Supplementary material

Prospective validation of the EASL management algorithm for acute kidney injury in cirrhosis

Ann Thu Ma, Cristina Solé, Adrià Juanola, Laia Escudé, Laura Napoleone, Emma Avitabile, Martina Pérez-Guasch, Marta Carol, Enrico Pompili, Jordi Gratacós-Ginés, Anna Soria, Ana Belén Rubio, Marta Cervera, Maria José Moreta, Manuel Morales-Ruiz, Elsa Solà, Esteban Poch, Núria Fabrellas, Isabel Graupera, Elisa Pose, Pere Ginès.

Table of contents

Supplementary Figure S1 EASL AKI diagnosis and management algorithm

Supplementary Figure S2 Boxplot of urinary NGAL by AKI phenotype

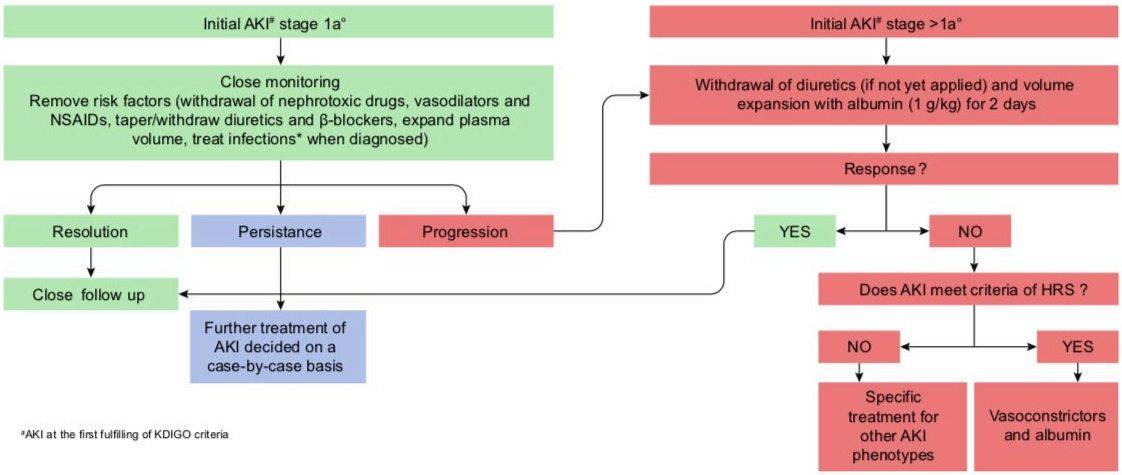
Supplementary Figure S3 Probability of 90-day transplant-free survival by AKI phenotype

Supplementary Table S1 Baseline characteristics of 202 AKI episodes at time of AKI diagnosis

Supplementary Table S2 Baseline characteristics of AKI that persists beyond 48h, by phenotype

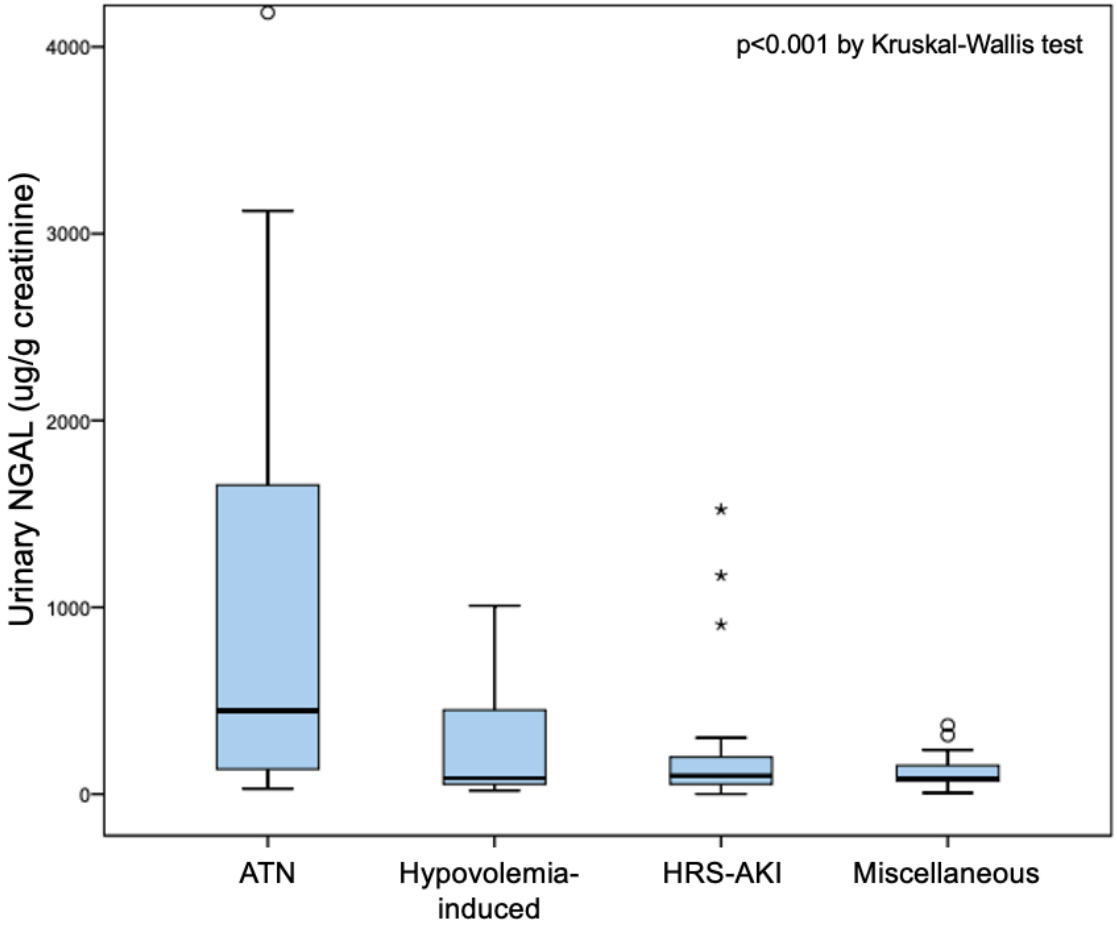
Supplementary Table S3 Multivariate Cox regression analysis for predictors of 90-day mortality

Supplementary Figure S1 EASL AKI diagnosis and management algorithm



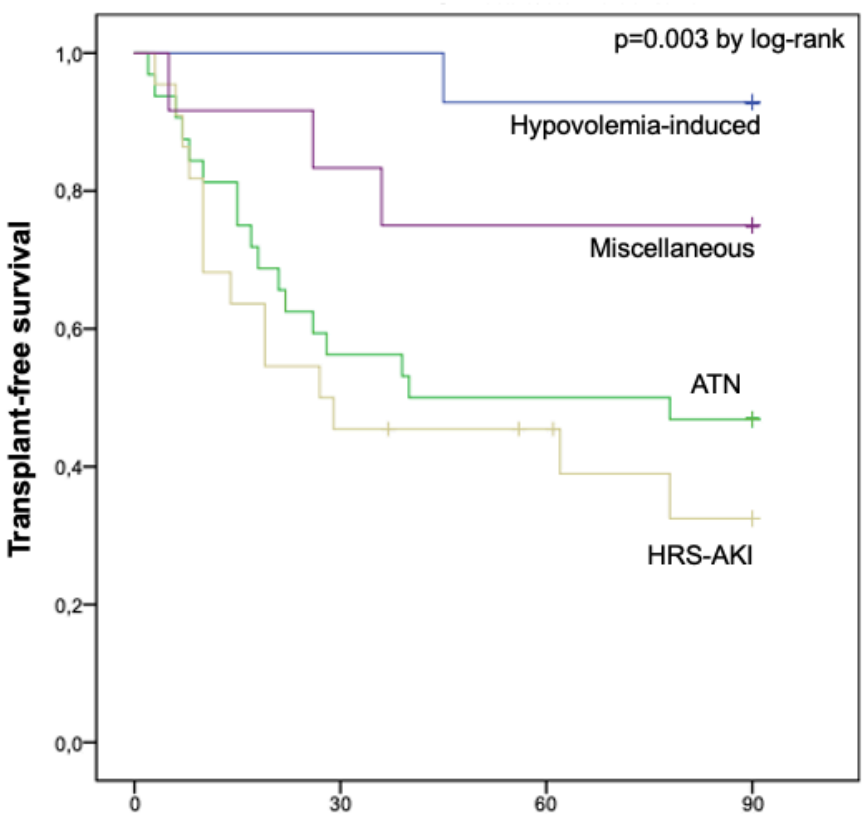
Supplementary Figure S2 Boxplot of urinary NGAL by AKI phenotype

Solid bold line represents median. Lower and upper limits of box represent 25th and 75th quartiles, respectively. Level of significance: p<0.001 (Kruskal-Wallis test).



Supplementary Figure S3 Probability of 90-day transplant-free survival by AKI phenotype in patients with persistent AKI ≥1B by day 3

Level of significance: p=0.003 (log rank).



N at risk				
Hypovolemia-induced	14	14	13	13
Miscellaneous	12	10	10	9
ATN	32	18	16	15
HRS-AKI	22	10	8	5

Supplementary Table S1 Baseline characteristics of 202 AKI episodes at time of AKI diagnosis

Characteristic		n=202 [a]
Age, years		62 [54-68]
Male gender		162 (80)
Cirrhosis etiology	Alcohol	123 (61)
	HCV	16 (8)
	MASLD	19 (9)
	Other	44 (22)
Type 2 diabetes		73 (36)
Chronic kidney disease		38 (19)
Ascites		160 (79)
Child-Pugh score	A / B / C	14 / 83 / 105 (7 / 41 / 52)
Infection		113 (56)
Gastrointestinal bleeding		18 (9)
Shock		31 (15)
Hospital-acquired AKI		74 (37)
AKI stage at diagnosis	1A / 1B / 2 / 3	42 / 90 / 36 / 34 (21 / 45 / 18 / 17)
MELD		23 [18-29]
MELD-Na		27 [22-31]
Creatinine (mg/dL)		1.9 [1.5-2.5]
Sodium (mEq/L)		133 [129-137]
Bilirubin (mg/dL)		2.9 [1.5-6.7]
Albumin (g/L)		29 [25-33]
CRP (mg/dL) [b]		3.0 [1.1-6.4]
WBC ($\times 10^9$/L)		6.8 [4.4-11.2]
Platelets ($\times 10^9$/L)		93 [56-150]
INR		1.6 [1.3-2.0]

[a] The 202 AKI episodes correspond to 139 individual patients.
[b] Available in 183/202 AKI episodes.
Continuous variables are presented as median [IQR], categorical as n (%).
CRP, C-reactive protein; HCV, hepatitis C virus; INR, international normalized ratio; MELD, model for end-stage; Na, sodium; MASLD, metabolic-associated steatotic liver disease; WBC, white blood count.

Supplementary Table S2 Baseline characteristics of AKI episodes that persisted beyond 48h, by phenotype

		Non HRS-AKI			HRS-AKI	p value
		Hypovolemia-induced	**ATN**	**Miscellaneous**		
		n=21	n=48	n=15	n=30	
Age, years		63 (58-72)	63 (52-70)	58 (49-64)	60 (50-64)	0.11
Male gender		17 (81)	38 (79)	9 (60)	28 (93)	0.06
Cirrhosis etiology	Alcohol	10 (48)	34 (71)	6 (40)	25 (83)	0.09
	HCV	1 (5)	2 (4)	1 (7)	1 (3)	
	MASLD	3 (15)	2 (4)	1 (7)	2 (7)	
Type 2 diabetes		8 (38)	13 (27)	3 (20)	11 (37)	0.55
CKD		6 (29)	10 (21)	3 (20)	8 (27)	0.86
Child-Pugh score	A / B / C	1 / 14 / 6 (5 / 67 / 29)	2 / 17 / 29 (4 / 35 / 60)	0 / 6 / 9 (0 / 40 / 60)	1 / 9 / 20 (3 / 30 / 67)	0.16
Ascites		16 (76)	37 (77)	14 (93)	30 (100)	0.06
Infection		9 (43)	36 (75)	7 (47)	18 (60)	**0.04**
MELD		23 [17-25]	28 [22-31]	28 [27-36]	28 [19-33]	**0.009**
MELD-Na		26 [18-28]	30 [26-32]	31 [28-36]	31 [23-36]	**<0.001**
Creatinine (mg/dL)		2.2 [1.9-3.1]	2.5 [1.7-4.0]	2.6 [2.3-3.6]	1.9 [1.6-2.2]	0.60
Sodium (mEq/L)		135 [131-138]	133 [128-137]	135 [127-139]	130 [125-134]	**0.02**
Bilirubin (mg/dL)		2.0 [0.8-3.1]	3.7 [1.5-6.6]	4.2 [1.0-6.7]	6.6 [1.8-26.1]	**0.03**
CRP (mg/dL)		6.5 [1.1-11.0]	5.3 [2.7-9.2]	3.8 [3.0-9.2]	2.5 [1.1-3.8]	0.05
WBC ($\times 10^9$/L)		6.6 [4.5-10.2]	8.2 [4.6-14.1]	9.1 [5.6-11.8]	7.1 [4.7-10.8]	0.70
Platelets ($\times 10^9$/L)		105 [69-173]	94 [49-149]	107 [61-161]	82 [55-123]	0.21
INR		1.4 [1.3-1.6]	1.7 [1.4-2.2]	1.8 [1.4-2.3]	1.8 [1.4-2.3]	0.13
uNGAL on day 3 (ug/g creat) **		86 [53-450]	446 [134-1654]	85 [69-153]	98 [53-198]	**<0.001**

** Available in 102/114 AKI episodes: 18/21 hypovolemia-induced, 41/48 ATN, 13/15 miscellaneous, 30/30 HRS-AKI,
Continuous variables are presented as median [p25-p75], categorical as n (%).
Statistical significance using Fisher's exact test, Mann-Whitney U test or Kruskal Wallis test, as appropriate.
ATN, acute tubular necrosis; CKD, chronic kidney disease; CRP, C-reactive protein; HCV, hepatitis C virus; HRS-AKI, hepatorenal syndrome-acute kidney injury; INR, international normalized ratio; MELD, model for end-stage; Na, sodium; MASLD, metabolic-associated steatotic liver disease; uNGAL, urinary neutrophil gelatinase-associated lipocalin; WBC, white blood count.

Supplementary Table S3 Multivariate Cox hazards regression analysis for predictors of 90-day mortality

	HR (95%CI)	p value
MODEL 1 [a]		
Age	1.05 (1.01-1.09)	0.007
MELD-Na	1.14 (1.08-1.21)	<0.001
ATN phenotype [b]	3.09 (1.37-6.97)	0.006
HRS-AKI phenotype [b]	4.19 (1.79-9.83)	0.001
MODEL 2 [a]		
Age	1.07 (1.02-1.11)	0.002
MELD-Na	1.14 (1.08-1.20)	<0.001
uNGAL	1.0002 (1.00006-1.0003)	0.023

ATN, acute tubular necrosis; MELD, model for end-stage; Na, sodium; OR, odds ratio; HR, hazard ratio. Statistical significance using likelihood ratio test.
[a] 139 patients included in Model 1, 82 in Model 2 (due to fewer patients with uNGAL measured on day 3). Of the 82 patients with uNGAL, 7 no longer had AKI ≥1B on day 3, but the uNGAL had been drawn prior to serum creatinine becoming available.
[b] Using hypovolemia-induced AKI as reference group.