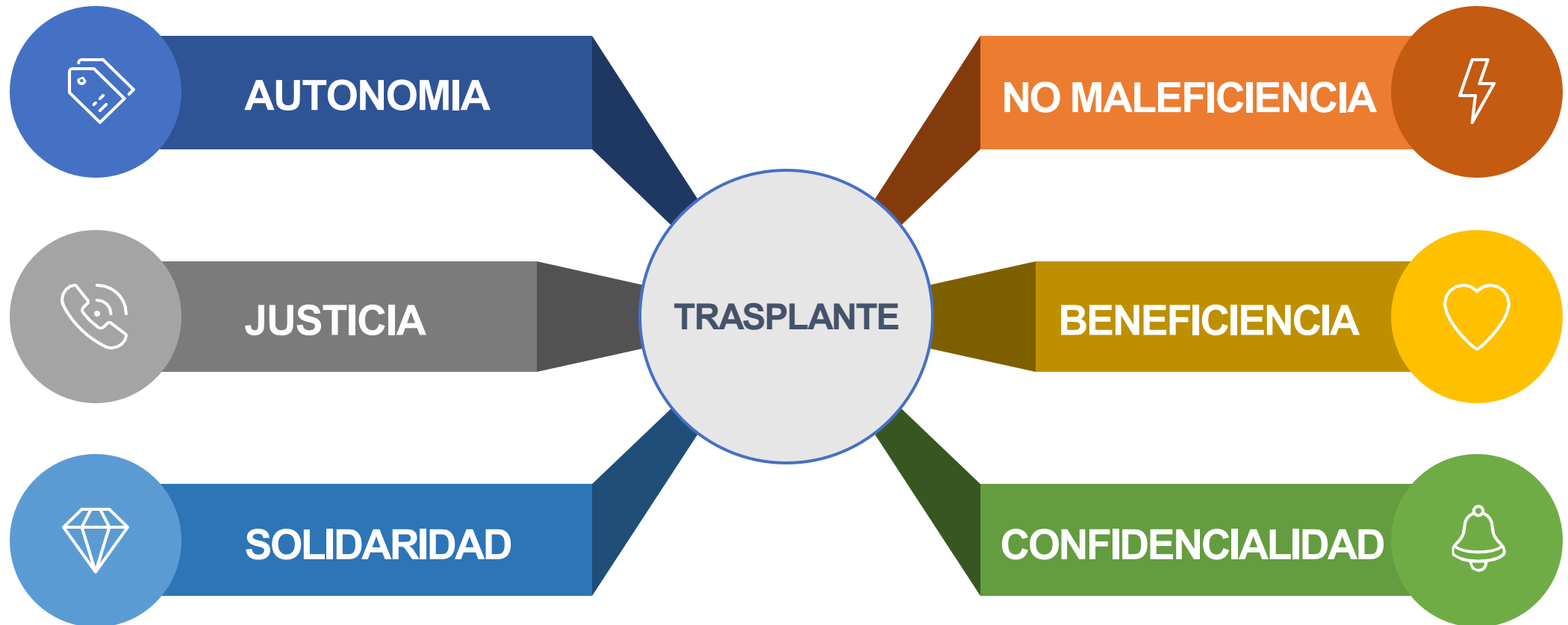# *ACLF y trasplante hepático. Utilidad y futilidad.*

Carmen Vinaixa Aunés

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Instituto de Salud Carlos III, CIBERehd

@SEThepatico

LaFe Hospital Universitari i Politècnic

ciberehd
Centro de Investigación Biomédica en Red
Enfermedades Hepáticas y Digestivas

seth
FUNDACIÓN SOCIEDAD ESPAÑOLA DE TRASPLANTE HEPÁTICO

Hospital General Universitario Dr. Balmis

GENERALITAT VALENCIANA

PRINCIPIOS ÉTICOS
EN MEDICINA

AUTONOMIA

JUSTICIA

SOLIDARIDAD

TRASPLANTE

NO MALEFICIENCIA

BENEFICIENCIA

CONFIDENCIALIDAD

Principios éticos en trasplante

- Beneficiencia

- Beneficiencia
- No maleficiencia

Resultados post-TH del receptor

Mortalidad en lista de espera

Seguridad del donante (LDLT)

Recursos sanitarios

- No maleficiencia

- Justicia
- Equidad

Utilidad en Trasplante: Definición

Beneficio en supervivencia

Beneficio económico para la comunidad

Beneficio en calidad de vida

Futilidad en Trasplante: Definición

No hay una cifra mágica….pero:

➢ **Supervivencia < 3 meses post-TH o durante ingreso**

➢ **Supervivencia < 50% a 1 del TH**

➢ **Supervivencia < 30% a los 6 meses**

….combinados con criterios clínicos objetivos y evaluación multidisciplinar.

ACLF: Definición CLIF-C / CANONIC

- Pacientes jóvenes (50-55 años) con cirrosis descompensada
- Desarrollo simultáneo de:
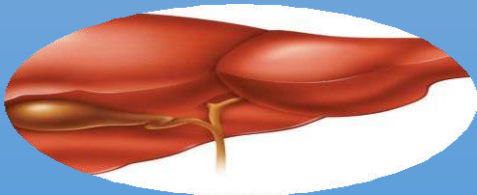
Descompensación hepática aguda

- Ascitis
- Encefalopatía
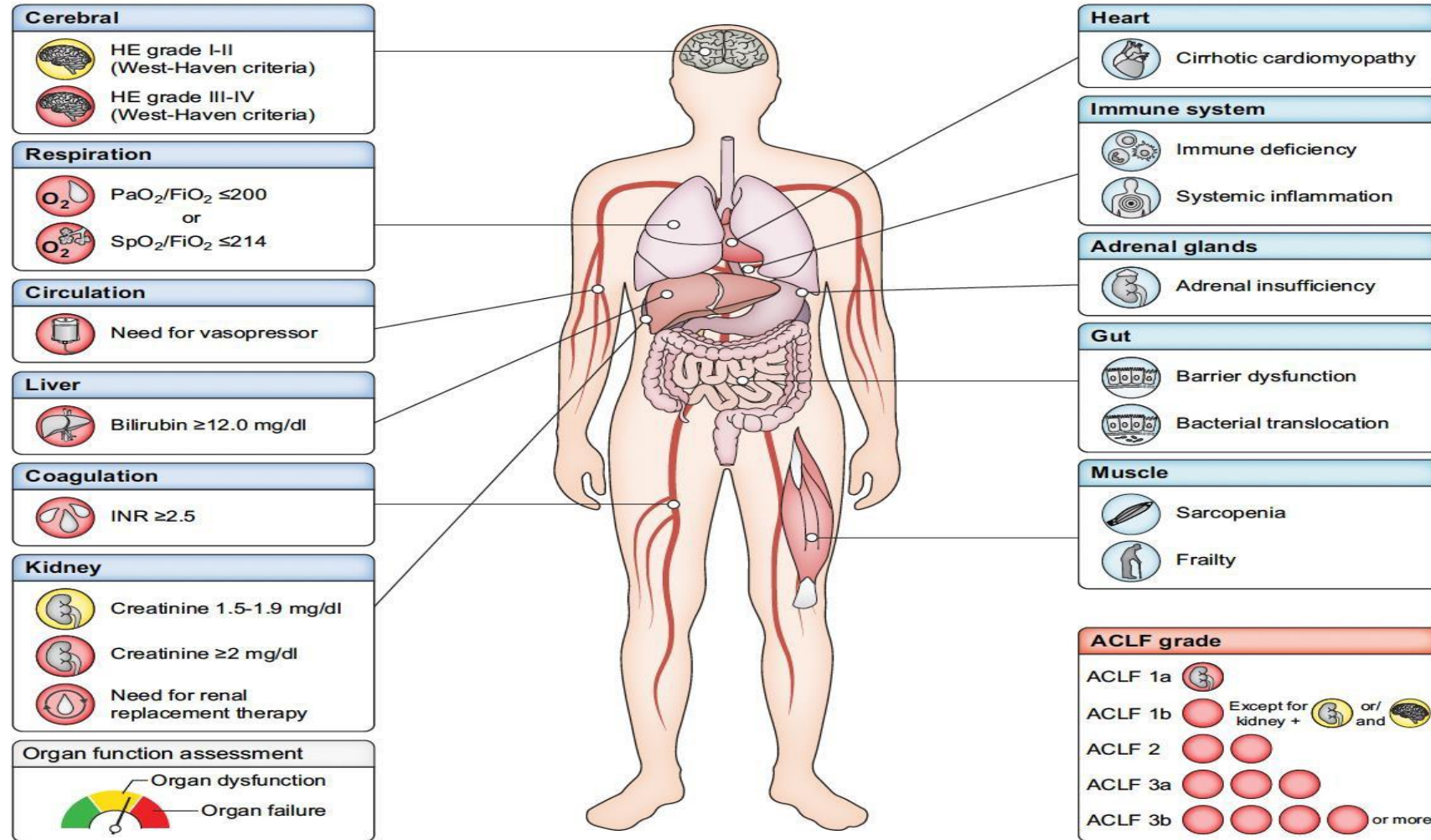- HDA
- +/- Infección bacteriana

Fracaso orgánico (1 o más órganos)

- Hígado
- Riñón
- Cerebro
- Coagulación
- Circulatorio
- Respiratorio

Inflamación sistémica severa

Peor pronóstico que descompensación aguda aislada

Moreau R et al. Gastroenterology 2013

ACLF: Fracasos orgánicos y clasificación pronóstica

Cerebral
- HE grade I-II (West-Haven criteria)
- HE grade III-IV (West-Haven criteria)

Respiration
- $PaO_2/FiO_2 \leq 200$ or
- $SpO_2/FiO_2 \leq 214$

Circulation
- Need for vasopressor

Liver
- Bilirubin ≥ 12.0 mg/dl

Coagulation
- INR ≥ 2.5

Kidney
- Creatinine 1.5-1.9 mg/dl
- Creatinine ≥ 2 mg/dl
- Need for renal replacement therapy

Organ function assessment
- Organ dysfunction
- Organ failure

Heart
- Cirrhotic cardiomyopathy

Immune system
- Immune deficiency
- Systemic inflammation

Adrenal glands
- Adrenal insufficiency

Gut
- Barrier dysfunction
- Bacterial translocation

Muscle
- Sarcopenia
- Frailty

ACLF grade
- ACLF 1a
- ACLF 1b — Except for kidney + or/ and
- ACLF 2
- ACLF 3a
- ACLF 3b — or more

CLIF-C ACLF score =

CLIF-C OF score
+
Edad
+
Recuento leucocitos

Estimación mortalidad 3, 6, 12 meses

Moreau R, EASL CPG ACLF 2023

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PRONÓSTICO ACLF: Estudio CANONIC

Grados de ACLF	Características clínicas	N	Mortalidad 28 días	Mortalidad 90 días
No ACLF	No hay fallo orgánico, o únicamente uno que no sea el riñón (Creatinina <1.5, no EH)	1040 (77%)	4,7%	14%
ACLF grado 1a	Fallo renal (Creat > 2 mg/dL)	148 (11%)	22%	40,7%
ACLF grado 1b	FO (no renal) + Cr. >1.5 y <2 y/o EH grado 1-2			
ACLF grado 2	2 fallos orgánicos	108 (8%)	32%	52%
ACLF grado 3	3 o más fallos orgánicos.	47 (3,5%)	76,7%	79,1%

Moreau R et al. Gastroenterology 2013

ACLF SIN TRASPLANTE HEPÁTICO

ACLF-3 : resultados pre y post-TH

Estudio/ Autor	Tipo de estudio	N ACLF-3	Mortalidad en LE	Supervivencia Post-TH	Comentarios
Artru (2017)	3 centros franceses Retrospectivo 2008-2014	73 TH	NA	73% (1 año)	Buenos resultados del TH en ACLF
Levesque (2017)	1 centro francés Retrospectivo 2008-2013	30 TH	NA	43% (1 año)	Confirma ACLF como factor de riesgo de mortalidad a 90 días
Tuluvath (2018)	UNOS Retrospectivo 2002-2016	2515 en LE 3556 TH	>92% a 30 días	81% (1 año)	Identificó predictores de superv post-TH *Tiempo LE corto
Sundaram (2018)	UNOS Retrospectivo 2005-2016	5355 LE 6381 TH	44% a 28 días	78% (1 año)	MELD no predice supervivencia post-TH
Sundaram (2019)	UNOS Retrospectivo 2002-2014	5009 en LE	33% a 28 días	NA	Mayor mortalidad en LE ACLF-3 q UNOS status 1a
Artzner (2020)	5 centros franceses Retrospectivo 2007-2017	152 TH	NA	83% (1 año)	TAM score Escasa info en datos donantes

Survival With and Without Liver Transplantation in Critically Ill Patients With Cirrhosis: A 20-Year Experience

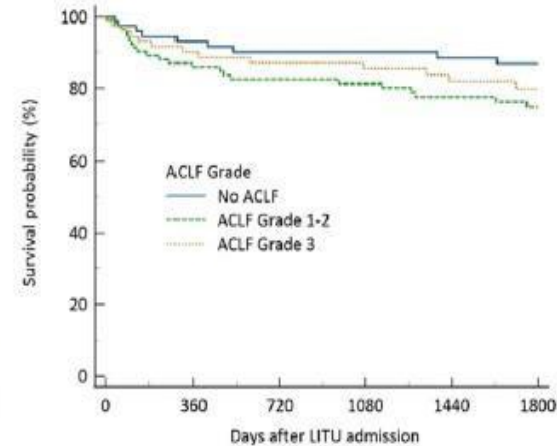Survival with and without liver transplantation in critically ill patients with cirrhosis: a twenty-year experience.
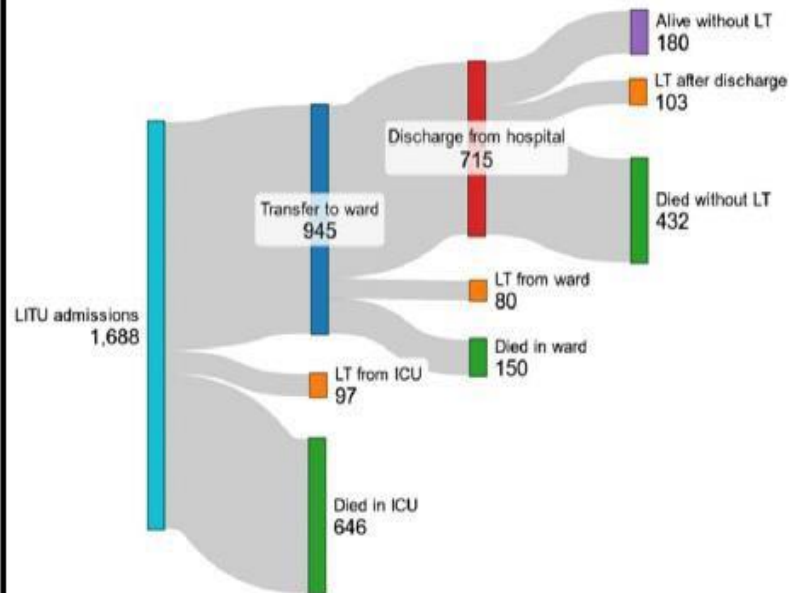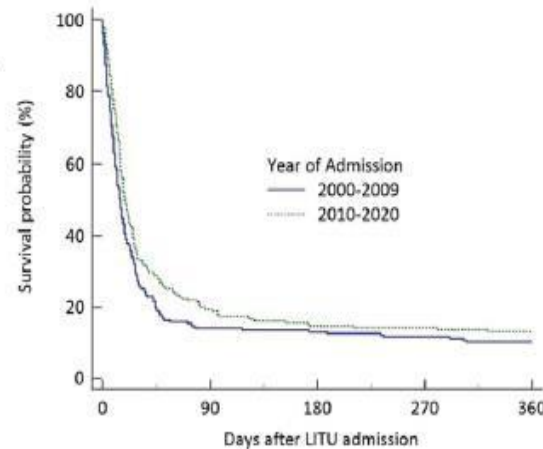
UK. King's College.
Restropectivo

N=1688
39% ACLF-3

Supervivencia > 1 año
ACLF-3 sin TH: **< 20%**

Bernal W et al. Clin Gastro and Hepatology 2025

ACLF y TRASPLANTE HEPÁTICO

Mortalidad pre y post-TH en ACLF

Belli L et al. *JHep* 2021

ACLF-3 : resultados pre y post-TH

Estudio/ Autor	Tipo de estudio	N ACLF-3	Mortalidad en LE	Supervivencia Post-TH	Comentarios
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Liver transplantation in the most severely ill cirrhotic patients: A multicenter study in acute-on-chronic liver failure grade 3

3 centros franceses
N = 73 ACLF-3
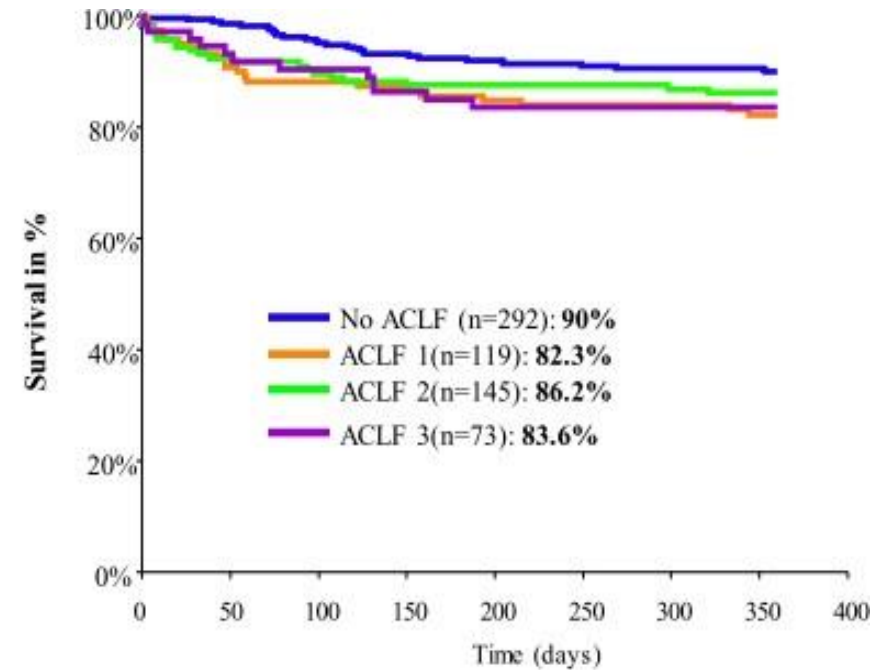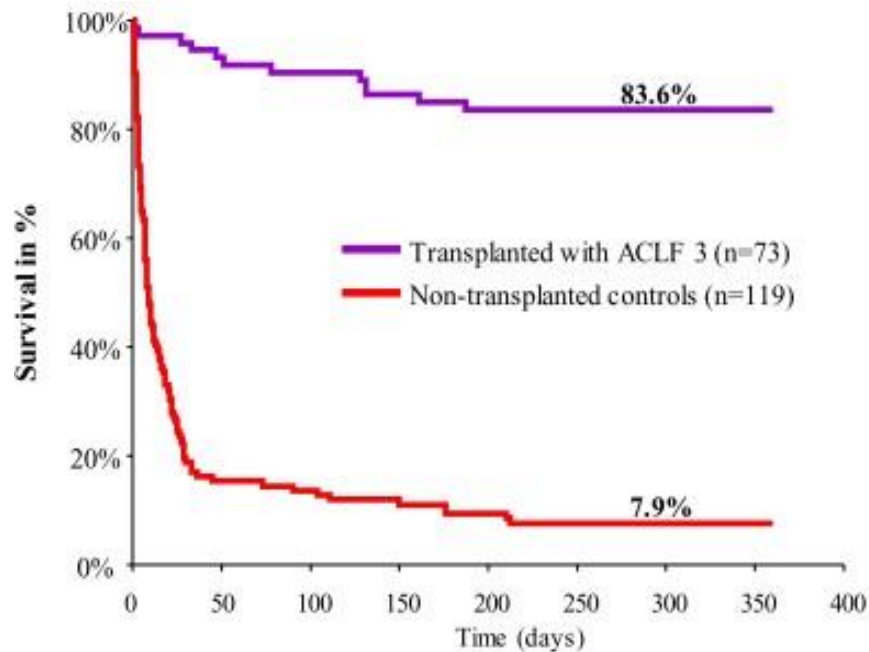
➔ *Pero mayor número de complicaciones post-TH*

Artru F, Louvet A, Ruiz I, et al. Liver transplantation in the most severely ill cirrhotic patients: A multicenter study in acute-on-chronic liver failure grade 3. *J Hepatol*. 2017;67(4):708-715.

Factors Associated with Survival of Patients With Severe Acute-On-Chronic Liver Failure Before and After Liver Transplantation

Vinay Sundaram,[1,*] **Rajiv Jalan**,[2,*] Tiffany Wu,[3] Michael L. Volk,[4] Sumeet K. Asrani,[5] Andrew S. Klein,[6] and Robert J. Wong[7]

- N=100.594 pacientes en LE; N= 50.552 TH entre 2005-2016, N=6.381 ACLF-3

- Base de datos UNOS, retrospectivo

➔ *Pacientes con ACLF-3 tenían más probabilidad de morir o salir de LE, independientemente del MELD-Na*
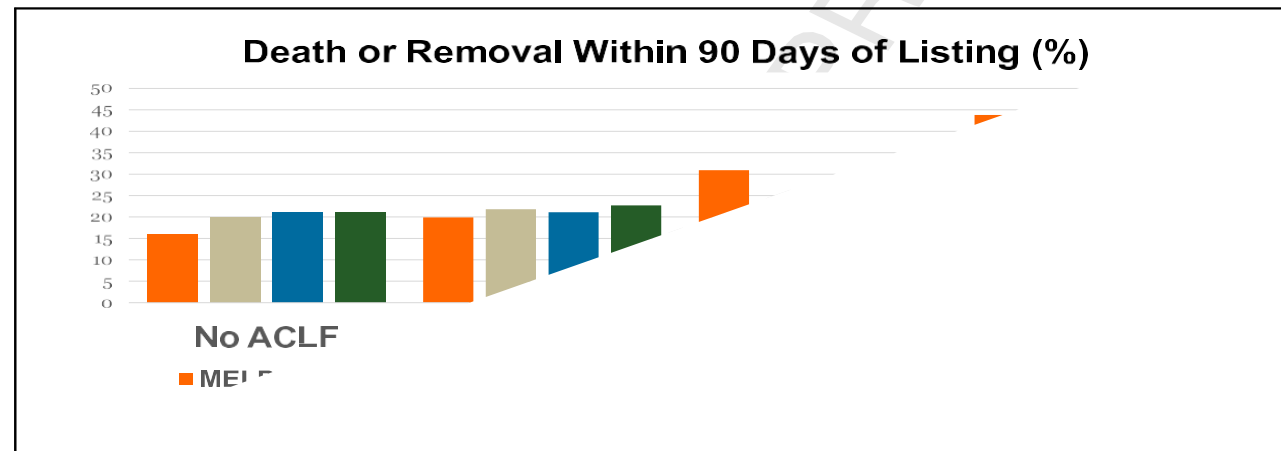
Death or Removal Within 90 Days of Listing (%)

Factors Associated with Survival of Patients With Severe Acute-On-Chronic Liver Failure Before and After Liver Transplantation

Vinay Sundaram,[1,*] **Rajiv Jalan**,[2,*] Tiffany Wu,[3] Michael L. Volk,[4] Sumeet K. Asrani,[5] Andrew S. Klein,[6] and Robert J. Wong[7]

Table 4. Univariable and Multivariable Cox Proportional Hazards Regression Evaluating Risk Factors for 1-Year Posttransplant Mortality Among Patients With ACLF-3
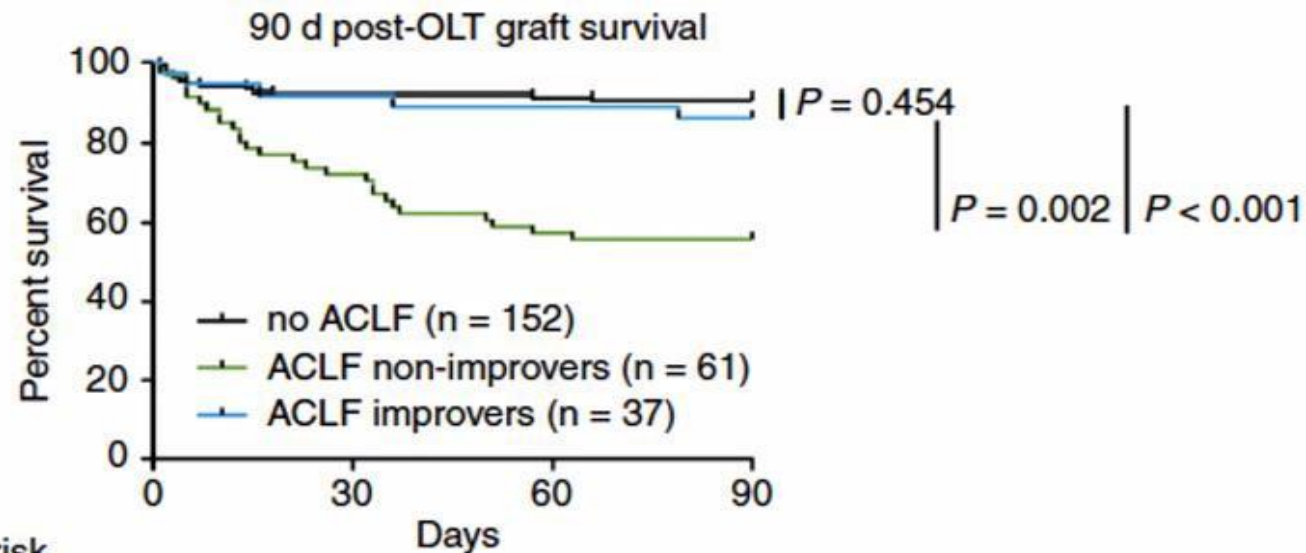
	Univariable analysis HR (95% CI)	Multivariable analysis[a] HR (95% CI)
Functional status ≥80%	0.65 (0.47–0.89)	0.76 (0.55–1.06)
Futility score >8 points	1.57 (1.42–1.74)	1.12 (0.97–1.30)
Donor risk index ≥1.7	1.25 (1.12–1.40)	1.22 (1.09–1.35)
Transplant within 30 days of listing	0.87 (0.79–0.96)	0.89 (0.81–0.98)
Mechanical ventilation	1.56 (1.42–1.72)	1.49 (1.22–1.84)
Circulatory failure	1.37 (1.24–1.51)	0.90 (0.78–1.05)
4 or more organ failures	1.28 (1.16–1.41)	1.04 (0.92–1.19)

ACLF: Evaluación dinámica

OLT-Survival score

- CLIF-C ACLF score
  +
- Mejoría clínica

(A) 90-day post-transplant survival in non-ACLF patients, ACLF improvers and ACLF non-improvers

90 d post-OLT graft survival

no ACLF (n = 152)
ACLF non-improvers (n = 61)
ACLF improvers (n = 37)

$P = 0.454$
$P = 0.002$ $P < 0.001$

patients at risk				
Non-ACLF	152	141	140	138
ACLF Improvers	37	35	34	32
ACLF non-improvers	61	45	36	34

Huebener et al. APT 2018

Liver transplantation for critically ill patients with acute on chronic liver failure: a prospective national programme of waitlist prioritisation. UK.
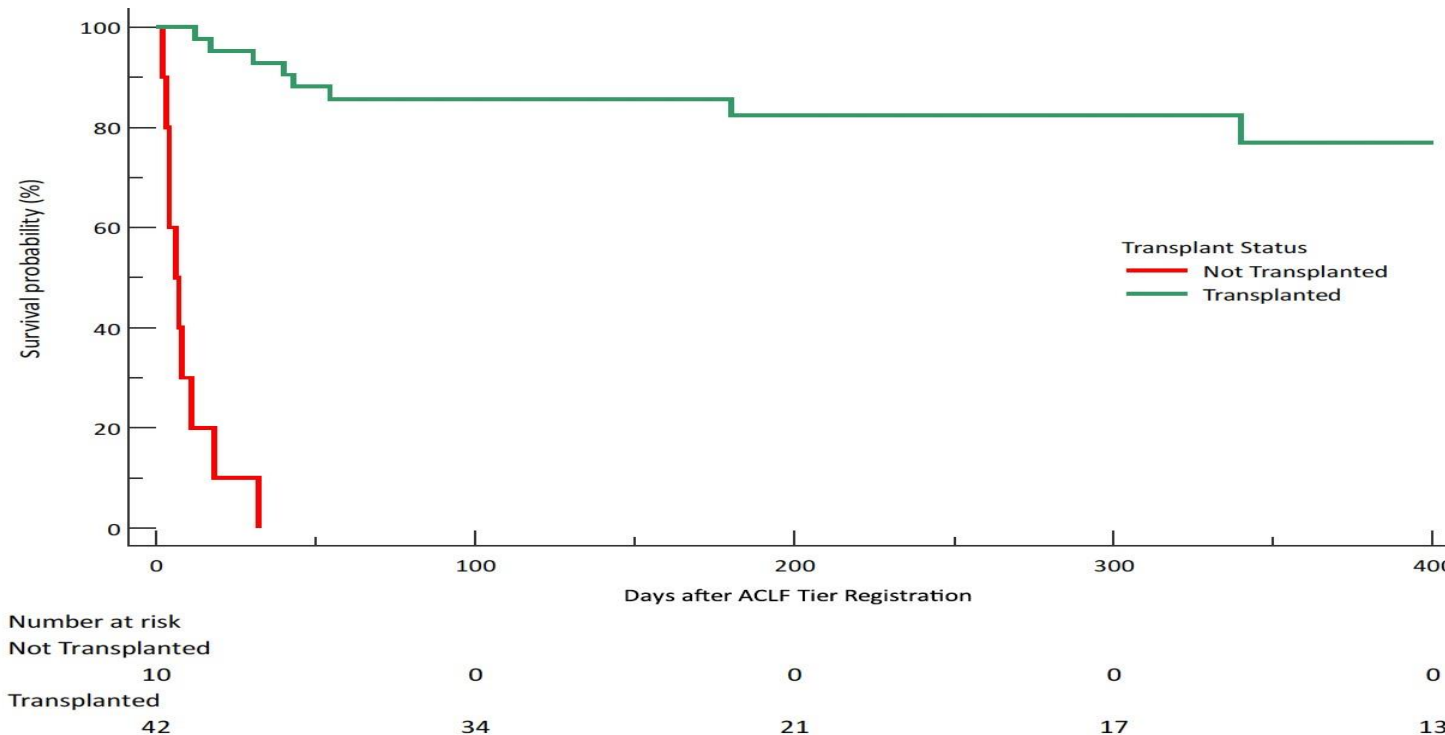

Fig. 1: Survival after ACLF tier registration according to Transplant Status. Note: p < 0.001 Log-rank.

UK. 7 centros.
Prospectivo.

N=52 ACLF-3 ➔ 42 TH

➔ Criterio de <u>futilidad</u> pre-establecido:
supervivencia < 60% al año

➔ <u>Priorización</u> si supervivencia esperada a 28 días < 50%

**Grupo TH:
Supervivencia 1 año 77%**

Bernal, W., Taylor, R., Rowe, I. A., Chauhan, A., Armstrong, M. J., Allison, M. E. D., Webb, G., Pirani, T., Moore, J., Burke, L., Masson, S., Cressy, D., Hogan, B. J., Westbrook, R., Jalan, R., Simpson, K. J., Isaac, J., & Thorburn, D. (2024). Liver transplantation for critically ill patients with acute on chronic liver failure: a prospective national programme of waitlist prioritisation. *The Lancet regional health. Europe, 46*, 101067. https://doi.org/10.1016/j.lanepe.2024.101067

Mortalidad post-TH en ACLF. EEUU.

Reduced short-term survival following liver transplant in patients with acute-on-chronic liver failure: Reevaluating OPTN data

Study Population and Methods

- Retrospective cohort study (OPTN: 1013-23)
- Included adult, first-time DDLT candidates
- Exposure: Severe ACLF (grade 3) at WL/LT
- Outcomes: Patient survival post-LT
- Marginal structural model (MSM) to address selection bias and time-varying exposure.
- Extended Cox PH models to account for non-proportional hazard over time

Directed Acyclic Graph: DAG to illustrate the MSM*
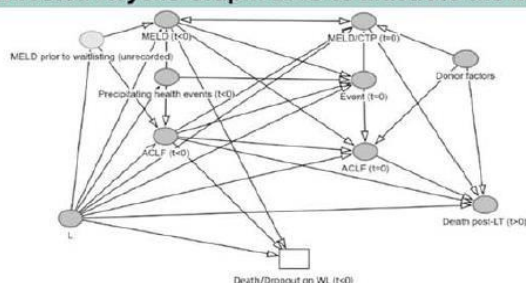
Outcomes
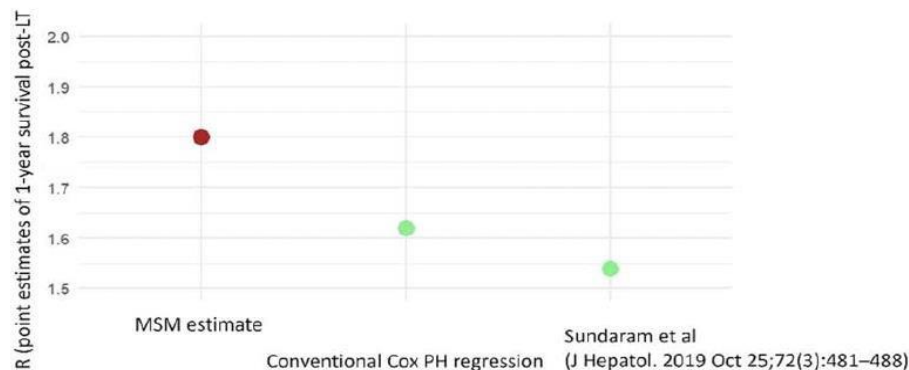
- 31,267 LT candidates: 11.3% (3,518) had ACLF-3 at listing
- 13.6% (4,243) died or dropped out on the waitlist
- 27,024 LT recipients: 12.3% (3,333) had ACLF-3 at LT
- **ACLF-3 at LT linked to higher 1-year post-LT death risk (HR 1.80, 95% CI 1.09–2.97) but not thereafter**
- MSM effect size 9% higher than literature and the conventional Cox PH model in this cohort (HR: ~1.5-1.6)

HR (point estimates of 1-year survival post-LT)

MSM estimate

Conventional Cox PH regression

Sundaram et al (J Hepatol. 2019 Oct 25;72(3):481–488)

AASLD Tanaka, et al | *Hepatology Communications.* 2025.

Hepatology Communications

OPTN. EEUU.
Restropectivo.
2013 - 2023

31,267 candidatos TH
11% ACLF-3 (inscripción)
14% excluidos LE

27,024 TH
12% ACLF-3 (en TH)
➔ mayor mortalidad 1 año post-TH
➔ Resultados favorables a largo plazo

eliminan sesgo selección

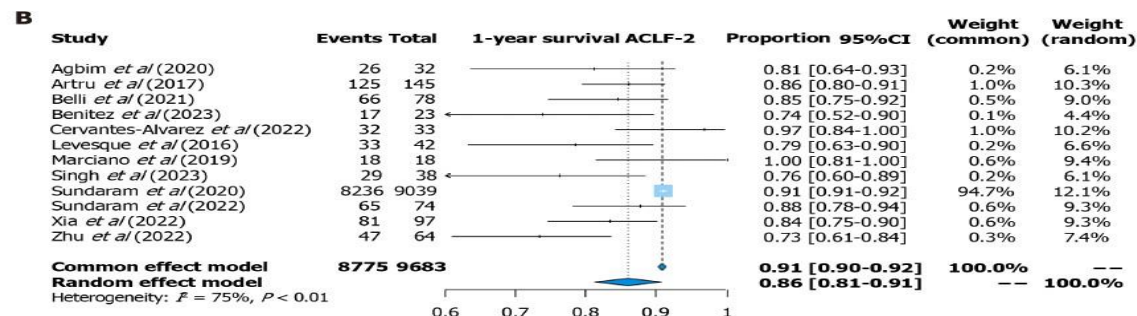# Meta-análisis supervivencia ACLF 1 año post-TH

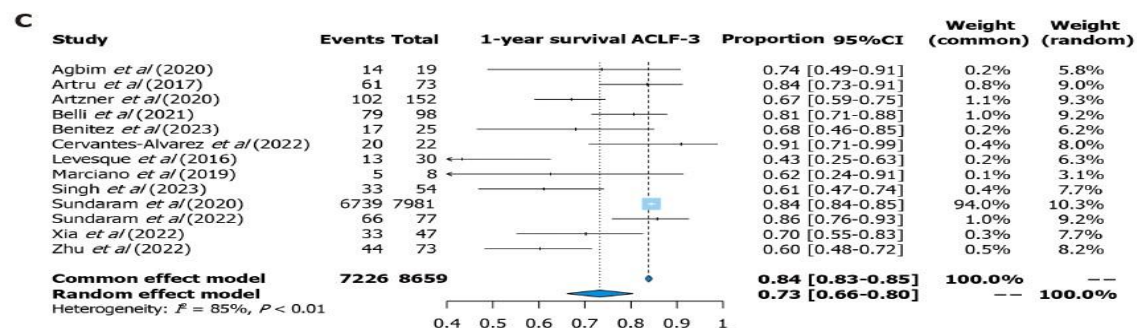17 estudios
28000 pacientes
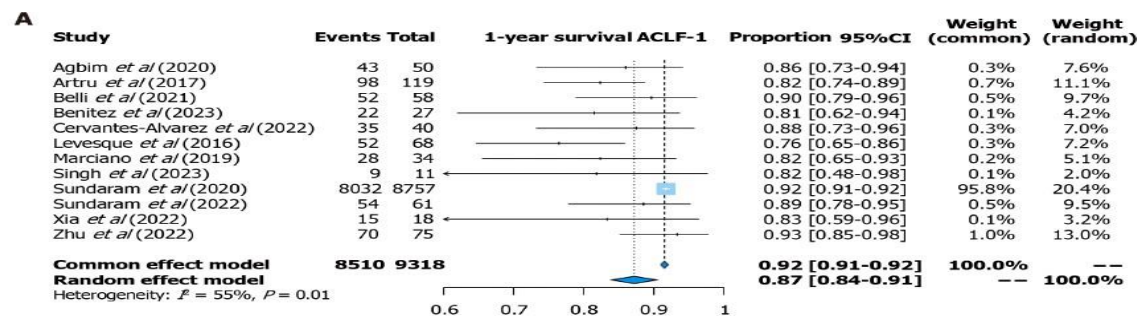
ACLF-1 — 87%

ACLF-2 — 86%

ACLF-3 — 73%

Figure 5 One-year survival following liver transplantation among acute-on-chronic liver failure patients stratified by severity grades. A: One-year survival for acute-on-chronic liver failure (ACLF)-1 patients; B: One-year survival for ACLF-2 patients; C: One-year survival for ACLF-3 patients. ACLF: Acute-on-chronic liver failure; CI: Confidence interval.

Li et al. WJG 2025

ACLF: Evolución según tipo de fracaso orgánico

Kaplan-Meier Curve of Overall Survival Stratified by Organ Failure Combinations

Organ Failure Combinations	Event	Total	HR (95% CI)
combination of circulatory and other OF	42	429	0.65 (0.47-0.91)
combination of circulatory and respiratory and other OF	226	1268	Reference
other combinations	460	3357	0.78 (0.66-0.91)

Logrank P-value: 0.0020

Kaplan-Meier Curve of Overall Survival Stratified by Organ Failure Combinations

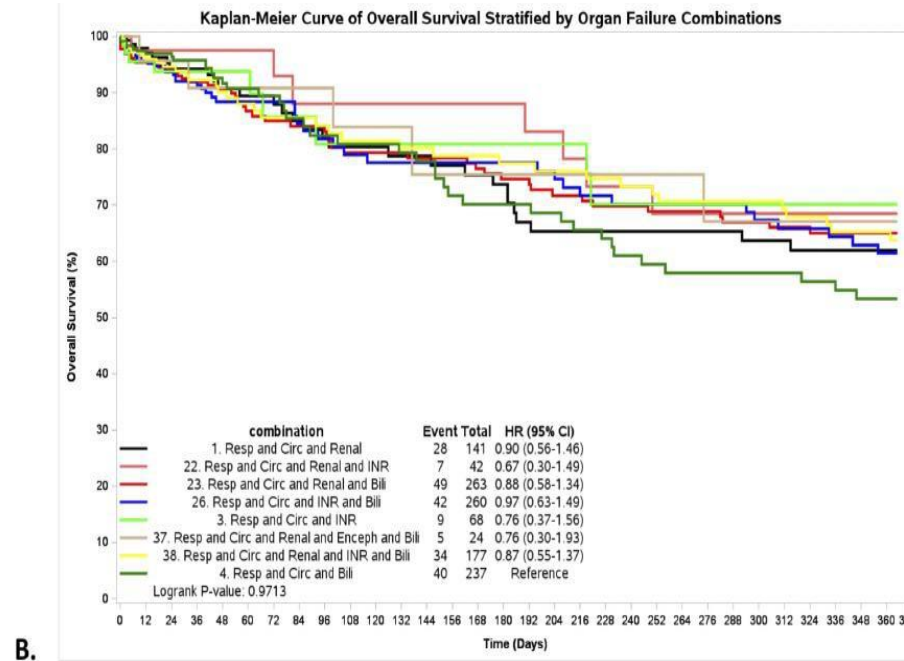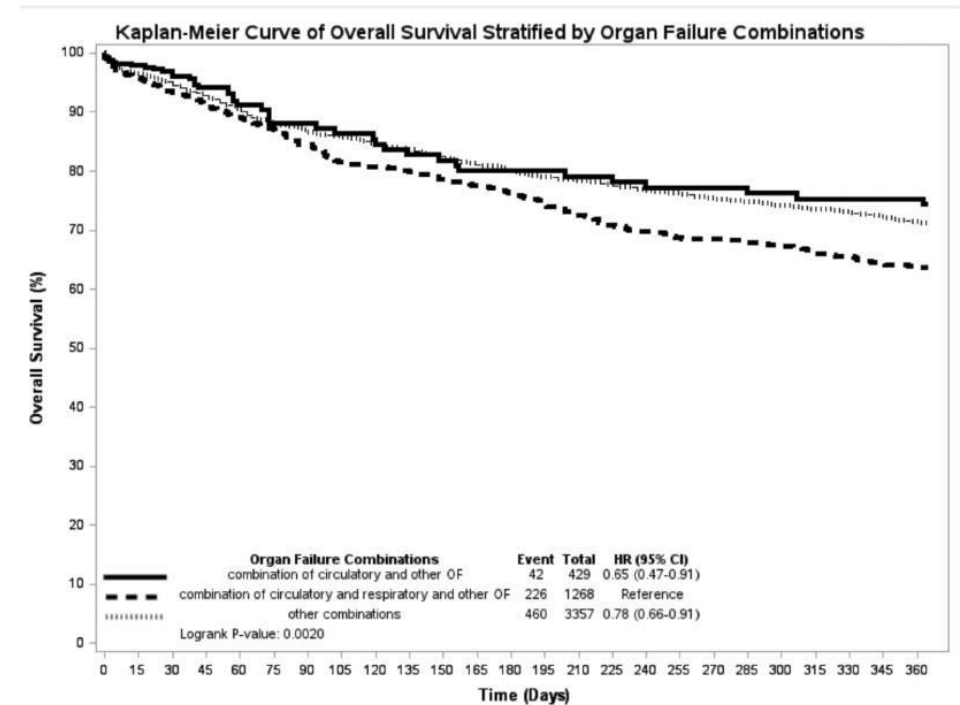| combination	Event	Total	HR (95% CI)
1. Resp and Circ and Renal	28	141	0.90 (0.56-1.46)
22. Resp and Circ and Renal and INR	7	42	0.67 (0.30-1.49)
23. Resp and Circ and Renal and Bili	49	263	0.88 (0.58-1.34)
26. Resp and Circ and INR and Bili	42	260	0.97 (0.63-1.49)
3. Resp and Circ and INR	9	68	0.76 (0.37-1.56)
37. Resp and Circ and Renal and Enceph and Bili	5	24	0.76 (0.30-1.93)
38. Resp and Circ and Renal and INR and Bili	34	177	0.87 (0.55-1.37)
4. Resp and Circ and Bili	40	237	Reference

Logrank P-value: 0.9713

B.

Fig. 2. Survival analysis of different groups of organ failures and 1-year mortality.
Panel A: Kaplan-Meier survival analysis for different organ failure groups and 1-year mortality. The analysis reveals a higher mortality rate in the group with both respiratory and circulatory failures compared to other groups. Panel B: Kaplan-Meier survival analysis within the respiratory and circulatory failure group, including only groups of permutation that contains at least 20 subjects. The analysis compares the survival rates of sub-groups, indicating no significant differences within this group.

SRTR. EEUU. Restropectivo.

N=5054 ACLF-3

Peor supervivencia y peor estadio funcional en pacientes con **fracaso circulatorio + respiratorio** independientemente del número de fracasos orgánicos

Wozniak, H., Zhao, X., Chen, S., Herridge, M. S., & Bhat, M. (2025). Stratifying risk in ACLF-3 patients: The impact of circulatory and respiratory failure on one-year post-transplant outcomes. *Journal of critical care*, *89*, 155129. https://doi.org/10.1016/j.jcrc.2025.155129

Mortalidad en LE de TH en ACLF

NT-proBNP predict the development of acute-on-chronic liver failure and mortality in patients with cirrhosis listed for liver transplantation

AIM: To evaluate N-terminal pro-B-type natriuretic peptide (NT-proBNP) as a predictor of acute-on-chronic liver failure (ACLF) and mortality in patients on the waiting list (WL) for liver transplantation (LT).

Single-center study (2014–2020, Hospital Italiano de Buenos Aires)

277 patients with cirrhosis included on the WL for LT.

NT-proBNP, clinical data, sarcopenia, CysC, and liver disease severity were collected at WL inclusion.

Median follow-up in WL: 10.5 (4–20.8) months

- 32% patients develop ACLF in WL.
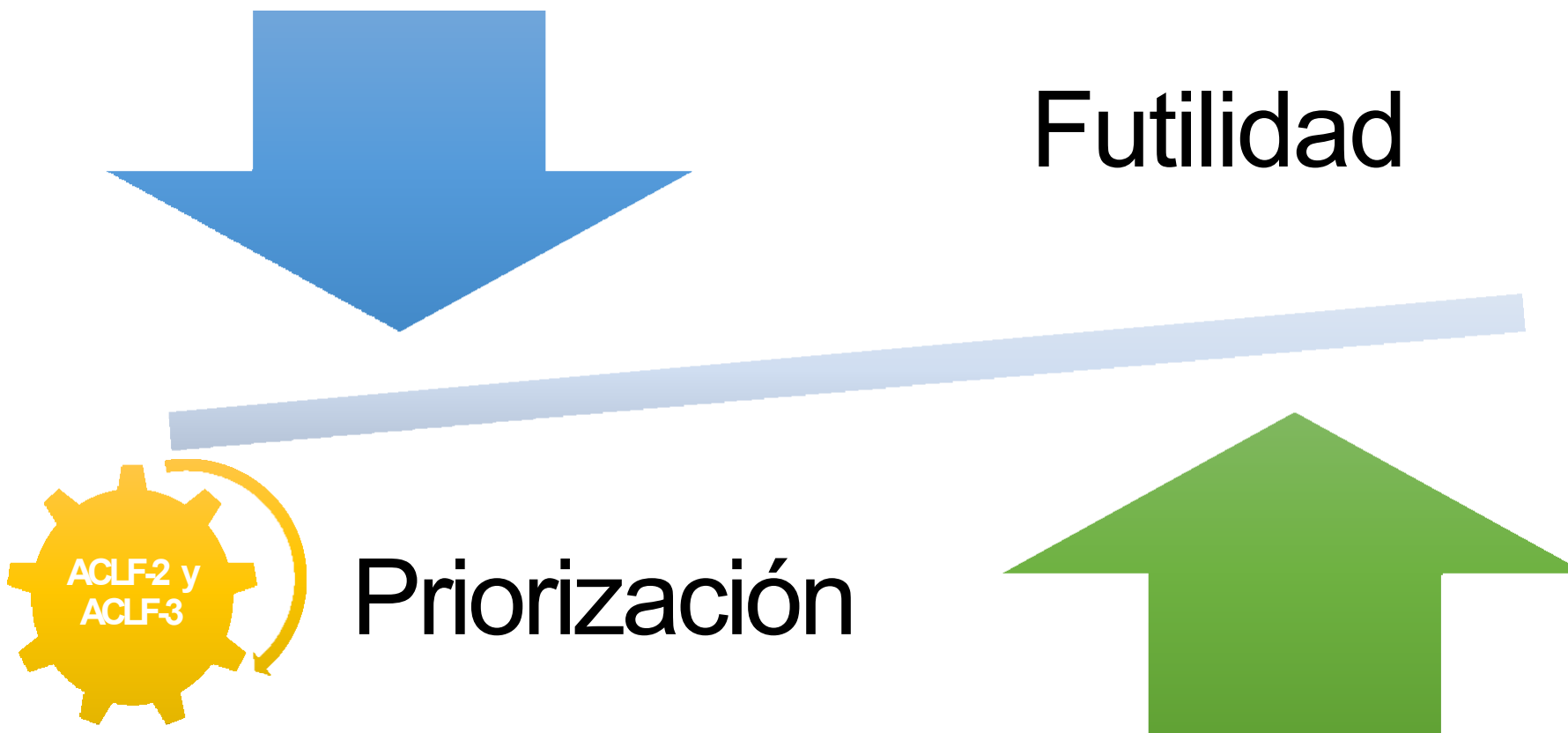- 31% patients underwent LT.
- 4% died/delisted without ACLF.

In competing risk analysis, after adjusting for MELD-Na and CysC, NT-proBNP was independently associated with ACLF and mortality on the WL.

	sub-HR (95% IC)	p-value
ACLF in WL		
NT-proBNP ≥ 125 pg/mL	4.00 (1.76-9.10)	0.001
CysC ≥ 1.5 mg/L, yes vs no	2.72 (1.43-5.14)	0.002
MELD-Na, in 1 units	1.16 (1.11-1.21)	<0.001
Death in WL		
NT-proBNP ≥ 125 pg/mL	3.89 (1.28-11.79)	0.016
CysC ≥ 1.5 mg/L, yes vs no	5.89 (2.17-15.99)	<0.001
MELD-Na, in 1 units	1.00 (0.94-1.05)	0.992
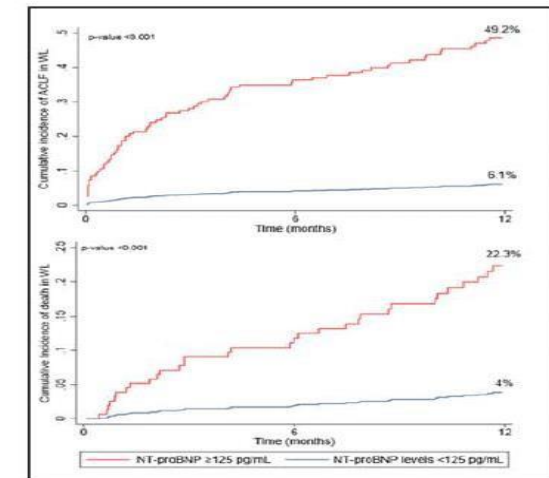
Incorporating NT-proBNP into clinical practice may improve risk stratification, enable early intervention, and optimize prioritization for LT candidates.
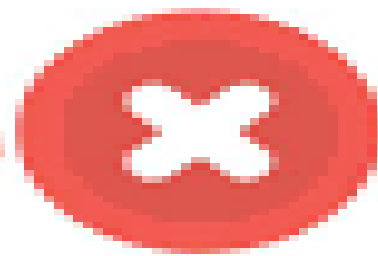
AASLD   Diaz, et at.| Liver Transplantation 2025   Liver Transplantation

ACLF y Trasplante

Futilidad

ACLF-2 y ACLF-3

Priorización

TH en ACLF

PROS

Beneficio en supervivencia a corto plazo

CONS

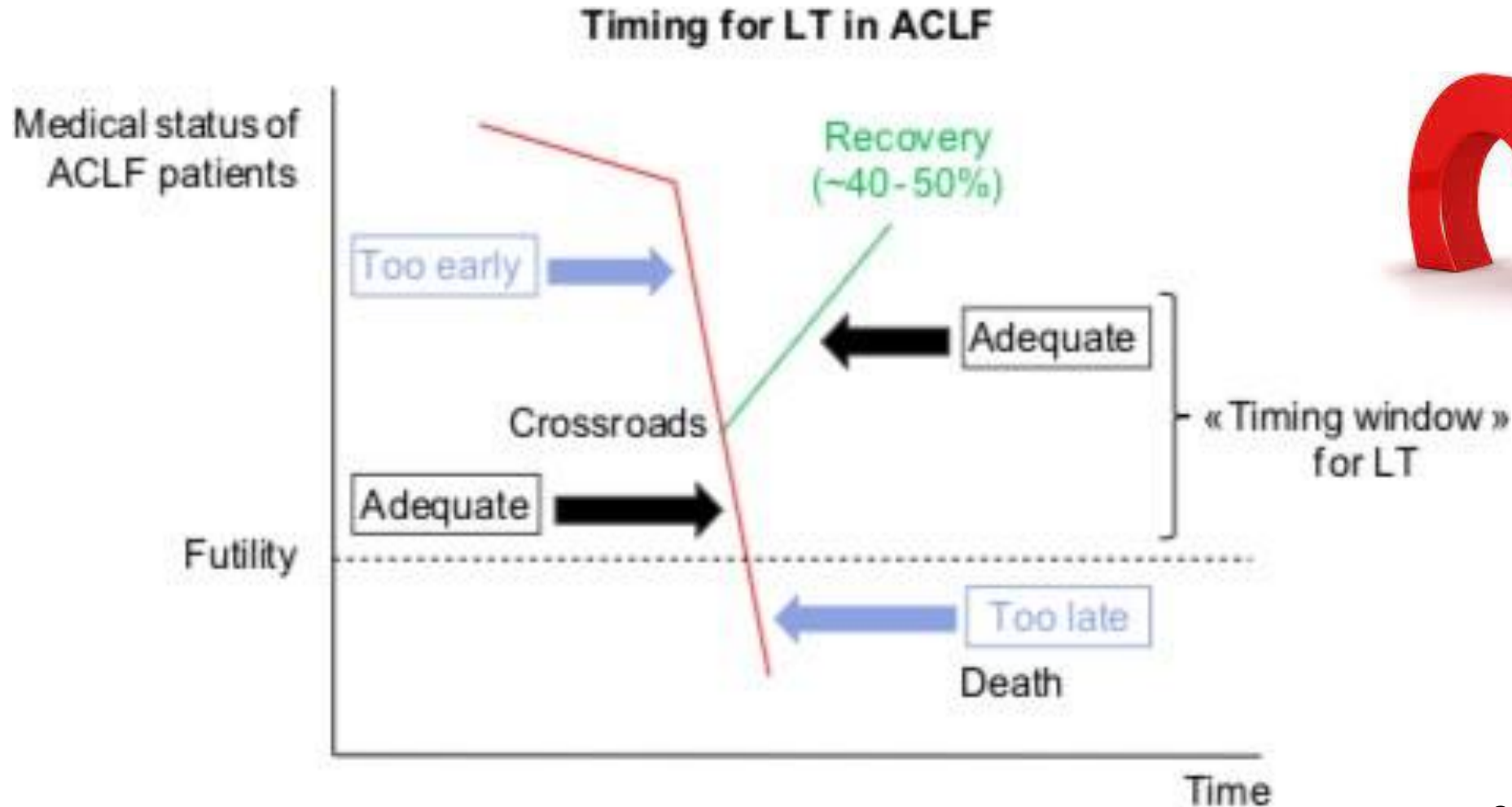Supervivencia y calidad de vida a largo plazo?

Empleo de órganos sobre otras indicaciones

Momento idóneo del TH: Ventana para TH

Timing for LT in ACLF

Momento idóneo del TH: Ventana para TH

FIGURE 1 | Concept of the "transplantation window" during a critical care hospitalization in severe ACLF with different scenari. **(A)** Rapid improvement of severe ACLF: patients must be referred to a LT center for evaluation as 1-year transplant-free survival is between 20% and 60%. **(B)** One transplantation window. **(C)** Two transplantation windows. The first "transplantation window" is likely more favorable ("greener") than the second, as the patient presents with fewer complications related to hospitalization (e.g., deconditioning, colonization by multidrug-resistant bacteria, etc.). **(D)** Absence of transplantation window commonly due to uncontrolled sepsis and organ failure. *Adapted from Artru, Trovato et al., Lancet Gastroenterol. Hepatol. 2024.* [64].

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Momento idóneo del TH: Priorización?

"short-term outcomes for ACLF recipients—especially those transplanted from the ICU—remain inferior to those of patients with decompensated cirrhosis transplanted outside of critical care. This raises concerns about the overall impact on transplant outcomes should the indication for ACLF broaden significantly."

Should patients with acute-on-chronic liver failure grade 3 receive higher priority for liver transplantation? Artru, Florent et al. Journal of Hepatology, Volume 78, Issue 6, 1118 - 1123

Futilidad del trasplante

➢ **Supervivencia < 3 meses (90 días) post-TH o durante ingreso**

➢ **Supervivencia < 50% a 1 año del TH**

➢ **Supervivencia < 30% a los 6 meses**

- En el estudio CANONIC, alcanzaron criterios de futilidad pacientes con ACLF-3 inicialmente y:
  - ≥4 fallos de órganos **(N=18)**
  - **CLIF-C ACLF score >64** a los 3-7 días del diagnóstico de ACLF

  ➜ Mortalidad 100% a los 90 días

Validación CLIF-C ACLF score

- Estudio CANONIC: (N=47 ACLF-3)
CLIF-C ACLF score > 64 puntos ➜
futilidad

- Estudio H.Royal Free,
retrospectivo
N = 202

AUC = 0.8 (mejor que MELD , Child-Pugh)

**CLIF-C score > 70 puntos + >3
fracasos de órganos➜ futilidad**
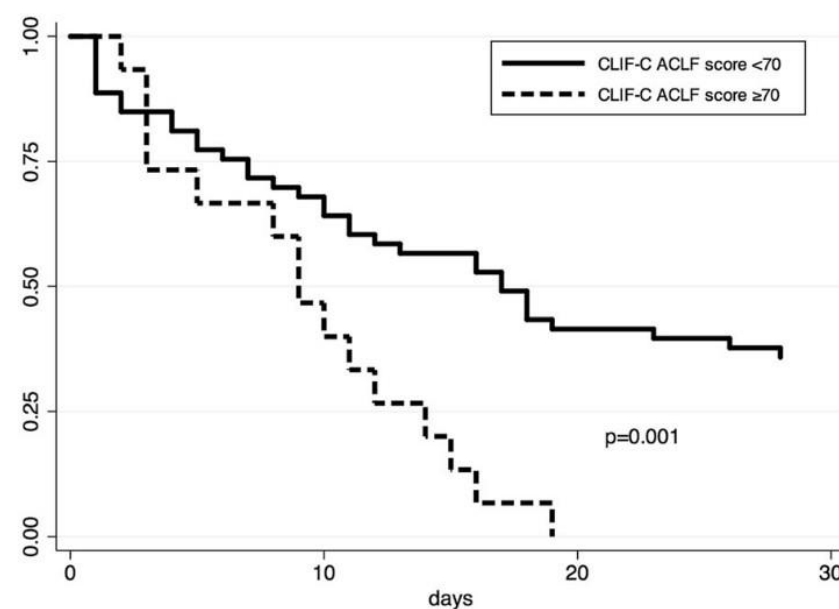
Fig. 3 Twenty-eight-day survival according to the European Foundation for the study of chronic liver failure (CLIF-C) Acute-on-Chronic Liver Failure (ACLF) score in ACLF grade 3. Low 28-day survival is noted in patients with CLIF-C ACLF score ≥ 70, 2 days after receiving full intensive treatment unit supportive therapy

"Futility risk score"

EEUU
N=31.289
2002-2015
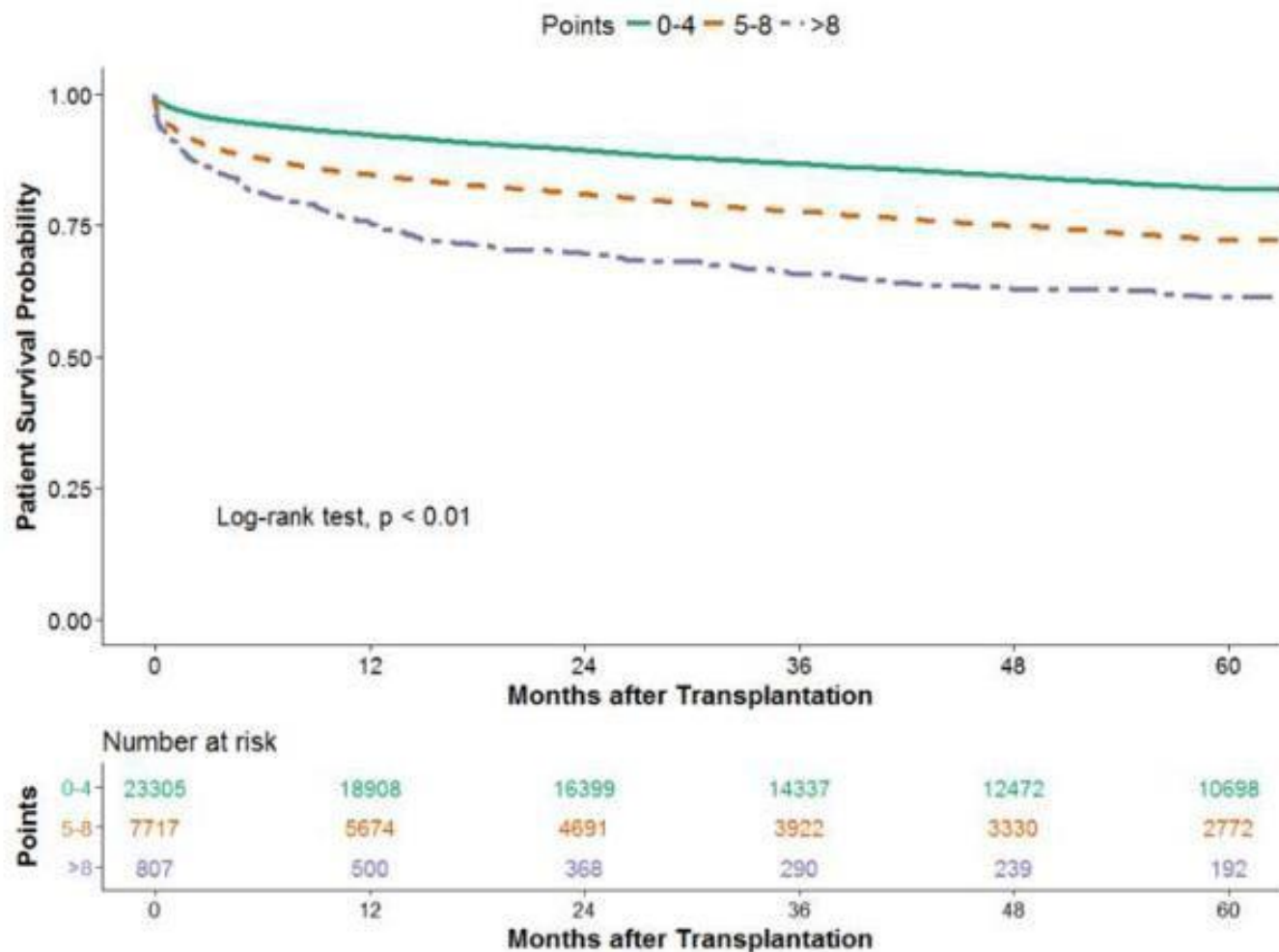
FACTORES DEL RECEPTOR:
- Necesidad de ventilación mecánica (5 ptos)
- Edad > 60 años (3 ptos)
- Hemodiálisis (3 ptos)
- Creatinina > 1.5 mg/dL (sin hemodiálisis) (2 ptos)
- Diabetes (2 ptos)

→ Asociados a fracaso del injerto

Asrani et al. J Hep 2018

ESCALAS predicción resultados post-TH

Score / autor	Componentes de la escala	Comentarios
TAM score (Artzner)	- Edad>53 años - Lactato arterial> 4 mmol/l - Ventilación mecánica con PaFi < 200 mmHg - Recuento leucos < 10,000	- aplica a ACLF-3 - predicción supervivencia 1 año post-TH
OLT-survival score (Huebener)	- CLIF-C score - Mejoría clínica previa al TH	- supervivencia a 90 días post-TH - aplica a todos los grados de ACLF
_ (Singal)	- Edad - Fracaso circulatorio - Fracaso respiratorio - Etiología: alcohol - Fracaso cerebral	- aplica a ACLF-3 - predicción supervivencia 1 año post-TH
_ (Levesque)	- Edad > 57 años & sexo masculino - Donante masculino - Indicación de TH (HCC vs cirrosis descompensada) - infección - presencia de ACLF	- mortalidad a 90 días post-TH
CT-score (Wackenthaler)	- Esplenomegalia - Atrofia hepática - Diámetro VCI	- aplica a ACLF-3
Normograma (Chen)	- Recuento de leucocitos - ratio GPT/GOT - número de fracasos orgánicos	- aplica solo a VHB - predicción supervivencia 1 año post-TH
SALT-M score (Hernáez)	- Edad > 50 años - Fracaso respiratorio - diabetes - Fracaso circulatorio - IMC	- aplica a ACLF-2 y ACLF-3 - predicción mortalidad a 1 año post-TH - predicción estancia hospitalaria post-TH

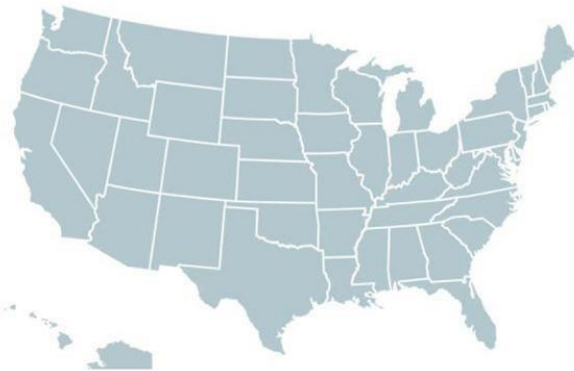# TAM ("Transplantation for ACLF-3 Model") score

	Points
Arterial lactate level (mmol/l)	
<4	0
≥4	1
Mechanical ventilation with PaO₂/FiO₂ ratio ≤ 200 mm Hg	
No	0
Yes	1
Age (years)	
<53	0
≥53	1
Leukocyte counts (G/l)	
>10	0
≤10	1
TAM score	= Σ

N=152
5 centros europeos
2007-2017

@SETHepatico
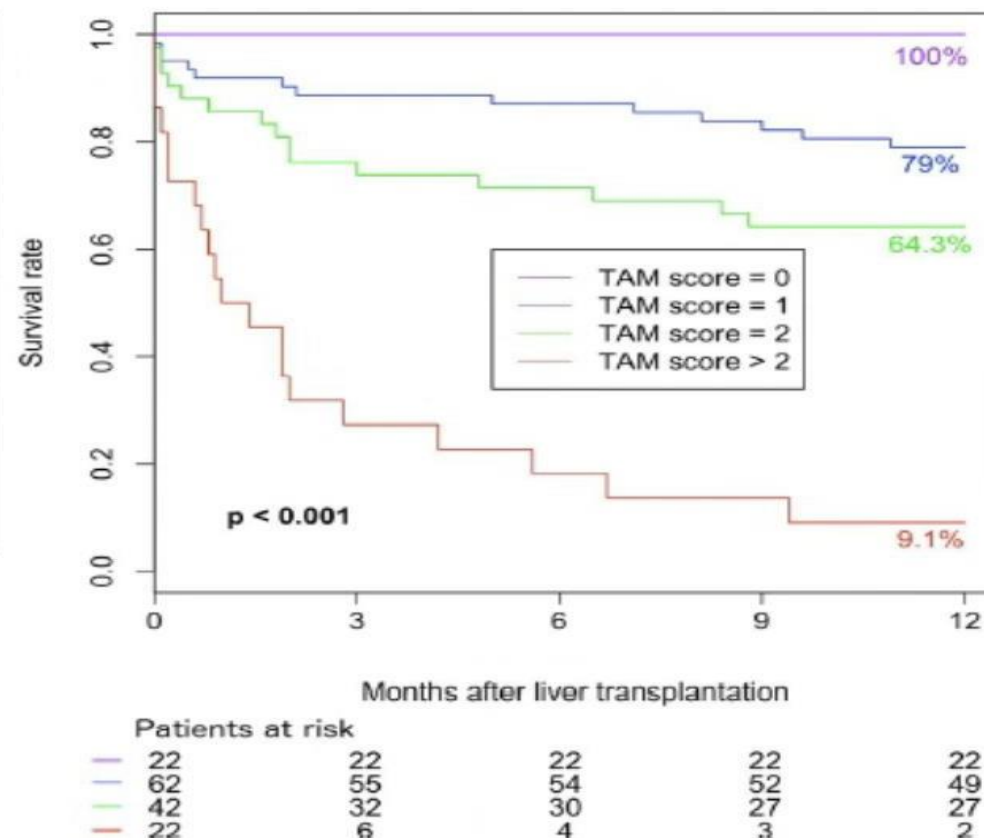
SALT-M (Sundaram ACLF-LT-Mortality) score

MODEL Consortium (development/internal validation)

15 Liver Transplant Centers, 521 patients with ACLF 2-3

External validation

France

Strasbourg and Villejuif, 120 patients with ACLF-3

Tool: logistic regression using clinically meaningful variable selection in addition to modern selection techniques. Adequate power for 5 predictors. Used median regression to estimate median length of stay using the same principles.

✓ Age 50+
✓ Diabetes mellitus
✓ Body mass index (continuous)
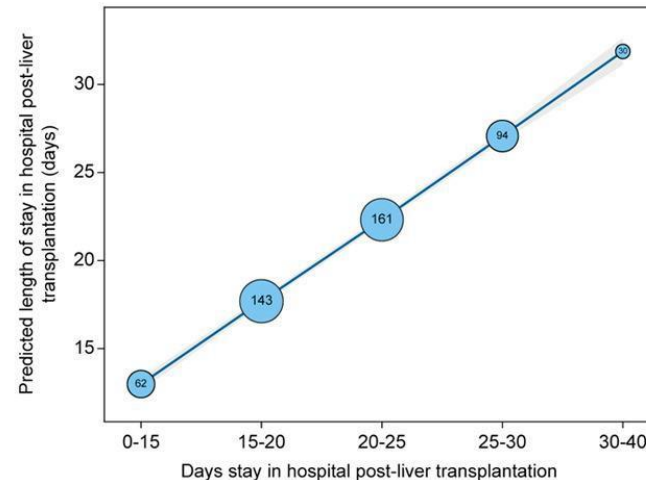✓ Circulatory failure (one or 2+ inotropes)
✓ Respiratory failure

Sundaram ACLF-LT (SALT)-Mortality score predicts 1-year mortality probability post-LT

AUROC 0.72 (development)
AUROC 0.80 (external validation)

Able to assess median length-of-stay in days post LT

Predicted length of stay in hospital post-liver transplantation (days) vs Days stay in hospital post-liver transplantation

Adjusted for age, body mass index, diabetes use of inotropes, respiratory failure, prior history of MDRB, RRT and WBC at LT

ACLF 2/3 & LT candidate?
→ The Sundaram score can help in the discussions of LT in these patients

MDRB, multidrug resistant bacteria; RRT, renal replacement therapy; WBC, white blood cell count

Hernáez R et al. J Hep 2023.

@SEThepatico

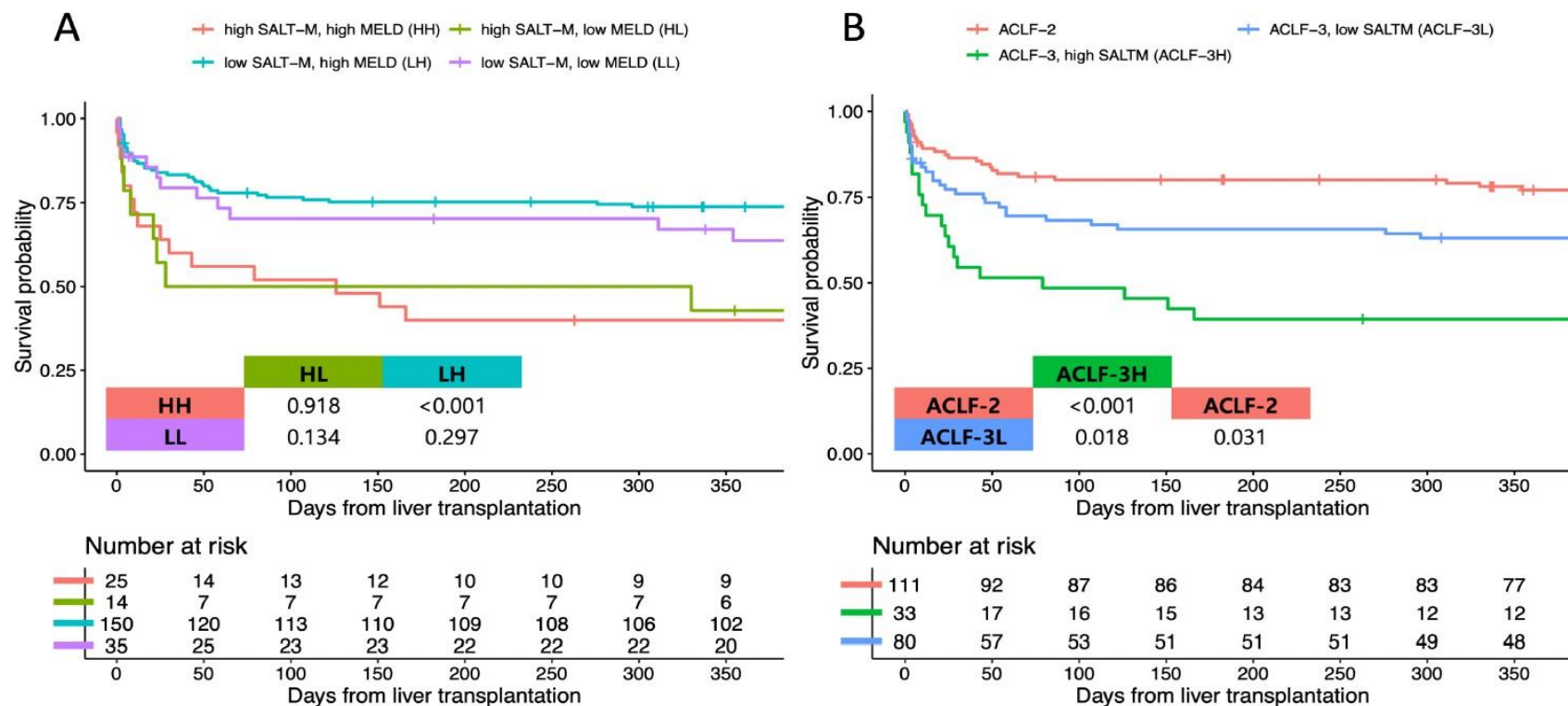# Validación SALT-M score en Asia

FIGURE 3 | Kaplan–Meier plot of the patients classified by (A) SALT-M and MELD score (B) ACLF grade and SALT-M. ACLF, acute-on-chronic liver failure; MELD, model for end-stage liver disease; SALT-M, Sundaram-ACLF-LT Mortality.

N=224

AUROC 0.691
C-index 0.650

> MELD, MELD-Na, MELD 3.0, delta-MELD

*SALT-M categoriza supervivencia independiente de MELD

Kim et al. AP&T 2024.

Factores de riesgo asociados a mortalidad elevada post-trasplante por ACLF:

CONSENSO DE EXPERTOS

Decision to proceed to LT in an already listed critically ill cirrhotic patient hospitalized in the ICU for an acute deterioration

Severely frail patient (clinical frailty scale ≥7) — Yes → CONSIDER POSTPONING OR WITHDRAWING LT

No ↓

One of the following
- Persistent fever >39°C
- Leucopenia < 0.5 G/l
- Appropriate antimicrobial treatment of SBP or PNE < 72 hours
- Previous infection related to PDR *Enterobacteriaceae*

Yes → CONSIDER POSTPONING OR WITHDRAWING LT

No ↓

One of the following:
- PaO2/FiO2 ratio <150
- Norepinephrine > 1.0 µg/kg/min
- Arterial lactate > 9 mmol/L

Yes → CONSIDER POSTPONING OR WITHDRAWING LT

No ↓

Worsening of the clinical course of the patient at the time of graft proposal — Yes → CONSIDER POSTPONING OR WITHDRAWING LT

No ↓

Multidisciplinary discussion to validate LT

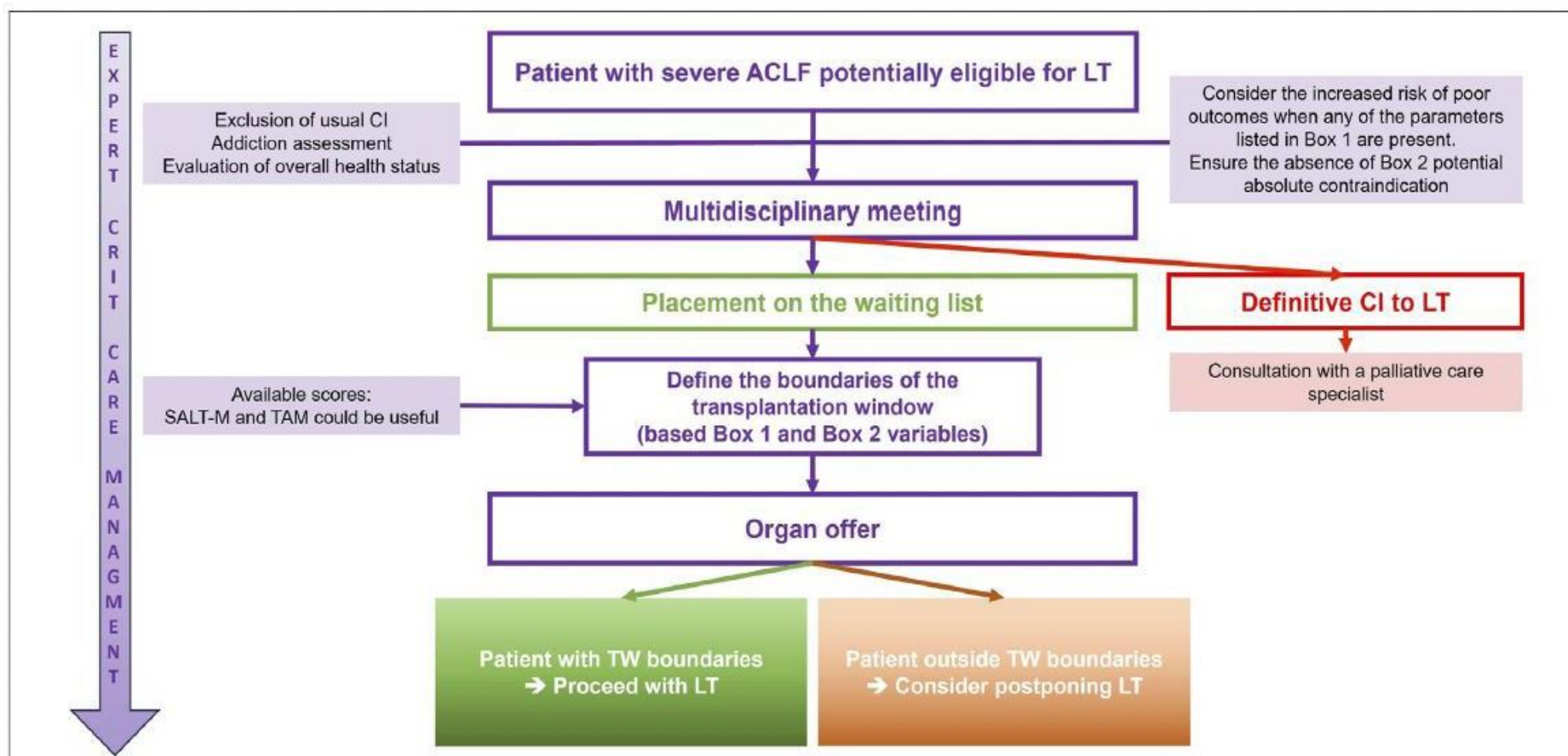Weiss E et al. *Transplantation* 2020

FIGURE 2 | Proposal for a management algorithm for a cirrhotic patient with severe ACLF and potential eligibility for liver transplantation (LT). Abbreviations: ACLF, Acute-on-chronic liver failure; CI, contraindication; LT, liver transplantation; SALT-M, Sundaram ACLF Liver Transplantation Mortality; TAM, Transplantation for ACLF-3 model *Adapted from Artru, Trovato et al., Lancet Gastroenterol. Hepatol. 2024* [64].

L´Hermite et al. Transplant International 2025

Patient with severe ACLF potentially eligible for LT

Consider the increased risk of poor outcomes when any of the parameters listed in Box 1 are present

BOX 1 | Predictive factors of mortality after liver transplantation for ACLF. *Limited scientific evidence. Abbreviations: ICU, intensive care unit; PVT, portal vein thrombosis; DRI, donor risk index.

Patient-related factors on admission to ICU
Age (especially when ≥60 years)
Diabetes mellitus
Body mass index
Cardiac risk factors (arrhythmias, severe valvular disease, coronary artery disease)
Cumulative comorbidities as expressed in Charlson Comorbidity Index
Frailty, malnutrition – sarcopenia
PVT*
Cirrhotic cardiomyopathy*

Factors related to a patient's stay in ICU
Respiratory failure as per EASL definition (PaO2/FiO2 ≤200)
Worsening organ failure, elevated arterial lactate (>4 mmol/L)
Vasopressor use and multiple vasopressors requirement
Infection with multidrug-resistant organisms during hospitalization
Prolonged time in ICU to transplantation (>15 days)*

Donor-related factors
High Donor Risk Index (e.g. DRI ≥1.7)
Age of the donor
Diabetes mellitus of the donor

BOX 2 | Proposed absolute contraindications to liver transplantation in the context of ACLF. *Based on Delphi consensus from Weiss et al. Transplantation 2020. [34]. #Based on the consensus document on UK ACLF Tier Bernal et al., Lancet Reg Health 2024. [18]. Abbreviations: LT, liver transplantation; ARDS, acute respiratory distress syndrome; ECMO, extra corporeal membrane oxygenation.

Potential absolute contraindications to LT in the context of ACLF
Non modifiable – related to the patient
Frailty with Clinical Frailty Scale ≥7 before admission*
Modifiable – related to the ICU stay
Norepinephrine requirement >1 γ/kg/min*
ARDS with PaO2/FiO2 ratio < 150*
Arterial lactate >9 mmol/L*
Active bacterial or fungal sepsis*
Severe irreversible neurological injury#
Patient under Extra Corporeal Membrane Oxygenation (ECMO) device#
Severe acute pancreatitis or intestinal ischemia#

FIGURE 2 | Proposal for a management algorithm for a cirrhotic patient with severe ACLF and potential eligibility for liver transplantation (LT). Abbreviations: ACLF, Acute-on-chronic liver failure; CI, contraindication; LT, liver transplantation; SALT-M, Sundaram ACLF Liver Transplantation Mortality; TAM, Transplantation for ACLF-3 model Adapted from Artru, Trovato et al., Lancet Gastroenterol. Hepatol. 2024 [64].

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ACLF y TRASPLANTE HEPÁTICO RESULTADOS A LARGO PLAZO

ACLF: resultados a largo plazo. EEUU.

Post–transplant survival probability

p < 0.0001

67.7% a 5 años
ACLF-3

Legend:
- No ACLF
- ACLF-1
- ACLF-2
- ACLF-3
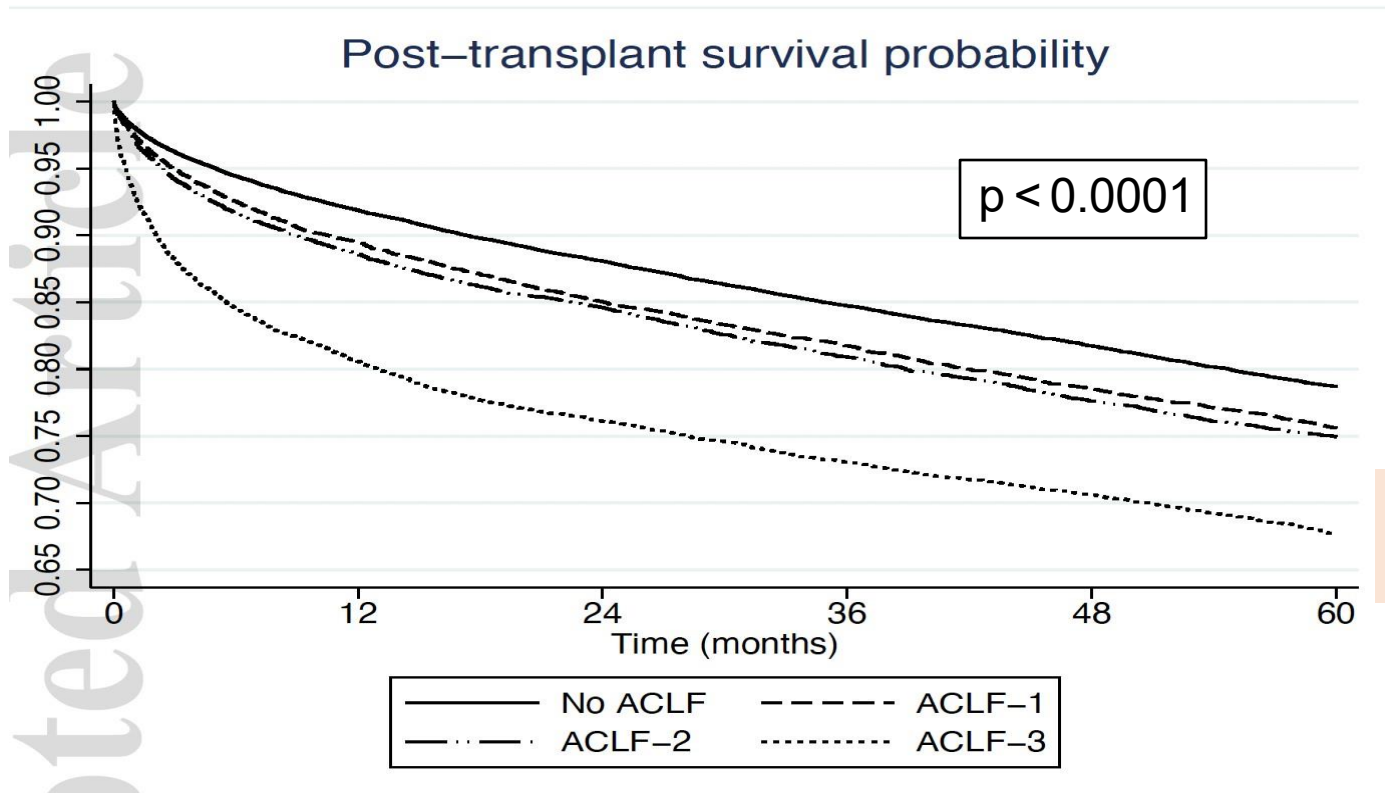
EEUU. 2004 – 2017.
N=56800, 14% ACLF-3

Después del 1er año post-TH, descenso similar de la supervivencia en todos los grupos

Sundaram, V., Mahmud, N., Perricone, G., Katarey, D., Wong, R. J., Karvellas, C. J., Fortune, B. E., Rahimi, R. S., Maddur, H., Jou, J. H., Kriss, M., Stein, L. L., Lee, M., Jalan, R., & Multi-Organ Dysfunction, Evaluation for Liver Transplantation (MODEL) Consortium (2020). Longterm Outcomes of Patients Undergoing Liver Transplantation for Acute-on-Chronic Liver Failure. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society*, *26*(12), 1594–1602. https://doi.org/10.1002/lt.25831

ACLF: resultados a largo plazo. ALEMANIA.

- 250 TH (98 ACLF)
- Seguimiento 8,7 años

- **Supervivencia**
    55% (5 años post-TH)
    49% (10 años post-TH)

- **Comorbilidades** a 5 años
    - sin diferencias significativas
   - La única diferencia ➔ *duración estancia hospitalaria tras alta post-TH*

Comorbidities 5 years after LT	Non-ACLF LT survivors (n = 120)	ACLF LT survivors (n = 61)	P value
Diabetes mellitus			
Total	60 (50.0%)	22 (38.6%)	.20
New-onset after LT	18 (15.0%)	15 (24.6%)	.15
Hypertension			
Total	99 (79.2%)	48 (84.2%)	.54
New-onset after LT	54 (45.0%)	33 (54.1%)	.27
Dyslipidemia	64 (46.0%)	33 (54.1%)	.36
Osteoporosis	51 (39.2%)	31 (50.8%)	.16
Body mass index	25.20 (22.13-29.13)	26.89 (23.67-29.20)	.10
Median no. of daily medications	9 (7-12)	9 (7-12)	.58
Days hospitalized during 60 months following discharge after LT	44.50 (26.25-73.00)	62.50 (35.25-110.50)	<.001

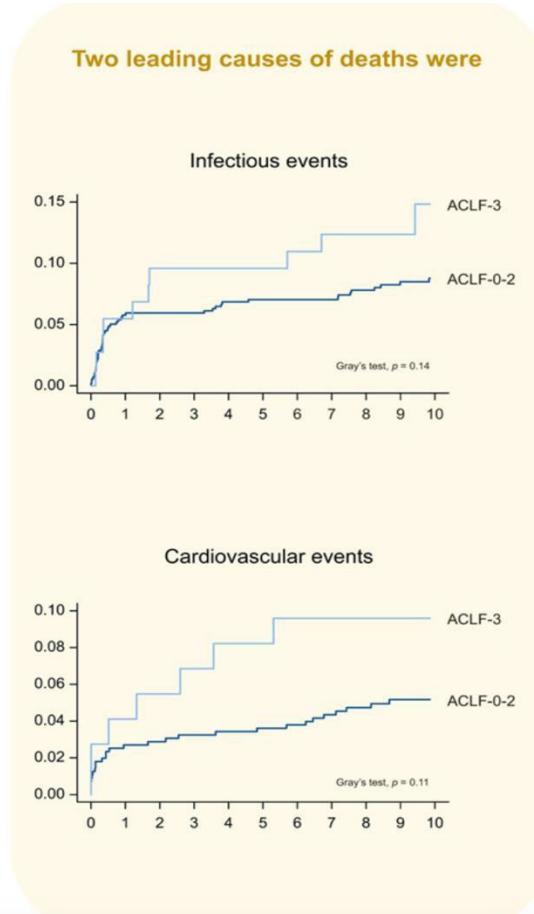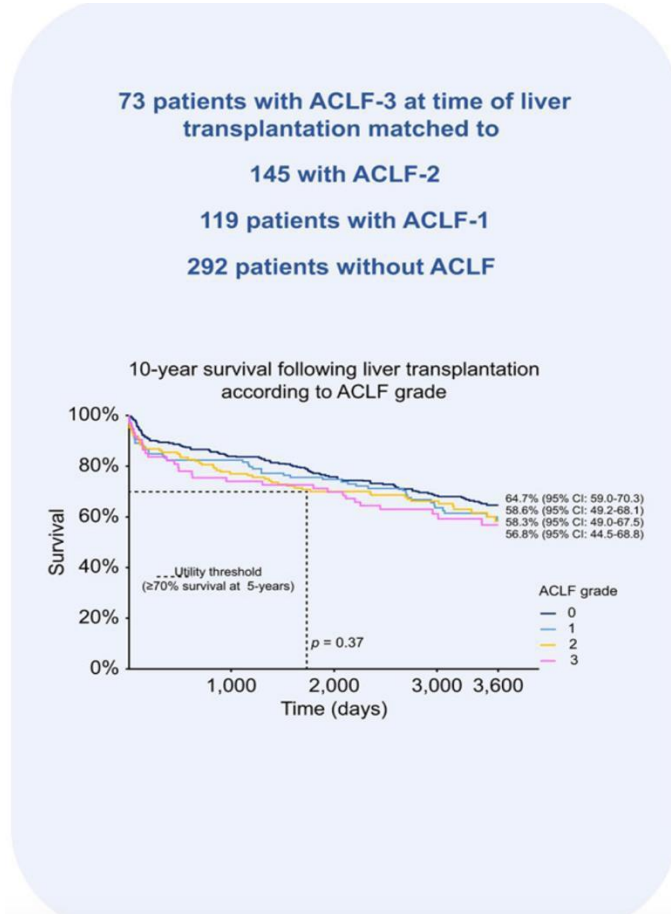# ACLF: resultados a largo plazo. ALEMANIA.

- ## Comparación **calidad de vida**
  - 60% pacientes respondieron
  - ACLF:
    - capacidad reducida para llevar a cabo ABVD
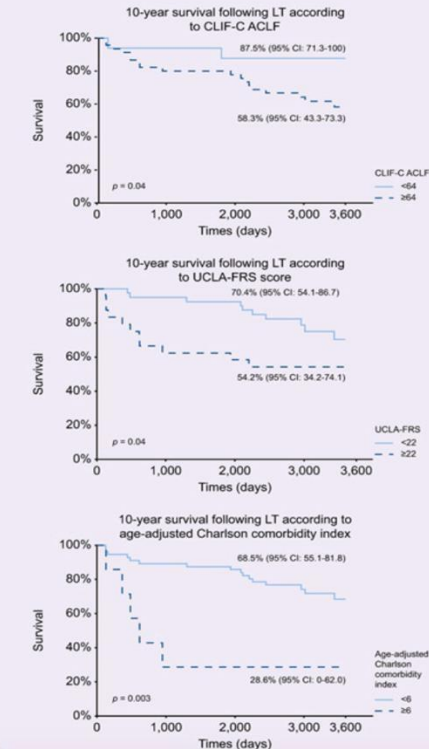   - Más depresión & ansiedad
    - <50% refieren salud "óptima"

  ➤ Relación inversa con duración estancia en UCI
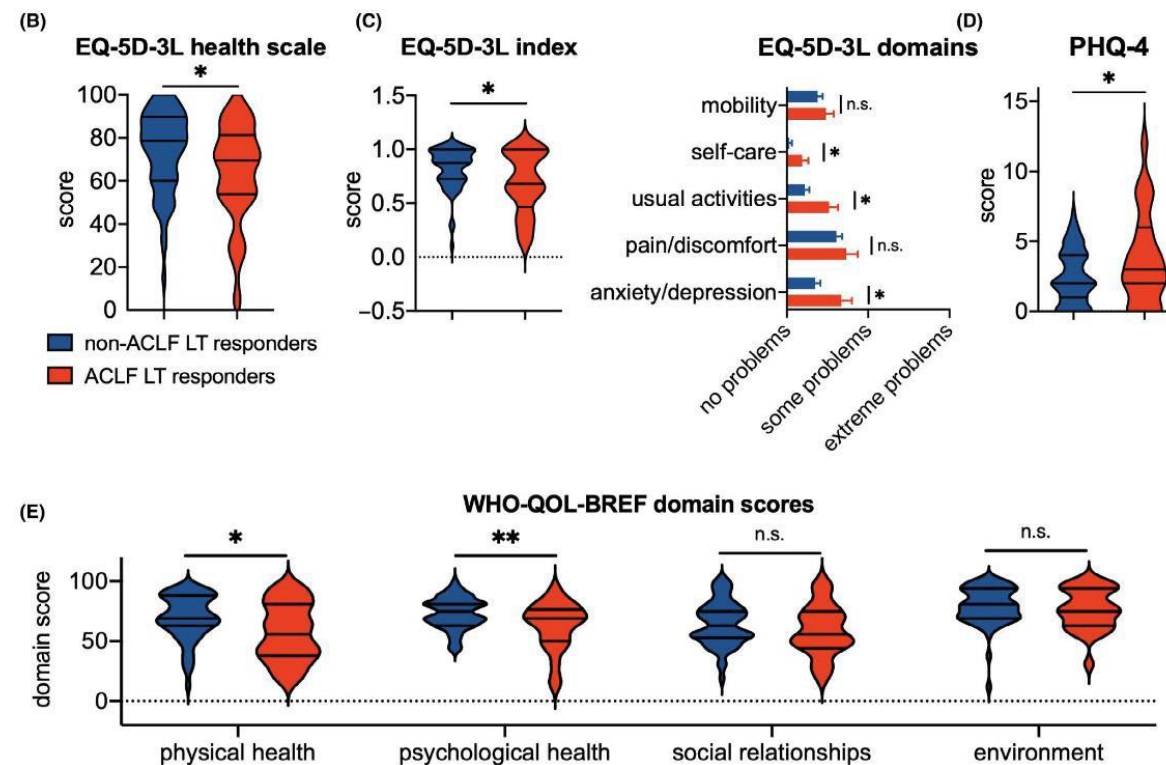
ACLF: resultados a largo plazo. FRANCIA

Artru, et al (2025). Long-term outcome following liver transplantation of patients with ACLF grade 3. *Journal of hepatology*, *82*(1), 62–71. https://doi.org/10.1016/j.jhep.2024.06.039
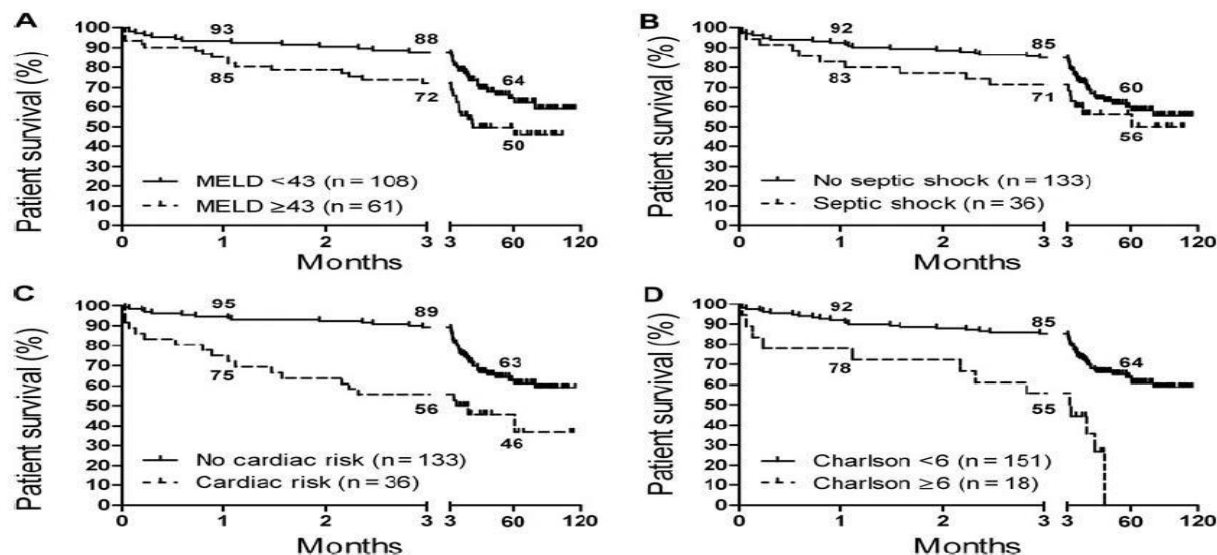
MELD > 40: UCLA-FRS score

FIGURE 3. Early posttransplant patients' survival stratified for independent predictors of futility. Kaplan-Meier survival plots illustrate patients' overall survival for patients with (A) MELD score of less than 43 versus 43 or more ($P = 0.0047$), (B) septic shock versus no septic shock ($P = 0.108$), (C) cardiac risk versus no cardiac risk ($P = 0.0001$), and (D) age-adjusted Charlson Comorbidity Index less than 6 versus 6 or more ($P = 0.0002$). The x axis is divided in early (0–3 months) and late (3–120 months) survival. P values for curve comparison are computed using the Gehan-Breslow-Wilcoxon test.

TABLE 5. Cumulative UCLA Futility Risk Score (UCLA-FRS)

Risk Factor	Log OR	Log OR (Ratio to Sepsis)	Points	Points (Ratio to Sepsis)
MELD (per point)	0.129	0.15	0.5	0.17
Pre-OLT septic shock	0.866	1.00	3	1.00
Cardiac risk	1.145	1.32	4	1.33
Age-adjusted Charlson Comorbidity Index ≥6	1.373	1.58	5	1.67

Cumulative UCLA Futility Risk Score = 0.5 × (MELD score) + 5 × (1 = Charlson Comorbidity Index ≥6; 0 = Charlson Comorbidity Index <6) + 4 × (1 = cardiac risk; 0 = no cardiac risk) + 3 × (1 = septic shock; 0 = no septic shock).

- MELD

- Shock séptico pre-TH

- Riesgo cardíaco

- Índice de comorbilidad de Charlson ajustado a edad > 6 puntos

Petrowsky H, Rana A, Kaldas FM, Sharma A, Hong JC, Agopian VG, et al. Liver Transplantation in Highest Acuity Recipients: Identifying Factors to Avoid Futility. *Ann Surg* (2014) 259(6):1186–94. doi:10.1097/SLA. 0000000000000265

30º CONGRESO SETH
SOCIEDAD ESPAÑOLA DE TRASPLANTE HEPÁTICO

@SETHepatico

ACLF post-TH: Supervivencia a corto y largo plazo

**TABLE 1 |** Outcomes of studies evaluating liver transplantation for ACLF.

Study	Study period	ACLF grades 1; 2; 3* (n)	1-year post-LT survival for ACLF grades 1; 2; 3*	Long-term post-LT survival for ACLF grades 1; 2; 3*
Deceased-donor liver transplantation				
Kwon et al. [11]	2008–2019	102; 129; 140	ACLF grade 3: 67.9%	5-year survival : 57.6%
Artru et al. [32]	2008–2014	ACLF grade 3 : 73	NA	5-year survival 76.4%; 69.7%; 72.6%; 10-year survival 58.6%; 58.3%; 56.8%;
Bernal et al. [30]	2021–2023	ACLF grade 3 : 42	ACLF grade 3 : 77%	NA
Alukal et al. [29]	2005–2021	ACLF grade 3 : 4806	ACLF grade 3: 86.2%	NA
Hernaez et al. [43]	2014–2019	0; 237; 284	84.4% for grade 2; 76.4% for grade 3	NA
Zhu et al. [12]	2018–2020	75; 64; 73	93.3%; 73.4%; 60.3%	NA
Xia et al. [13]	2015–2021	18; 97; 47	83.0%; 83.2%; 69.8%	3-year survival 83.0%; 80.3%; 69.8%
Sundaram et al. [28]	2018–2019	61; 74; 77	88.5%; 87.8%; 85.7%	NA
Cervantes-Alvarez et al. [14]	2015–2019	40; 33; 22	87.5%; 97.0%; 90.9%	6-year survival 80.0%; 93.9%; 77.3%
Artzner et al. [39]	2018–2019	ACLF grade 3 : 98	ACLF grade 3: 79%	NA
Goosmann et al. [15]	2009–2014	All grades : 98	NA	5-year survival 55.1%
Belli et al. [27]	2018–2019	58; 78; 98	88.6% for grade 1; 78.9% for grade 3	NA
Sundaram et al. [26]	2004–2017	ACLF grade 3 : 2744	ACLF grade 3: 82%	NA
Artzner et al. [47]	2007–2017	ACLF grade 3 : 152	ACLF grade 3: 67.1%	NA
Agbim et al. [16]	2006–2013	50; 32; 19	86%; 81%; 74%	NA
Sundaram et al. [26]	2004–2017	8757: 9039; 7981	89.5%; 88.6%; 80.6%	5-year survival 75.2%; 74.9%; 67.7%
Sundaram et al. [41]	2002–2014	ACLF grade 3 : 2349	ACLF grade 3: 79.8%	NA
Marciano et al. [17]	2010–2016	34; 18; 8	82.3%; 100.0%; 62.5%	NA
Sundaram et al. [25]	2005–2016	7375; 7513; 6381	89.1%; 88.1%; 81.8%	NA
Thuluvath et al. [24]	2002–2016	4330; 3557; 3556	88%; 88%; 83%	5-year survival 74%; 74%; 70%
Huebener et al. [48]	2009–2014	24; 45; 29	3-month survival 72.4%	2-year survival : 60.2%
Artru et al. [6]	2008–2014	ACLF grade 3 : 73	ACLF grade 3: 83.6%	NA
Levesque et al. [18]	2008–2013	68; 42; 30	76.5%; 78.6%; 43.3%	NA
Michard et al. [19]	2007–2014	All grades : 55	60%	NA
Finkenstedt et al. [20]	2002–2010	All grades : 33	87%	5-year survival 82%
Xing et al. [21]	2001–2009	All grades : 133	75.9%	5-year survival 72.1%
Living-donor liver transplantation				
Kwon et al. [11]	2008–2019	261; 147; 75	ACLF grade 3: 72%	5-year survival : 67.5%
Kulkarni et al. [22]	2019–2021	All grades : 55	72.7%	NA

*Overall results across all ACLF grades if individual grade-specific data are unavailable.
Abbreviations ACLF, Acute-on-chronic liver failure; NA, not available.

1 año: 60-80%

5 años: 55-70 (80) %

L´Hermite et al. Transplant International 2025

Curva de aprendizaje

89.5%

72.5%
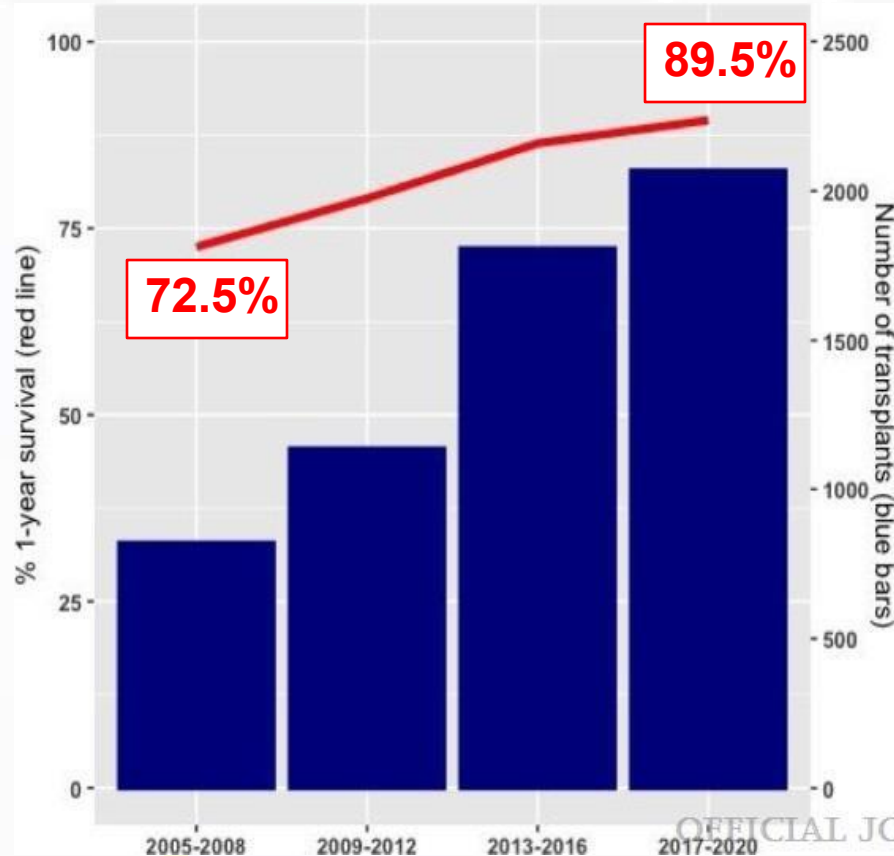
Between 2005 and 2020:

- The number of critically ill patients with cirrhosis who were transplanted in the United States increased (blue bars)

- Their one-year post-transplant survival increased by 17 percentage points (red line)

- This has led to a decrease in the post-transplant survival gap between critically ill patients and non critically ill patients with cirrhosis

- These results are in favor of advocating access to liver transplantation for carefully selected critically ill patients with cirrhosis

TH en ACLF: Necesidades no cubiertas…

- priorización
- distribución de órganos

Búsqueda de equidad

- comorbilidades
- categorización tipo de fracaso orgánico

Optimización de modelos pronósticos predictores

Manejo peri-trasplante

- papel de terapias extracorpóreas
- mitigar complicaciones infecciosas y cardiovasculares

Estandarización de estudio pre-trasplante

- Comorbilidad cardiovascular
- Perfil adicciones y social

MENSAJES PARA LLEVAR A CASA…

- ACLF: elevada mortalidad a corto plazo

  - Impacto de las infecciones (pre, post)

  - Buenos resultados trasplante hepático, también a largo plazo

- Centro experto, equipo multidisciplinar (UCI)

- Determinar criterios de priorización en LE de TH

ESTUDIO MULTICÉNTRICO NACIONAL - SETH
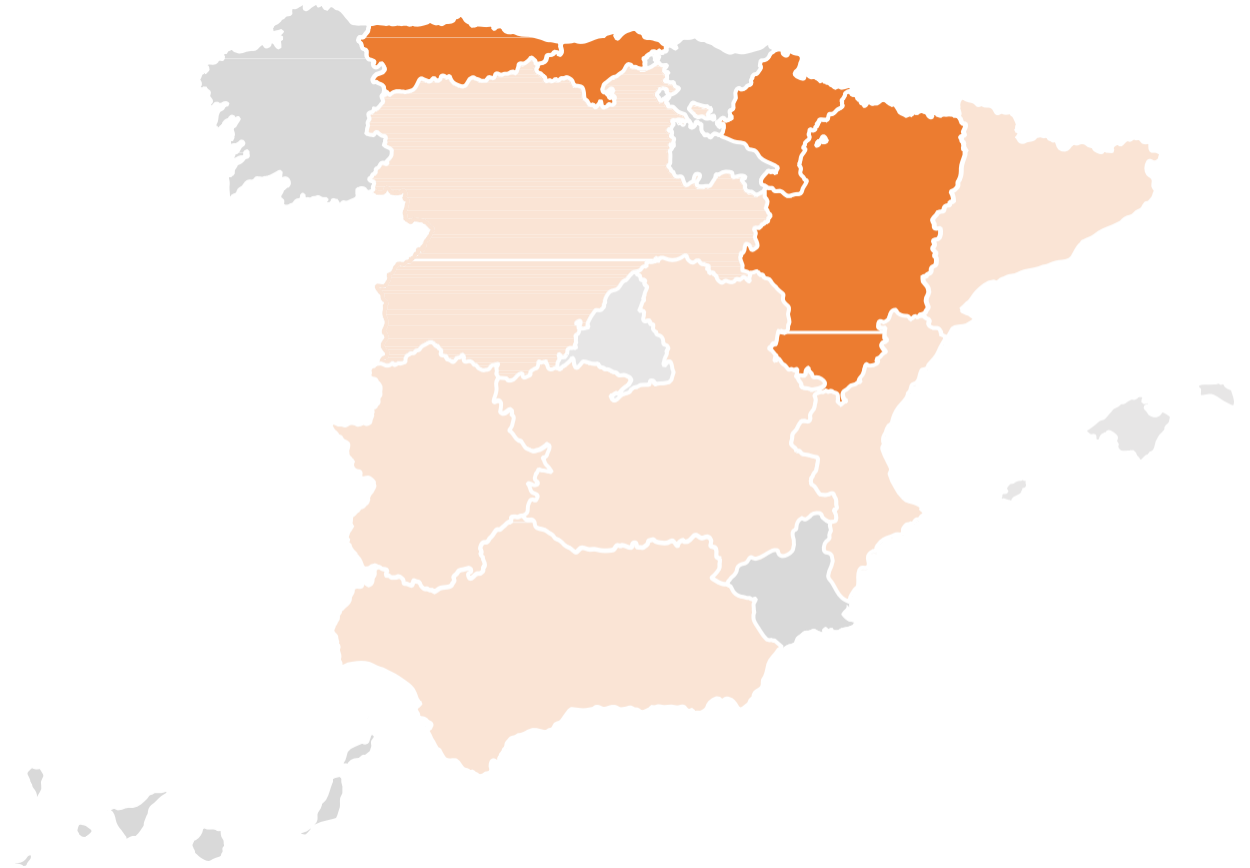
Población de estudio: ACLF-2 y 3

Población control: MELD > 20, no ACLF

Objetivos del estudio

- **Conocer datos en España de supervivencia a medio y largo plazo**
- **Validación TAM score, SALT-M score**
- Calidad de vida
- Complicaciones post-TH

ESTUDIO MULTICÉNTRICO NACIONAL - SETH

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GRACIAS POR VUESTRA ATENCIÓN

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