

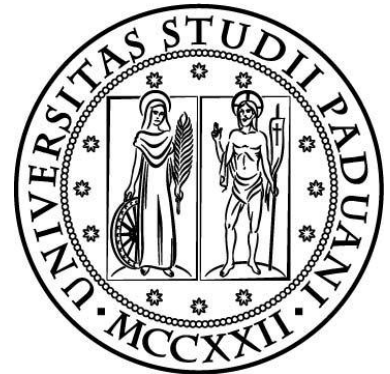
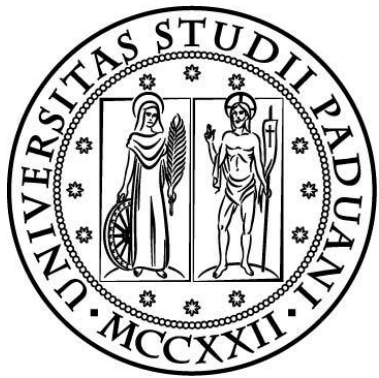
Stati Generali CNT

Roma 6-8 Novembre 2019

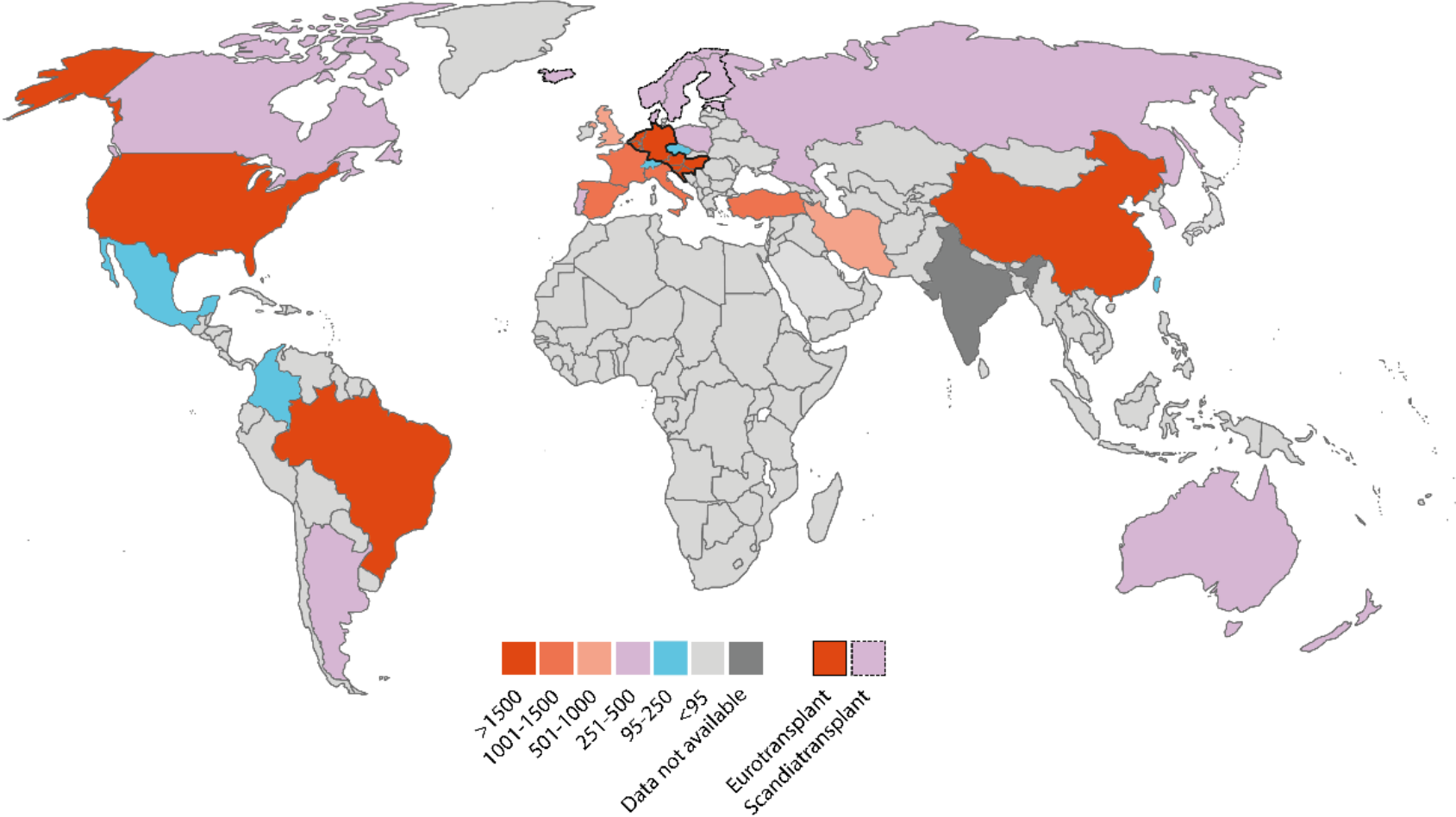
L'indicazione al trapianto di fegato da vivente e problematiche post-trapianto

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Deceased donor liver transplantation per year









Tschuor C, Ferrarese A, Kümmerli C, Dutkowski P, Burra P & Clavien PA, J Hepatol 2019



Specific issues concerning the management of patients on the waiting list and after liver transplantation



Patrizia Burra¹  | Edoardo G. Giannini²  | Paolo Caraceni³  | Stefano Ginanni Corradini⁴  | Maria Rendina⁵ | Riccardo Volpes⁶  | Pierluigi Toniutto⁷ 

Liver International 2018

5.1 | The donor 5.1.1 | Question

Which general donor selection criteria are accepted to obtain an adequate partial allograft while also ensuring an acceptable donor safety?

Statements

In Italy donors must be from 18 to 60 years old.

The medical work-up for older donors should be particularly strict (not graded).

All potential donors should be screened for cardiovascular disease, and there should be a low threshold for their exclusion if significant risk factors are found. **(B, I)**







The goals of donor assessment are to ensure that:

- (a) an adequate partial allograft can be safely procured;
- (b) there is no risk of disease transmission from donor to recipient;
- (c) the donor understands the process and would be able to overcome any psychological consequences. **(C, I)**



Specific issues concerning the management of patients on the waiting list and after liver transplantation



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Liver International 2018

5.2 | The recipient 5.2.1 | Question

What should be the specific approach to the management of recipients of a living donation?

Statements

Living donor liver transplantation should only be performed at specialist centres by a multidisciplinary transplant team. **(A, I)**

Decision-making should be multidisciplinary and meet the standards for transplant services in European countries. **(A, I)**

The Italian standard for transplant benefit, an overall graft and patient survival of more than 50% at 5 years, is the recommended standard for both deceased donor LT (DDLT) and LDLT. **(B, I)**

New indications for LDLT?

New indications for LDLT?

Acute alcoholic hepatitis

Clinical Syndrome of Alcoholic Hepatitis

- Jaundice
- Weight loss
- Malnutrition
- Renal failure
- Sepsis (role of steroids)



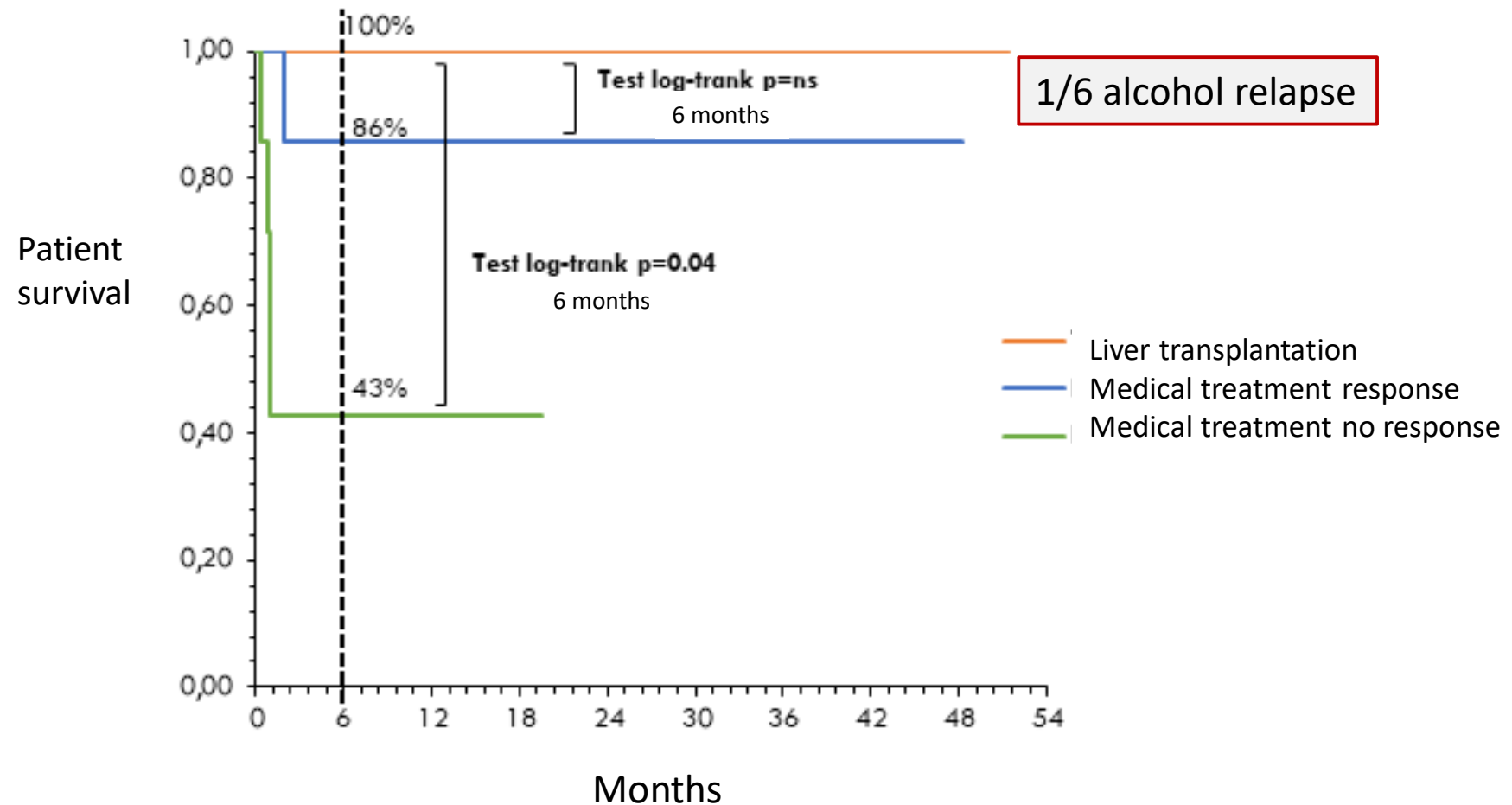
Impact on the waiting list of patients with alcoholic hepatitis proposed for early transplantation

Patients with severe alcoholic hepatitis have very high MELD scores and are likely to rank at the top of the transplant waiting list.

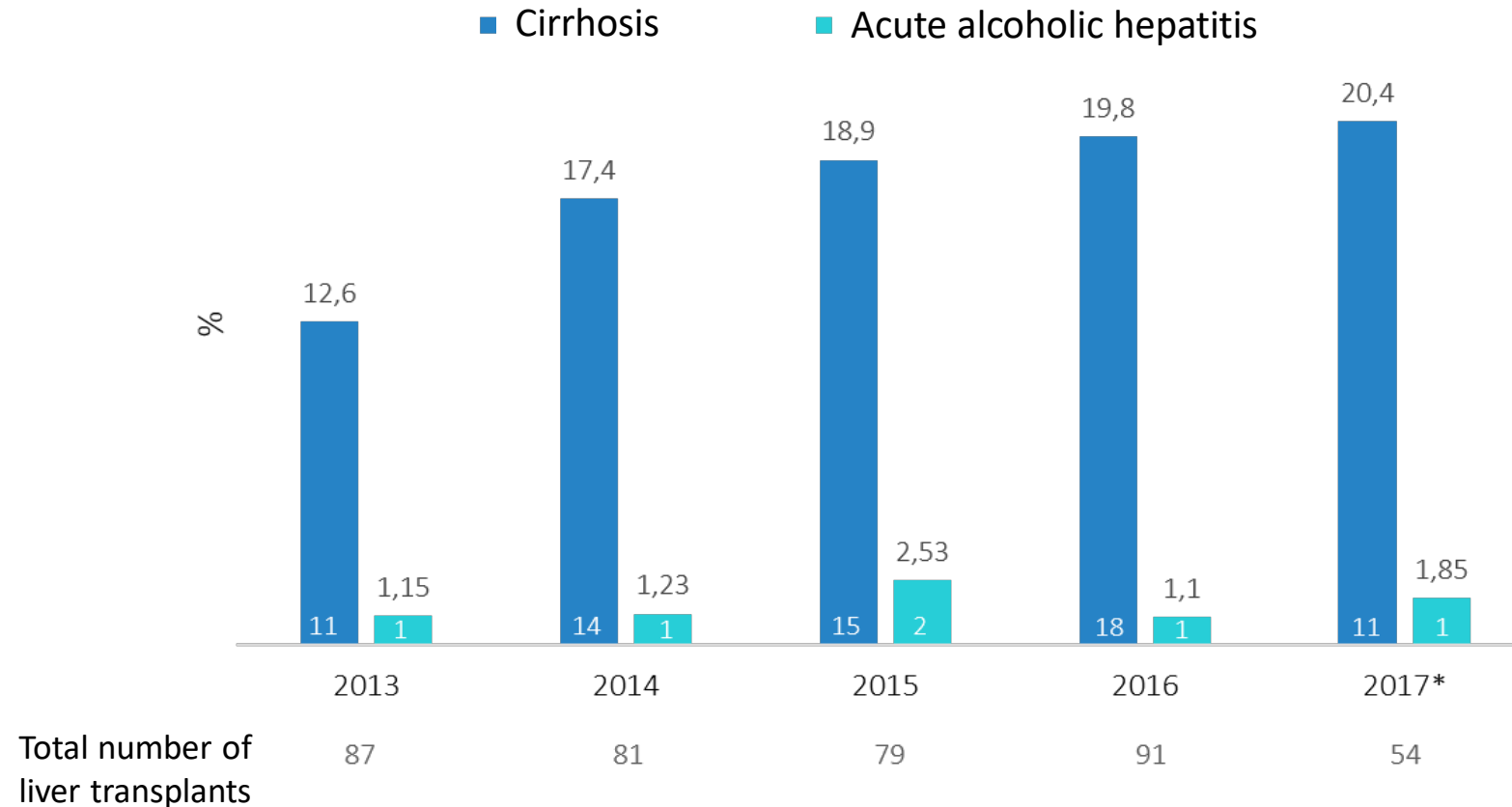


Burra P, Belli LS, Ginanni Corradini S, Volpes R, Marzioni M, Giannini E, Toniutto P. DLD 2017

Patient survival in severe alcoholic hepatitis: medical treatment (responder/no responder) vs early liver transplantation



Percentage of liver transplants yearly performed for alcoholic liver disease: Padua Experience



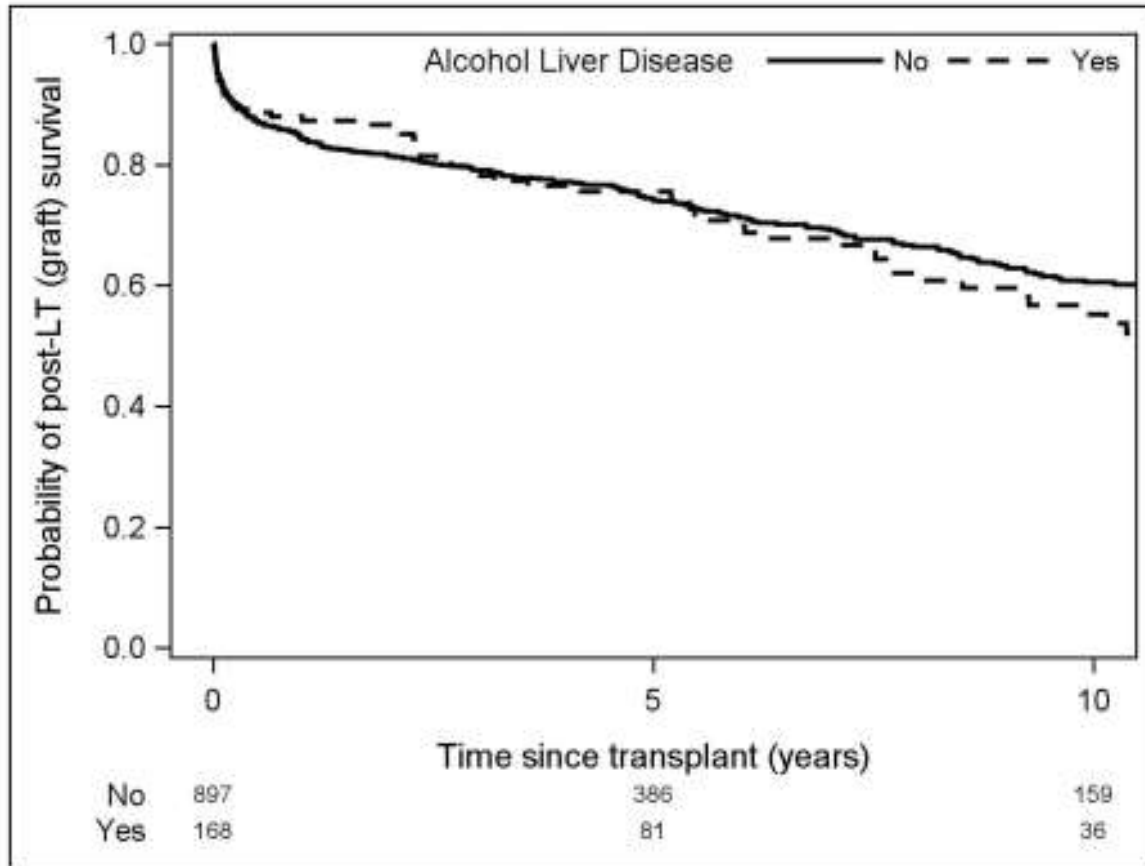
Adult to Adult Living Donor Liver Transplantation Study (A2ALL) for alcohol-related liver disease (ALD)

1065 patients underwent LDLT

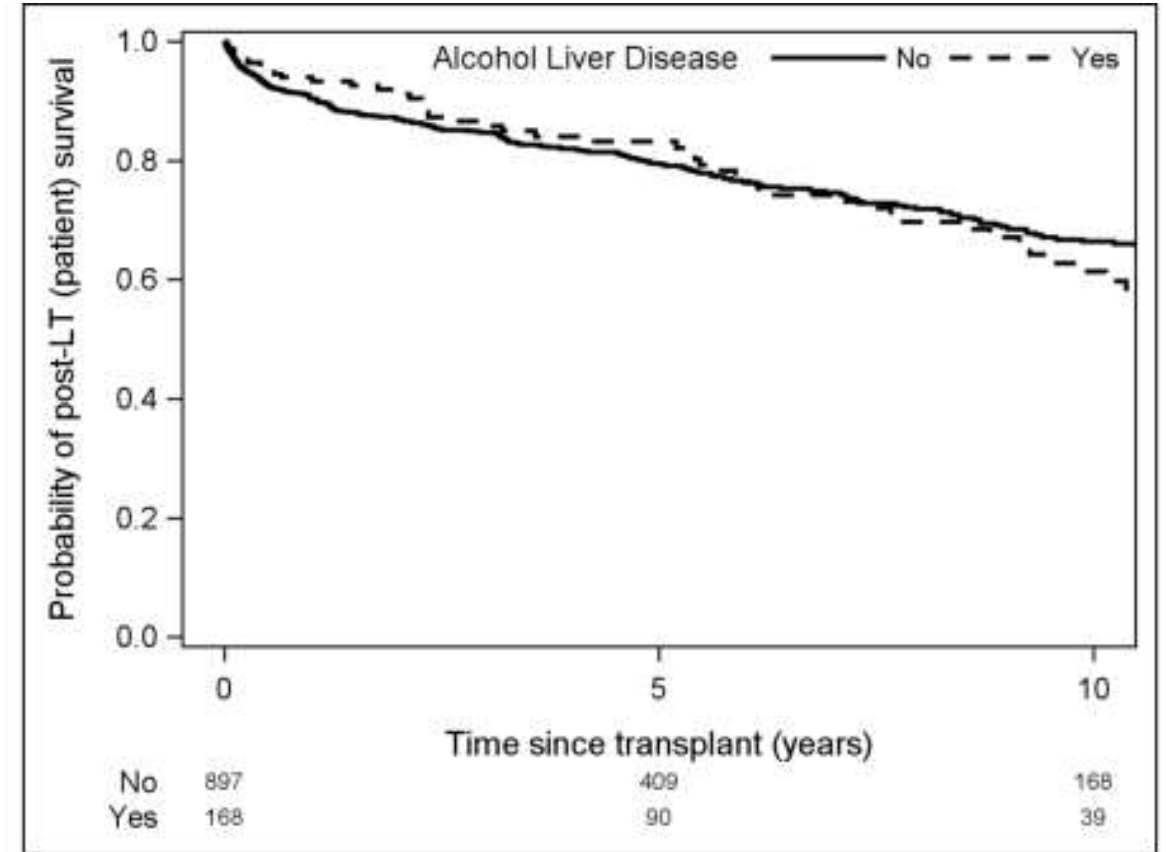
168 (15.8%) were transplanted for ALD

168 LDLT for alcohol-related liver disease (ALD) (data from A2ALL Study)

Graft survival



Patient survival



Should LDLT be carried out in acute alcoholic hepatitis (AAH)?

Patients selected according to **approved protocols** are ideal to be considered for LDLT, given that these patients are younger and in the most productive time of their life.

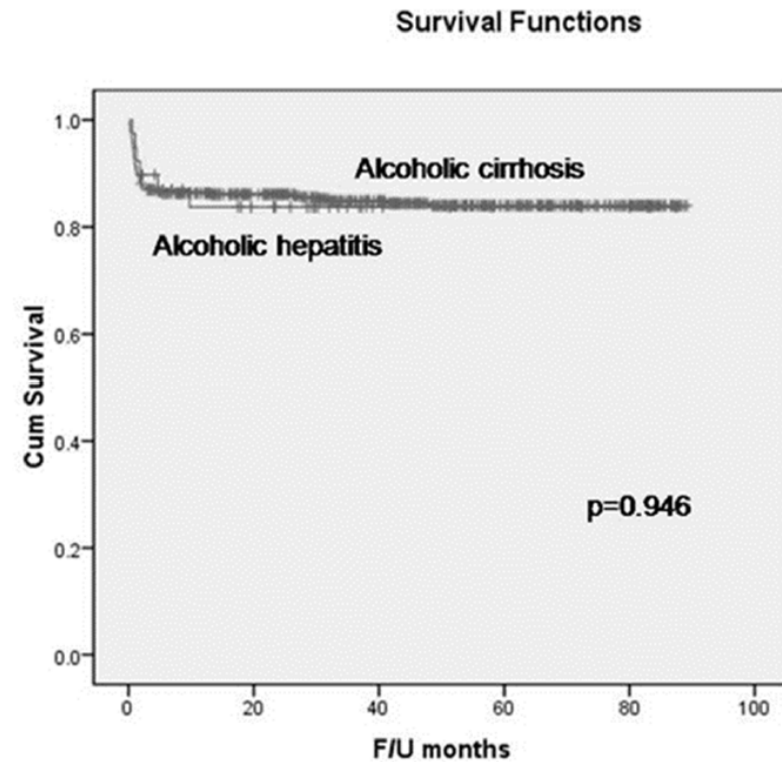
LDLT may be considered if a **well-informed donor** is available and the patient is **unlikely to receive a deceased** organ for LT.

LDLT for severe AAH

- LDLT in 39 AAH patients and 461 ALD patients
- AAH vs ALD recipients at the time of LT:
 - Younger (43 vs 48 yrs, $p=0.001$)
 - Sicker (CTP 11 vs 10; MELD 22 vs 18; $p=0.000$)

Outcome of LDLT for AAH vs ALD

- Survival was not different between AAH and ALD recipients
- Post-operative infections more common in AAH vs ALD (71.7% vs 51.6%, $p=0.018$)
- Alcohol relapse rate in AAH: 12.8%



New indications for LDLT?

- HIGH MELD
- ACLF
- ALF

LDLT for decompensated end stage liver disease is controversial

	Patient No.						
	1	2	3	4	5	6	7
Age (yr)	56	45	61	52	62	43	62
Sex	M	F	M	F	M	M	M
Liver disease	ETOH	ETOH	HBV	Autoimmune	ETOH, HCC stage IV	HCV	HCV
CPT score	13	14	13	9	13	14	13
CPT classification	C	C	C	B	C	C	C
ICU	No	No	Yes	No	No	Yes	No
Mechanical ventilation	No	No	No	No	No	Yes	No
Renal failure	No	Compensated	Decompensated hemodialysis	No	Compensated	Compensated	No
MELD	21	39	45	14	18	40	30

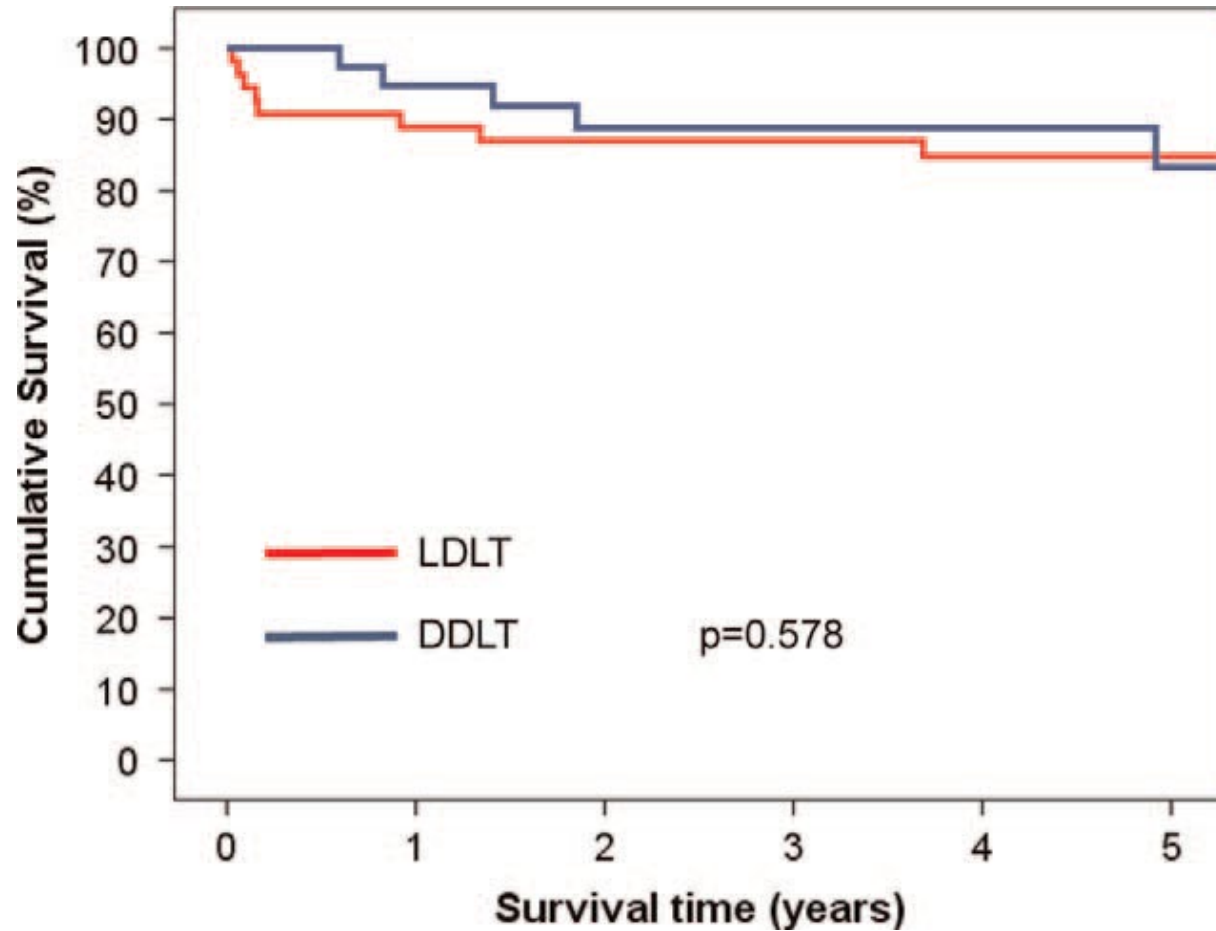
7 cases

Post-LT intubation 6 days, ICU stay 23 days, hospital stay 69 days

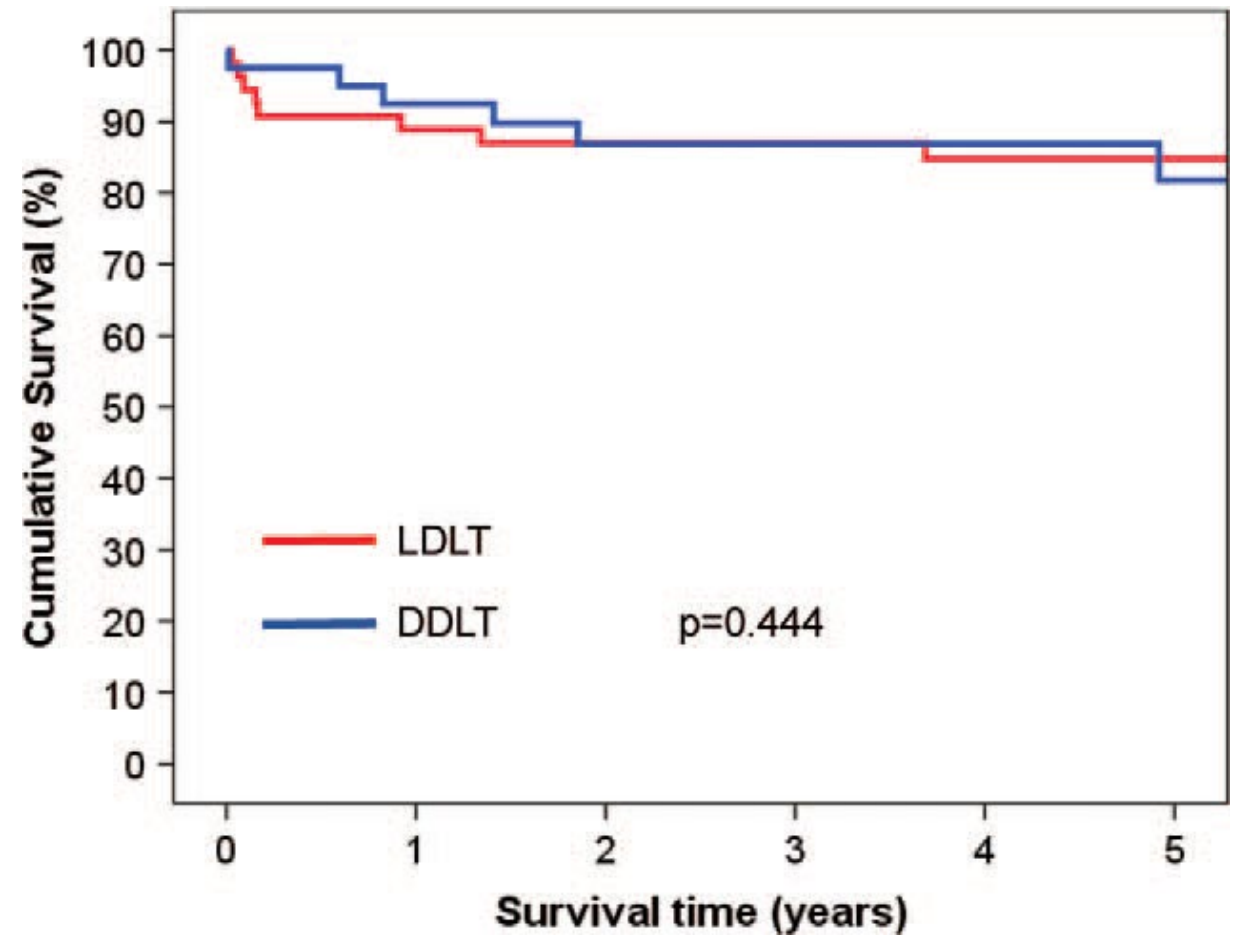
Patient and graft survival rates were 43% at 15 months post-LT

54 LDLT vs. 40 DDLT for patients with MELD ≥ 35

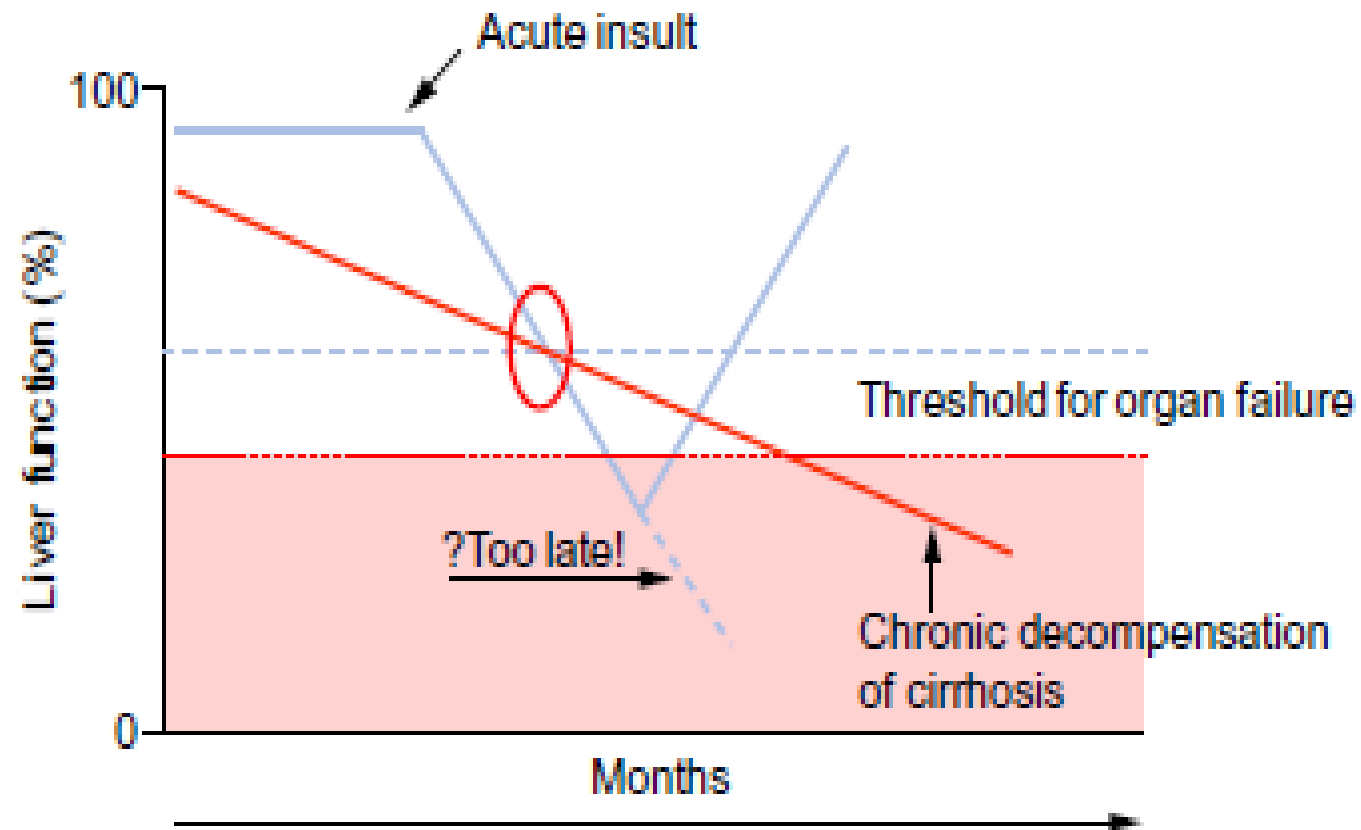
Patient Survival



Graft Survival



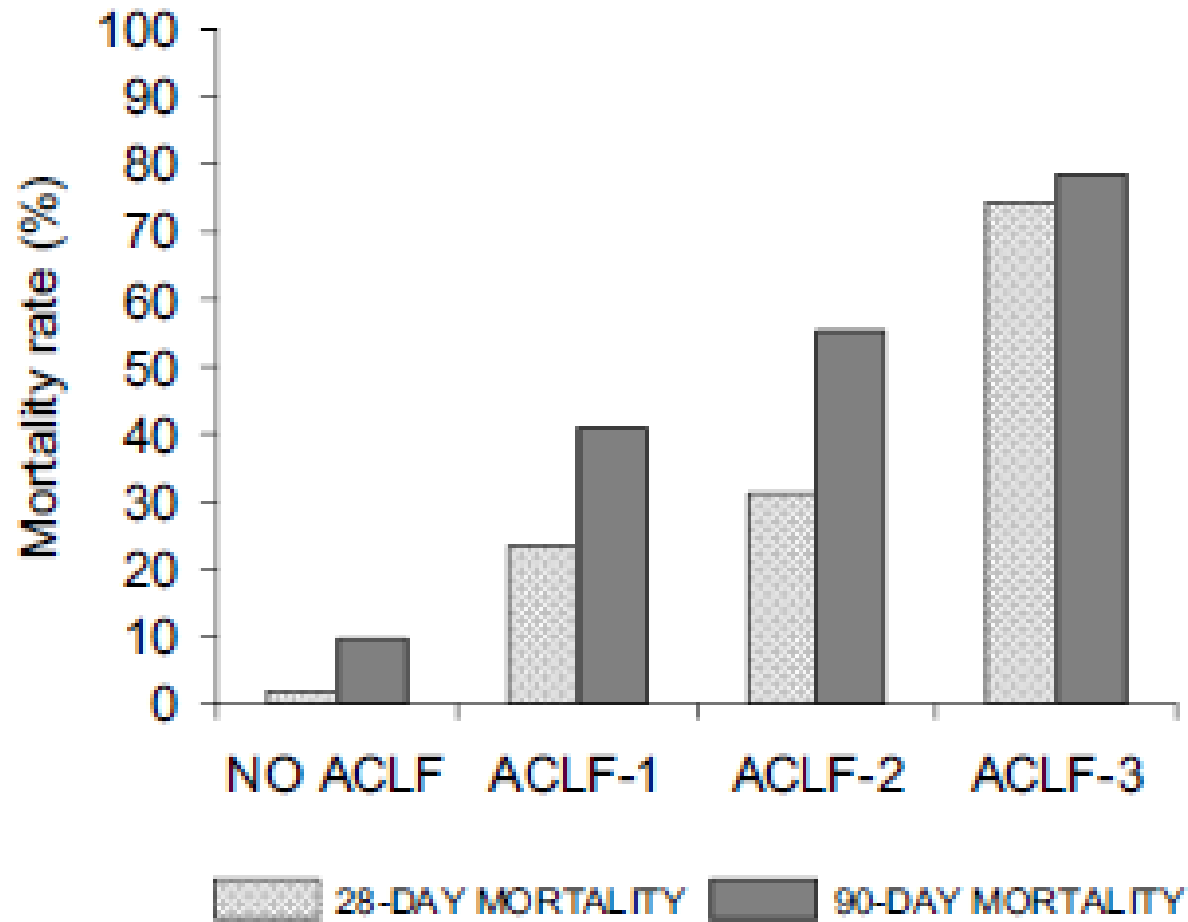
Acute on Chronic Liver Failure is a distinct syndrome than chronic decompensation




Grading of acute on chronic liver failure – CLIF SOFA

Grade of ACLF	Definition
Grade 1-Type a	Single kidney failure
Grade 1-Type b	One “non-kidney” organ failure with serum creatinine between 1.5 to 1.9 mg/dL and/or mild-to moderate hepatic encephalopathy
Grade 2	Two organ failures
Grade 3	Three or more organ failures

28-day ad 90-day mortality according to ACLF stages

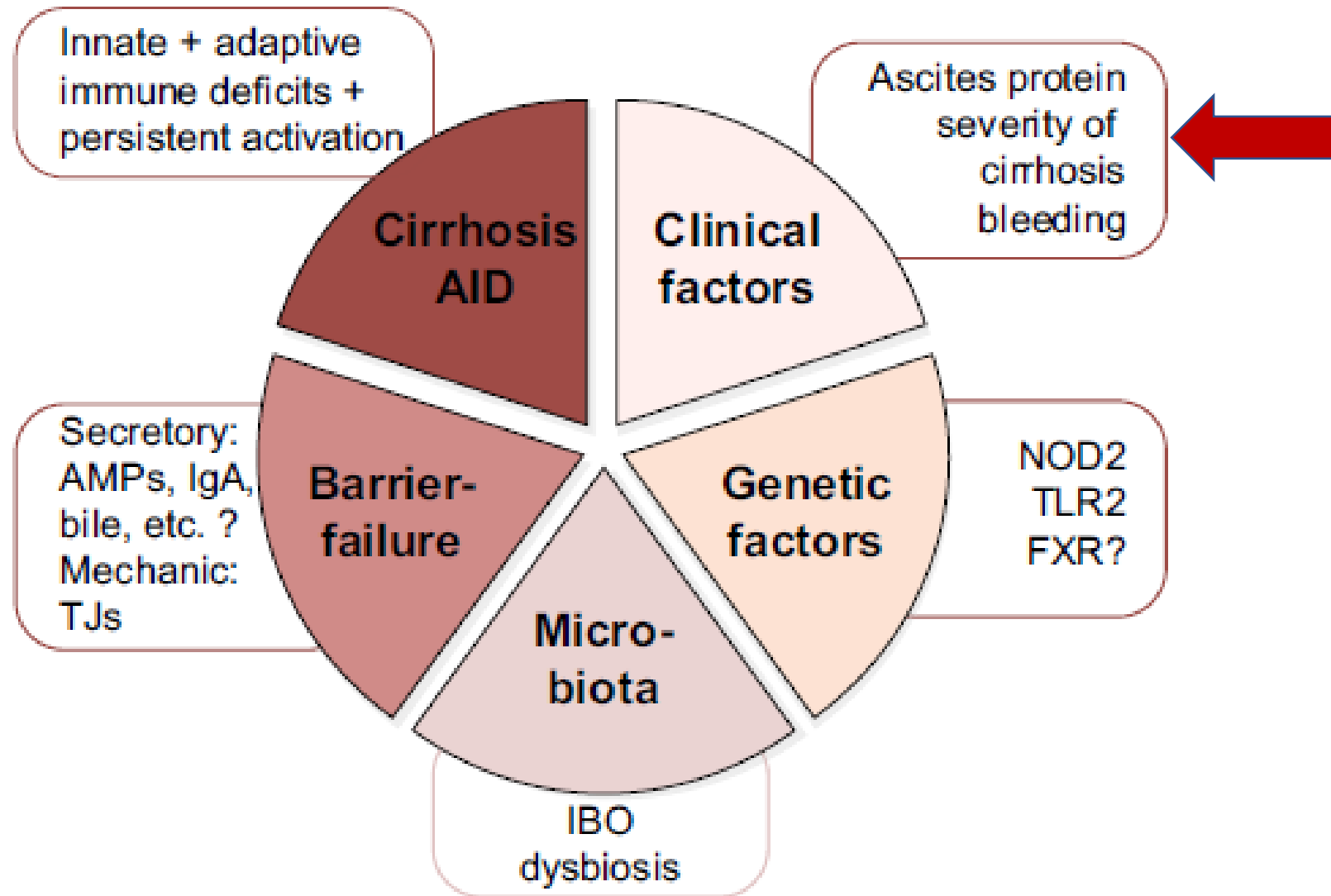


Causes of death in ACLF

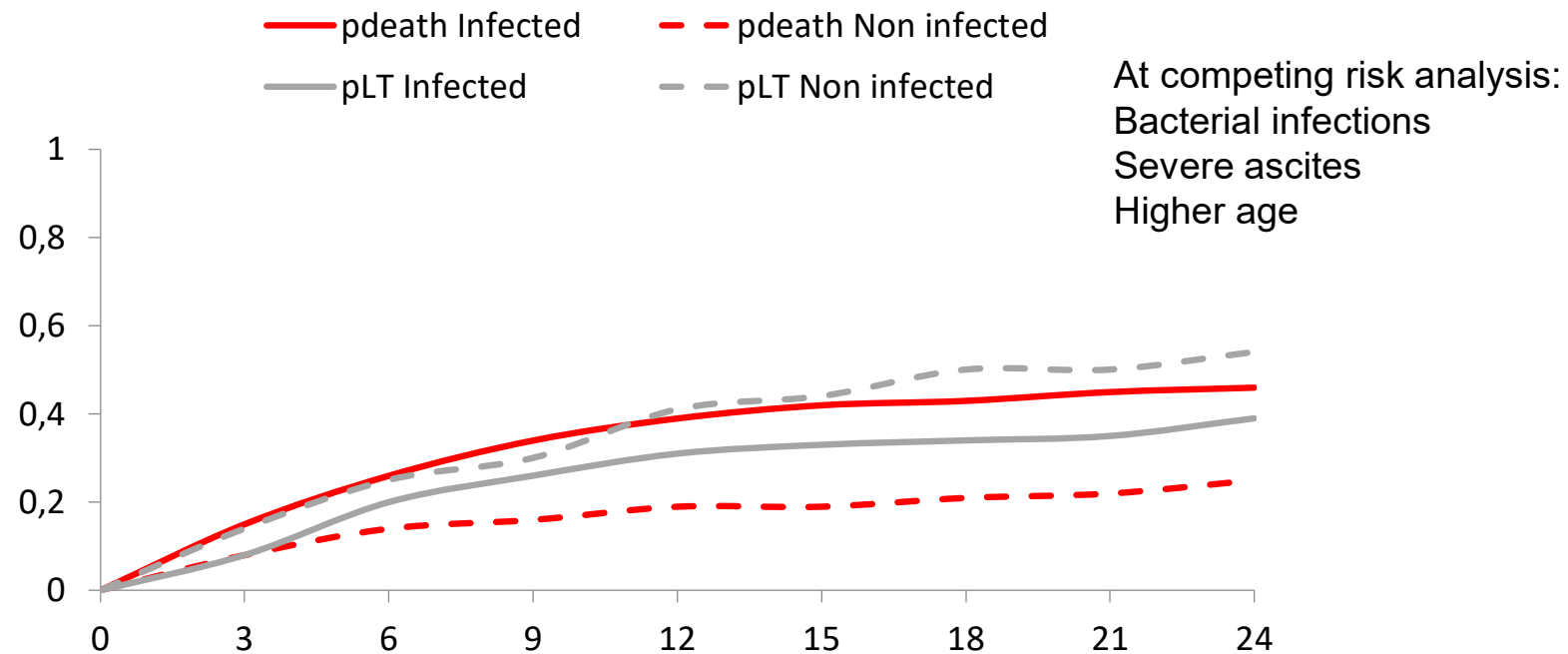


Causes of death	Deaths at 28 days (n = 144)	Deaths at 90 days (n = 265)
Multiple organ failure without septic or hypovolemic shock	63 (43.8)	99 (37.4)
Septic shock	40 (27.8)	62 (23.4)
Hypovolemic shock	12 (8.3)	19 (7.2)
Cirrhosis ^a	0	7 (2.6)
Cerebral hemorrhage	2 (1.4)	4 (1.5)
Myocardial infarction	1 (0.7)	4 (1.5)
Hepatocellular carcinoma	1 (0.7)	4 (1.5)
Non-liver cancer	2 (1.4)	2 (0.8)
Massive pulmonary inhalation	1 (0.7)	2 (0.8)
Epileptic status	1 (0.7)	2 (0.8)
Pulmonary embolism	0	2 (0.8)
Other causes ^b	7 (4.9)	11 (4.2)
Cause unknown	11 (7.6)	42 (15.8)

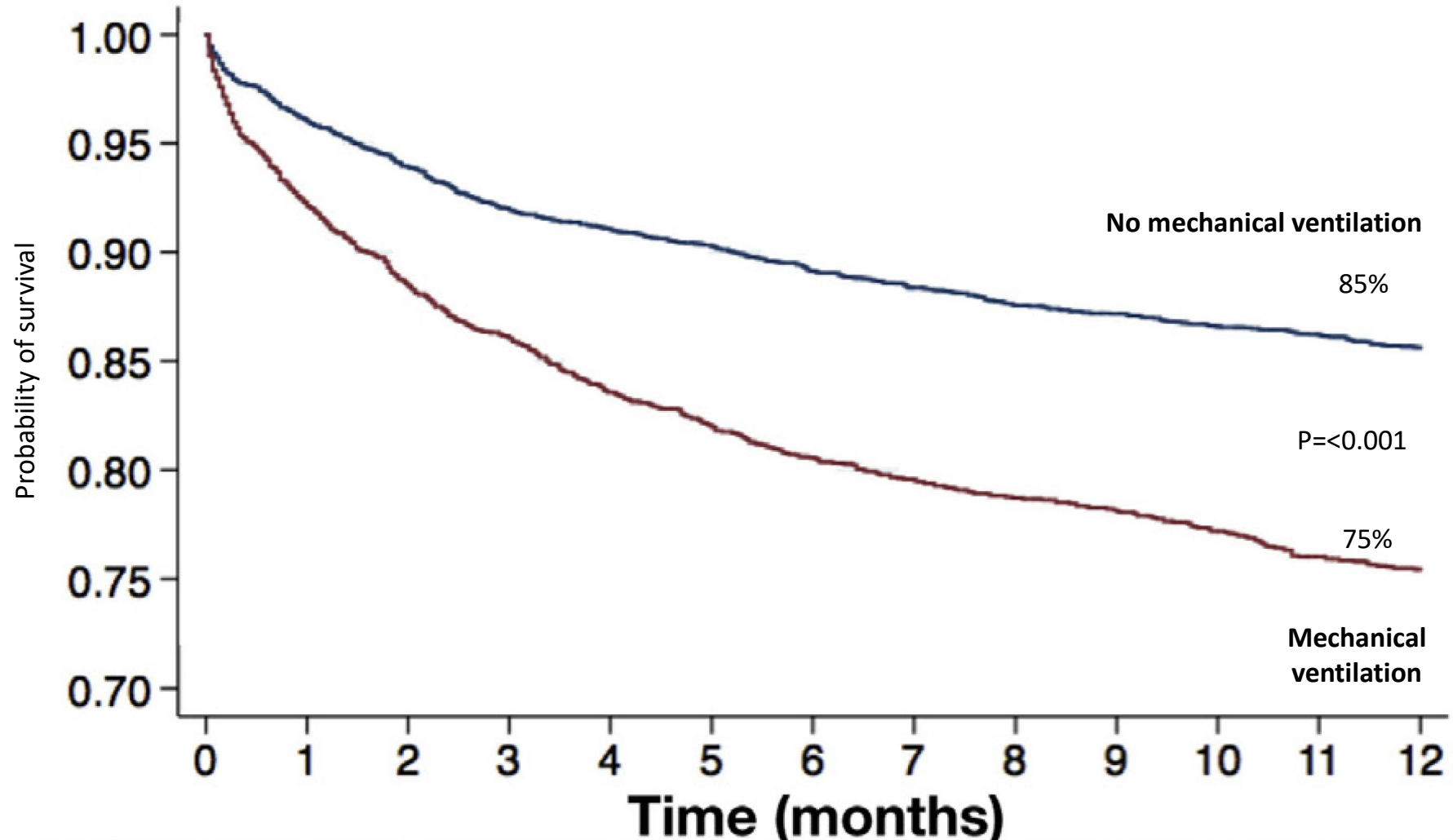
Pathogenesis of bacterial infections in cirrhosis



The impact of bacterial infections at Padua Liver Transplant Center on waiting list management: 114 candidates with bacterial infection had a higher probability of death ($p=0.004$) and a lower probability of undergoing liver transplantation ($p=0.01$) when compared with 762 matched candidates with no bacterial infection.



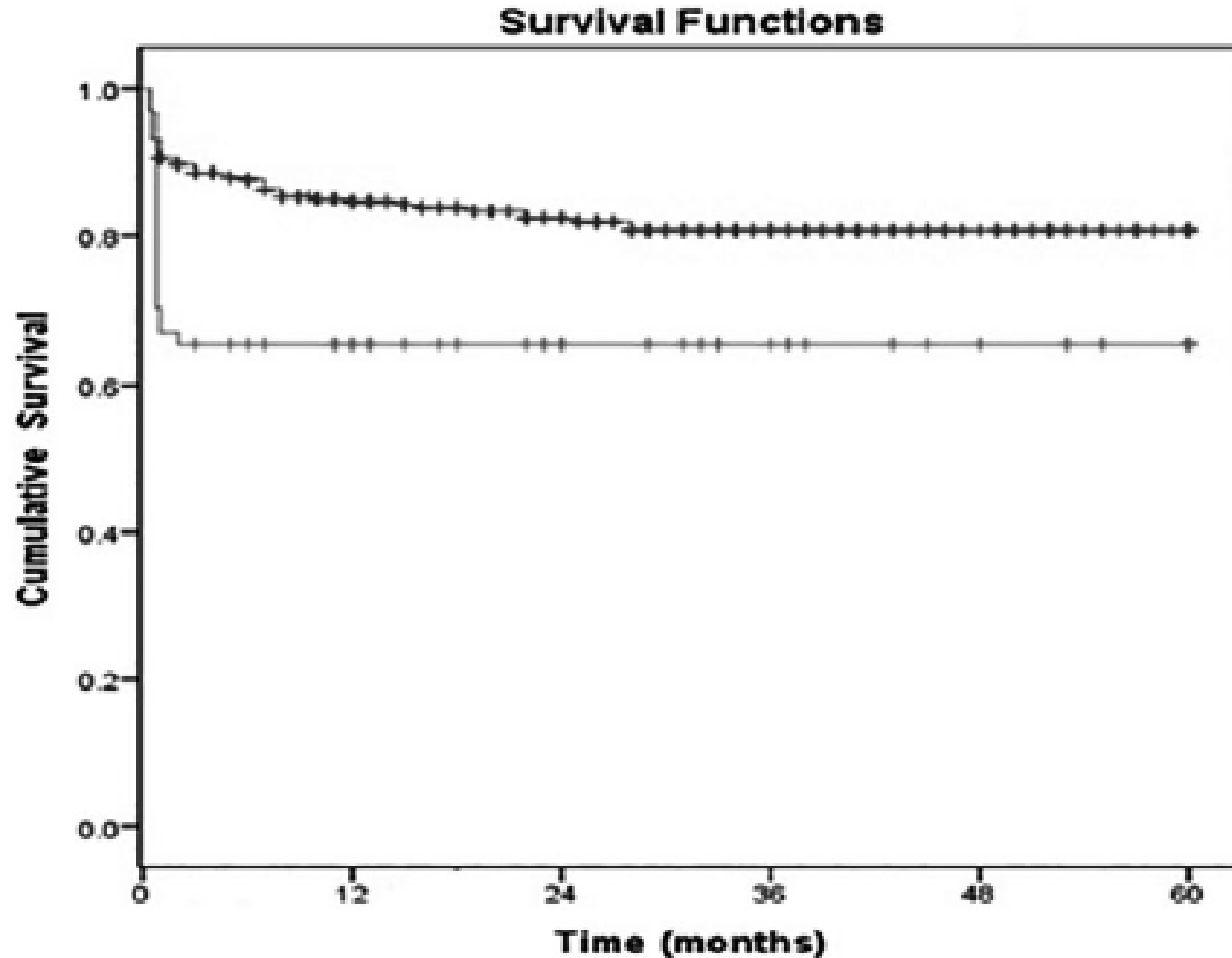
Probability of survival after liver transplantation in patients with ACLF grade 3 according to the presence of mechanical ventilation at transplantation



Living Donor Liver Transplantation for Acute Liver Failure

In countries where deceased organ donation is sparse, emergency living donor liver transplantation is the only lifesaving option in selected patients with acute liver failure.

LDLT for Acute Liver Failure



349 LDLT for ESLD

61 (14.9%) LDLT for ALF

65% 5-year survival

Predicted outcome:

postoperative worsening of cerebral edema

preoperative SIRS

sepsis

“...livers do not grow on trees...”

David Mulligan Hepatology 2016

Lower 5-year survival?

40% likelihood of 5-year survival as a cut-off for LDLT in recipient **ineligible** for DDLT

Re-transplantation for acute liver failure?

Using a deceased organ from the common pool to transplant a patient who was determined to be **ineligible** for that organ would be **unjust to another patient** who is entitled to the gift of life because of the great likelihood of deriving a significant benefit from it.

Transplant teams **should not offer a deceased organ to a living donor recipient with acute graft failure given the injustice to others on the transplant list.**

Should living donor liver transplantation be an option when deceased donation is not?

Situations do arise in which **it is unclear whether living donor liver transplant should be offered**, and what the ethical standard for making such decisions should be.

When an **liver transplant candidate is declined for listing** to receive a deceased donor liver transplantation, sometimes a loved one comes forward and offers to be a living donor.

This raises the ethical question of whether a patient who is not eligible for deceased donor liver transplant **should be eligible for living donor liver transplant**.

Should living donor liver transplantation be an option when deceased donation is not?

- Should the same standards that are used to decline or accept patients on waiting list, also be used to determine whether an LDLT should be performed?
- Should the criteria be more or less rigorous?

Should living donor liver transplantation be an option when deceased donation is not?

- Should the same standards that are used to decline or accept patients on waiting list, also be used to determine whether an LDLT should be performed?
- Should the criteria be more or less rigorous?
- **No clear and compelling recommendation has emerged.**
- **Transplant centres have been left uncertain how to proceed in these difficult situations.**

Trust and setting limits in LDLT

Living donation does not involve taking an organ from the deceased donor pool. There are other important ethical considerations that warrant setting limits in LDLT:

- 1) Medical team:** they must independently assess the benefits and burdens and conclude that the promised benefits are worth the foreseeable risks involved.
- 2) It is essential that society trusts the transplantation community** and that the integrity and reputation of transplantation programmes is upheld to preserve the future of LDLT.
- 3) The third reason to set limits in LDLT is to preserve the future availability of this practice.**

Donor Outcomes in Anonymous Live Liver Donation

- 50 anonymous live liver transplants (2005-2017).
- The median hospital stay for the donor was 6 days.
- There was 1 Dindo-Clavien Grade 3 complication that completely resolved.
- One-year recipient survival was 91% in 22 adults.
- One-year recipient survival was 97% in 28 children.
- No donor reported regretting their decision.