Time-dependent area under the curve of APRI, FIB4 and ALBI score in the outcome of mortality



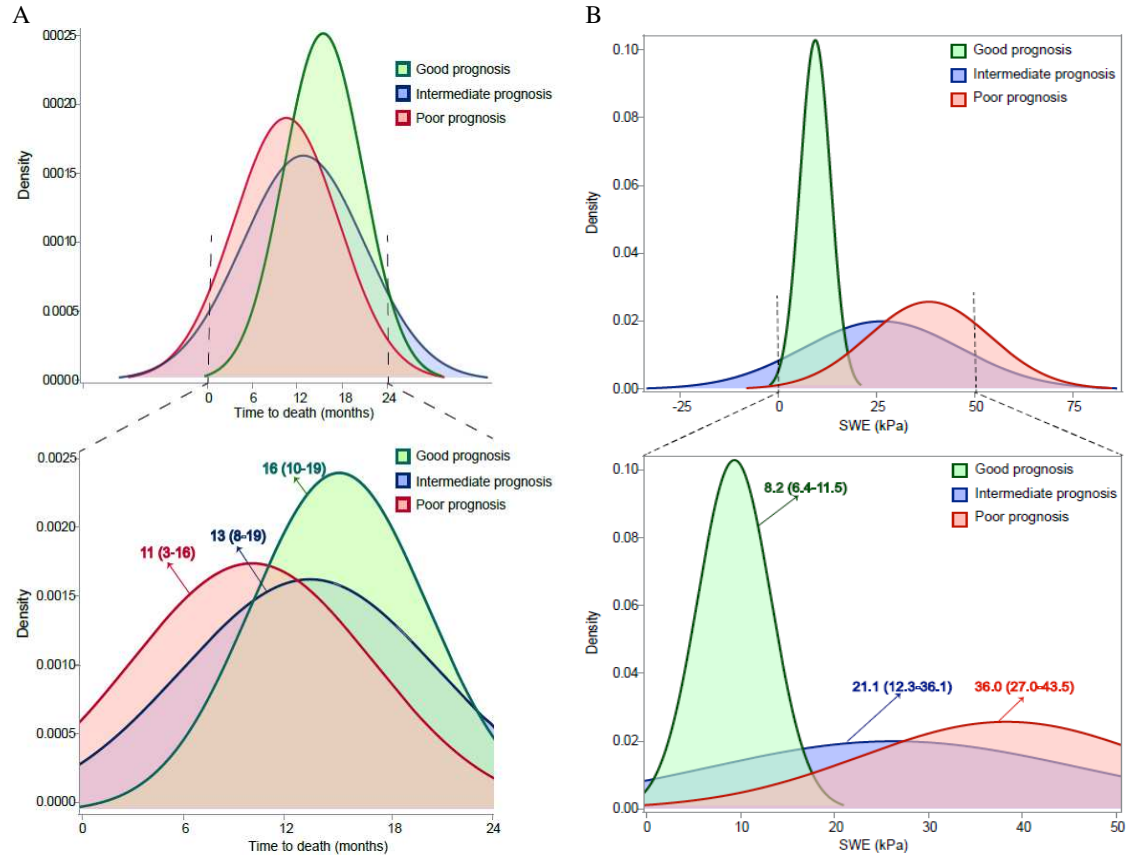
Supplementary Figure 4. Panel A. ROC curve of combination of SWE and MELD, SWE, MELD score and Child-Pugh score in prediction of mortality. Panel B. Calibration plot of MELD score and SWE combined with MELD score. Panel C. Kaplan Meier curve of patients with MELD score < 10, comparison between SWE > 20 kPa < 20 kPa; Panel D. Kaplan Meier curve of patients with MELD score > 10, comparison between SWE > 20 kPa and < 20 kPa



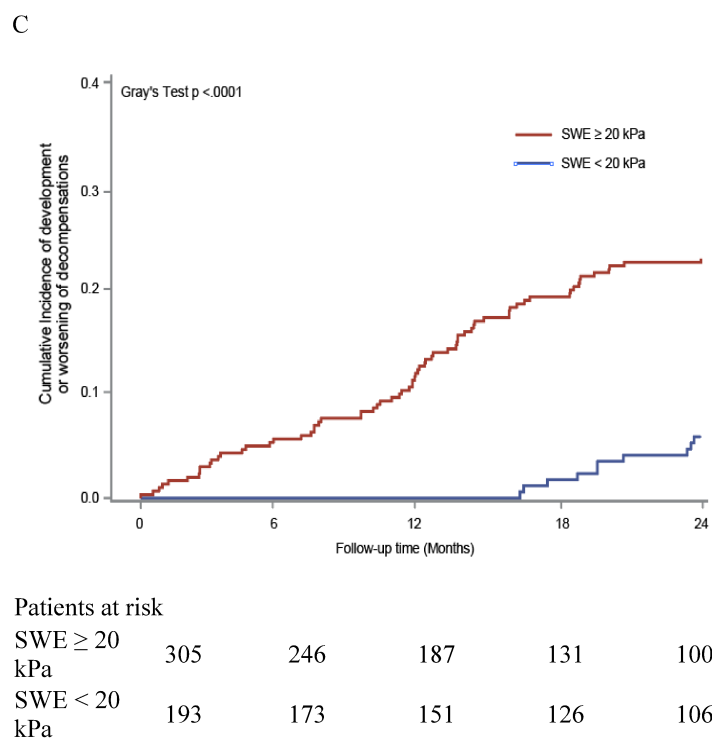
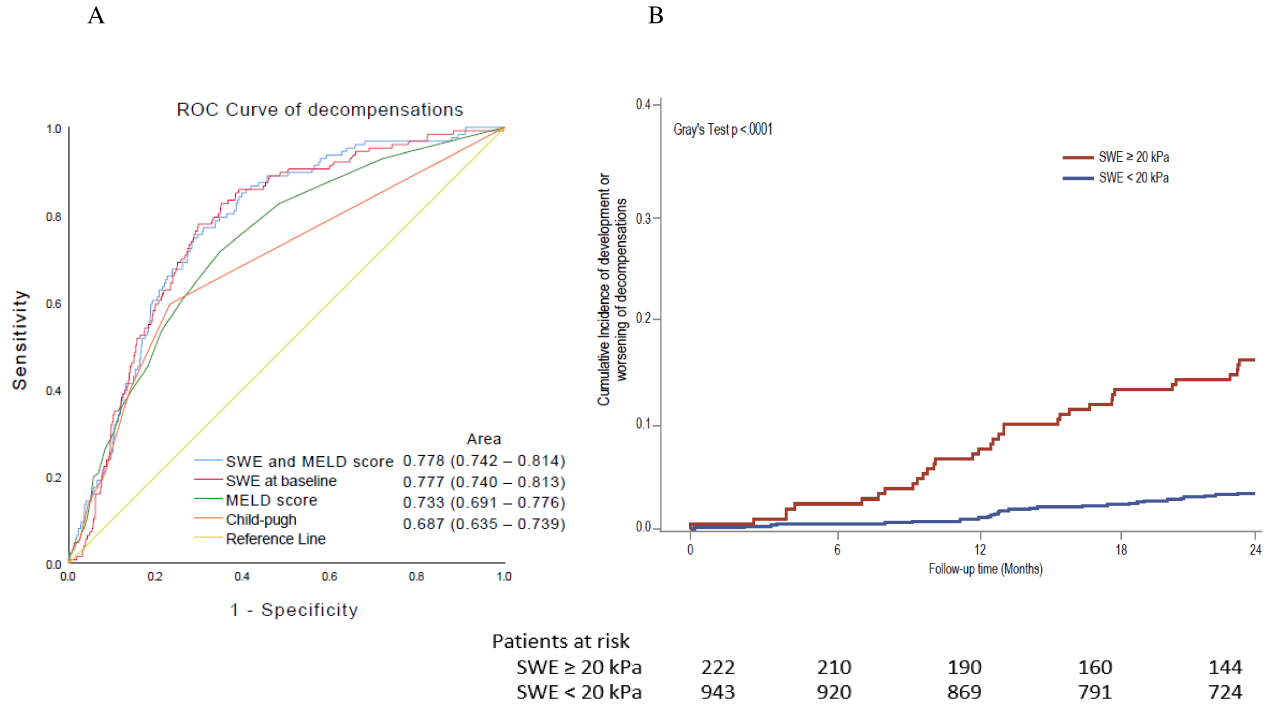
Patients at risk	Follow-up time (Months)				Patients at risk
	0	3	6	9	
SWE < 20 kPa	943	920	870	794	713
SWE ≥ 20 kPa	222	210	190	160	141

Patients at risk	Follow-up time (Months)				Patients at risk
	0	3	6	9	
SWE > 20 kPa	193	173	151	126	105
SWE ≥ 20 kPa	305	246	187	134	97

Supplementary figure 5. Panel A. Density curve of patients died days during 2-year of follow-up. The length of follow-up days of each group was described as median and interquartile range. Panel B. Density curve of L-SWE distribution of patients with good, intermediate and poor prognosis. The L-SWE value of each group was described as median and interquartile range.

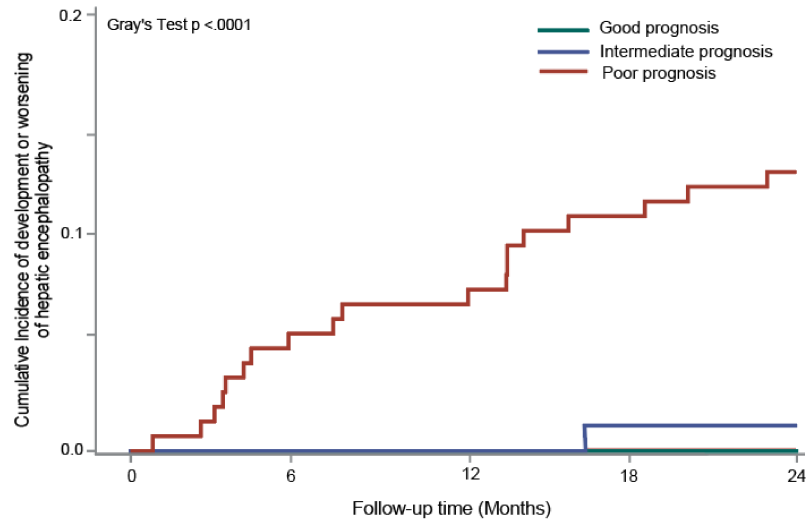


Supplementary Figure 6. Panel A. ROC curve of decompensation development; Panel B. Cumulative incidence of decompensation in patients with MELD score < 10, comparison between SWE > 20 kPa and < 20 kPa; Panel C. Cumulative incidence of decompensation in patients with MELD score > 10, comparison between SWE > 20 kPa and < 20 kPa;



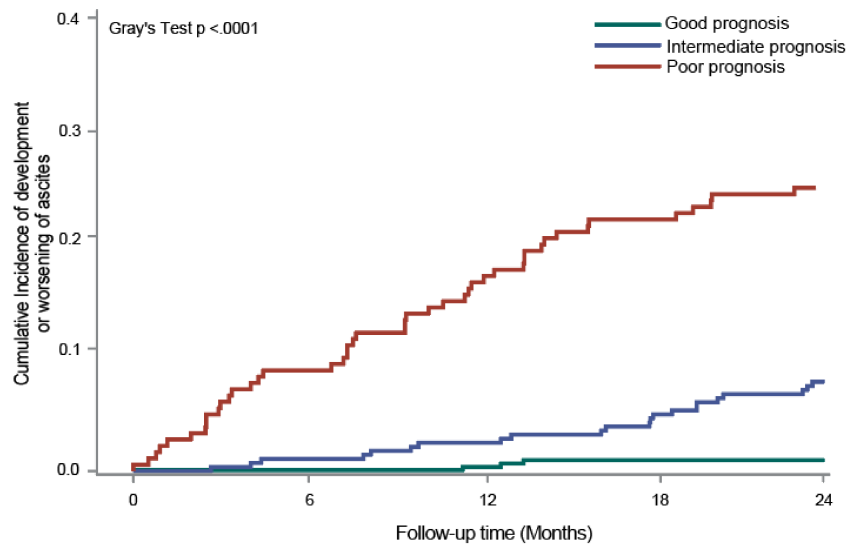
Supplementary Figure 7. Cumulative incidence of development of Panel A ascites (death as competing risk), Panel B, hepatic encephalopathy (death as competing risk) over two years in patients with good, intermediate and poor prognosis.

A



Patients at risk					
Good prognosis	943	927	916	878	853
Intermediate prognosis	415	412	403	388	377
Poor prognosis	305	305	304	301	297

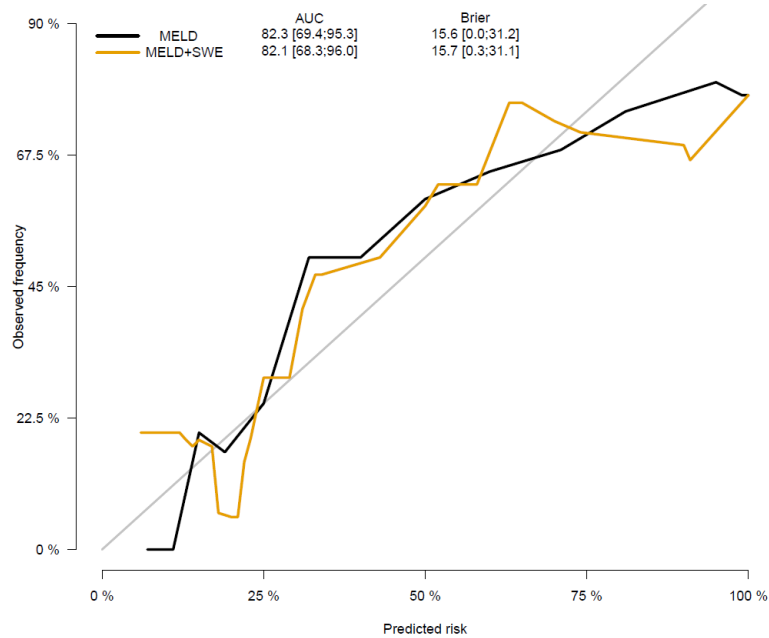
B



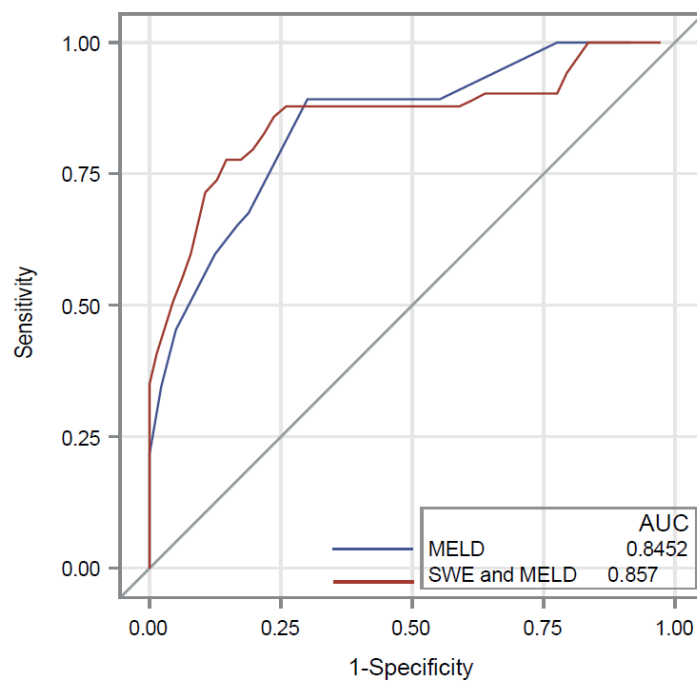
Patients at risk					
Good prognosis	943	920	869	791	725
Intermediate prognosis	415	383	341	286	251
Poor prognosis	305	246	187	134	100

Supplementary figure 8 Panel A. Calibration plot of the SWE and MELD in the mortality outcome prediction of validation cohort; Panel B. ROC curve of MELD score and SWE combined with MELD score in prediction 2-year mortality of validation cohort

A.

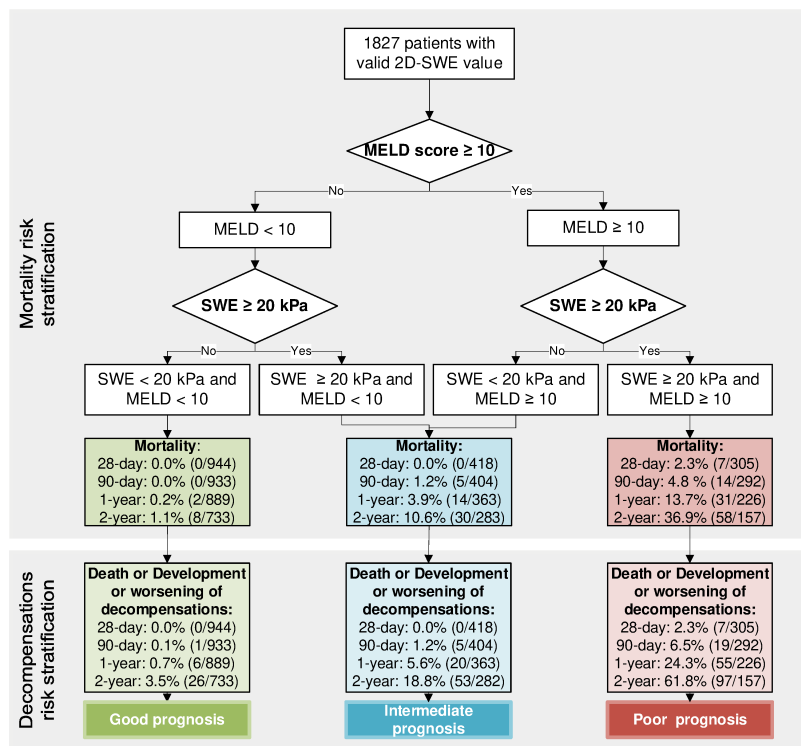


B

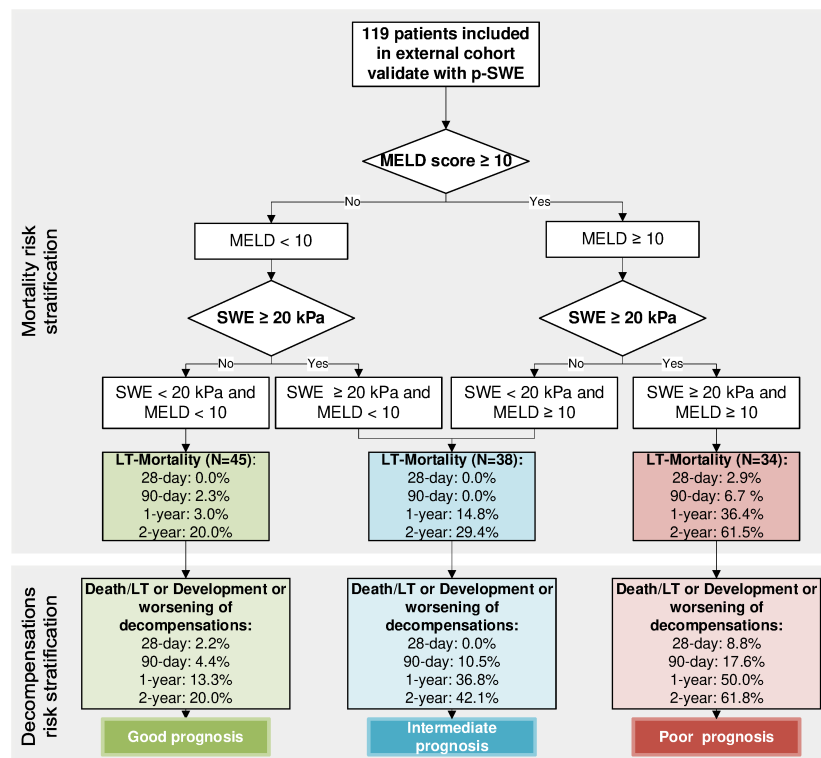


Supplementary figure 9. Panel A. Decision tree of the cohort with 2D-SWE. Panel B. Decision tree of the additional cohort with p-SWE

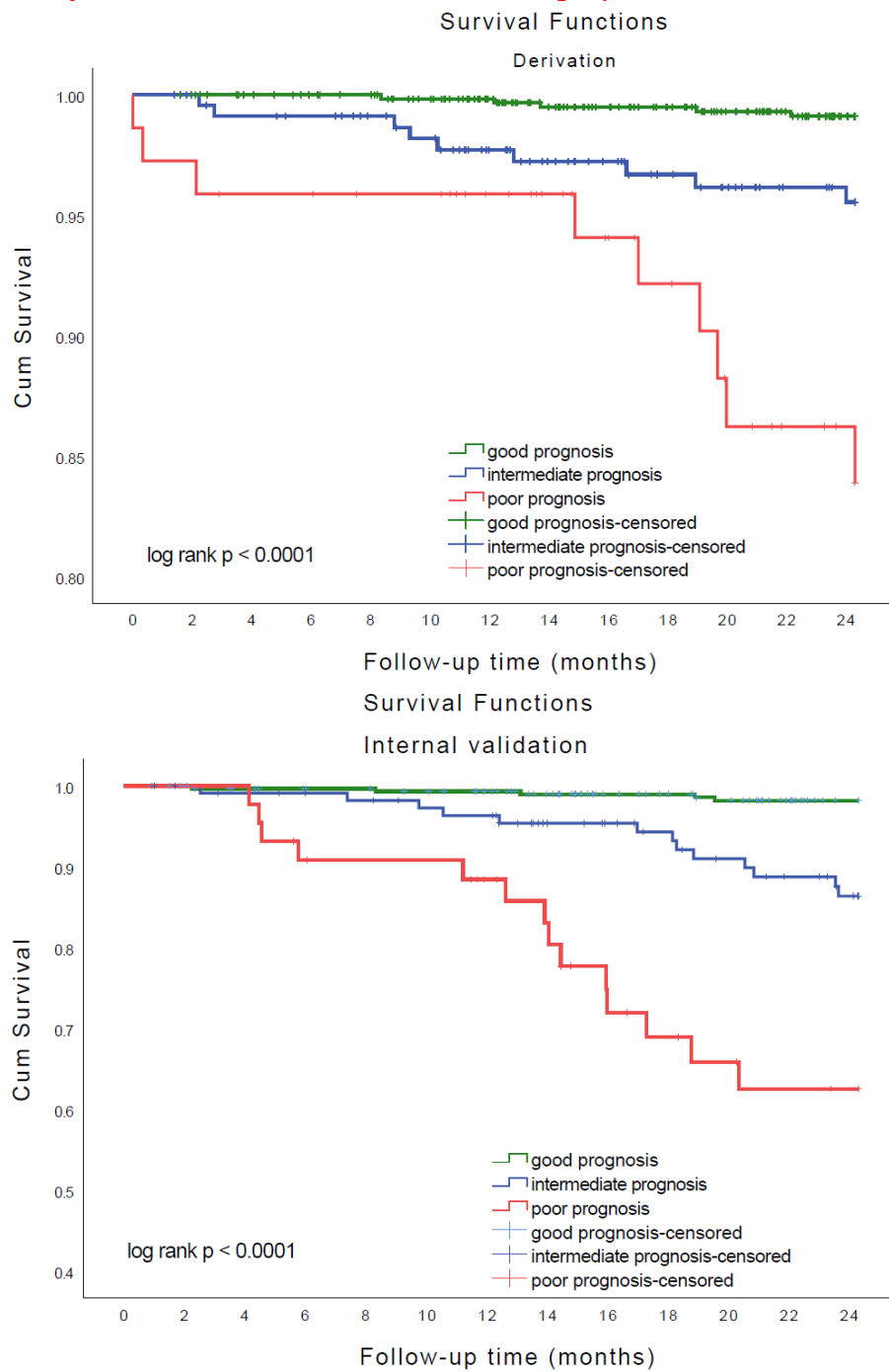
A



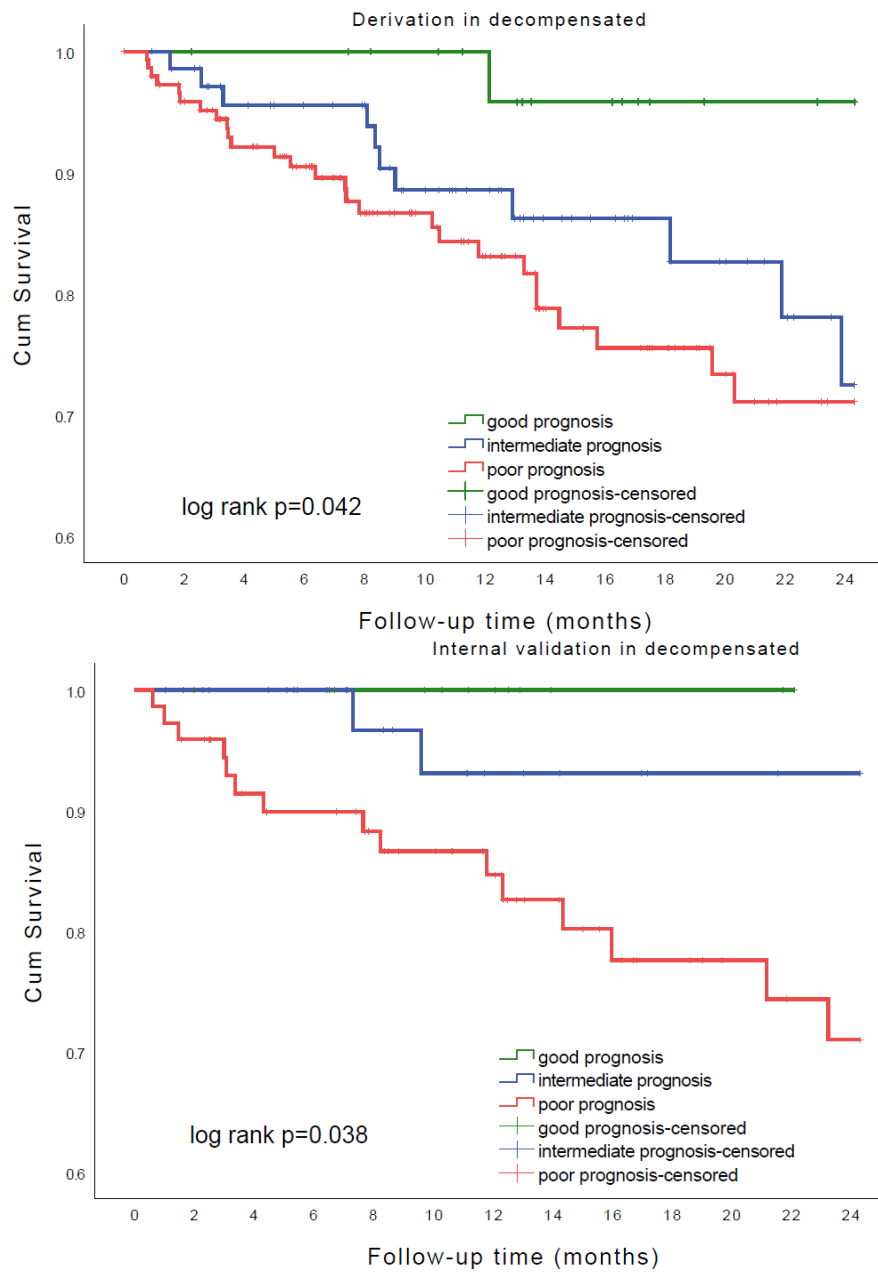
B



Supplementary figure 10. Kaplan Meier curve of 2-year survival in compensated patients randomly selected into derivation and internal validation groups

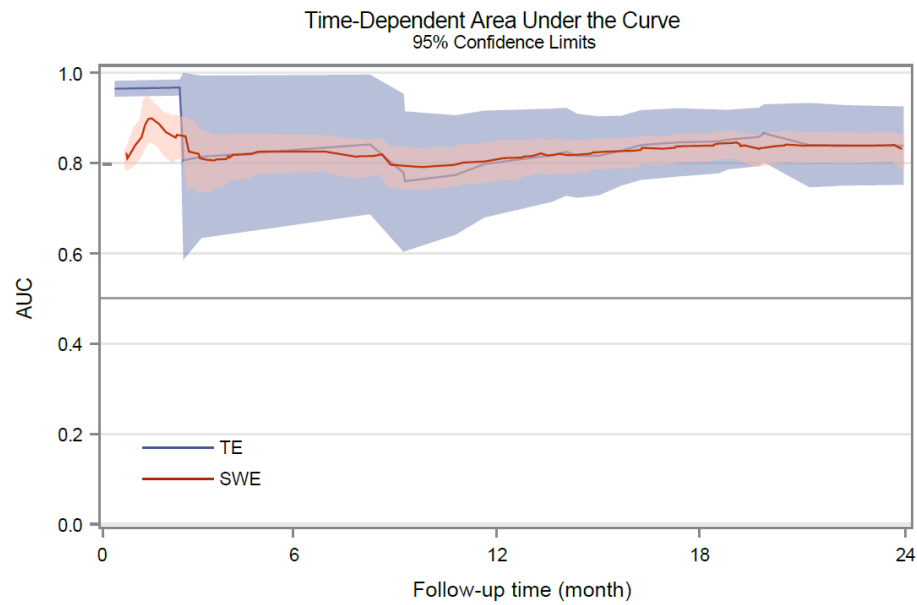


Supplementary figure 11. Kaplan Meier curve of 2-year survival in decompensated patients randomly selected into derivation and internal validation groups

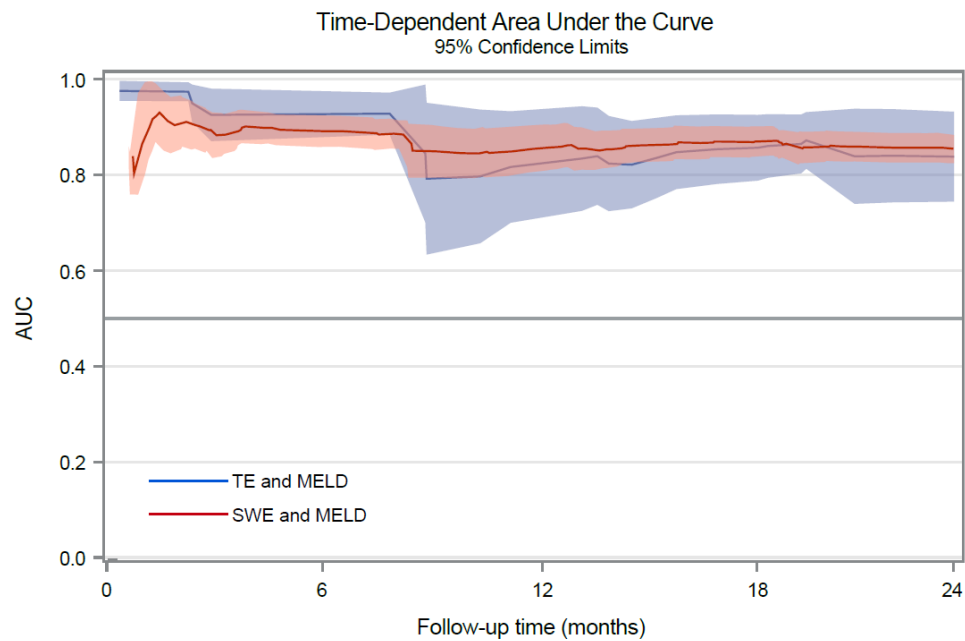


Supplementary figure 12. Panel A. Time-dependent area under the curve of TE and SWE. Panel B. Time-dependent area under the curve of TE combined with MELD score and SWE combined with MELD score.

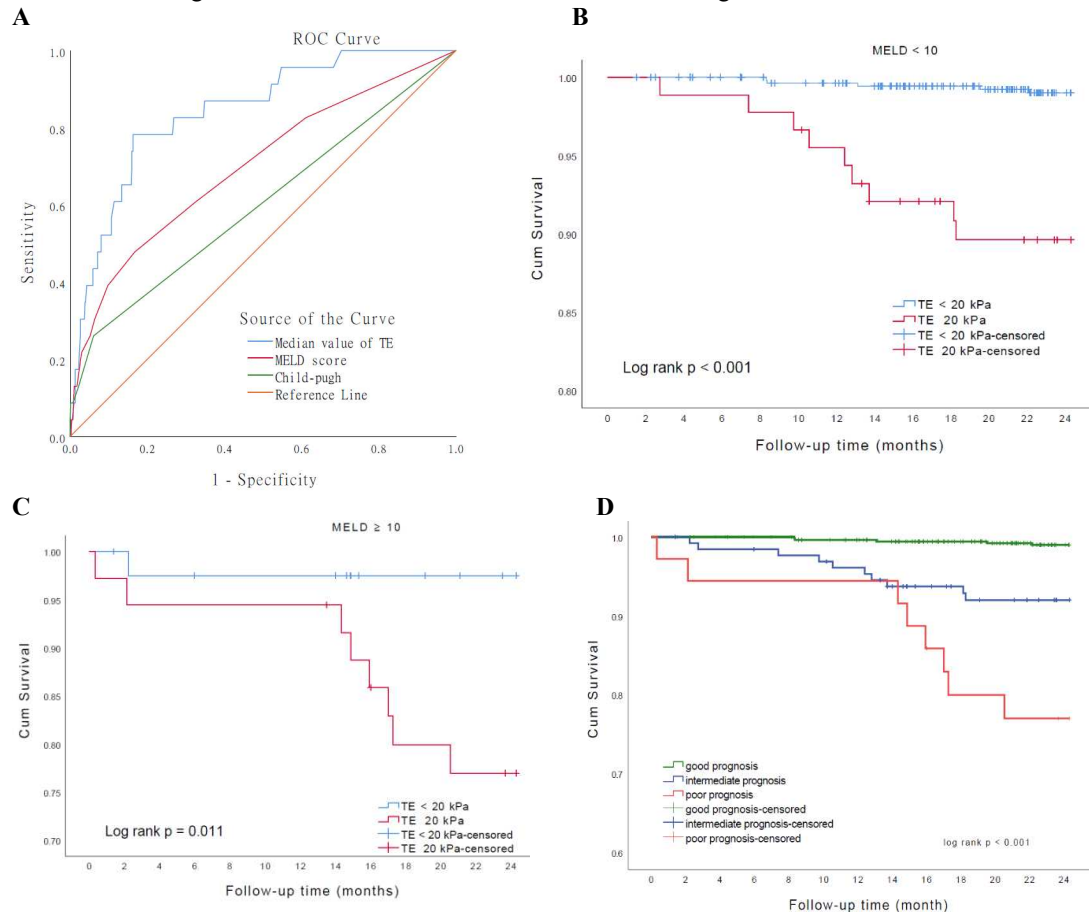
A



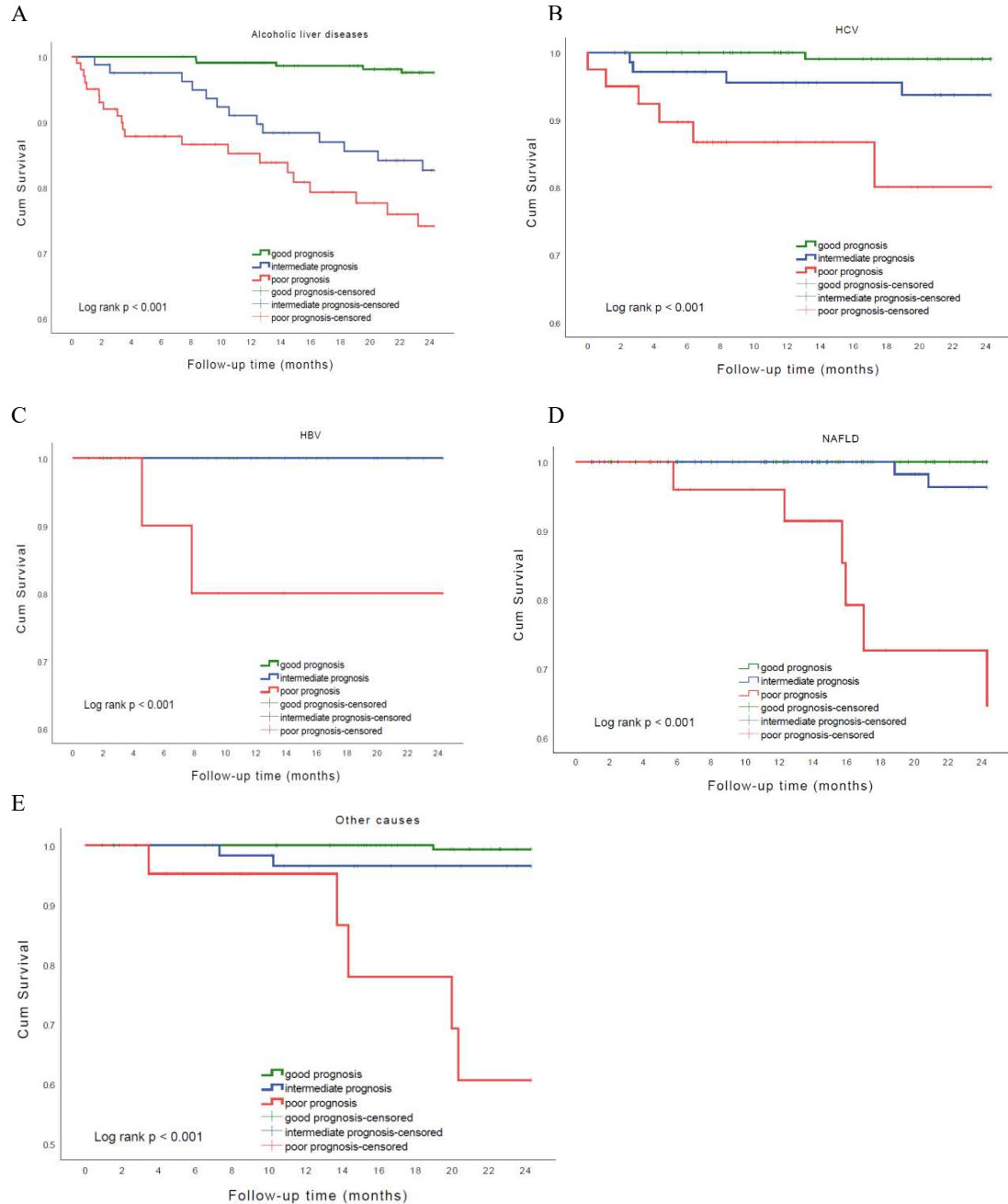
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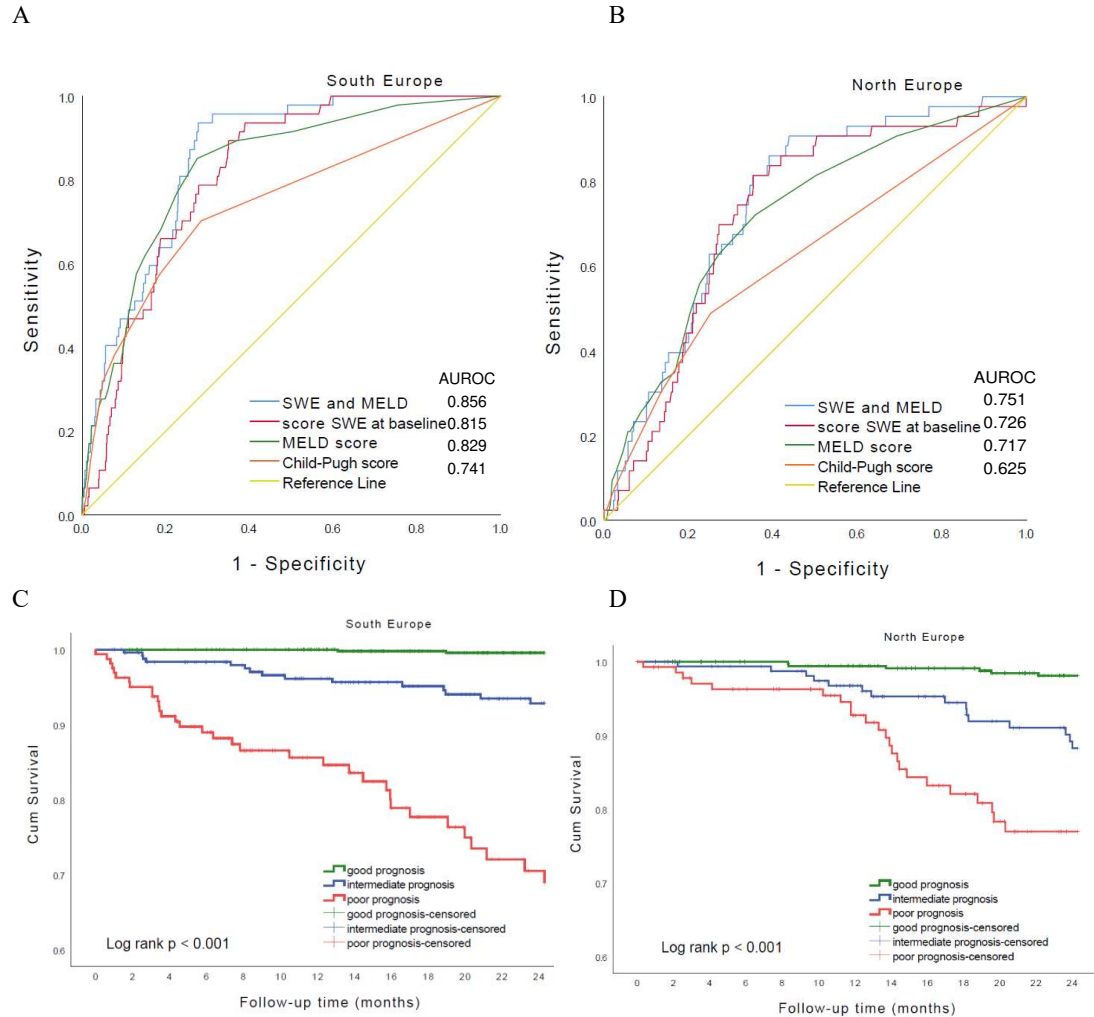
Supplementary figure 13. Panel A. ROC curve of TE in the outcome prediction and compared with other models. Panel B. Kaplan Meier curve of patients with MELD lower than 10, compared by TE lower and greater than 20kPa; Panel C. Kaplan Meier curve of patients with MELD equal and higher than 10, compared by TE lower and greater than 20kPa; Panel D. Kaplan Meier curve of patients with TE lower or greater than 20kPa, combined with MELD lower or greater than 10.



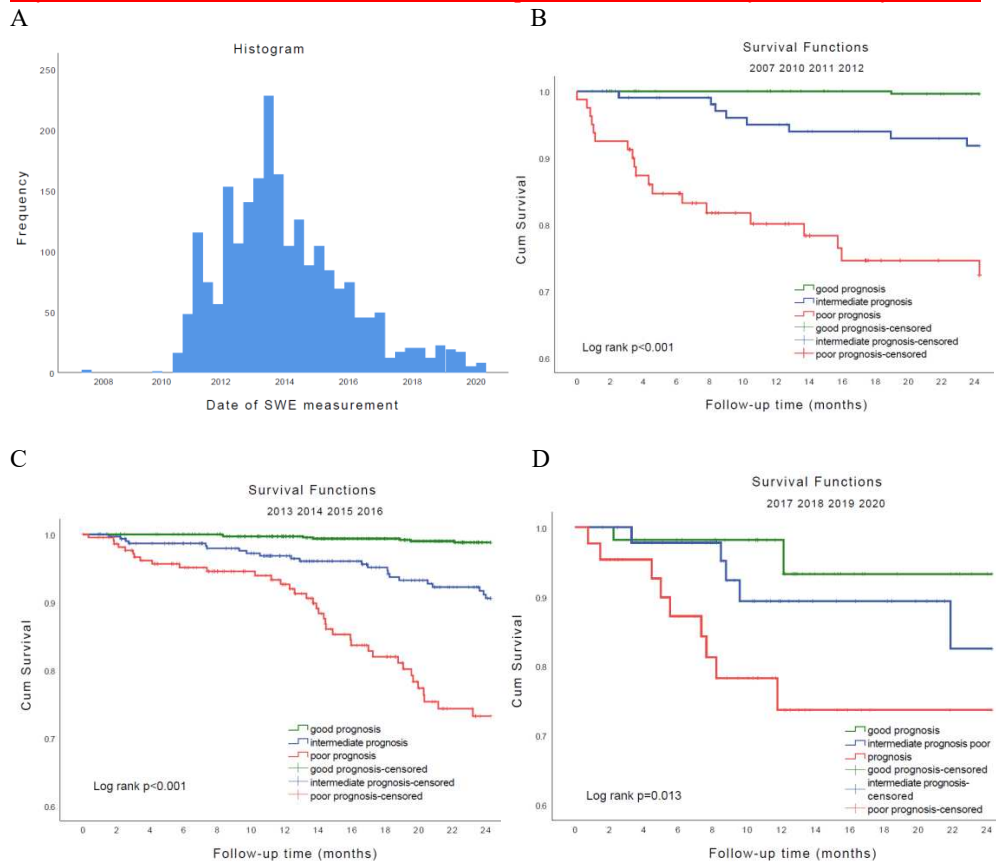
Supplementary figure 14. Etiology sensitive analysis of Kaplan Meier survival curve in different causes of chronic liver disease, compared among different prognosis groups. Panel A. in alcohol-related chronic liver diseases; Panel B. in HCV; Panel C. in HBV; Panel D. in NAFLD; Panel E. in other causes.



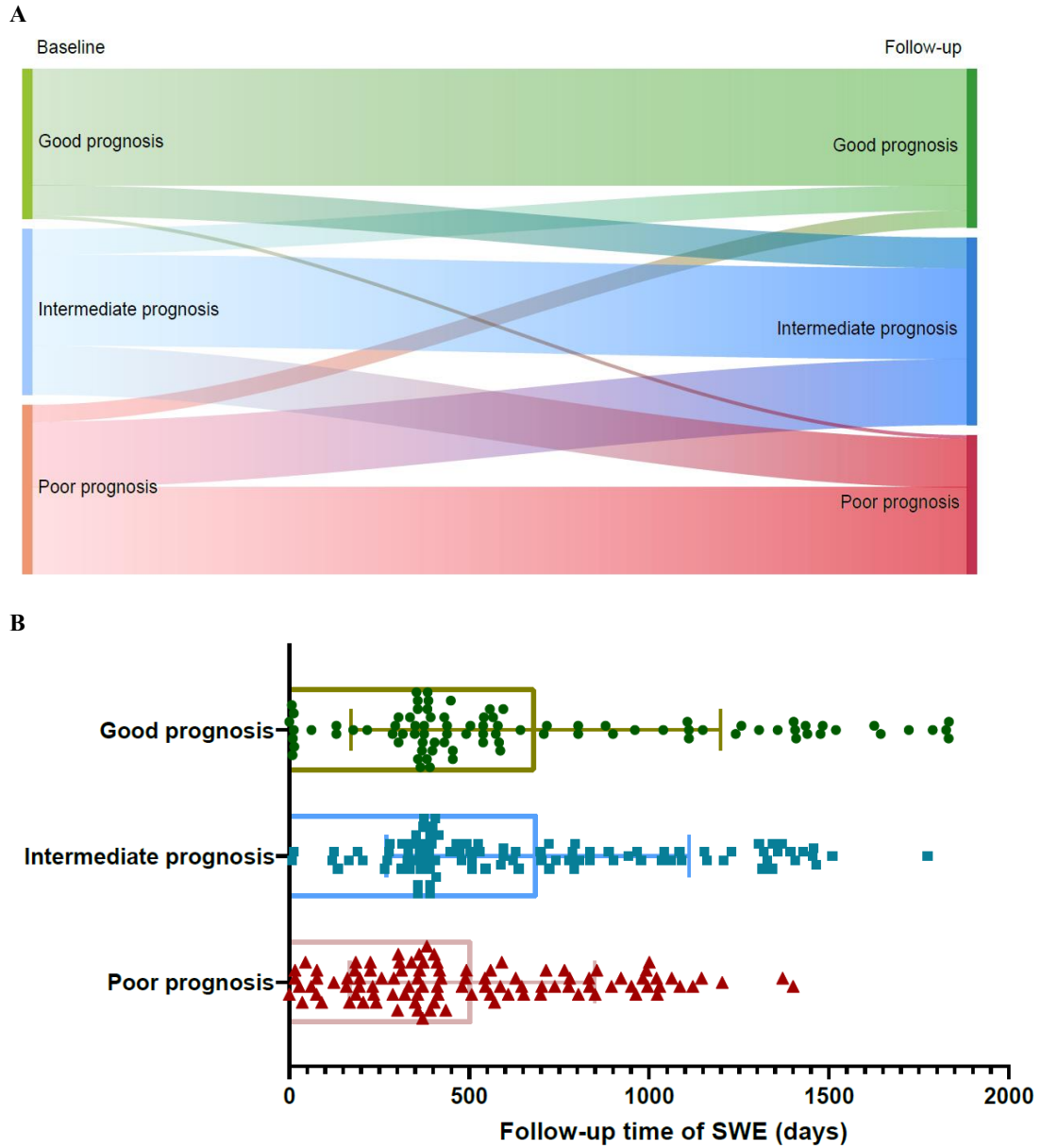
Supplementary figure 15. Center sensitivity analysis. Panel A. ROC curve in South Europe of 2-year mortality; Panel B. ROC curve in North Europe of 2-year mortality. Panel C. Kaplan Meier curve of South Europe in three group of different prognoses; Panel D. Kaplan Meier curve of North Europe in three group of different prognoses



Supplementary figure 16. Panel A. Histogram of date distribution of the SWE measurement of patients included from all participated centers; Panel B. Survival function curve of patients included from year 2007 to year 2012; Panel C. Survival function curve of patients included from year 2013 to year 2016; Panel D. Survival function curve of patients included from year 2017 to year 2020



Supplementary figure 17. Panel A. River diagram of dynamic changes at baseline and during follow-up of the patients with good prognosis, intermediate prognosis and poor prognosis; Panel B. Distribution of the follow-up time of patients with good prognosis, intermediate prognosis and poor prognosis



Supplementary reference

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