

Risk of further decompensation/mortality in patients with cirrhosis and ascites as the first single decompensation event

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Table S1

	Grade-2 moderate ascites (n=323)	Grade-3 severe ascites (n=299)	SHR (95%CI) Grade 3 vs. 2	p-value
Child-Pugh Score – median (IQR)	7 (6-9)	9 (8-10)	-	-
MELD – mean ± SD	13.6±5.4	16.8±6.0	-	-
Non-selective betablocker, n (%)	119 (37%)	105 (31%)	-	-
Diuretics, n (%)	277 (86%)	277 (93%)		
- Furosemide	29 (9%)	24 (8%)	-	-
- Antialdosteronic	67 (21%)	58 (19%)		
- Both	181 (56%)	195 (65%)		
Any further decompensation, n (%)	121 (37%)	229 (77%)	3.64 (2.93-4.51)	<0.001
First further decompensation event, n (%)				
- Refractory ascites	18 (6%)	112 (37%)		
- SBP	11 (3%)	21 (7%)		
- HRS-AKI	9 (3%)	20 (7%)	-	-
- Variceal bleeding	18 (6%)	9 (3%)		
- Hepatic encephalopathy	55 (17%)	57 (19%)		
- ≥2 simultaneous further decompensation events	10 (3%)	10 (3%)		
All further decompensation events, n (%)				
- Refractory ascites	39 (12%)	165 (55%)	6.90 (4.92-9.67)	<0.001
- SBP	30 (9%)	75 (25%)	3.36 (2.22-5.08)	<0.001
- HRS-AKI	24 (7%)	57 (19%)	2.96 (1.86-4.72)	<0.001
- Variceal bleeding	26 (8%)	28 (9%)	1.42 (0.82-2.45)	0.210
- Hepatic encephalopathy	73 (23%)	110 (37%)	2.08 (1.56-2.78)	<0.001
Hyponatremia¹, n (%)	86 (27%)	129 (43%)	2.08 (1.59-2.71)	<0.001
ACLF, n (%)	46 (14%)	100 (33%)	3.08 (2.18-4.36)	<0.001
PVT, n (%)	34 (11%)	28 (9%)	1.01 (0.62-1.65)	<0.001
HCC, n (%)	53 (16%)	26 (9%)	0.63 (0.39-1.00)	0.048
TIPS, n (%)	28 (9%)	53 (18%)	-	-
LT, n (%)	52 (16%)	53 (18%)	-	-
Death, n (%)	126 (39%)	136 (45%)	1.40 (1.10-1.79)	0.006
- Liver-related	102 (81%)	122 (90%)		
- Non-liver-related	22 (17%)	14 (10%)	-	-
- Unknown	2 (2%)	-		

¹ defined as serum sodium <130 mmol x L⁻¹

Table S1. Follow-up characteristics compared between patients with grade-2 and grade-3 ascites.

Abbreviations: n number; ACLF acute-on-chronic liver failure; HCC hepatocellular carcinoma; HRS-AKI hepatorenal syndrome-acute kidney injury; IQR interquartile range; OLT orthotopic liver transplantation; PVT portal vein thrombosis; SBP spontaneous bacterial peritonitis; SHR subdistribution hazard ratio; TIPS transjugular intrahepatic portosystemic shunt

Table S2

Variable	CPS-A (n=93)	CPS-B (n=359)	CPS-C (n=170)	p-value
Any further decompensation, n (%)	24 (26%)	207 (58%)	119 (70%)	<0.001
First further decompensation event, n (%)				
- Refractory ascites	4 (4%)	81 (23%)	45 (26%)	<0.001
- SBP	1 (1%)	25 (7%)	6 (4%)	
- HRS-AKI	1 (1%)	11 (3%)	17 (10%)	
- Variceal bleeding	3 (3%)	19 (5%)	5 (3%)	
- Hepatic encephalopathy	13 (14%)	59 (16%)	40 (24%)	
- More than one decompensation event	2 (2%)	12 (3%)	6 (4%)	
All further decompensation events (occurring ever), n (%)				
- Refractory ascites	10 (11%)	122 (34%)	72 (42%)	<0.001
- SBP	4 (4%)	68 (19%)	33 (19%)	0.002
- HRS-AKI	4 (4%)	42 (12%)	35 (21%)	<0.001
- Variceal bleeding	4 (4%)	35 (10%)	15 (9%)	0.250
- Hepatic encephalopathy	16 (17%)	97 (27%)	70 (41%)	<0.001
Hyponatremia ¹ , n (%)	17 (18%)	116 (32%)	82 (48%)	<0.001
Number of paracenteses, median (IQR)	0 (0-1)	1 (0-5)	2 (0-5)	<0.001
ACLF, n (%)	7 (8%)	77 (21%)	62 (36%)	<0.001
PVT, n (%)	12 (13%)	36 (10%)	14 (8%)	0.481
HCC, n (%)	19 (20%)	48 (13%)	12 (7%)	0.007
TIPS, n (%)	9 (10%)	54 (15%)	18 (11%)	0.212
OLT, n (%)	14 (15%)	60 (17%)	31 (18%)	0.798
Death, n (%)	28 (30%)	162 (45%)	72 (42%)	0.033
Type of deaths, n (%)				
- Liver-related	22 (79%)	136 (84%)	66 (92%)	<0.001
- Non-liver related	5 (18%)	25 (15%)	6 (8%)	
- Unknown	1 (4%)	1 (1%)	-	

¹ defined as serum sodium <130 mmol x L⁻¹

Table S2. Follow-up characteristics compared among CPS stages.

Abbreviations: n number; ACLF acute-on-chronic liver failure; HCC hepatocellular carcinoma; HRS-AKI hepatorenal syndrome-acute kidney injury; IQR interquartile range; OLT orthotopic liver transplantation; PVT portal vein thrombosis; SBP spontaneous bacterial peritonitis; TIPS transjugular intrahepatic portosystemic shunt

Table S3

	MELD <10 (n=126)	MELD 10-14 (n=237)	MELD ≥15 (n=259)	p-value
Any further decompensation, n (%)	49 (39%)	126 (53%)	175 (68%)	<0.001
First further decompensation event, n (%)				
- Refractory ascites	14 (11%)	49 (21%)	67 (26%)	<0.001
- SBP	8 (6%)	16 (7%)	8 (3%)	
- HRS-AKI	2 (2%)	4 (2%)	23 (9%)	
- Variceal bleeding	6 (5%)	9 (4%)	12 (5%)	
- Hepatic encephalopathy	14 (11%)	42 (18%)	56 (22%)	
- More than one decompensation event	5 (4%)	6 (3%)	9 (3%)	
All further decompensation events, n (%)				
- Refractory ascites	24 (19%)	72 (30%)	108 (42%)	<0.001
- SBP	15 (12%)	38 (16%)	52 (20%)	0.121
- HRS-AKI	10 (8%)	19 (8%)	52 (20%)	<0.001
- Variceal bleeding	7 (6%)	16 (7%)	31 (12%)	0.045
- Hepatic encephalopathy	22 (18%)	61 (26%)	100 (39%)	<0.001
Hyponatremia¹, n (%)	24 (19%)	73 (31%)	118 (46%)	<0.001
Number of paracenteses, median (IQR)	1 (0-3)	1 (0-5)	2 (0-6)	0.002
ACLF, n (%)	16 (13%)	41 (17%)	89 (34%)	<0.001
PVT, n (%)	15 (12%)	24 (10%)	23 (9%)	0.729
HCC, n (%)	17 (%)	33 (14%)	29 (11%)	0.632
TIPS, n (%)	12 (10%)	35 (15%)	34 (13%)	0.368
OLT, n (%)	14 (11%)	41 (17%)	50 (19%)	0.128
Death, n (%)	38 (30%)	103 (44%)	121 (47%)	0.007
Type of deaths, n (%)				
- Liver-related	30 (79%)	87 (84%)	107 (88%)	0.257
- Non-liver related	8 (21%)	14 (14%)	14 (12%)	
- Unknown	-	2 (2%)	-	

¹ defined as serum sodium <130 mmol x L⁻¹

Table S3. Follow-up characteristics compared among MELD strata.

Abbreviations: n number; ACLF acute-on-chronic liver failure; HCC hepatocellular carcinoma; HRS-AKI hepatorenal syndrome-acute kidney injury; IQR interquartile range; OLT orthotopic liver transplantation; PVT portal vein thrombosis; SBP spontaneous bacterial peritonitis; TIPS transjugular intrahepatic portosystemic shunt

Table S4

Patients – n (%)	Included < 2014 n=320 (51%)	Included ≥ 2014 n=302 (49%)	p-value
Age (years) – mean ± SD	55.0±11.2	58.1±11.0	<0.001
Sex (M) – n (%)	216 (68%)	207 (69%)	0.780
Etiology¹			
Alcohol – n (%)	173 (54%)	193 (64%)	0.013
HCV – n (%)	92 (29%)	50 (17%)	<0.001
HBV – n (%)	42 (13%)	16 (5%)	<0.001
NAFLD – n (%)	28 (9%)	47 (16%)	0.009
Autoimmune – n (%)	15 (5%)	15 (5%)	0.871
Other – n (%)	13 (4%)	23 (8%)	0.058
Ascites grade			
Grade-2/moderate – n (%)	165 (52%)	158 (52%)	0.851
Grade-3/severe – n (%)	155 (48%)	144 (48%)	
Varices² (yes vs. no) – n (%)			
None – n (%)	98 (31%)	95 (32%)	0.051
Small – n (%)	108 (34%)	90 (30%)	
Large – n (%)	95 (30%)	109 (36%)	
Child-Pugh Stage			
A – n (%)	52 (16%)	41 (14%)	0.410
B – n (%)	187 (58%)	172 (57%)	
C – n (%)	81 (25%)	89 (30%)	
Child-Pugh Score – median (IQR)	8 (7-10)	8 (7-10)	0.455
MELD – mean ± SD	15.3±6.0	14.9±5.7	0.407
Non-selective betablocker, n (%)	118 (37%)	106 (35%)	0.645
Diuretics, n (%)	274 (86%)	280 (93%)	0.017
- Furosemide	22 (7%)	31 (10%)	
- Aldosterone antagonists	67 (21%)	58 (19%)	
- Both	185 (58%)	191 (63%)	
Albumin (g x L⁻¹) – mean ± SD	32.7±6.2	31.5±5.9	0.014
Bilirubin (mg x dL⁻¹) – median (IQR)	2.01 (1.17-3.58)	1.92 (1.02-3.50)	0.367
INR – mean ± SD	1.41±0.32	1.42±0.30	0.544
Platelets (G x L⁻¹) – median (IQR)	103 (65-152)	122 (85-175)	<0.001

¹ patients may have more than one liver disease etiology

² missing information in 27 (4%) patients

Table S4. Comparison of patient characteristics according to time of inclusion (prior vs. after 2014).

Abbreviations: M male; F female; n number; Alcohol alcohol-related liver disease; HCV hepatitis C virus; HBV hepatitis B virus; NASH non-alcoholic steatohepatitis; SD standard deviation; MELD Model for end-stage liver disease; IQR interquartile range; INR international normalized ratio

Table S5

Patients – n (%)	Padova n=315 (51%)	Vienna n=307 (49%)	p-value
Age (years) – mean ± SD	56.9±11.9	56.1±10.5	0.342
Sex (M) – n (%)	215 (68%)	208 (68%)	0.893
Etiology¹			
Alcohol – n (%)	162 (51%)	204 (66%)	<0.001
HCV – n (%)	90 (29%)	52 (17%)	<0.001
HBV – n (%)	48 (15%)	10 (3%)	<0.001
NAFLD – n (%)	44 (14%)	31 (10%)	0.138
Autoimmune – n (%)	19 (6%)	11 (4%)	0.154
Other – n (%)	10 (3%)	26 (9%)	0.005
Ascites grade			
Grade-2/moderate – n (%)	187 (59%)	136 (44%)	<0.001
Grade-3/severe – n (%)	128 (41%)	171 (56%)	
Varices² (yes vs. no) – n (%)			
None – n (%)	112 (36%)	81 (26%)	<0.001
Small – n (%)	118 (38%)	80 (26%)	
Large – n (%)	73 (24%)	131 (43%)	
Child-Pugh Stage			
A – n (%)	68 (22%)	25 (8%)	<0.001
B – n (%)	184 (58%)	175 (57%)	
C – n (%)	63 (20%)	107 (35%)	
Child-Pugh Score – median (IQR)	8 (7-9)	9 (7-10)	<0.001
MELD – mean ± SD	14.1±6.0	16.2±5.6	<0.001
Non-selective betablocker, n (%)	112 (36%)	106 (35%)	0.810
Diuretics, n (%)	254 (81%)	280 (93%)	<0.001
- Furosemide	27 (9%)	31 (10%)	
- Aldosterone antagonists	29 (9%)	58 (19%)	
- Both	198 (63%)	191 (63%)	
Albumin (g x L⁻¹) – mean ± SD	33.8±5.9	30.6±5.9	<0.001
Bilirubin (mg x dL⁻¹) – median (IQR)	1.57 (0.91-2.90)	2.30 (1.41-4.17)	<0.001
INR – mean ± SD	1.37±0.33	1.46±0.29	<0.001
Platelets (G x L⁻¹) – median (IQR)	104 (65-146)	126 (81-183)	<0.001

¹ patients may have more than one liver disease etiology

² missing information in 27 (4%) patients

Table S5. Baseline characteristics in the subgroups of patients from Padova (n=315) and Vienna (n=307).

Abbreviations: M male; F female; n number; HCV hepatitis C virus; HBV hepatitis B virus; NASH non-alcoholic steatohepatitis; SD standard deviation; CTP Child-Turcotte-Pugh score; MELD Model for end-stage liver disease; IQR interquartile range; INR international normalized ratio; PLT platelet count; SBP spontaneous bacterial peritonitis

Fig. S1

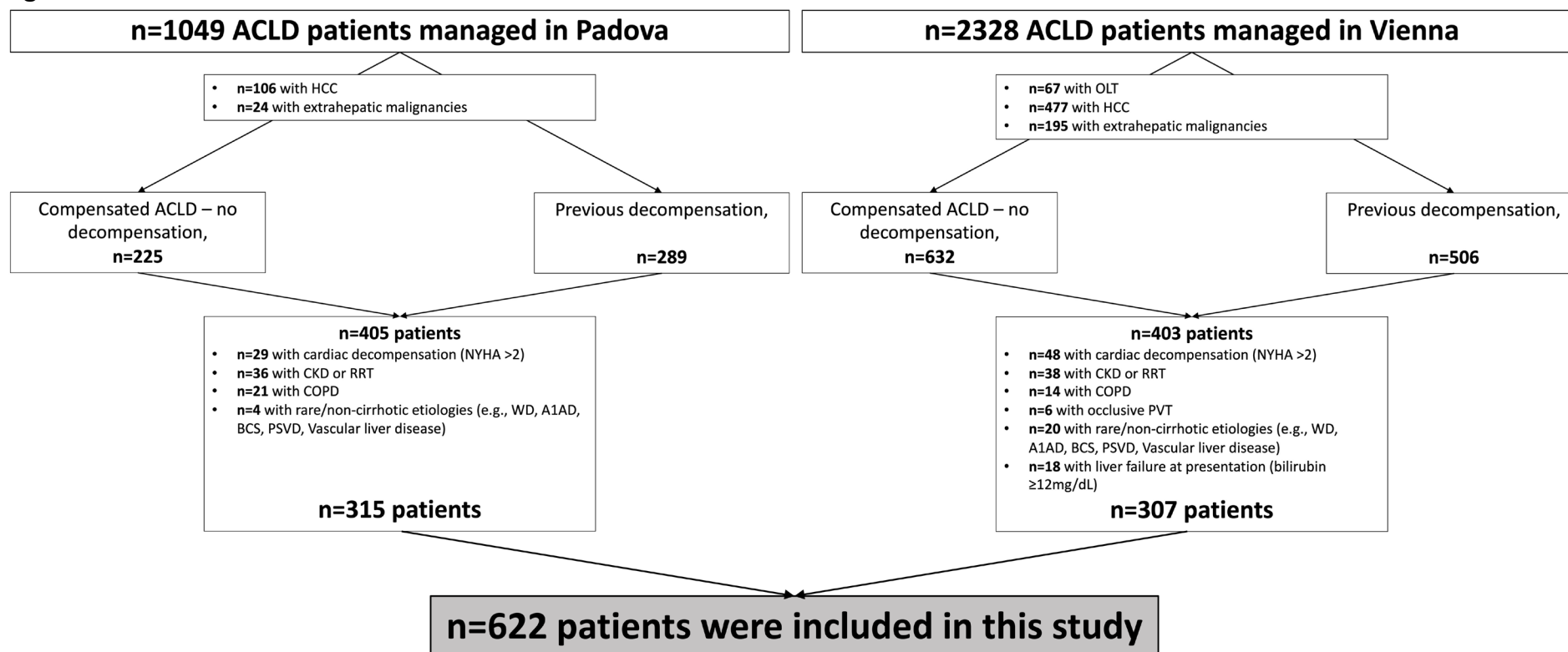


Fig. S1. Patient flowchart of the centres in Padova and Vienna.

Abbreviations: A1AD alpha-1 antitrypsin deficiency; ACLD advanced chronic liver disease; ACLF acute-on-chronic liver failure; BCS Budd-Chiari syndrome; BL baseline; CKD chronic kidney disease; COPD chronic obstructive pulmonary disease; HCC hepatocellular carcinoma; NYHA New York Heart Association; OLT orthotopic liver transplantation; PSVD porto-sinusoidal vascular disease; PVT portal vein thrombosis; RRT renal replacement therapy; WD Wilson's disease

Fig. S2

Cumulative incidence plot of single decompensating events

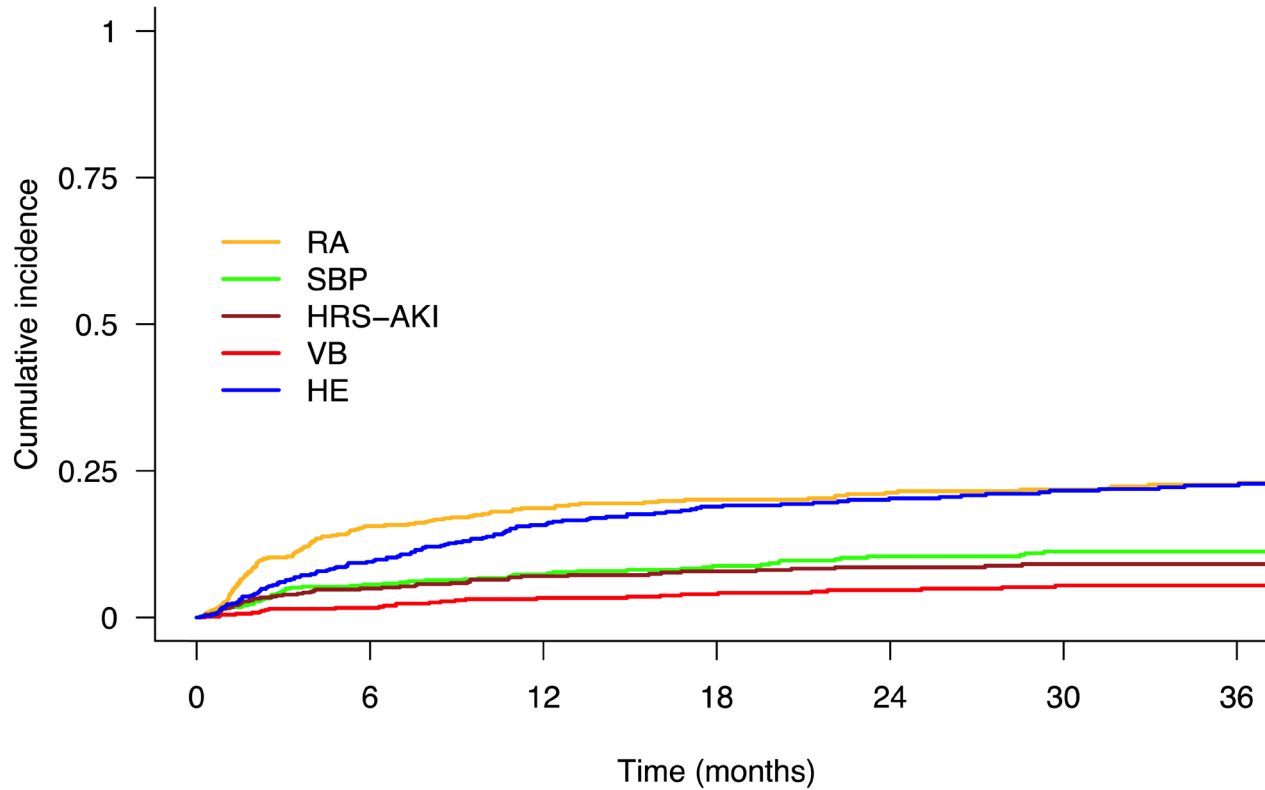


Fig. S2. Cumulative incidence plots of each first/further decompensation event.

Abbreviations: RA – refractory ascites; SBP – spontaneous bacterial peritonitis; HRS-AKI – hepatorenal syndrome-acute kidney injury; VB – variceal bleeding; HE – hepatic encephalopathy

Fig. S3

Cumulative incidence plot for death and liver transplantation

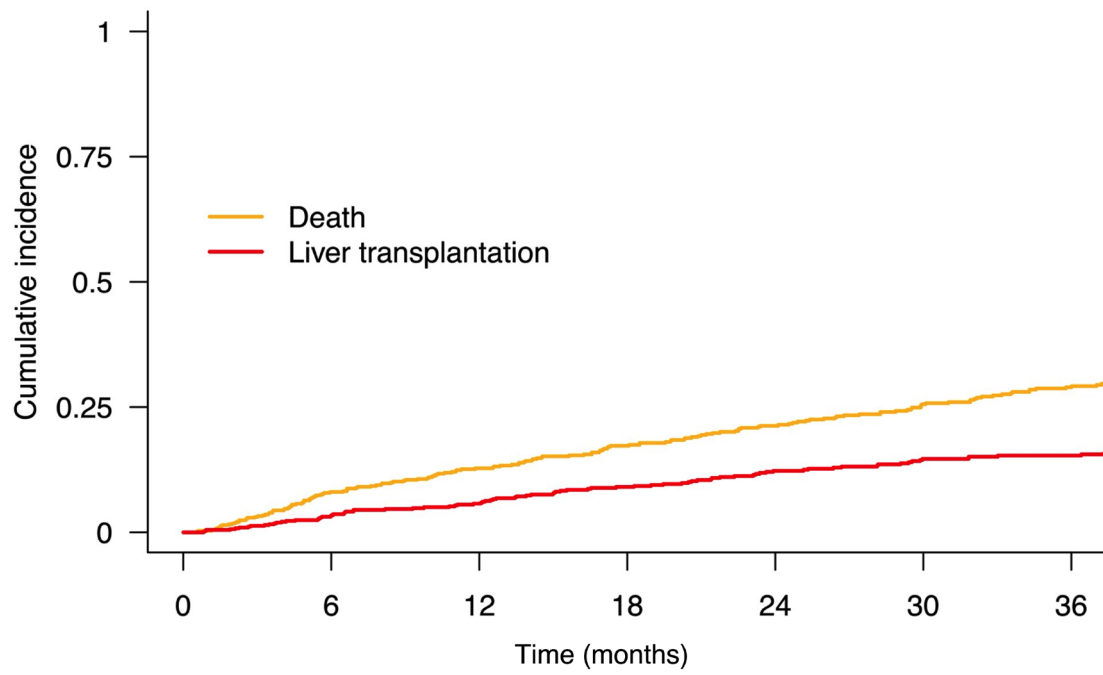
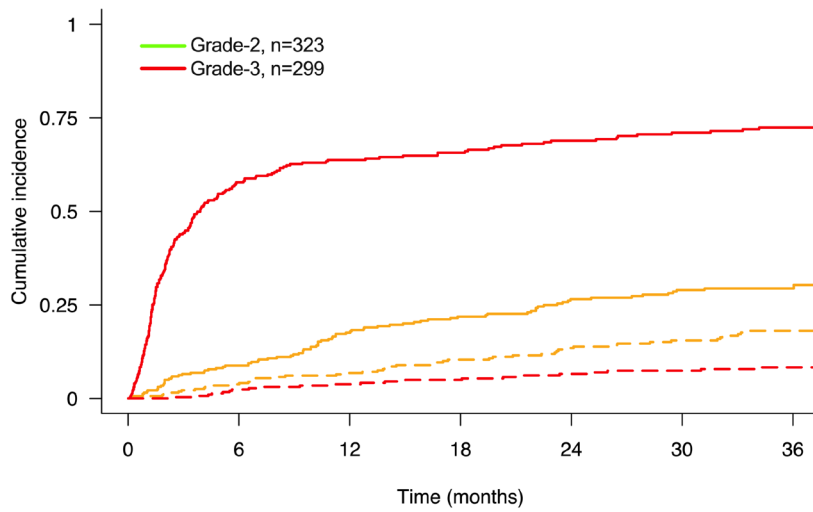


Fig. S3. Cumulative incidence plot for death and liver transplantation.

Fig. S4

[A] Cumulative incidence plot of further decompensation according to ascites grade

SHR: 3.64 (2.93-4.51), p<0.001



[B] Cumulative incidence plot of transplant-free survival according to ascites grade

SHR: 1.40 (1.10-1.79), p=0.006

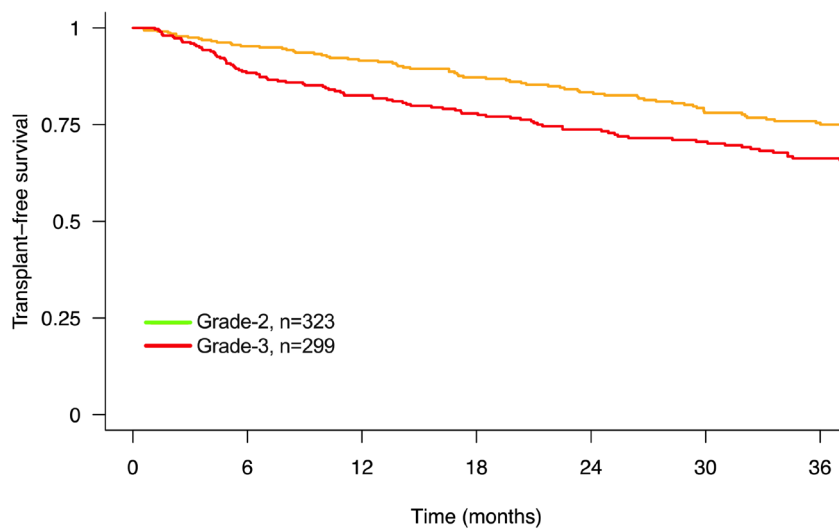


Fig. S4. Cumulative incidence plot of further decompensation (**A**) and probability of transplant-free survival (**B**) stratified according to the severity of ascites.

Fig. S5

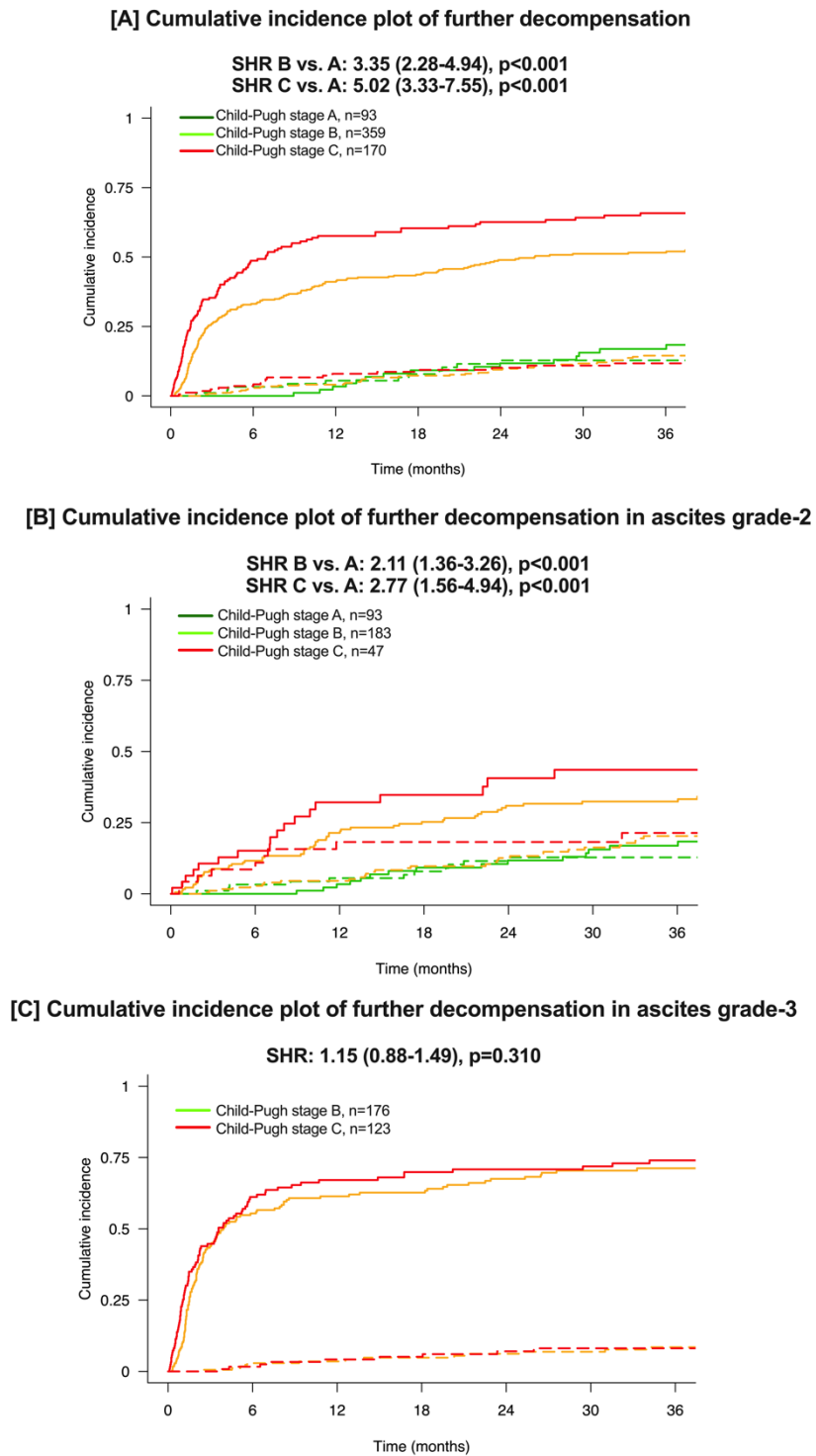


Fig. S5. Cumulative incidence plot of further decompensation stratified according to CPS stages in the study cohort (**A**), in patients with grade-2 ascites (**B**), and in patients with grade-3 ascites (**C**).

Fig. S6

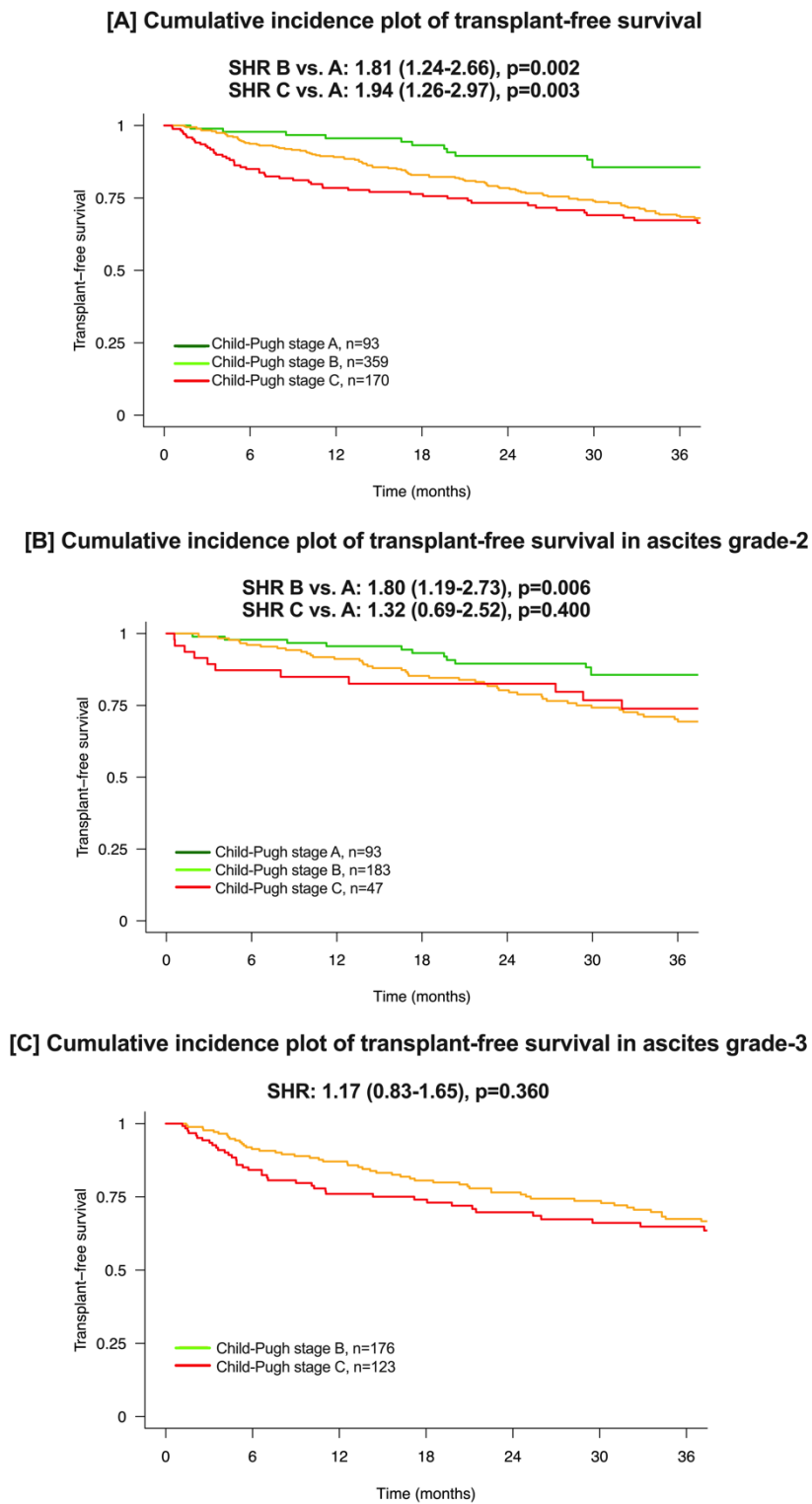
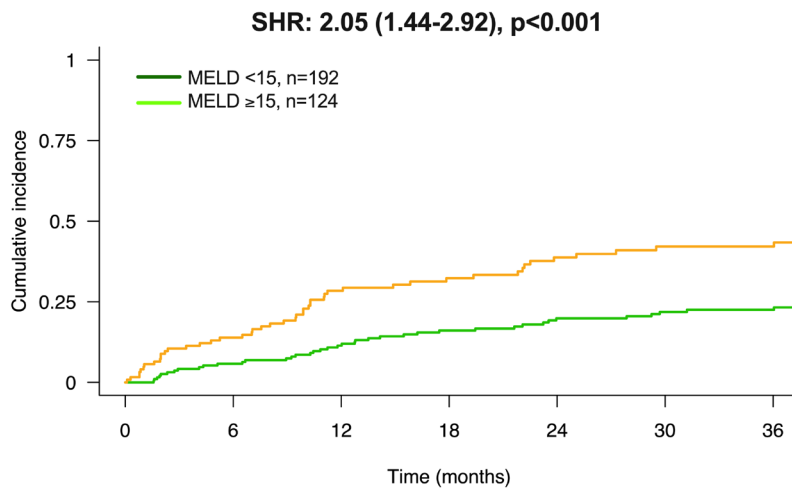


Fig. S6. Probability of transplant-free survival stratified according to CPS stages in the study cohort (A), in patients with grade-2 ascites (B), and in patients with grade-3 ascites (C).

Fig. S7

[A] Cumulative incidence plot of further decompensation in patients with ascites grade-2



[B] Cumulative incidence plot of transplant-free survival in patients with ascites grade-2

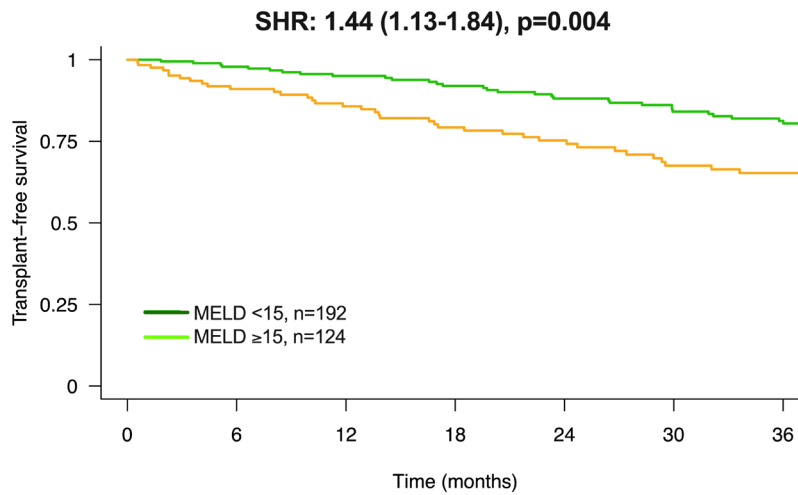


Fig. S7. Cumulative incidence plot of further decompensation (**A**) and transplant-free survival (**B**) in patients with grade-2 ascites stratified by MELD <15 vs. ≥15.