



Decompensated Liver Disease in the Hospitalized Patient

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NW Regional Hospital Medicine Conference

Outline

- Definitions
 - Acute Liver Failure (ALF)
 - Acute on Chronic Liver Failure (ACLF)
- Prognostication in ACLF
- EtOH hepatitis
 - Liver Transplantation

Case

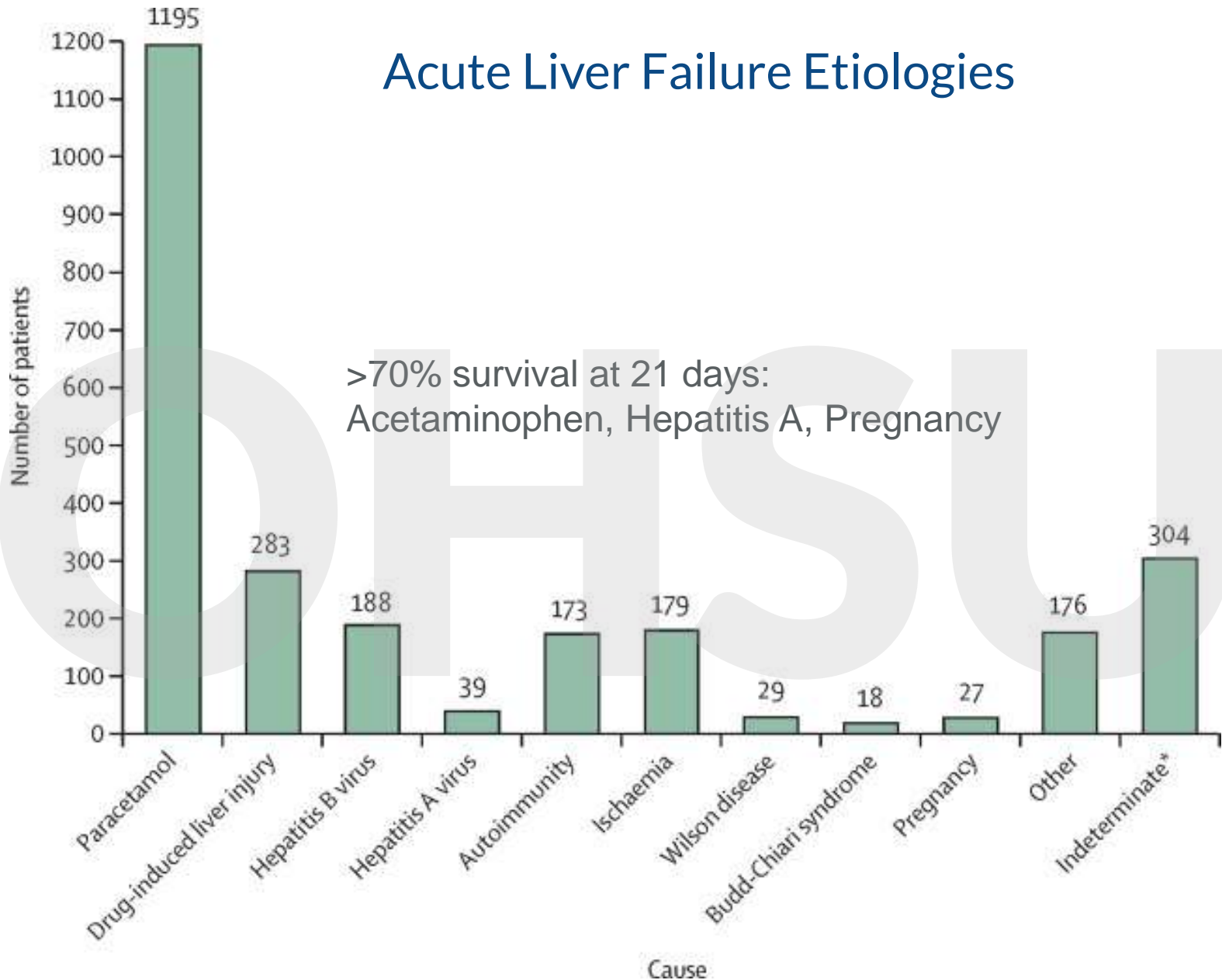
- 42yo female with a diagnosis of EtOH hepatitis and cirrhosis 3 months prior to presentation, now admitted for worsening ascites. She is awake but has slow speech
- Exam: Jaundiced, distended abd but not tense, +asterixis
- Tbili 13.5 (stable), Alk phos 127, AST 119, ALT 64
- INR 2.9 (Baseline 1.8 ~1 week ago)
- Cr 2.1 (Baseline 1.1 ~ 1 week ago)
- Alb 2.7
- Hgb stable
- Outpatient medications:
 - Furosemide 40mg, Spironolactone 100mg
 - Lactulose 2 tsp BID

Acute Liver Failure

General Definition:

- No pre-existing liver disease
 - Acute hepatocellular damage
 - Coagulopathy
 - Encephalopathy
- Uncommon entity
 - 1 case per million people
 - If a patient doesn't have encephalopathy, then it's not ALF!
 - Severe *acute liver injury* only
 - Decompensated chronic liver disease that can present as fulminant disease
 - Wilson
 - Autoimmune hepatitis
 - HBV

Acute Liver Failure Etiologies



Stravitz RT, Lee WM. Lancet 2019



Acute-on-chronic liver failure (ACLF)- What is it?

- *“I know it when I see it!”*
- *“The entity is not new. All physicians who have followed hospitalized patients with cirrhosis have been seeing this type of patient over their entire career....ACLF has taken on a life of its own and has led to a vast body of literature...However, it has also led to confusion because ACLF is considered by many as a new diagnostic entity rather than, what it really is, an old entity of prognostic significance that is still in search of a unifying definition.”*

- Guadalupe Garcia-Tsao

ACLF- general definition

- Very common entity
- No consensus definition
- Decompensation of liver disease in a patient with underlying chronic liver disease/cirrhosis with extrahepatic organ failures
 - Liver failure- coagulopathy, encephalopathy
- Extrahepatic Organ failures:
 - Kidney
 - Cerebral (hepatic encephalopathy)
 - Circulation
 - Pulmonary
- Thought to secondary to proinflammatory state with increased cytokine production leading to multiorgan failure

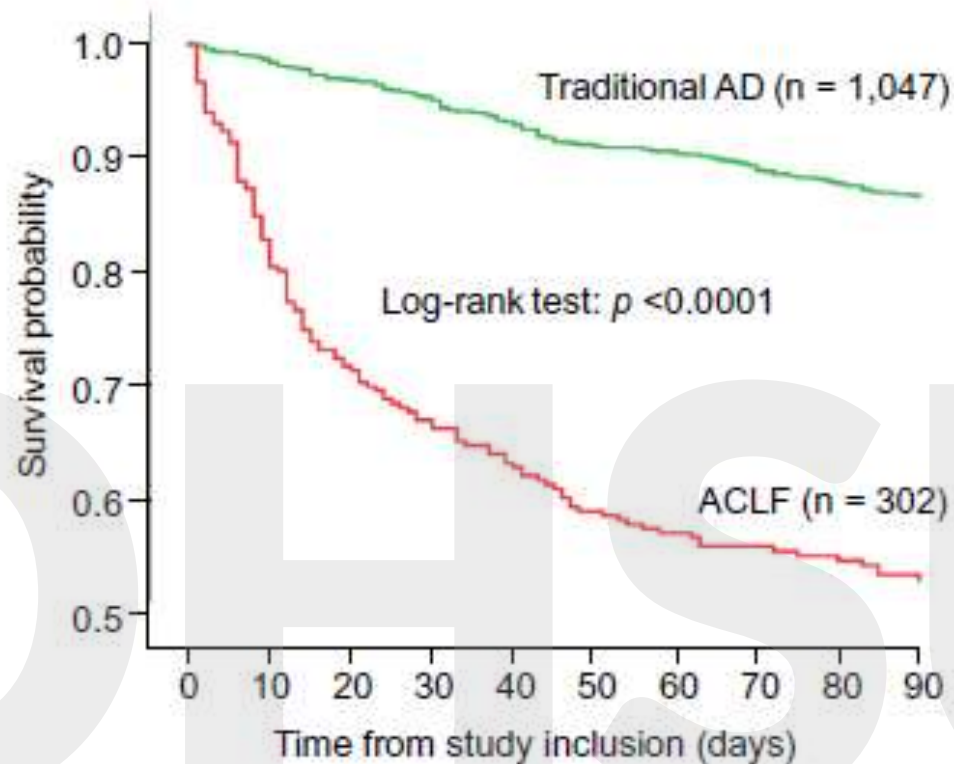


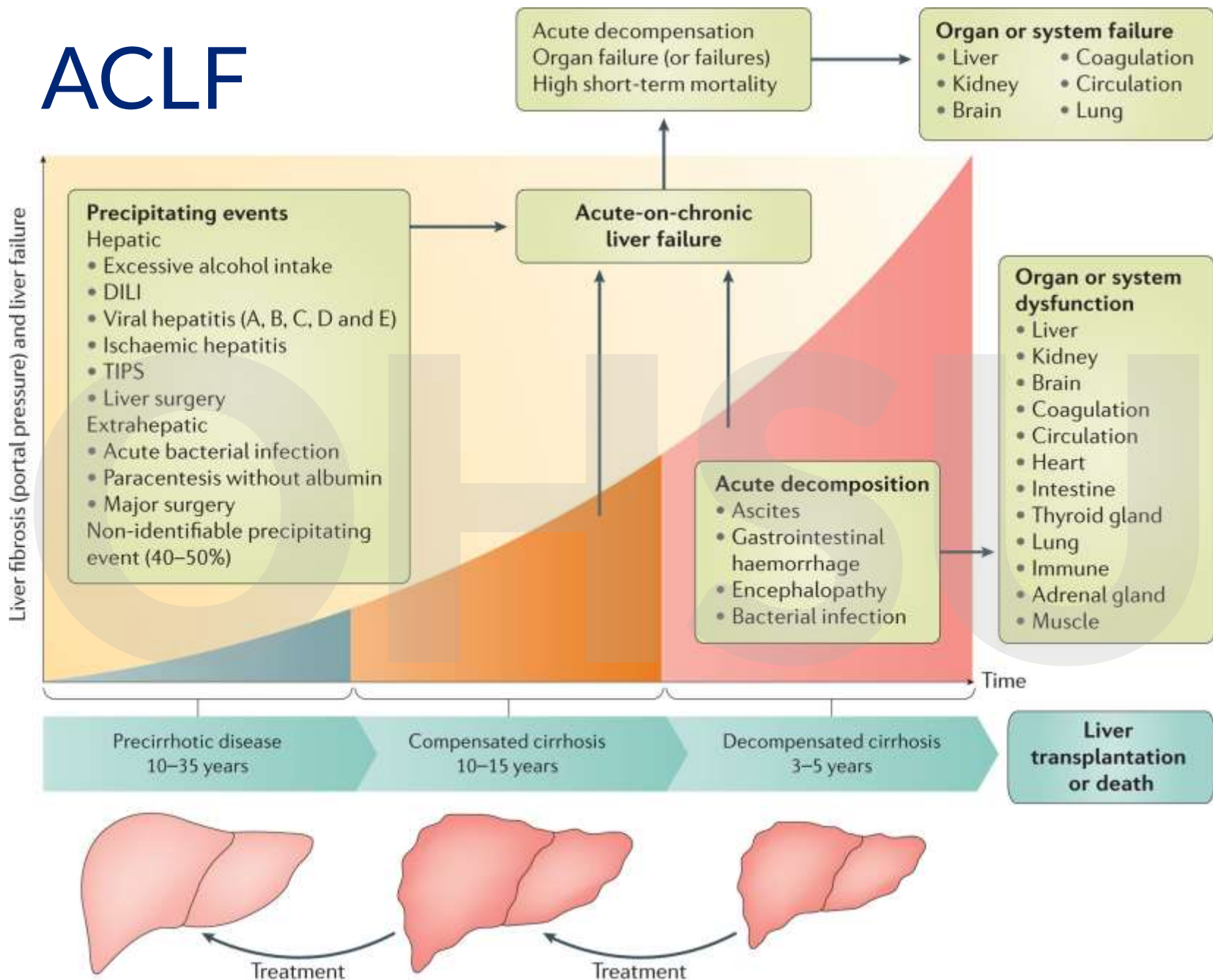
Fig. 1. Cumulative transplant-free survival curves of patients from the CANONIC study. Kaplan-Meier 90-day transplant-free cumulative survival curves of patients from the CANONIC study⁷ with or without ACLF (traditional AD). Kaplan-Meier Curves were compared using the log-rank test. ACLF, acute-on-chronic liver failure; AD, acute decompensation.

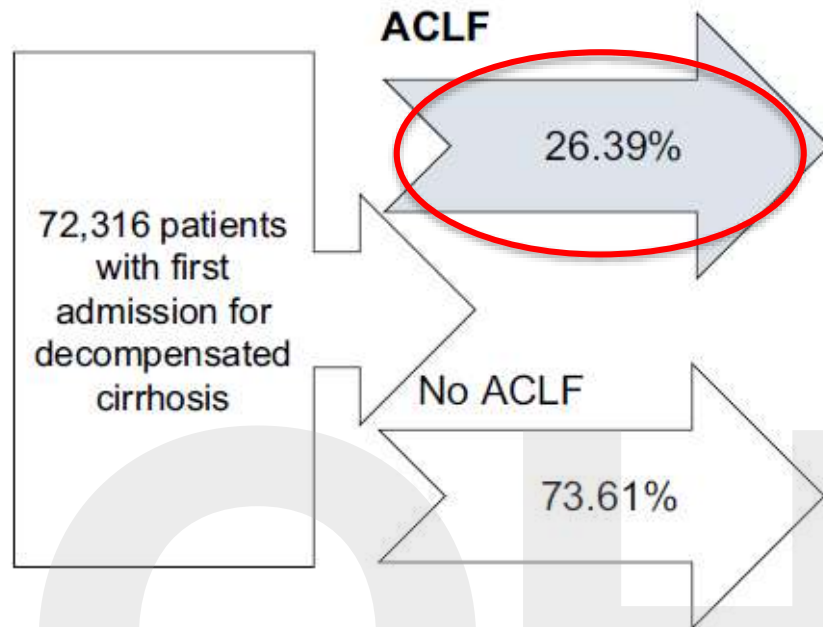
Grading ACLF

- Most accepted grading system
 - European CANONIC study definition (Moreau et al.)
 - ACLF 1
 - (i) single kidney failure (sCr \geq 2.0), (ii) single failure of the liver, coagulation, circulation, or respiration who had a sCr 1.5 to 1.9 mg/dl, and (iii) single cerebral failure who had a sCr 1.5 to 1.9 mg/dl.
 - ACLF Grade 2- 2 organ failures
 - ACLF Grade 3- 3 organ failures
 - North American Consortium for the Study of End-Stage Liver Disease (NACSELD)
 - 2 of 4 organ failures as kidney, brain, circulatory, and respiratory failures

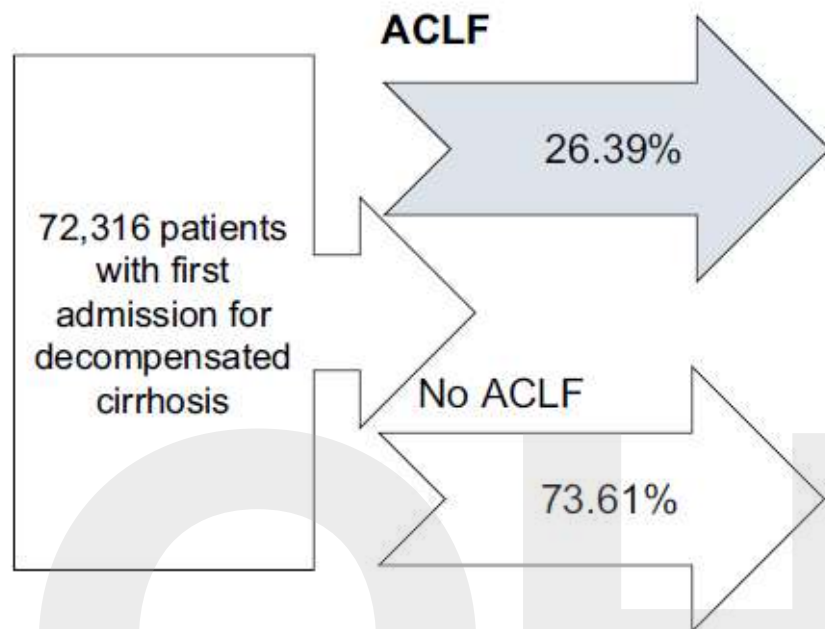
Failing organ	European Association for the Study of Liver-Chronic Liver failure organ failures definition (9)
Liver	Bilirubin level of >12 mg/dL
Kidney	Creatinine level of ≥ 2.0 mg/dL or renal replacement
Brain	West-Haven hepatic encephalopathy grade 3–4
Coagulation	INR ≥ 2.5
Circulation	Use of vasopressor (terlipressin and/or catecholamines)
Respiration	PaO ₂ /FiO ₂ of ≤ 200 or SpO ₂ /FiO ₂ of ≤ 214 or need for mechanical ventilation

ACLF



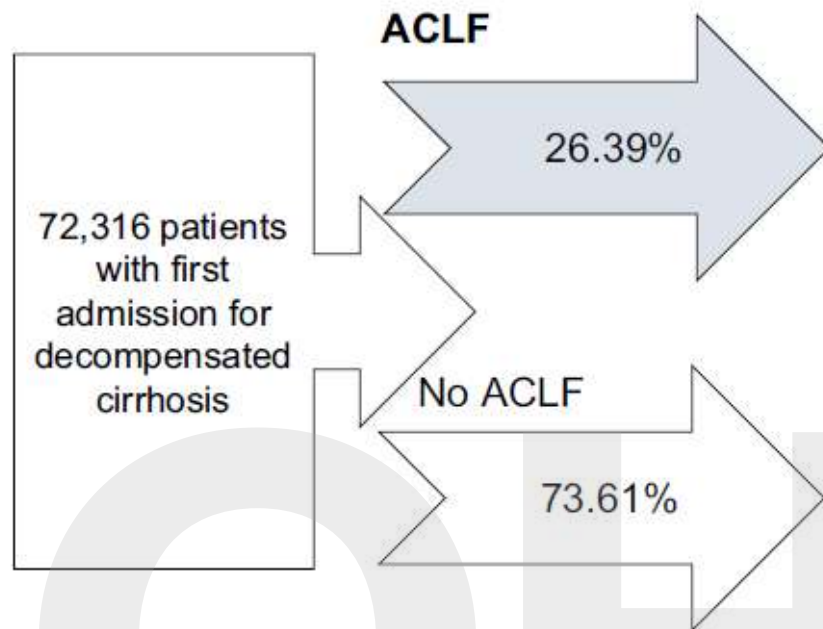


	No ACLF	ACLF
Potential precipitating events of ACLF		
Bacterial infection	5,587 (10.50)	2,762 (14.47)
Gastrointestinal haemorrhage	4,596 (8.63)	1,632 (8.55)
Alcoholism 1 year prior to cirrhosis index date	19,338 (36.33)	5,469 (28.66)
Infection or gastrointestinal bleeding or alcohol	25,192 (47.32)	7,936 (41.59)
Organ failures		
Liver	1,144 (2.15)	2,342 (12.27)
Kidney	0 (0.00)	13,718 (71.89)
Cerebral	10,481 (19.69)	6,870 (36.00)
Coagulation	1,314 (2.47)	2,644 (13.86)
Circulation	602 (1.13)	3,362 (17.62)
Lungs	918 (1.72)	3,227 (16.91)
Arterial pressure (mmHg), median (p25–p75)	93.17 (84.33–102.33)	87.17 (76.83–98.50)



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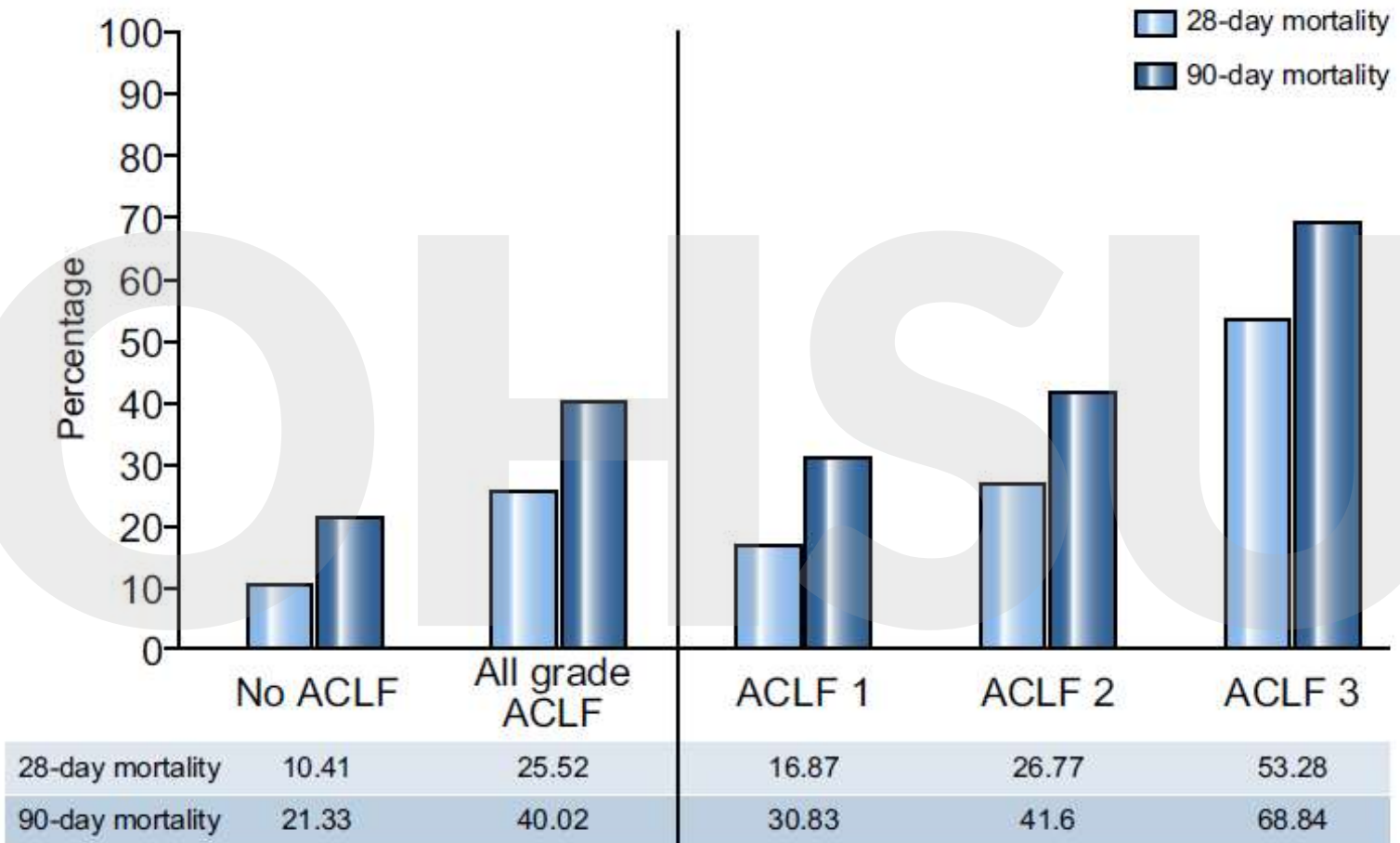


Fig. 1. Mortality rate* at 28 and 90 days in patients with and without ACLF and by grade. To examine the difference between ACLF and ACLF grades, the

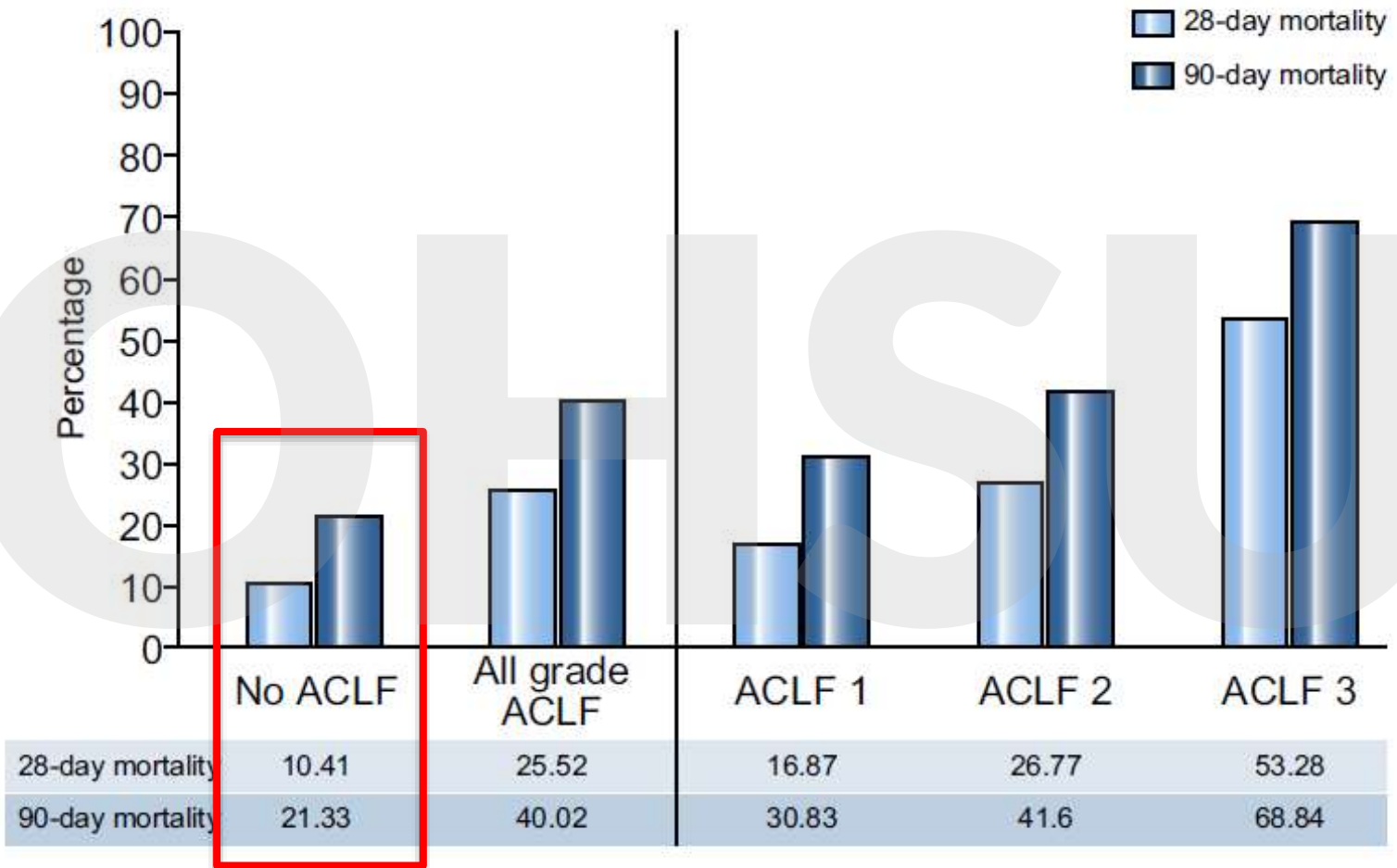


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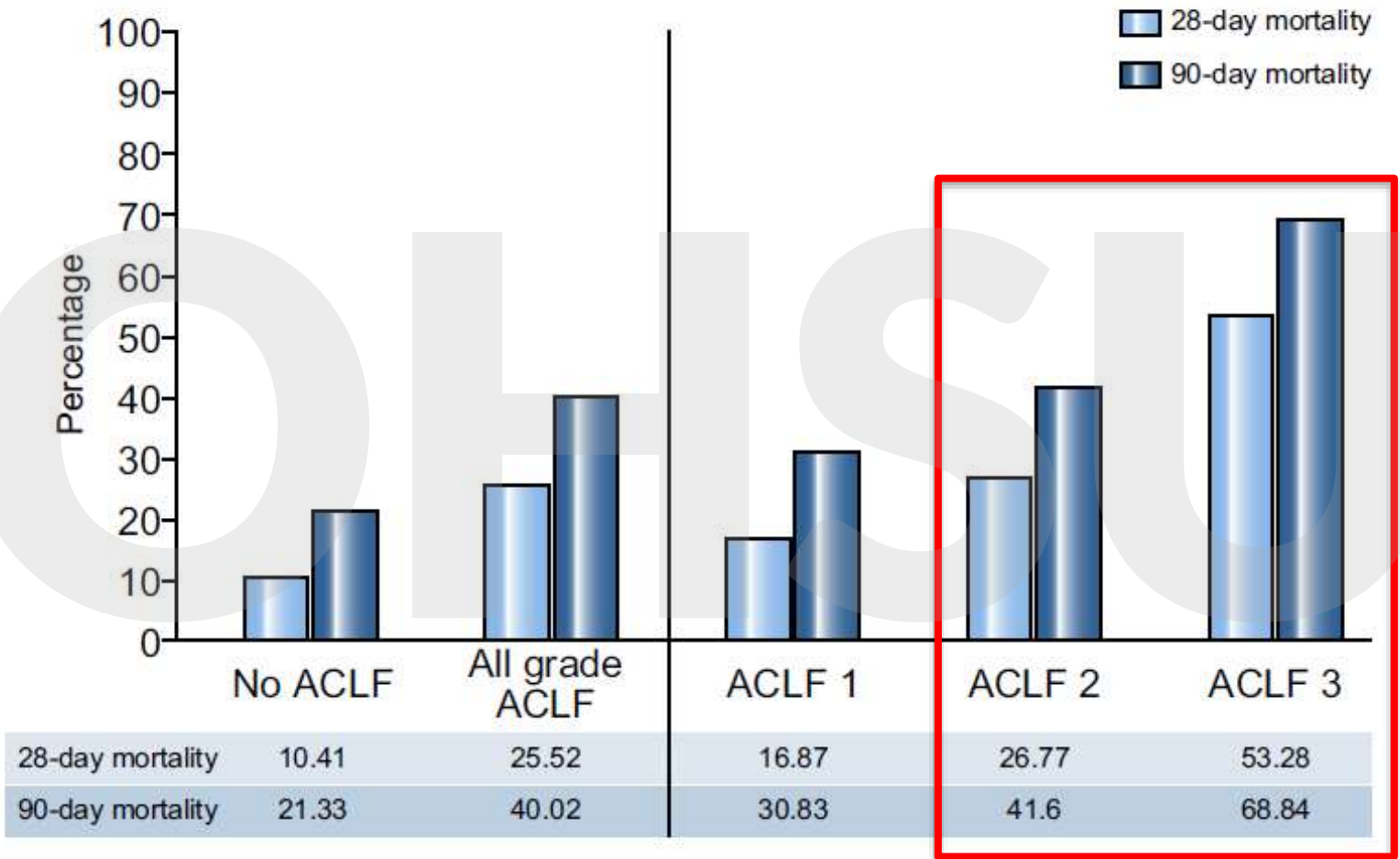
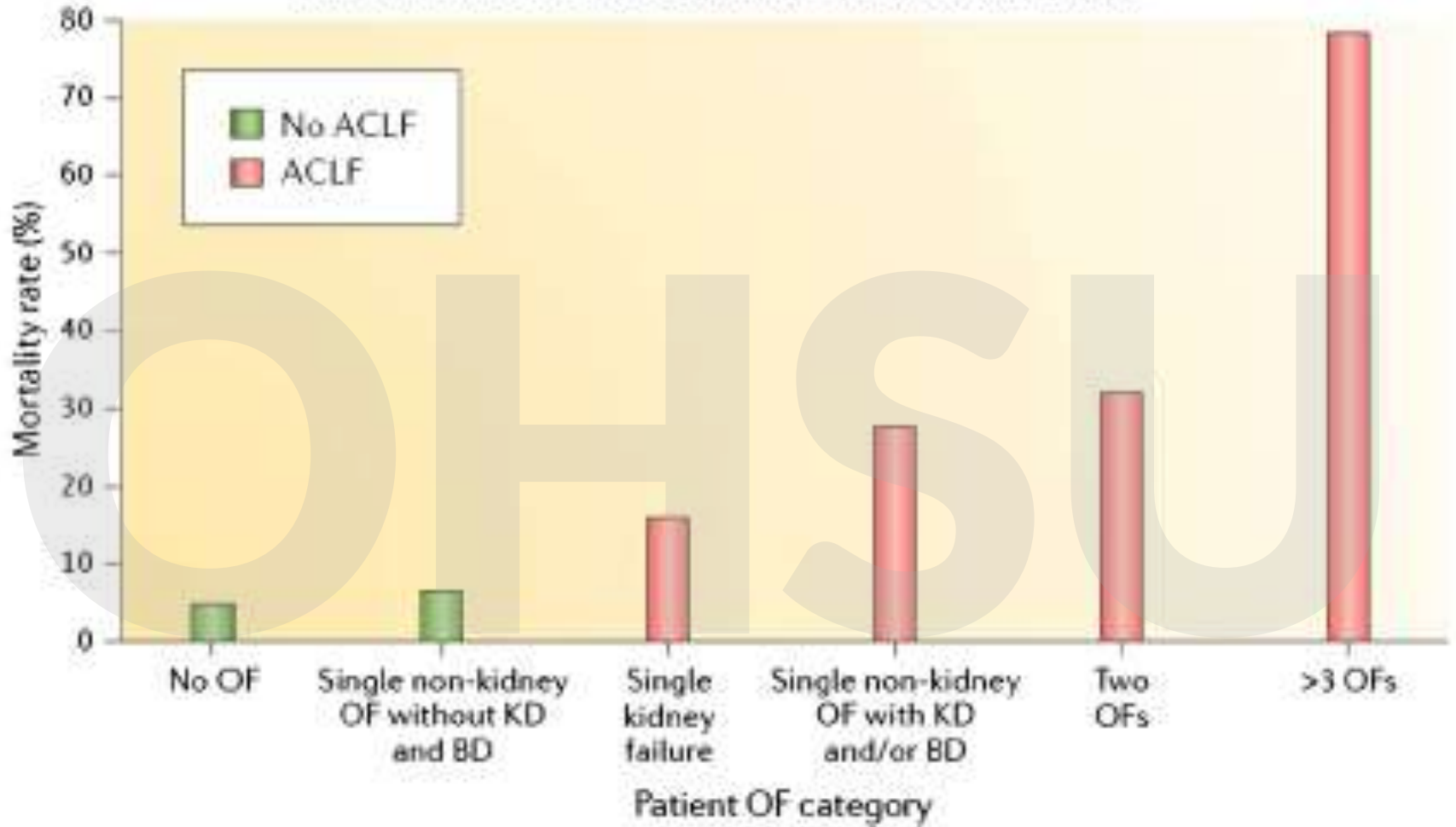


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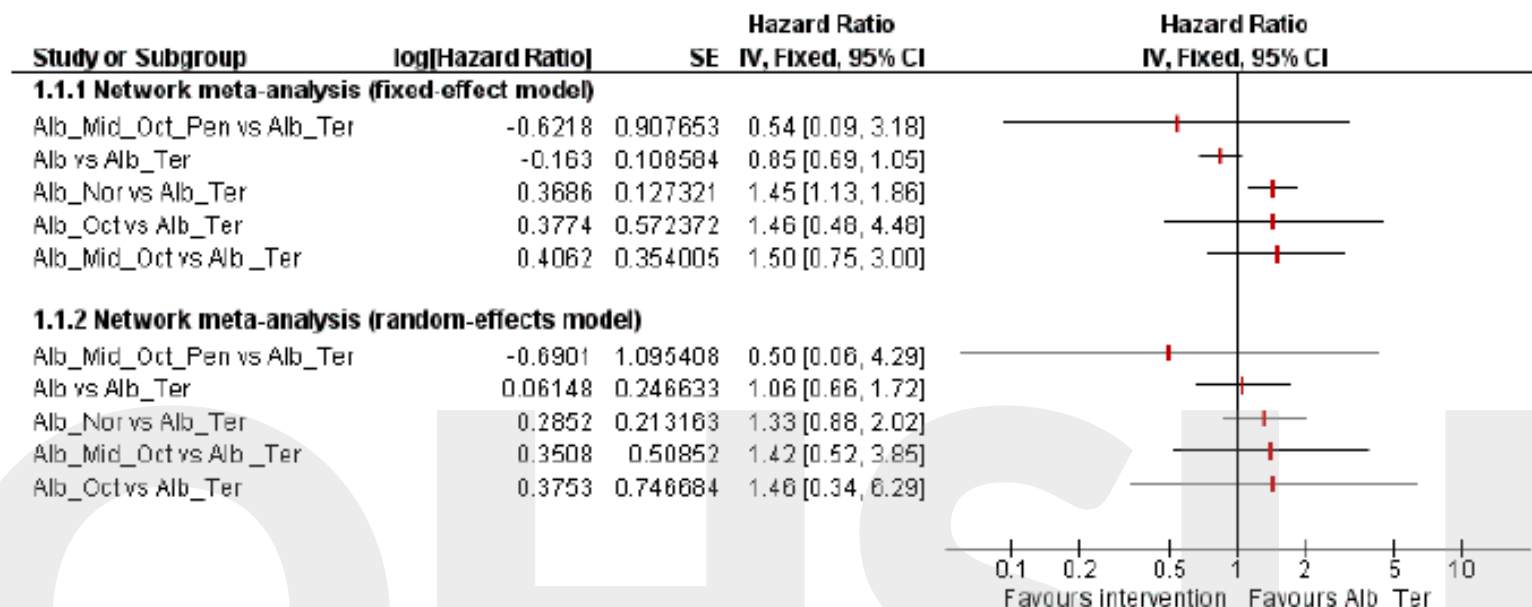
Relationship between organ failure and mortality in ACLF



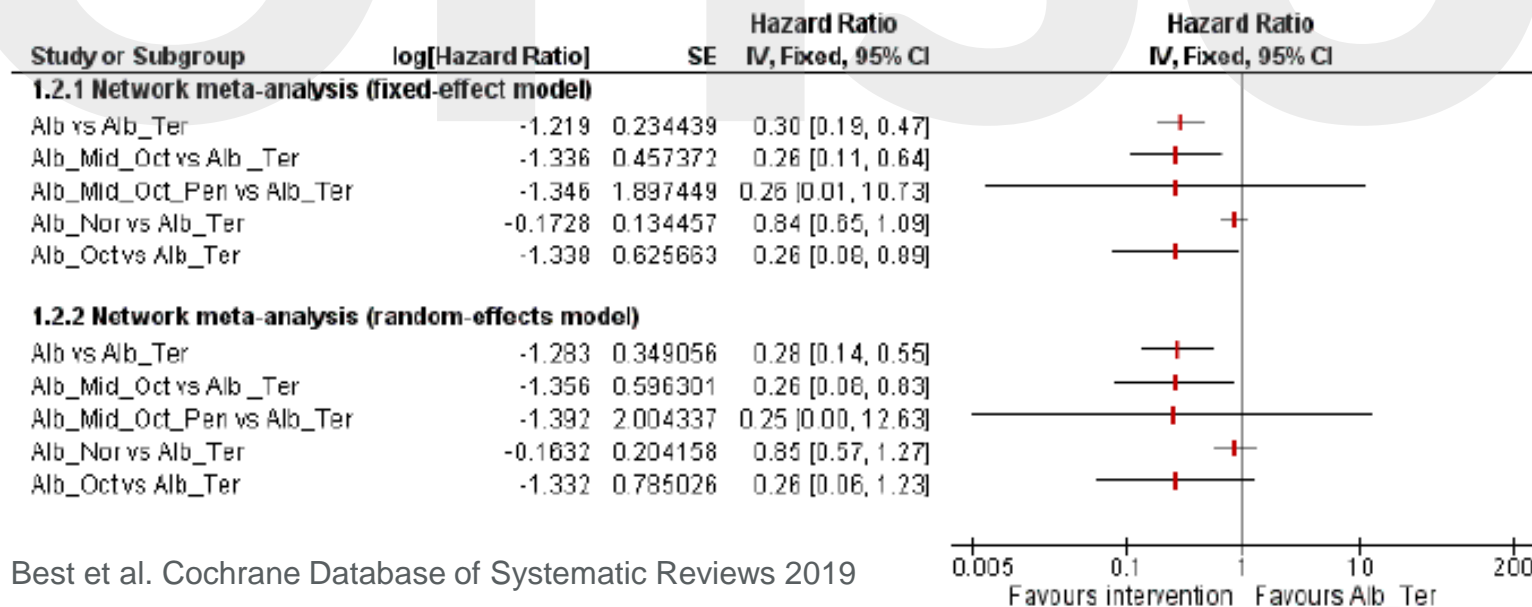
Acute Kidney Injury and Hepatorenal Syndrome Definitions in cirrhosis

- Acute Kidney Injury
 - Stage 1 Increase in sCr \geq 0.3 mg/dL in 48 hours, or \geq 50% increase in sCr over baseline over 7 days
 - Stage 2- sCr 2-3x baseline
 - Stage 3- sCr $>$ 3x baseline
- Resolution of AKI – sCr within 0.3mg/dL of baseline
- Hepatorenal syndrome
 - Cirrhosis AND ascites
 - Meets AKI criteria
 - Absence of shock
 - No nephrotoxic drugs
 - No macroscopic signs of structural kidney injury

All-cause mortality



Recovery from hepatorenal syndrome



CLIF ACLF calculator

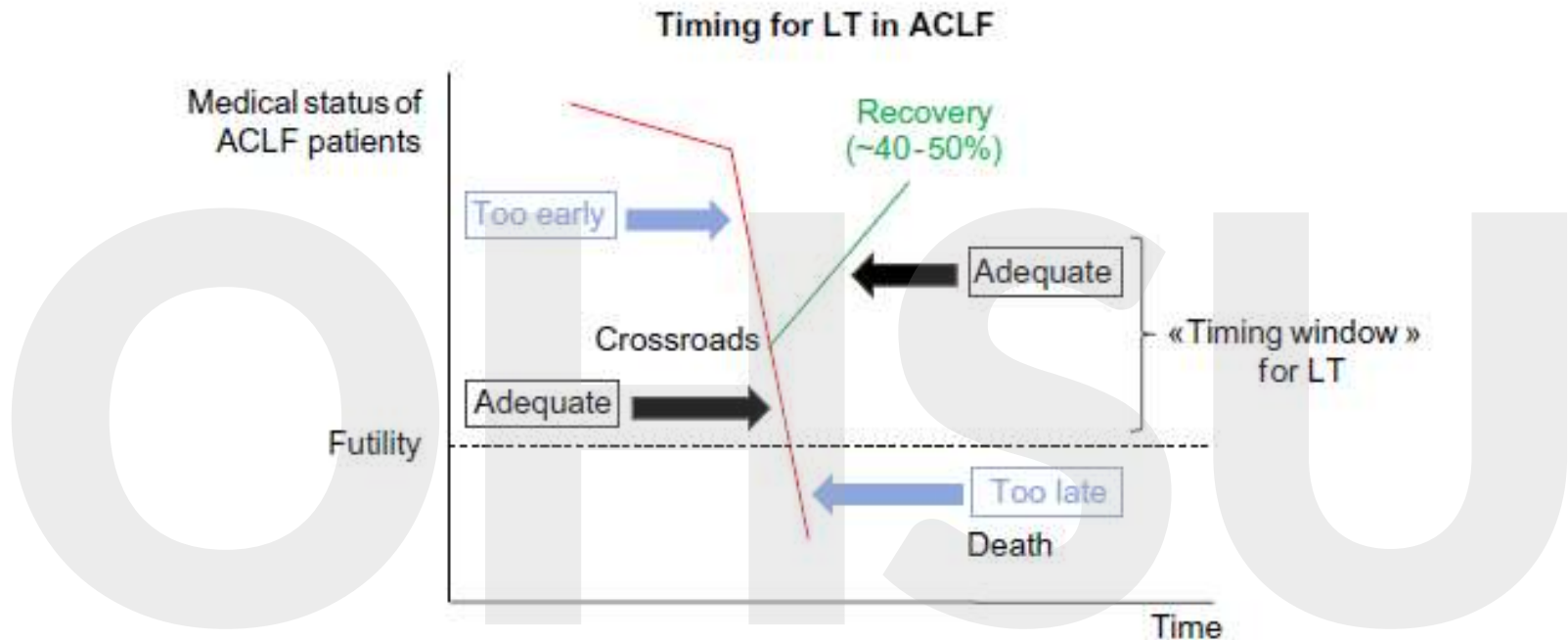
- <http://www.efclif.com/scientific-activity/score-calculators/clif-c-aclf>
- Google: CLIF ACLF calculator

The screenshot displays the EF Clif website's navigation bar and the CLIF-C ACLF calculator interface. The navigation bar includes the EF Clif logo (European Foundation for the Study of Chronic Liver Failure) and menu items for FOUNDATION, SCIENTIFIC ACTIVITY, and SCORE CALCULATORS. The main heading is "CLIF-C ACLF CALCULATOR". Below this, the text reads: "CLIF-C ACLF (Acute-on-Chronic Liver Failure) score and expected mortality rates" and "ACLF Grade, CLIF-C OF (Organ Failure) Score and CLIF-C ACLF (ACLF patients) or CLIF-C AD Score (non-ACLF patients with Acute Decompensation)". A link "See score formula" is provided. The calculator form is divided into two sections: "DATA" and "CLIF-C Organ Failure Sub-scores". The "DATA" section includes a field for "Bilirubin" with a unit of "mg/dl". The "CLIF-C Organ Failure Sub-scores" section includes a "Liver score" field and a "Liver failure" field with radio buttons for "Yes" and "No". At the bottom of the page, there is a cookie consent notice: "We use first and third party cookies to improve the services by analysing your browsing habits. If you continue browsing the website, you accept their installation and use as aforesaid. You may modify the settings and obtain more information in the Cookies Policy." and an "ACCEPT" button.

Management of ACLF

- Best conservative care
 - Difficult entity to study
 - Quality of data are not adequate to draw conclusions
- Treat infection, support GI bleed
- Aggressively treat renal failure
 - Albumin 1mg/kg up to 100g IV daily x 2 days, then 50g thereafter
 - If HRS, Midodrine and octreotide
 - IV octreotide vs. subcut (usually stop if not effective after 2 weeks)
 - Midodrine 15mg po TID- can be continued as outpatient
 - Norepinephrine can be used to increase renal perfusion
 - Terlipressin not available in the US

ACLF and Liver Transplantation



- Patients can be too sick for LT evaluation or if listed then become too sick for LT
- If renal failure ONLY, consider liver transplant evaluation
- Typically, only ACLF 1 patients can be transplanted
 - Can patients survive the operation?

Back to our case...

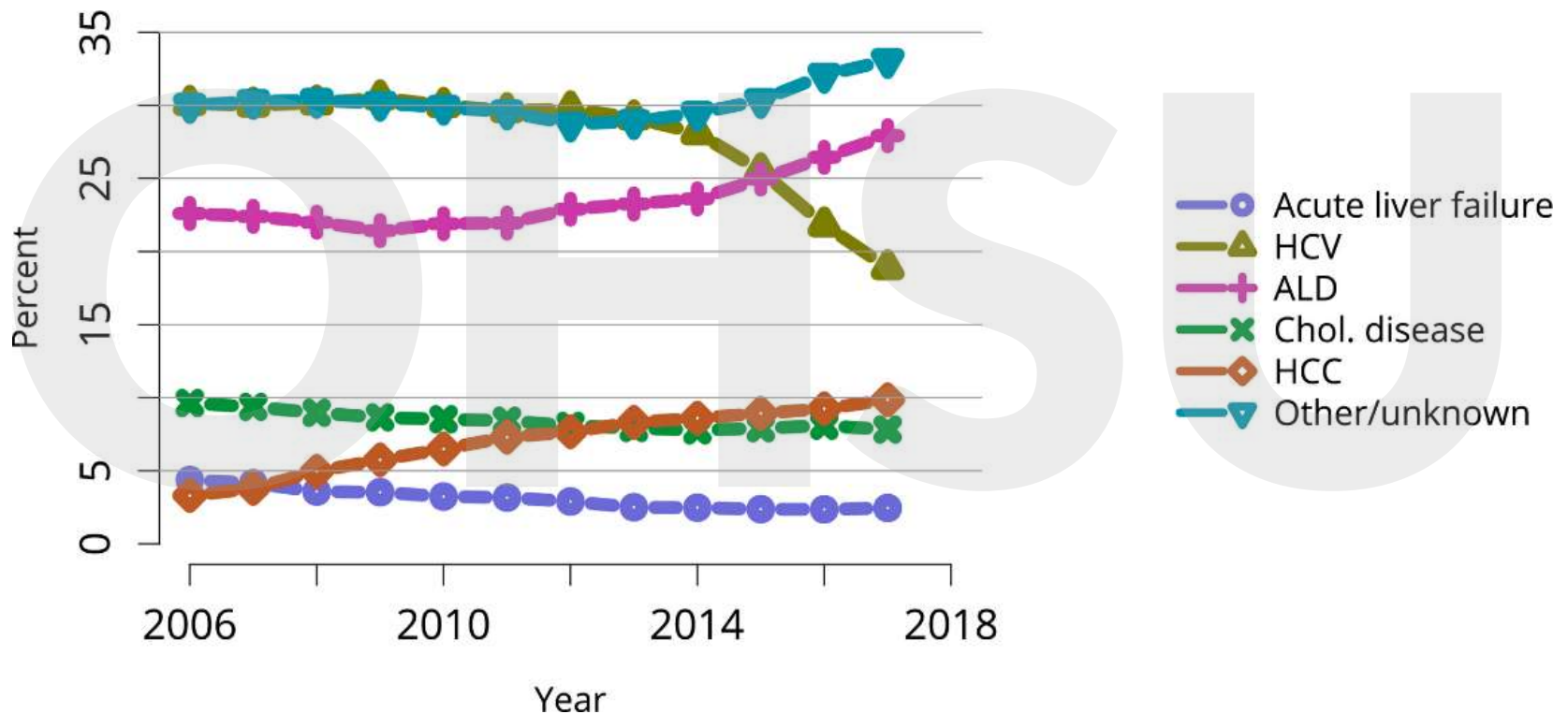
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Case: ACLF

- Reportedly abstinent x 3 months
- Current decompensation could be either due progression of disease vs. precipitant
- Plan:
 - R/O infection (diagnostic tap, blood cultures, UA, CXR)
 - Check ETG/PeTH
 - U/S with dopplers (due to AKI can't get contrasted imaging)
 - Hold diuretics
 - Albumin IV 100g x 2 days
- Grade 3 ACLF
 - 56% mortality at 1 month, 75% at 3 months
 - Kidney, Cerebral (Grade 1 encephalopathy), Coagulation
 - Better short term mortality prediction than MELD

Distribution of adults waiting for liver transplant by diagnosis

OPTN/SRTR 2017 Annual Data Report: Liver

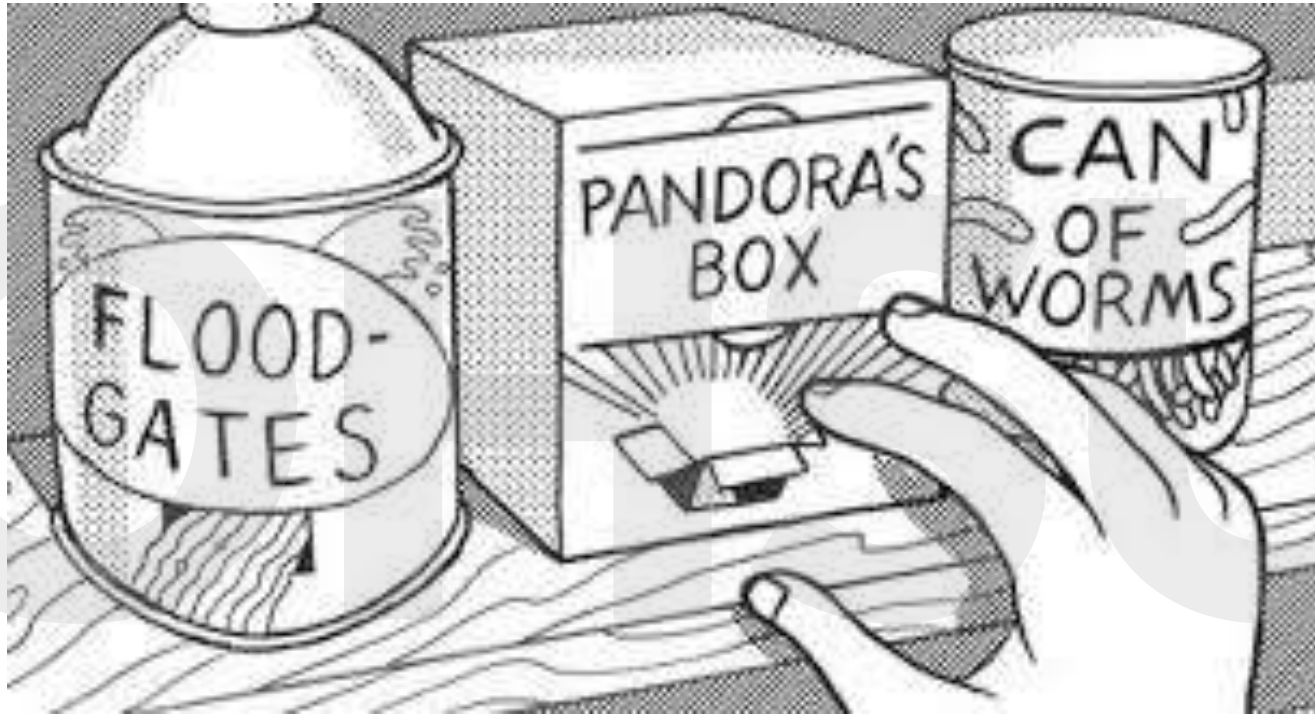


ACLF: EtOH Hepatitis

- EtOH hepatitis is a classic ACLF entity
- Corticosteroids?
 - Multiple meta-analyses including a Cochrane review without any significant short or long term mortality benefit
 - If any contraindication, most would not use steroids
 - If discriminant function >32 , most are still using steroids if no contraindications with low threshold to stop
 - Lille score at 7 days and stop if Lille score is >0.45
 - Steroids+NAC or NAC alone
 - No high quality data

Liver transplantation for acute alcoholic hepatitis

- Landmark NEJM article 2011
- N=26 patients transplanted in 7 centers (mostly French)
- Severe alcoholic hepatitis at high risk of death (median Lille score, 0.88) were selected and placed on the list for a liver transplant
- Fewer than 2% of patients admitted for an episode of severe alcoholic hepatitis were selected
- Protective factors: all patients transplanted had supportive family members, no severe coexisting conditions, and a commitment to alcohol abstinence.
- 5 returned to drinking, but all >720 days after LT



LT for EtOH hepatitis:

Areas of uncertainty

- What are the long term outcomes?
- Selection criteria in the study different from our real life practice?
- Are these patients overly advantaged?
 - EtOH hepatitis patients often have labs that over estimate their global degree of clinical instability
 - Particularly in those with minimal to no kidney failure

Is my patient with EtOH Liver Disease a liver transplant candidate?

- Patients who we previously did not consider LT candidates who MAY be candidates
 - Every center has their own criteria for considering evaluation for liver transplantation
- Acute EtOH hepatitis related liver failure
 - No sobriety by definition
 - No cirrhosis
 - Must be first episode of EtOH related decompensation
- Acute on chronic EtOH liver disease/cirrhosis with abstinence with at least 2 months of sobriety OUT OF THE HOSPITAL

Case: ACLF, precipitated by EtOH

- Grade 3 ACLF – 56% mortality at 1 month, 75% at 3 months
 - Kidney, Cerebral (Grade 1 encephalopathy), Coagulation
- MELD 40
- Liver Transplant evaluation
 - Does not guarantee listing for transplant
- Palliative Care Consult
 - Stay tuned for Dr. Arnab Mitra tomorrow!

Summary

- Acute liver failure
 - Uncommon, and overall survival especially with acetaminophen is surprisingly favorable
- Acute on Chronic liver failure
 - Defining the syndrome is helpful for prognostication
 - Decompensated liver disease with chronic liver disease/cirrhosis WITH extrahepatic organ failure
 - 1/4 hospitalized decompensated cirrhotics
 - With 2 organ failures, 30% 28 day, 50% survival at 90 days
 - For example: Kidney and cerebral

Summary

- Liver transplantation is an option for patients with ACLF with 2 or less organ failures
- EtOH hepatitis is an emerging indication for liver transplantation
 - Highly selected patient population
- Consider Palliative Care consult for patients who have ACLF and are not LT candidates



OHSU

Thank You

OHSU Consult Line

503-494-4567