

Supplementary Material

Dynamic Course and Outcomes of Acute-on-Chronic Liver Failure in the Intensive Care Unit: Insights from a Real-World Cohort

Supplementary Table S1. Basic characteristics according to the years of ICU admission.

Patient characteristics	Total population	2013 - 2017	2018 - 2023	p-value
Total, N (%)	228 (100)	112 (49.1)	116 (50.9)	
Age [years], median (IQR)	56 (45-65)	56 (47-66)	55 (43-63)	0.264
Sex				
Male, n (%)	161 (70.6)	79 (70.5)	82 (70.7)	0.950
Female, n (%)	67 (29.4)	33 (29.5)	34 (29.3)	
BMI [kg/m²], median (IQR)	25.9 (22.9-29.0)	26.7 (24.3-31.1)	25.0 (21.6-28.0)	0.001
Etiology of liver disease				
Alcohol-associated liver disease, n (%)	128 (56.1)	60 (53.6)	68 (58.6)	0.442
Viral disease, n (%)	18 (7.9)	14 (12.5)	4 (3.4)	0.011
Autoimmune hepatitis, n (%)	11 (4.8)	7 (6.3)	4 (3.4)	0.324
MASH, n (%)	9 (3.9)	5 (4.5)	4 (3.4)	0.694
Wilson disease, n (%)	7 (3.1)	2 (1.8)	5 (4.3)	0.269
Other, n (%)*	31 (13.6)	9 (8.0)	22 (19.0)	0.016
Unknown, n (%)	24 (10.5)	15 (13.4)	9 (7.8)	0.166
Disease specific characteristics				
Ascites at admission, n (%)	166 (72.8)	74 (66.1)	92 (79.3)	0.025
Varices, n (%)	135 (59.2)	62 (55.4)	73 (62.9)	0.245
HE at admission, n (%)	116 (50.9)	55 (49.1)	61 (52.6)	0.599
Splenomegaly, n (%)	108 (47.4)	40 (35.7)	68 (58.6)	<0.001
Portal vein thrombosis, n (%)	34 (14.9)	13 (11.6)	21 (18.1)	0.169
Reasons for ICU admission				
Acute decompensation, n (%)	53 (23.2)	34 (30.4)	19 (16.4)	0.014
Respiratory failure, n (%)	25 (11.0)	14 (12.5)	11 (9.5)	0.466
Cardiac reason, n (%)	22 (9.6)	9 (8.0)	13 (11.2)	0.418
Bleeding, n (%)	54 (23.7)	23 (20.5)	31 (26.7)	0.272
Septic shock, n (%)	59 (25.9)	26 (23.2)	33 (28.4)	0.367
Other, n (%)**	15 (6.6)	6 (5.4)	9 (7.8)	0.465
Organ failures at ICU admission***				
Liver, n (%)	56 (24.6)	25 (22.3)	31 (26.7)	0.440
Kidney, n (%)	35 (15.4)	13 (11.6)	22 (19.0)	0.123
Brain, n (%)	63 (27.6)	38 (33.9)	25 (21.6)	0.037
Coagulation, n (%)	44 (19.3)	19 (17.0)	25 (21.6)	0.380
Circulation, n (%)	192 (84.2)	85 (75.9)	107 (92.2)	<0.001
Respiration, n (%)	138 (60.5)	61 (54.5)	77 (66.4)	0.066
Disease specific scores				
Child-Turcotte-Pugh, Median (IQR)	11 (9-13)	12 (9-13)	11 (9-13)	0.782
MELD-Na, Median (IQR)	27 (20-33)	26 (20-33)	28 (21-36)	0.185
ACLF Grade 1, n (%)	29 (12.7)	18 (16.1)	11 (9.5)	0.136
ACLF Grade 2, n (%)	75 (32.9)	36 (32.1)	39 (33.6)	0.812
ACLF Grade 3, n (%)	124 (54.4)	58 (51.8)	66 (56.9)	0.439
CLIF-C ACLF, Median (IQR)	56 (49-62)	54 (46-61)	57 (50-63)	0.130
CLIF-C OF, Median (IQR)	12 (10-13)	11.5 (10-13)	12 (10-14)	0.042
ICU-specific scores				
SOFA, Median (IQR)	11 (9-15)	11 (8-14)	12 (9-15)	0.222
SAPS II, Median (IQR)	48 (38-59)	46 (32-60)	49 (41-57)	0.180

Abbreviations: ACLF, acute-on-chronic liver failure; BMI, body mass index; CLIF-C, Chronic Liver Failure Consortium; HE, hepatic encephalopathy; IQR, interquartile range; MASH, Metabolic dysfunction associated steatohepatitis; MELD-Na, Model for End-Stage Liver Disease sodium; N, number; OF, Organ Failure; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment.

*Other reasons for cirrhosis are cholestatic liver diseases (n = 12, 5.3%), vascular/hypoxic liver diseases (n = 7, 3.1%), genetic/metabolic diseases (n = 7, 3.1%), post-transplant cirrhosis (n = 5, 2.2%). **Other reasons for admissions are Cerebral infarction (n=2), postoperative care after surgery (n=6), epileptic seizure (n=2), acute abdomen (n=1), non-hepatic coma (n=4). ***Organ failures were defined according to the EF CLIF-C OF score, as bilirubin ≥ 12 mg/dL for liver failure, creatinine ≥ 2 mg/dL or need for renal replacement therapy for renal failure, grade III/IV hepatic encephalopathy for brain failure, INR ≥ 2.5 for coagulation failure, use of vasopressors or MAP < 65 mmHg for circulation failure and PaO₂/FiO₂ ≤ 200 or need for mechanical ventilation for respiratory failure.

Supplementary Table S2. ICU-specific characteristics and laboratory parameters according to the years of ICU admission.

ICU specific parameters	Total population	2013 - 2017	2018 - 2023	p-value
ICU LOS [days], median (IQR)	6 (3-13)	6 (3-13)	6.5 (3-13)	0.574
IMV, n (%)	136 (59.6)	63 (56.3)	73 (62.9)	0.304
IMV [days], median (IQR)	6 (2-13)	5 (2-13)	7 (2-13)	0.347
Reason for IMV				
Respiratory failure	106 (77.9)	47 (74.6)	59 (80.8)	0.383
Hepatic encephalopathy	24 (17.6)	15 (23.8)	9 (12.3)	0.080
Acute variceal bleeding	6 (4.4)	1 (1.6)	5 (6.8)	0.213
EC therapy, n (%)	122 (53.5)	64 (57.1)	58 (50.0)	0.280
ECMO therapy, n (%)	5 (2.2)	2 (1.8)	3 (2.6)	1.000
RRT, n (%)	122 (53.5)	64 (57.1)	58 (50.0)	0.280
Cytosorb therapy, n (%)	37 (16.2)	3 (2.7)	34 (29.3)	<0.001
Vasopressor therapy, n (%)	198 (86.8)	90 (80.4)	108 (93.1)	0.004
Noradrenaline, n (%)	190 (83.3)	89 (79.5)	101 (87.1)	0.123
Vasopressin, n (%)	71 (31.1)	28 (25.0)	43 (37.1)	0.049
Dobutamine, n (%)	13 (5.7)	4 (3.6)	9 (7.8)	0.173
Terlipressin, n (%)	49 (21.5)	4 (3.6)	45 (38.8)	<0.001
Noradrenaline peak dose [µg/kg/min], median (IQR)	0.27 (0.12-0.64)	0.22 (0.10-0.65)	0.29 (0.14-0.59)	0.220
Noradrenaline 24 hours [µg/kg/min], median (IQR)	0.16 (0.07-0.42)	0.13 (0.06-0.32)	0.19 (0.10-0.42)	0.044
Vasopressin peak dose [I.U./h], median (IQR)	2 (2-2)	2 (2-2)	2 (2-2)	0.547
Dobutamine peak dose [µg/kg/min], median (IQR)	3.13 (2.7-7.4)	9.4 (4.2 - 10.5)	3.13 (2.5-4.2)	0.106
Terlipressin peak dose [mg/h], median (IQR)	0.2 (0.10-0.29)	0.04 (0.03-0.06)	0.2 (0.10-0.3)	<0.001
28-day survival, n (%)	121 (53.1)	58 (51.8)	63 (54.3)	0.556
90-day survival, n (%)	78 (34.2)	43 (38.4)	35 (30.2)	0.098
180-day survival, n (%)	63 (27.6)	36 (32.1)	27 (23.3)	0.082
1-year survival, n (%)	56 (24.6)	29 (25.9)	27 (23.3)	0.248
ICU survival, n (%)	128 (56.1)	63 (56.3)	65 (56.0)	0.974
Laboratory Parameters at ICU admission*	Total population	2013 - 2017	2018 - 2023	p-value
White blood cell count [G/L], median (IQR)	10.8 (6.7-17.3)	9.8 (5.8-15.7)	11.2 (7.5-17.7)	0.253
Platelets [G/L], median (IQR)	107 (60-169)	88 (53-152)	120 (65-179)	0.012
Hemoglobin [g/dL], median (IQR)	9.1 (7.9-10.3)	9.3 (8.2-10.6)	8.9 (7.8-10)	0.146
Creatinine [mg/dL], median (IQR)	1.7 (1.0-3.2)	1.7 (1.0-3.0)	1.6 (1.0-3.3)	0.736
Bilirubin [mg/dL], median (IQR)	4.5 (1.8-13.4)	4.3 (1.9-12.1)	4.7 (1.6-13.6)	0.888
AST [U/L], median (IQR)	83 (41-155)	83 (42-143)	84 (40-180)	0.978
ALT [U/L], median (IQR)	37 (23-81)	38 (22-81)	37 (23-80)	0.479
GGT [U/L], median (IQR)	94.0 (39.0-187.8)	91.0 (42.2-181.0)	104.0 (38.2-200.8)	0.551
CRP [mg/dL], median (IQR)	4 (1.7-8.4)	3.7 (1.7-8.0)	4.5 (1.7-9.1)	0.683
INR, median (IQR)	1.8 (1.4-2.5)	1.7 (1.4-2.3)	2 (1.6-2.8)	0.003
Fibrinogen [mg/dL], median (IQR)	230 (144-336)	228 (144-320)	231 (146-339)	0.511

Abbreviations: ACLF, acute-on-chronic liver failure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; EC, extracorporeal circulation; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; GGT, Gamma-glutamyl transferase; IMV, invasive mechanical ventilation; INR, international normalized ratio; IQR, interquartile range; LOS, length of stay; n, number; RRT, renal replacement therapy.

* Missing values: Hemoglobin: n=1, Bilirubin: n=1, AST: n=1, ALT: n=2, GGT: n=4, INR: n=3, Fibrinogen: n=9. ** ECMO therapy was conducted as venovenous ECMO in all cases.*** Cytosorb was always conducted in combination with conventional dialysis as adjunctive therapy. The initiation has been available as part of clinical routine since 2017, with initiation decided on an individual basis by the treating physician.

Supplementary Table S3. Basic characteristics according to CLIF-C ACLF grade at admission.

Patient characteristics	ACLF Grade 1	ACLF Grade 2	ACLF Grade 3	p-value
Total, N (%)	29 (12.7)	75 (32.9)	124 (54.4)	
Age [years], median (IQR)	53 (44-64)	60 (52-67)	55 (43-62)	0.008
Sex				
Male, n (%)	21 (72.4)	51 (68.0)	89 (71.8)	0.830
Female, n (%)	8 (27.6)	24 (32.0)	35 (28.2)	
BMI [kg/m²], median (IQR)	27.7 (23.8-29.2)	25.3 (21.7-28.4)	26.1 (22.6-29.9)	0.253
Etiology of liver disease				
Alcohol-associated liver disease, n (%)	17 (58.6)	40 (53.3)	71 (57.3)	0.829
Viral disease, n (%)	1 (3.4)	7 (9.3)	10 (8.1)	0.604
Autoimmune hepatitis, n (%)	2 (6.9)	5 (6.7)	4 (3.2)	0.469
MASH, n (%)	1 (3.4)	3 (4.0)	5 (4.0)	0.989
Wilson disease, n (%)	1 (3.4)	2 (2.7)	4 (3.2)	0.968
Other, n (%)*	4 (13.8)	8 (10.7)	19 (15.3)	0.649
Unknown, n (%)	3 (10.3)	10 (13.3)	11 (8.9)	0.610
Disease specific characteristics				
Ascites at admission, n (%)	17 (58.6)	50 (66.7)	99 (79.8)	0.024
Varices, n (%)	15 (51.7)	41 (54.7)	79 (63.7)	0.308
HE at admission, n (%)	8 (27.6)	27 (36.0)	81 (65.3)	<0.001
Splenomegaly, n (%)	14 (48.3)	40 (53.3)	54 (43.5)	0.405
Portal vein thrombosis, n (%)	5 (17.2)	9 (12.0)	20 (16.1)	0.680
Reasons for ICU admission				
Acute decompensation, n (%)	9 (31.0)	14 (18.7)	30 (24.2)	0.377
Respiratory failure, n (%)	4 (13.8)	10 (13.3)	11 (8.9)	0.542
Cardiac reason, n (%)	2 (6.9)	7 (9.3)	13 (10.5)	0.835
Bleeding, n (%)	10 (34.5)	20 (26.7)	24 (19.4)	0.172
Septic shock, n (%)	2 (6.9)	18 (24.0)	39 (31.5)	0.022
Other, n (%)**	2 (6.9)	6 (8.0)	7 (5.6)	0.808
Organ failures at ICU admission***				
Liver, n (%)	6 (20.7)	8 (10.7)	42 (33.9)	<0.001
Kidney, n (%)	4 (13.8)	6 (8.0)	25 (20.2)	0.068
Brain, n (%)	1 (3.4)	9 (12.0)	53 (42.7)	<0.001
Coagulation, n (%)	1 (3.4)	5 (6.7)	38 (30.6)	<0.001
Circulation, n (%)	14 (48.3)	64 (85.3)	114 (91.9)	<0.001
Respiration, n (%)	6 (20.7)	41 (54.7)	91 (73.4)	<0.001
Disease specific scores				
Child-Turcotte-Pugh, Median (IQR)	10 (8-12)	10 (9-12)	13 (11-14)	<0.001
MELD-Na, Median (IQR)	21 (16-26)	24 (15-28)	31 (24-37)	<0.001
CLIF-C ACLF, Median (IQR)	41 (37-45)	53 (48-58)	61 (55-66)	<0.001
CLIF OF, Median (IQR)	8 (8-10)	10 (10-11)	13 (12-15)	<0.001
ICU-specific scores				
SOFA, Median (IQR)	8 (7-9)	10 (8-12)	14 (11-17)	<0.001
SAPS II, Median (IQR)	34 (29-45)	46 (39-52)	53 (42-63)	<0.001

Abbreviations: ACLF, acute-on-chronic liver failure; BMI, body mass index; CLIF-C, Chronic Liver Failure Consortium; HE, hepatic encephalopathy; IQR, interquartile range; MASH, Metabolic dysfunction associated steatohepatitis; MELD-Na, Model for End-Stage Liver Disease sodium; N, number; OF, Organ Failure; SAPS II, Simplified Acute Physiology Score II; SOFA, Sequential Organ Failure Assessment.

*Other reasons for cirrhosis are cholestatic liver diseases (n = 12, 5.3%), vascular/hypoxic liver diseases (n = 7, 3.1%), genetic/metabolic diseases (n = 7, 3.1%), post-transplant cirrhosis (n = 5, 2.2%). **Other reasons for admissions are Cerebral infarction (n=2), postoperative care after surgery (n=6), epileptic seizure (n=2), acute abdomen (n=1), non-hepatic coma (n=4). ***Organ failures were defined according to the EF CLIF-C OF score, as bilirubin ≥ 12 mg/dL for liver failure, creatinine ≥ 2 mg/dL or need for renal replacement therapy for renal failure, grade III/IV hepatic encephalopathy for brain failure, INR ≥ 2.5 for coagulation failure, use of vasopressors or MAP < 65 mmHg for circulation failure and PaO₂/FiO₂ ≤ 200 or need for mechanical ventilation for respiratory failure.

Supplementary Table S4. ICU-specific characteristics laboratory parameters according to CLIF-C ACLF grade at admission.

ICU specific parameters	ACLF Grade 1	ACLF Grade 2	ACLF Grade 3	p-value
ICU LOS [days], median (IQR)	4 (2-7)	6 (3-15)	7 (3-15)	0.007
IMV, n (%)	2 (6.9)	39 (52.0)	95 (76.6)	<0.001
IMV [days], median (IQR)	1.5 (1-2)	8 (3-16)	5 (2-10)	0.064
Reason for IMV				
Respiratory failure	2 (100)	39 (100)	65 (68.4)	<0.001
Hepatic encephalopathy	0 (0)	0 (0)	24 (25.3)	0.002
Acute variceal bleeding	0 (0)	0 (0)	6 (6.3)	0.258
EC therapy, n (%)	8 (27.6)	29 (38.7)	85 (68.5)	<0.001
ECMO therapy, n (%)**	0 (0)	0 (0)	5 (4.0)	0.162
RRT, n (%)	8 (27.6)	29 (38.7)	85 (68.5)	<0.001
Cytosorb therapy, n (%)	1 (3.4)	4 (5.3)	32 (25.8)	<0.001
Vasopressor therapy, n (%)	12 (41.4)	66 (88.0)	120 (96.8)	<0.001
Noradrenaline, n (%)	10 (34.5)	64 (85.3)	116 (93.5)	<0.001
Vasopressin, n (%)	2 (6.9)	18 (24)	51 (41.1)	<0.001
Dobutamine, n (%)	1 (3.4)	5 (6.7)	7 (5.6)	0.818
Terlipressin, n (%)	1 (3.4)	15 (20.0)	33 (26.6)	0.021
Noradrenaline peak dose [µg/kg/min], median (IQR)	0.07 (0.04-0.15)	0.24 (0.10-0.49)	0.33 (0.15-0.70)	<0.001
Noradrenaline 24 hours [µg/kg/min], median (IQR)	0.03 (0.02-0.08)	0.14 (0.07-0.27)	0.18 (0.10-0.57)	<0.001
Vasopressin peak dose [I.U./h], median (IQR)	1.3 (0.5-2.0)	2.0 (2.0-2.0)	2.0 (2.0-2.0)	0.164
Dobutamine peak dose [µg/kg/min], median (IQR)	3.0 (3.0-3.0)	4.8 (2.9-9.8)	3.1 (2.3-5.9)	0.445
Terlipressin peak dose [mg/h], median (IQR)	0.03 (0.03-0.03)	0.2 (0.07-0.21)	0.2 (0.10-0.30)	0.117
28-day survival, n (%)	25 (86.2)	45 (60.0)	51 (41.1)	<0.001
90-day survival, n (%)	19 (65.5)	26 (34.7)	33 (26.6)	<0.001
180-day survival, n (%)	18 (62.1)	19 (25.3)	26 (21.0)	<0.001
1-year survival, n (%)	17 (58.6)	15 (20.0)	24 (19.4)	<0.001
ICU survival, n (%)	26 (89.7)	46 (61.3)	56 (45.2)	<0.001
Laboratory Parameters at ICU admission*	ACLF Grade 1	ACLF Grade 2	ACLF Grade 3	p-value
White blood cell count [G/L], median (IQR)	8.1 (4.3-11.7)	10.2 (6.8-14.9)	12.2 (7.0-19.6)	0.007
Platelets [G/L], median (IQR)	96 (51-174)	141 (75-200)	87 (54-138)	0.008
Hemoglobin [g/dL], median (IQR)	9.1 (8-9.6)	9.1 (8-10.4)	9 (7.8-10.3)	0.763
Creatinine [mg/dL], median (IQR)	1.1 (0.8-1.8)	1.3 (0.8-2.3)	2.2 (1.4-3.9)	<0.001
Bilirubin [mg/dL], median (IQR)	4.6 (1.2-10.2)	2.5 (1.0- 5.9)	6.8 (2.8-20.0)	<0.001
AST [U/L], median (IQR)	46 (33-104)	59 (38-103.5)	112 (45-201)	<0.001
ALT [U/L], median (IQR)	24 (18-57)	32 (17-60)	47 (27-88)	<0.001
GGT [U/L], median (IQR)	91.0 (48.5-157.5)	113.0 (45.0-222.0)	79.5 (31.2-183.8)	0.336
CRP [mg/dL], median (IQR)	2.7 (1.7-5.9)	3.2 (1.8-7.4)	4.6 (1.7-9.3)	0.431
INR, median (IQR)	1.8 (1.4-2.3)	1.6 (1.4-2.2)	2.1 (1.6-2.8)	0.001
Fibrinogen [mg/dL], median (IQR)	229 (181-307)	253 (151-388)	220 (138-312)	0.250

Abbreviations: ACLF, acute-on-chronic liver failure; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; EC, extracorporeal circulation; ECMO, extracorporeal membrane oxygenation; GGT, Gamma-glutamyl transferase; ICU, intensive care unit; IMV, invasive mechanical ventilation; INR, international normalized ratio; IQR, interquartile range; LOS, length of stay; n, number; RRT, renal replacement therapy.

* Missing values: Hemoglobin: n=1, Bilirubin: n=1, AST: n=1, ALT: n=2, GGT: n=4, INR: n=3, Fibrinogen: n=9. ** ECMO therapy was conducted as venovenous ECMO in all cases.*** Cytosorb was always conducted in combination with conventional dialysis as adjunctive therapy. The initiation has been available as part of clinical routine since 2017, with initiation decided on an individual basis by the treating physician.

Supplementary Table S5. Disease specific scores at ICU admission, after 24 hours and at ICU discharge for total population, ICU survivors and nonsurvivors.

Disease specific scores, median (IQR)	ICU Admission	after 24 hours	ICU Discharge
Total population (n=228)			
Child-Turcotte-Pugh	11 (9-13)	12 (9-13)	11 (9-13)
MELD-Na	27 (20-33)	26 (20-32)	25 (17-32)
CLIF-C ACLF	56 (49-62)	55 (49-62)	54 (47-62)
CLIF-C OF	12 (10-13)	12 (10-13)	12 (10-13)
ICU survivors (n=128)			
Child-Turcotte-Pugh	11 (9-13)	11 (9-13)	10 (8-12)
MELD-Na	25 (19-32)	24 (17 -31)	23 (15-27)
CLIF-C ACLF	54 (46-60)	52 (46-59)	50 (44-55)
CLIF-C OF	11 (10-13)	11 (10-12)	11 (10-12)
ICU nonsurvivors (n=100)			
Child-Turcotte-Pugh	12 (10-14)	12 (10-13)	13 (10-14)
MELD-Na	29 (22-37)	29 (22-35)	29 (22-36)
CLIF-C ACLF	59 (53-65)	60 (53-65)	61 (54-69)
CLIF-C OF	13 (11-14)	12 (11-14)	13 (11-15)

Abbreviations: ACLF, acute-on-chronic liver failure; CLIF-C ACLF, Chronic Liver Failure Consortium ACLF score; CLIF-C OF, Chronic Liver Failure Consortium Organ Failure score; IQR, interquartile range; MELD-Na, Model for End-Stage Liver Disease sodium score; n, number.

Supplementary Table S6. Outcome rates among single and multiple ICU admissions.

	Single ICU admissions	Multiple ICU admissions*
Individual patients, n (%)	191	18**
ICU survival, n (%)	100 (52.4)	9 (50.0)
28-day survival, n (%)	97 (50.8)	10 (55.6)
90-day survival, n (%)	67 (35.1)	5 (27.8)
180-day survival, n (%)	55 (28.8)	4 (22.2)

Abbreviations: ICU, intensive care unit.

* Survival rates were calculated for the last ICU admission.

** 17 patients were admitted twice to the ICU, while one patient was admitted three-times.

Supplementary Table S7. Binary logistic regression of clinically relevant variables as predictors for 90-day mortality.

Variable	n	Univariate analysis			Multivariate analysis		
		OR	CI of 95%	p-value	OR	CI of 95%	p-value
CLIF-C ACLF score	228	1.09	1.06 - 1.13	<0.001	1.07	1.03-1.11	<0.001
Gender	228	0.95	0.53 - 1.72	0.854			
BMI	228	1.01	0.96 - 1.06	0.722			
Septic shock*	228	2.50	1.29 - 5.14	0.009	1.51	0.64-3.72	0.350
Respiratory failure*	228	0.84	0.36 - 2.03	0.692			
IMV	228	1.59	0.92 - 2.75	0.100	0.57	0.26-1.20	0.145
RRT	228	2.61	1.51 - 4.58	<0.001	1.89	1.00-3.62	0.052
Noradrenaline peak dose	228	16.20	5.33 - 57.39	<0.001	13.5	3.18-69.7	<0.001
CRP**	228	1.01	0.97 - 1.04	0.746			
Platelets**	228	1.00	1.00 - 1.00	0.290			
Fibrinogen**	219	1.00	1.00 - 1.00	0.038	0.998	0.995-1.00	0.061

Univariate & multivariate analysis were conducted as binary logistic regression with odds ratio (OR) and 95% confidence interval. P-values <0.05 were determined as significant. After checking for multicollinearity (all variance inflation factors ≤ 1.3), multivariate analysis was conducted for parameters with a p-value ≤ 0.1 . Model performance of the multivariate logistic regression was given with an AUC=0.755 (95% CI 0.692-0.818). Noradrenaline peak dose is given as $\mu\text{g/kg/min}$, CRP and fibrinogen in mg/dL , and platelets were given in G/L .

Abbreviations: ACLF, acute-on-chronic liver failure; BMI, Body mass index; CLIF-C ACLF, Chronic Liver Failure Consortium ACLF score; CRP, C-reactive protein; CI, Confidence Interval; IMV, invasive mechanical ventilation; RRT, Renal replacement therapy; OR, Odds Ratio.

* Septic shock and respiratory failure as reasons for ICU admission. ** Laboratory values (i.e., CRP, Platelets and Fibrinogen) collected at ICU admission.

Supplementary Table S8. Binary logistic regression of clinically relevant variables as predictors for 90-day mortality including noradrenaline dose after 24 hours.

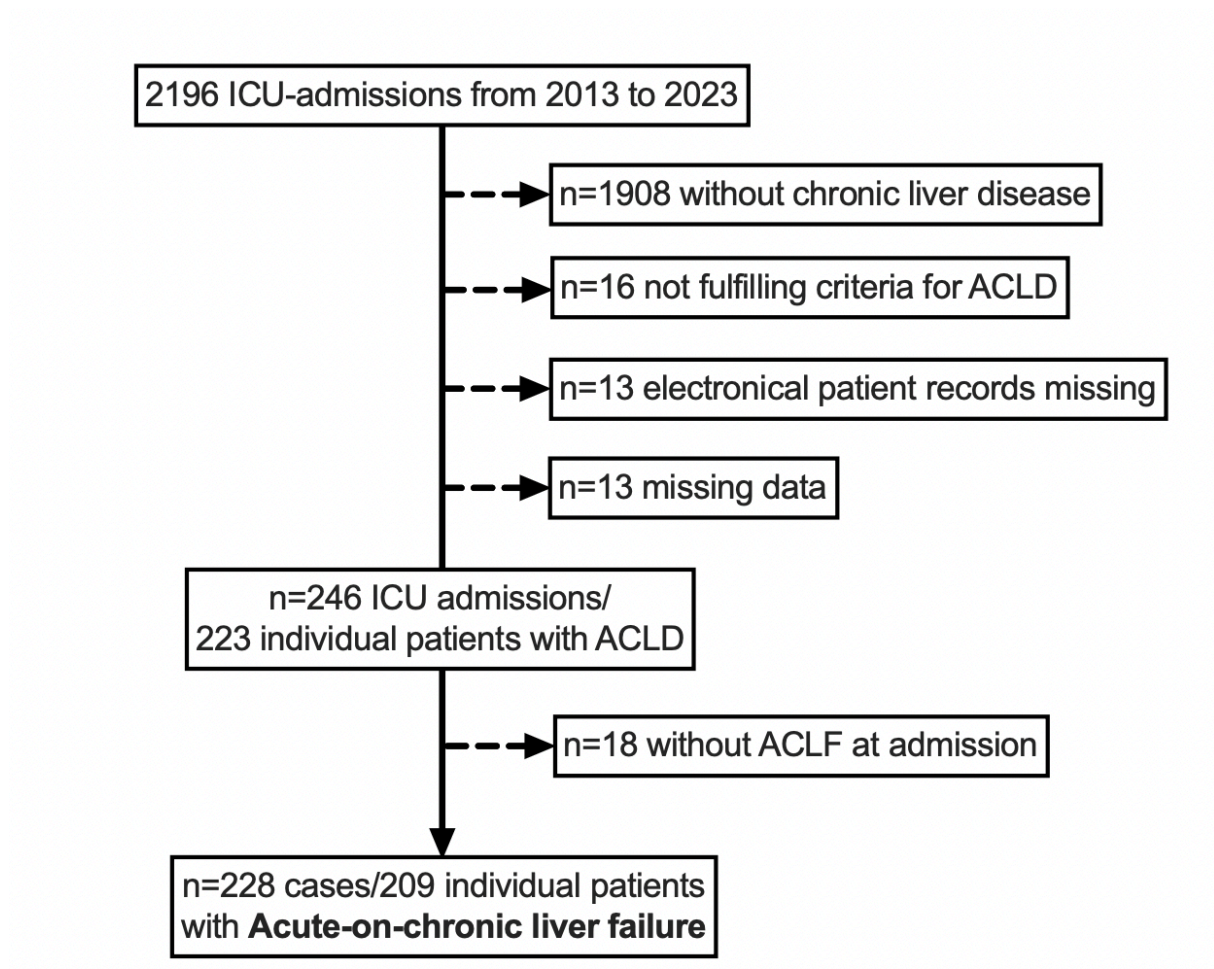
Variable	n	Univariate analysis			Multivariate analysis		
		OR	CI of 95%	p-value	OR	CI of 95%	p-value
CLIF-C ACLF score	228	1.09	1.06 - 1.13	<0.001	1.07	1.03 - 1.11	<0.001
Gender	228	0.95	0.53 - 1.72	0.854			
BMI	228	1.01	0.96 - 1.06	0.722			
Septic shock*	228	2.50	1.29 - 5.14	0.009	1.5	0.61 - 3.66	0.375
Respiratory failure*	228	0.84	0.36 - 2.03	0.692			
IMV	228	1.59	0.92 - 2.75	0.100	0.6	0.29 - 1.25	0.172
RRT	228	2.61	1.51 - 4.58	<0.001	1.91	1.00 - 3.66	0.050
Noradrenaline dose after 24 hours	228	32.7	6 - 178.48	<0.001	36.4	4.45 - 336.54	0.002
CRP**	228	1.01	0.97 - 1.04	0.746			
Platelets**	228	1.00	1.00 - 1.00	0.290			
Fibrinogen**	219	1.00	1.00 - 1.00	0.038	1.00	1.00 - 1.00	0.089

Univariate & multivariate analysis were conducted as binary logistic regression with odds ratio (OR) and 95% confidence interval. P-values <0.05 were determined as significant. After checking for multicollinearity (all variance inflation factors ≤ 1.3), multivariate analysis was conducted for parameters with a p-value ≤ 0.1 . Model performance of the multivariate logistic regression was given with an AUC = 0.793 (95% CI 0.733-0.852). Noradrenaline dose after 24 hours is given as $\mu\text{g/kg/min}$, CRP and fibrinogen in mg/dL , and platelets were given in G/L .

Abbreviations: ACLF, acute-on-chronic liver failure; BMI, Body mass index; CLIF-C ACLF, Chronic Liver Failure Consortium ACLF score; CRP, C-reactive protein; CI, Confidence Interval; IMV, invasive mechanical ventilation; RRT, Renal replacement therapy; OR, Odds Ratio.

* Septic shock and respiratory failure as reasons for ICU admission. ** Laboratory values (i.e., CRP, Platelets and Fibrinogen) collected at ICU admission.

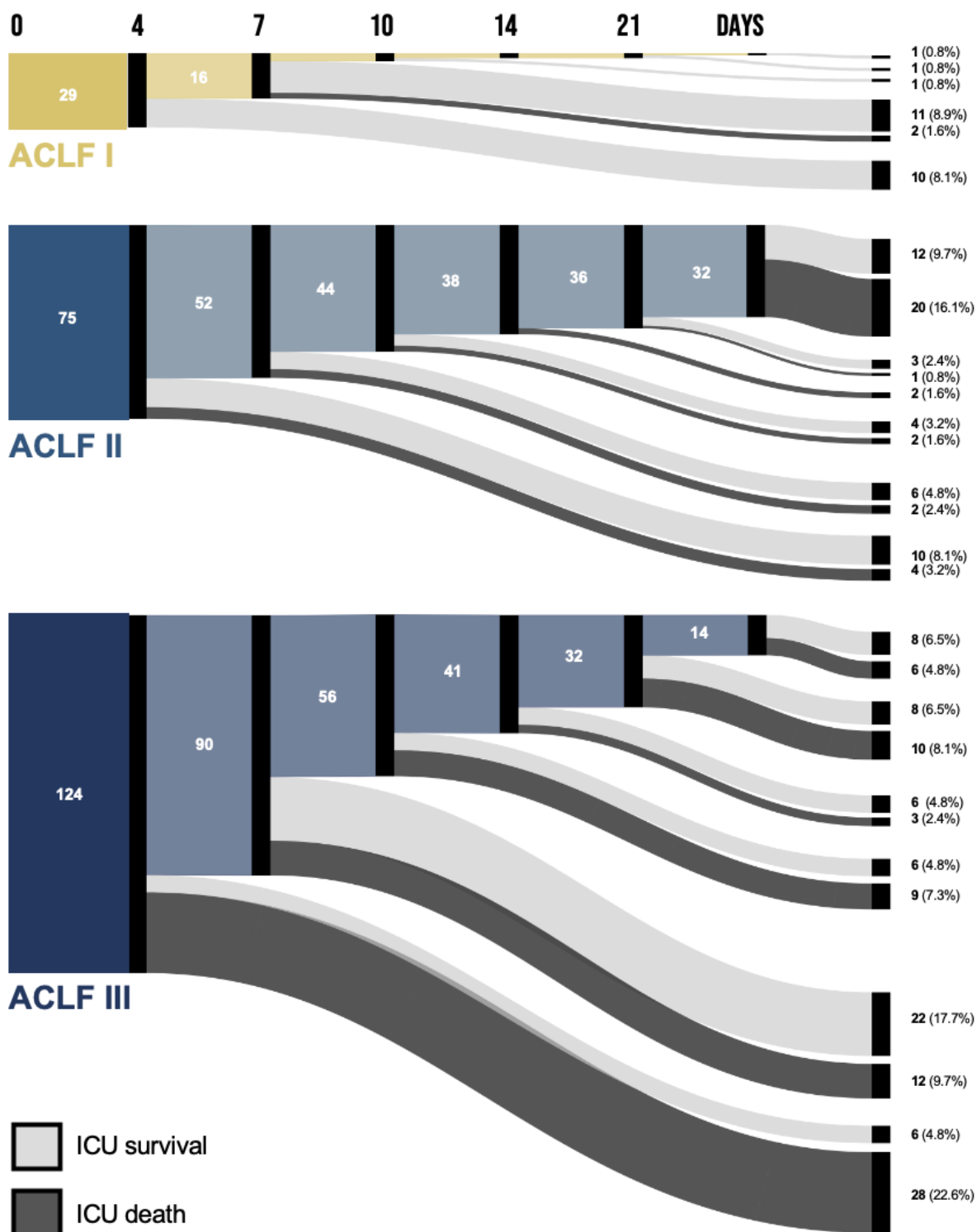
Supplementary Figure S1. Flowchart of the study population.



Supplementary Figure S1: Flow chart of the study population. All admitted patients to the ICU at the Department of Gastroenterology and Hepatology at the Medical University of Vienna from 2013 until 2023 were screened according to the predefined inclusion and exclusion criteria. All patients with criteria for ACLD, without significant lack of data and ACLF at ICU admission, were included in our study. 209 individual patients accounting for 228 cases were included.

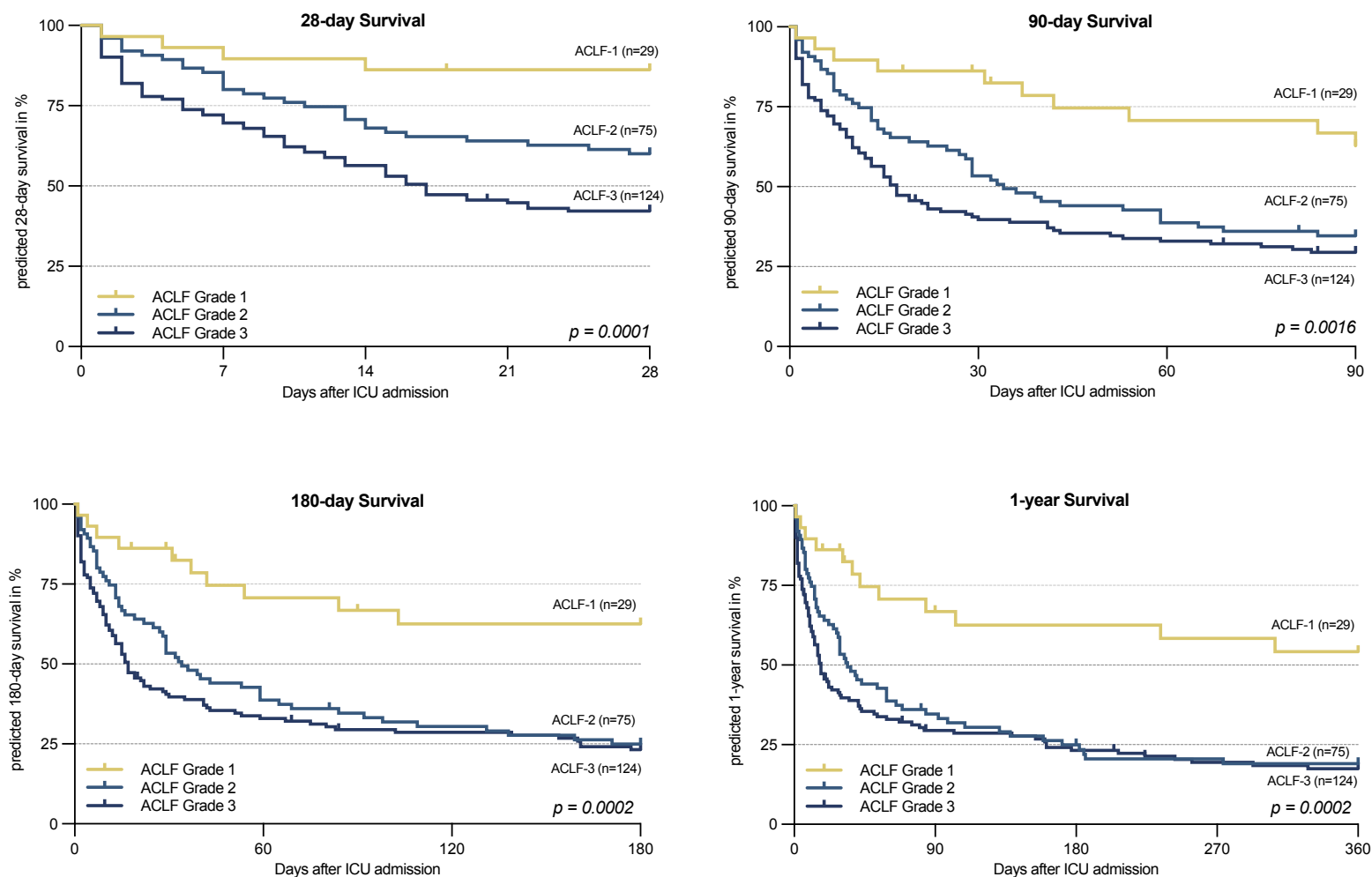
Supplementary Figure S2. Flow analysis of ICU survival or death after ICU-admission.

ICU ADMISSION



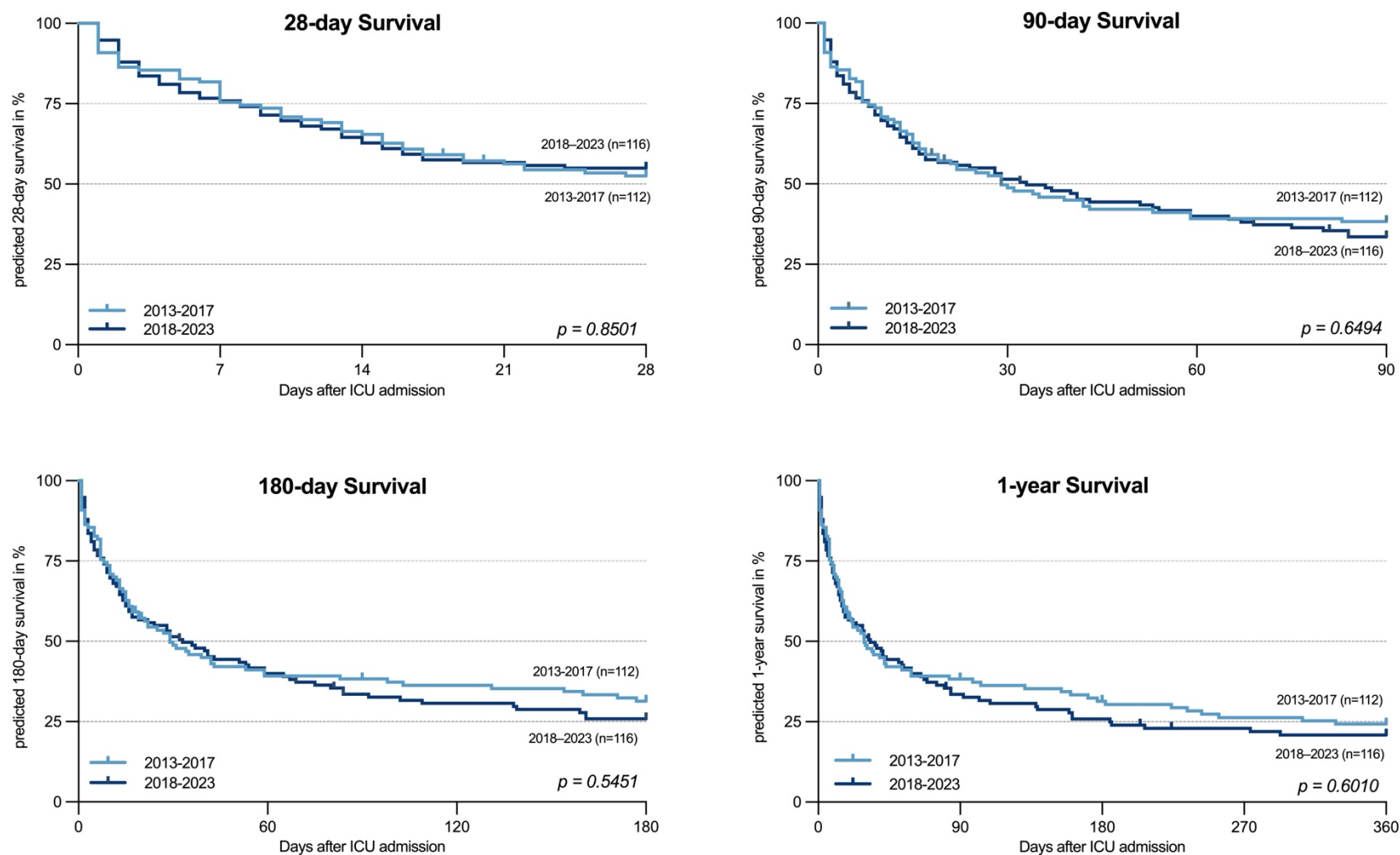
Supplementary Figure S2: Flow analysis of ICU survival or death after ICU-admission. Flow diagram illustrating ICU survival and mortality across patients stratified by ACLF grade (I-III) at admission. Light grey flows represent ICU survivors, and dark grey flows represent ICU deaths. The x-axis indicates time intervals after ICU admission (0-4, 5-7, 8-10, 11-14, 15-21, and >21 days). Absolute patient numbers and corresponding percentages are shown within each flow segment.

Supplementary Figure S3: Short- and long-term survival rates of ACLF grades.



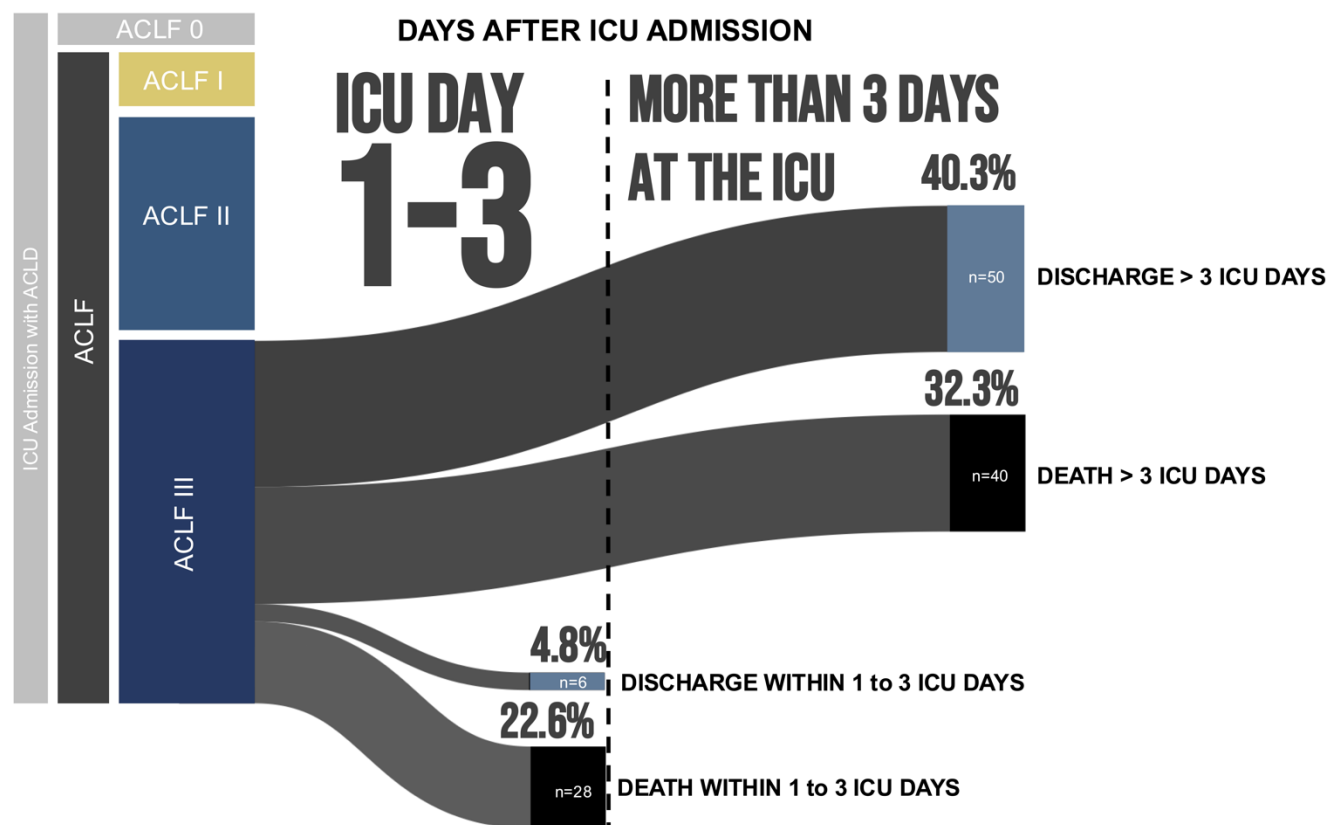
Supplementary Figure S3: Short- and long-term survival of ACLF grades. All included patients were separated into ACLF grades I, II, and III, as indicated. Survival analysis is given for 28-day, 90-day, 180-day, and 1-year survival. All survivals were calculated using a Kaplan-Meier analysis and log-rank test.

Supplementary Figure S4: Short- and long-term survival of early (2013-2017) vs. late admission (2018-2023).



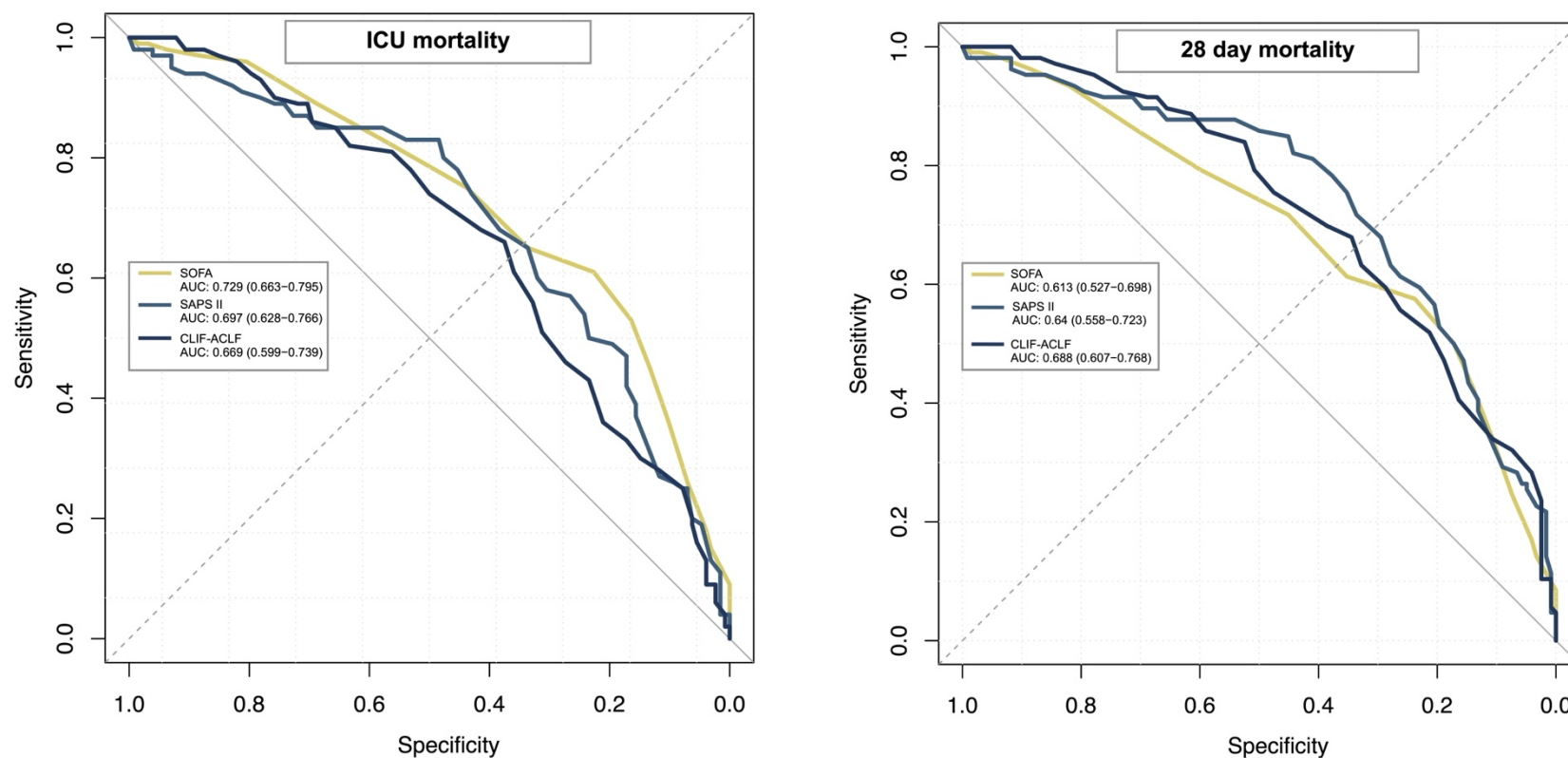
Supplementary Figure S4: Short- and long-term survival of early (2013-2017) vs. late admission (2018-2023). All included patients were separated according to admission dates (2013-2017 vs. 2018-2023), highlighted as light blue line for early admission (2013-2017) and dark blue line for late admission (2018-2023). Survival analysis is given for 28-day survival, 90-day, 180-day and 1-year survival. All survivals were calculated using a Kaplan-Meier analysis and log-rank test.

Figure S5: Outcome of patients with ACLF grade III depending on ICU LOS.



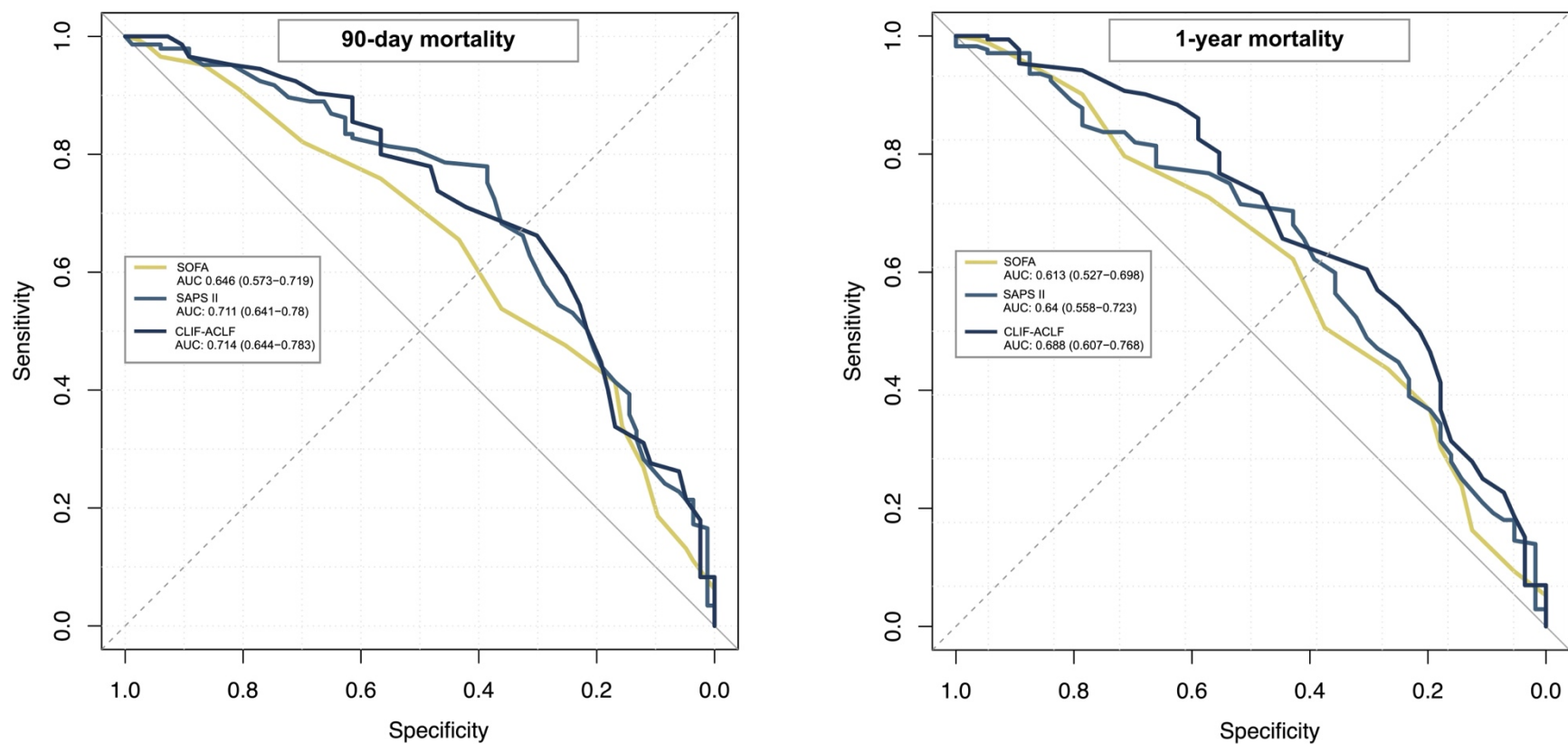
Supplementary Figure S5: Outcome of patients with ACLF grade III depending on ICU LOS. Patients with ACLF grade III were stratified by ICU stay duration (1-3 days vs. >3 days) and further categorized by outcome. Grey nodes indicate patients surviving ICU discharge, while black nodes represent ICU deaths. Absolute patient numbers are shown within each node.

Supplementary Figure S6: ROC analysis of CLIF-C ACLF and ICU-specific scores according to ICU and 28-day mortality.



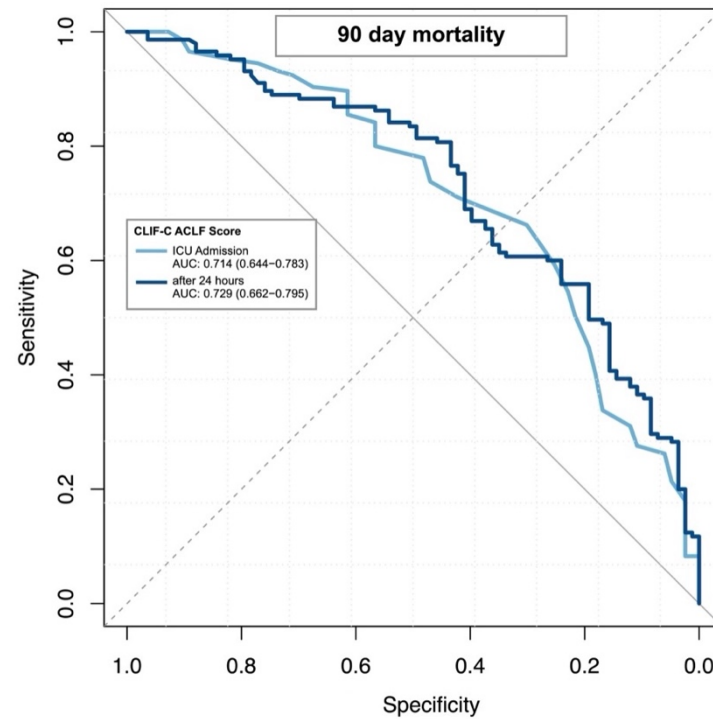
Supplementary Figure S6: ROC analysis of CLIF-C ACLF and ICU-specific scores according to ICU and 28-day mortality. Receiver operating characteristic (ROC) were given for Sequential Organ Failure Assessment (SOFA) score, Simplified Acute Physiology Score (SAPS) II and Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure (CLIF-C ACLF) score as indicated, predicting ICU- and 28-day mortality. Differences between AUCs did not reach statistical significance (DeLong $p > 0.05$).

Supplementary Figure S7: ROC analysis of CLIF-C ACLF and ICU-specific scores according to 90-day and 1-year mortality.



Supplementary Figure S7: ROC analysis of CLIF-C ACLF and ICU-specific scores according to 90-day and 1-year mortality. Receiver operating characteristic (ROC) curves for Sequential Organ Failure Assessment (SOFA) score, Simplified Acute Physiology Score (SAPS) II, and Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure (CLIF-C ACLF) score were provided as indicated, predicting 90-day and 1-year mortality. Differences between AUCs did not reach statistical significance (DeLong $p > 0.05$).

Supplementary Figure S8: ROC analysis of CLIF-C ACLF score at admission and after 24 hours according to 90-day mortality



Supplementary Figure S8: ROC analysis of CLIF-C ACLF score at admission and after 24 hours according to 90-day mortality. Receiver operating characteristic (ROC) curves were provided for the Chronic Liver Failure Consortium Acute-on-Chronic Liver Failure (CLIF-C ACLF) score, with a light blue line at admission and a dark blue line after 24 hours, predicting 90-day mortality. Differences between AUCs did not reach statistical significance (DeLong $p > 0.05$).