12th UMEM Critical Care Symposium
Wednesday, May 21, 2025
Presentation by Dr. Daniel Boutsikaris

PEARLS & PITFALLS OF CRITICALLY ILL CIRRHOTIC PATIENT

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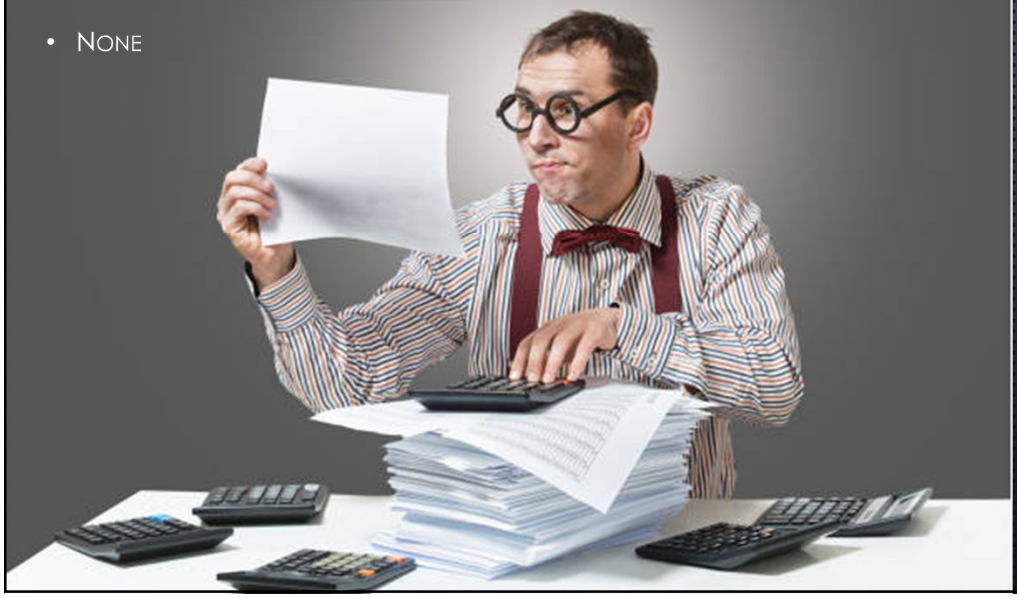
DR. DANIEL BOUTSIKARIS, M.D.
MEDICAL DIRECTOR OF MICU
RUTGERS ROBERT WOOD JOHNSON UNIVERSITY HOSPITAL
NEW BRUNSWICK, NJ

1

DISCLOSURES

- NONE



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OBJECTIVES:

- Diagnostic Considerations
- Review of Cirrhotic Physiology
- Management considerations of the Critically Ill Cirrhotic Patient

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DIAGNOSIS:

Acute on Chronic Liver Failure

- The Asian Pacific Association for the Study of the Liver (APASL)
- The European Association for the Study of Chronic Liver Failure (EASL-CLIF)
- The North American Consortium for the Study of End-Stage Liver Disease (NACSELD)

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Expert Opinion

JOURNAL
OF HEPATOLOGY

Towards a new definition of decompensated cirrhosis

Gennaro D'Amico[1], Mauro Bernardi[2], Paolo Angeli[3,*]

Decompensated Cirrhosis:
"Complications related to portal hypertension and impaired liver function such as GI bleeding, hepatic encephalopathy, jaundice and ascites formation."

"However, although there is an almost unanimous consensus on the prognostic weight of decompensation, a corresponding consensus on its definition is still lacking."

Journal of Hepatology 2022 vol. 76 | 202-207

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AASLD
AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

Guidance statement:

1. We suggest that the presence of all of the following elements are minimum critical components for the definition of ACLF: (1) acute onset with rapid deterioration in clinical condition, (2) the presence of liver failure defined by elevated bilirubin and elevated INR in patients with chronic liver disease with or without cirrhosis, and (3) the presence of at least one extrahepatic (neurologic, circulatory, respiratory, or renal) organ failure.

Hepatology. 2024;79:1463–1502.

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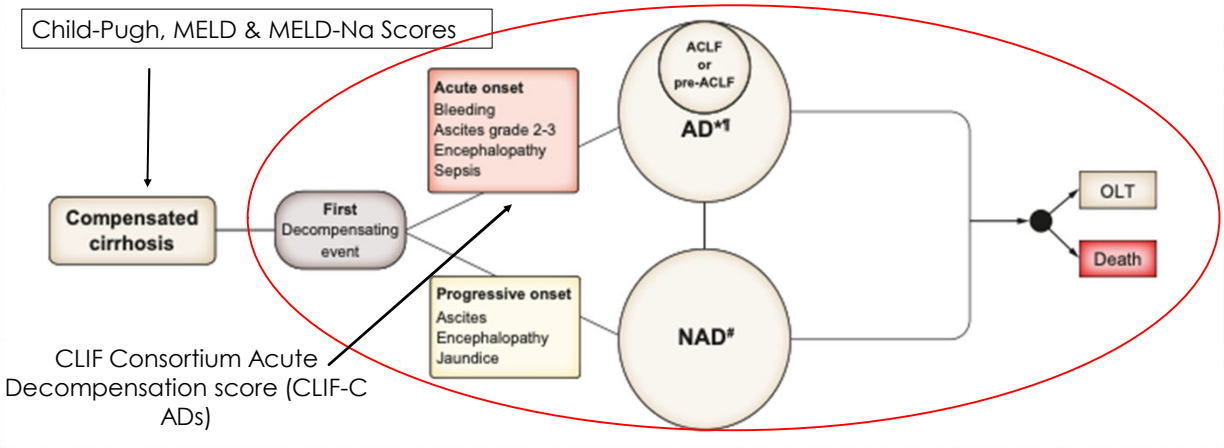
COMPENSATED vs DECOMPENSATED



Journal of Hepatology 2022 vol. 76 | p.204

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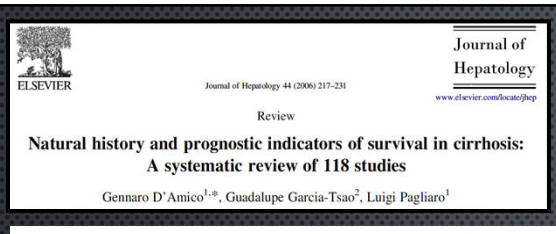
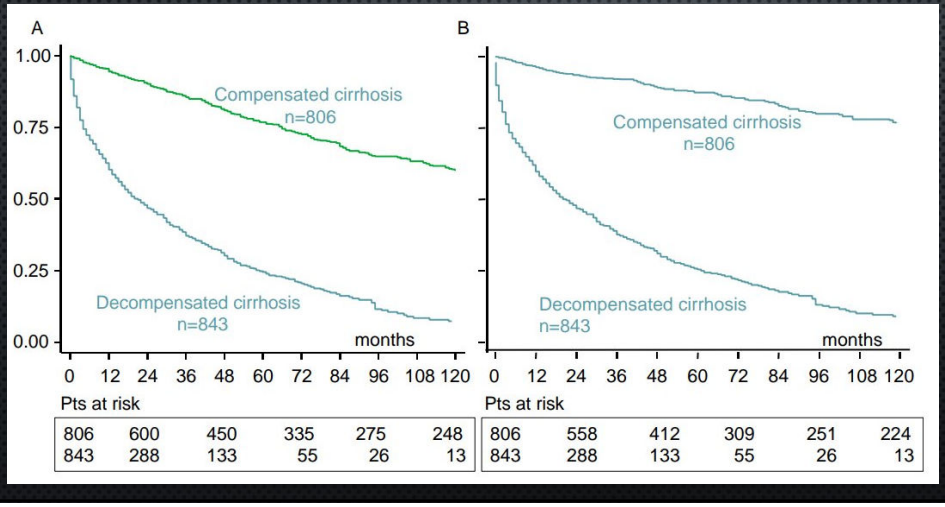

ELSEVIER
Journal of Hepatology 44 (2006) 217–231
Journal of Hepatology
www.elsevier.com/locate/jhep

Review

Natural history and prognostic indicators of survival in cirrhosis: A systematic review of 118 studies

Gennaro D'Amico[1,*], Guadalupe Garcia-Tsao[2], Luigi Pagliaro[1]

COMPENSATED vs DECOMPENSATED



Compensated – Median Survival 12 years

Decompensated – Median Survival 2 years

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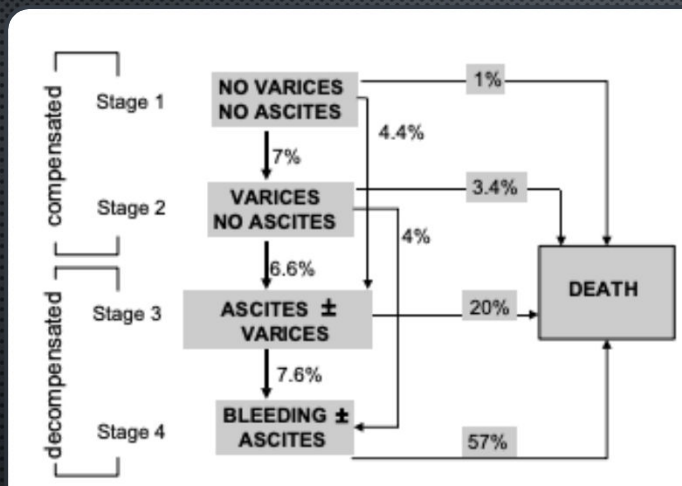

Fig. 4. Clinical course of cirrhosis: 1-year outcome probabilities according to clinical stages.

G. D'AMICO ET AL. / JOURNAL OF HEPATOLOGY 44 (2006) 217–231

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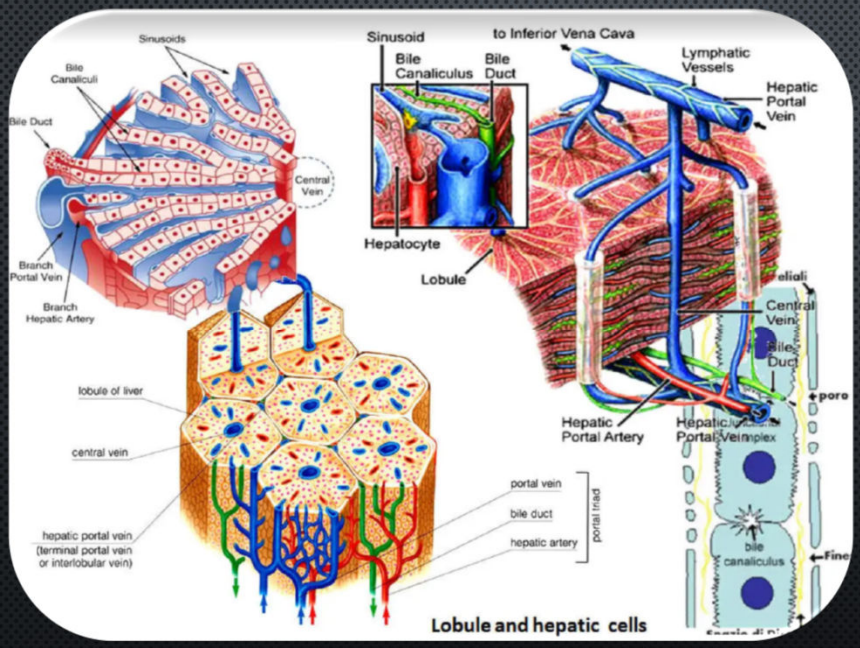

REVIEW OF ANATOMY

https://www.gastroepato.it/en_lobulo_epatico.htm

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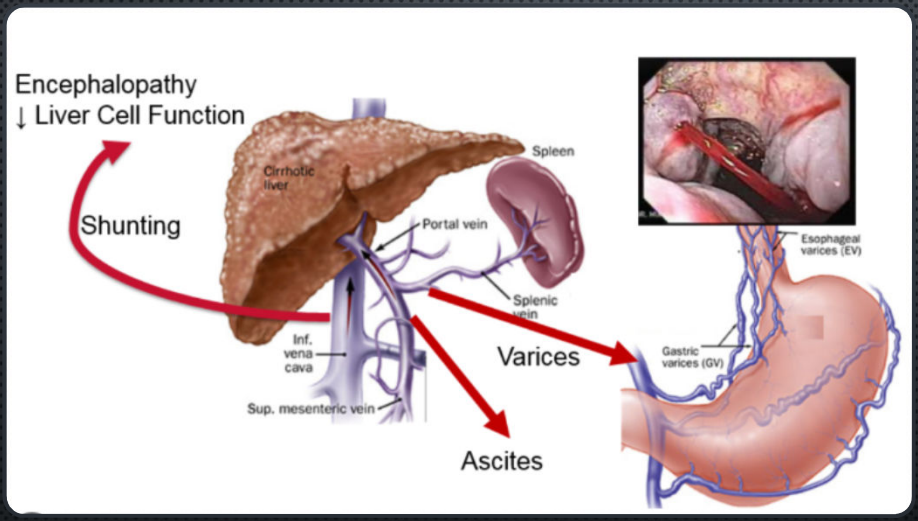

REVIEW OF ANATOMY

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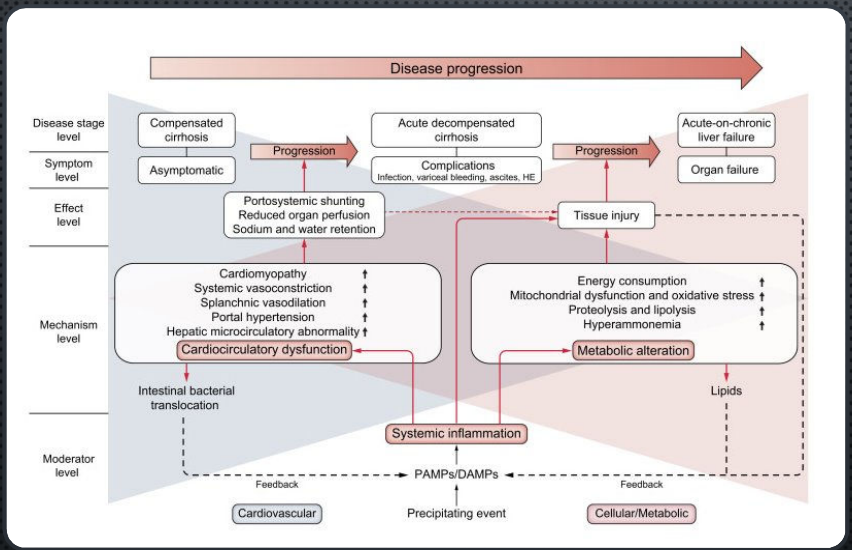

PHYSIOLOGY OF CIRRHOSIS

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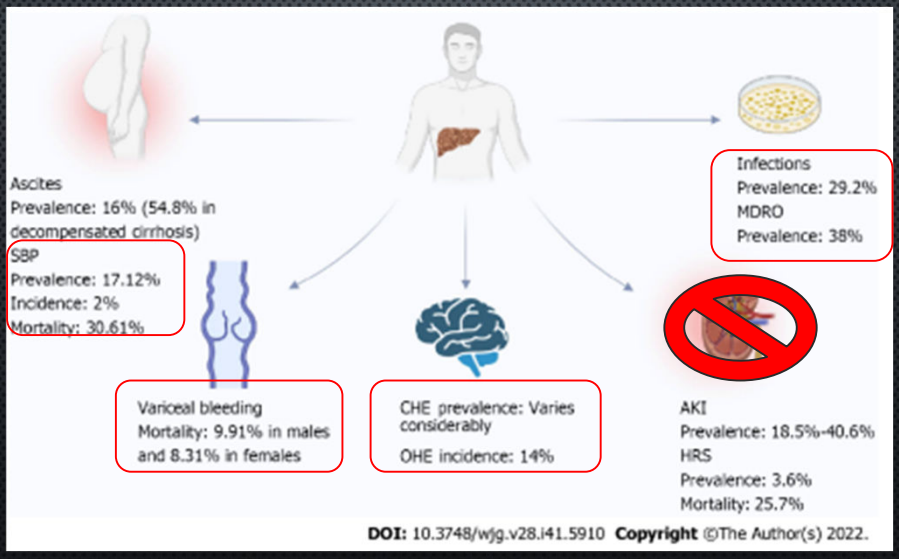
COMMON CAUSES OF DEATH



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INFECTIONS:

- INFECTION IS THE MOST COMMON PRECIPITANT OF ACLF WORLDWIDE, WITH A PREVALENCE OF 48%.
  - MOST COMMON INFECTIONS
    - SBP (36%)
    - UTI (22%)
    - RESPIRATORY INFECTIONS (19%)
    - SKIN AND SOFT TISSUE INFECTION (8%)

"Let me guess...it's contagious!"

Hepatology. 2024;79:1463–1502
AASLD PRACTICE GUIDANCE ON ACUTE-ON-CHRONIC LIVER FAILURE

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HEPATOLOGY
Official Journal of the American Association for the Study of Liver Diseases

Antimicrobial Therapeutic Determinants of Outcomes From Septic Shock Among Patients With Cirrhosis

Yaseen M. Arabi,[1,2] Saqib I. Dara,[1] Ziad Memish,[3,4] Abdulmajeed Al Abdulkareem,[5] Hani M. Tamim,[6] Nehad Al-Shirawi,[1] Joseph E. Parrillo,[7] Peter Dodek,[8] Stephen Lapinsky,[9] Daniel Feinstein,[10] Gordon Wood,[11] Sandra Dial,[12] Sergio Zanotti,[13] and Anand Kumar[14,15] for the Cooperative Antimicrobial Therapy of Septic Shock (CATSS) Database Research Group

Predictors of delay in initial antimicrobial therapy

1) Lower presenting temperature (P = 0.003)
2) Higher initial Bicarbonate (P = 0.02)
3) Nosocomial infections (P = 0.0009)
4) Female (P = 0.05)

Other Findings:

- SBP - 17.6% present at time of shock
- Escherichia coli & Staphylococcus Aureus most common pathogens
- High number of fungal Infections (9.3%)
- Use of Corticosteroids (30.2%) - relatively low compared to general cohort

HEPATOLOGY, VOL. 56, NO. 6, 2012

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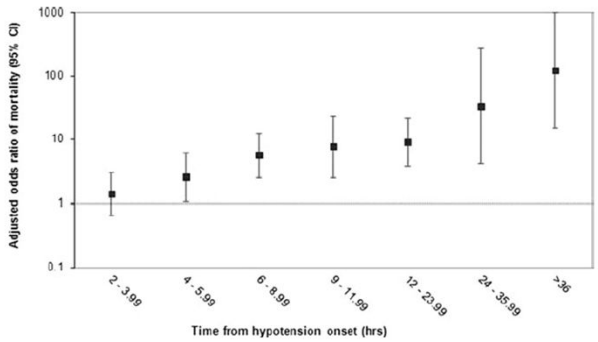
HEPATOLOGY, Vol. 56, No. 6, 2012



"In ICU patients with ACLF, lack of clinical improvement after 48 h should trigger broadening of antibiotic coverage and consideration of fungal coverage."

Hepatology. 2024;79:1463–1502, AASLD PRACTICE GUIDANCE ON ACUTE-ON-CHRONIC LIVER FAILURE

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"SPONTANEOUS" BACTERIAL PERITONITIS

- SBP – IS A CELLULAR DIAGNOSIS
- 33% HAVE ***NO*** SYMPTOMS AT ALL
- IF ADMITTED -> PARACENTESIS
  - ABSOLUTE NEUTROPHIL COUNT > 250/MM3

Hepatology, VOL . 74, NO. 2, 2021

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Early Diagnostic Paracentesis Improves Outcomes of Hospitalized Patients With Cirrhosis and Ascites: A Systematic Review and Meta-Analysis

Azizullah Beran, MD[1], Mouhand F.H. Mohamed, MD[2], Alejandra Vargas, MD[3], Tarek Aboursheid, MD[4], Muhammad Aziz, MD[5], Ruben Hernaez, MD[6], Kavish R. Patidar, DO[6], Lauren D. Nephew, MD[1], Archita P. Desai, MD[1], Eric Orman, MD[1], Naga Chalasani, MD, FACG[1] and Marwan S. Ghabril, MD[1]

Am J Gastroenterol 2024;119:2259–2266.

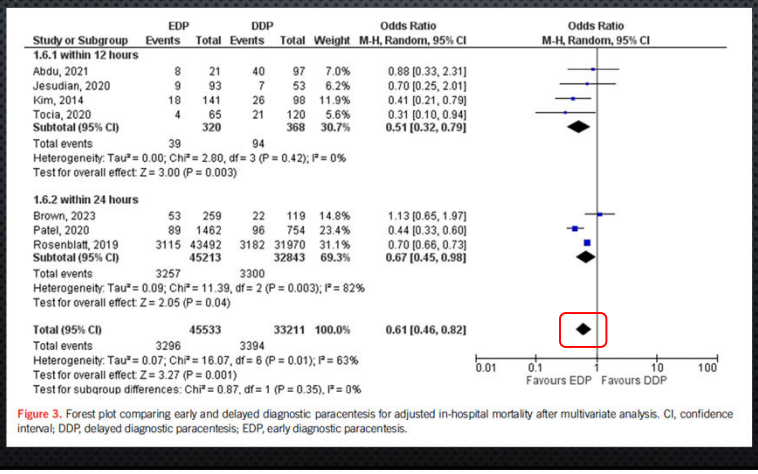

Figure 3. Forest plot comparing early and delayed diagnostic paracentesis for adjusted in-hospital mortality after multivariate analysis. CI, confidence interval; DDP, delayed diagnostic paracentesis; EDP, early diagnostic paracentesis.

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"SPONTANEOUS" BACTERIAL ***EMPYEMA***

Empirical antibiotics should also be started in patients with SBE (pleural fluid PMN count >250/mm^3).

Although the term “empyema” carries the implicit need for drainage, a chest tube should not be placed in patients with SBE.

Ref: Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases

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SBP – SPECIMEN CONSIDERATIONS

- BEDSIDE INOCULATION OF AT LEAST 10 mL OF THE ASCITIC SAMPLE INTO BLOOD CULTURE BOTTLES INCREASES THE SENSITIVITY OF THE CULTURE TO >90% IN THE DIAGNOSIS OF SBP.
- OBTAINING SIMULTANEOUS BLOOD SAMPLES FOR CULTURE INCREASES THE POSSIBILITY OF ISOLATING A CAUSATIVE ORGANISM.

Ref: Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases

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SBP TREATMENT

TABLE 9 - Antibiotics for Infections in Cirrhosis

Recommended antibiotics in hospitalized patients with cirrhosis and infection

(1) Spontaneous infections (peritonitis, bacteremia, empyema)

Community acquired	Nosocomial
• Third-generation cephalosporin	• Piperacillin/tazobactam AND
	• Daptomycin (if known VRE in past or evidence of GI colonization) OR
	• Meropenem if known to harbor MDR gram-negative organisms

Ref: Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases

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DON'T FORGET THE ALBUMIN

TABLE 4. IN-HOSPITAL MORTALITY ACCORDING TO VARIABLES WITH INDEPENDENT PREDICTIVE VALUE.*

VARIABLE	CEFOTAXIME (N=63)		CEFOTAXIME PLUS ALBUMIN (N=63)	
	BUN <30 mg/dl	BUN ≥30 mg/dl	BUN <30 mg/dl	BUN ≥30 mg/dl
	no. of patients who died/total no. (%)			
Bilirubin <4 mg/dl				
Prothrombin time ≥60% of control	0/13	3/6 (50)	0/10	1/10 (10)
Prothrombin time <60% of control	0/7	2/8 (25)	0/14	2/5 (40)
Bilirubin ≥4 mg/dl				
Prothrombin time ≥60% of control	1/3 (33)	1/5 (20)	0/0	0/1
Prothrombin time <60% of control	4/12 (33)	7/9 (78)	0/16	3/7 (43)
Total	5/35 (14)	13/28 (46)	0/40	6/23 (26)

*The cutoff points for the predictive variables are the median values in the overall group of patients. To convert the values for blood urea nitrogen (BUN) to millimoles per liter, multiply by 0.357; to convert the values for bilirubin to micromoles per liter, multiply by 17.1.

The New England Journal of Medicine August 1999 Volume 341 Number 6 · 405

(Mortality – 10% Combo vs. 29% antibiotics alone, P=0.01)

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EARLY SEPSIS IS HARD TO DIAGNOSIS

1) Impaired Lactate Clearance
2) Vasodilator Production from portal hypertension lower MAP
3) Alcohol Associated hepatitis increases WBC and other markers of inflammation
4) Relative Adrenal Insufficiency is common in Cirrhotic patients
5) Fever is often absent

Consider infection esp when a patient with cirrhosis deteriorates, particularly with encephalopathy, AKI, and/or jaundice

- PT WITH ACLF WHO SURVIVE INFECTION –> 45% WILL HAVE ANOTHER INFECTION WITHIN 6 MONTHS.
- 1/3RD OF HOSPITALIZED CIRRHOTIC PATIENTS WILL HAVE BACTERIAL INFECTIONS (35% ARE MDRO).

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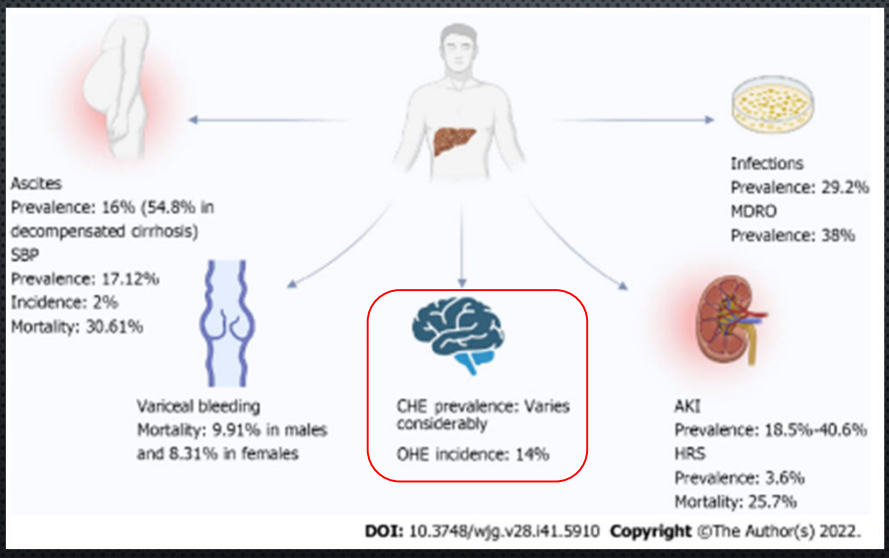
COMMON CAUSES OF DEATH



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ALTERED MENTAL STATUS

- HEPATIC ENCEPHALOPATHY -> DIAGNOSIS OF EXCLUSION
  - DRUG RELATED
  - INFECTIONS
  - DIABETIC KETOACIDOSIS/HYPEROSMOLAR HYPERKETOTIC STATE
  - ELECTROLYTE DISORDERS (HYPONATREMIA)
  - INTRACRANIAL PATHOLOGY SUCH AS BLEED
  - NONEPILEPTIC SEIZURES
    - SOME CAN COEXIST WITH HE

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DIAGNOSTICS:

What about Ammonia ?

- ROUTINE AMMONIA TESTING IN PATIENTS WITH KNOWN CIRRHOSIS AND AMS IS NOT RECOMMENDED.
  - HOWEVER, A LOW AMMONIA LEVEL IN PATIENTS WITH COMA OR CONFUSION SHOULD POINT TOWARD ETIOLOGIES OTHER THAN HE.

Hepatology. 2024;79:1463–1502, AASLD PRACTICE GUIDANCE ONACUTE-ON-CHRONIC LIVER FAILURE

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Hepatic Encephalopathy Grades/Stages

West Haven Criteria. Defines criteria for the stages of hepatic encephalopathy.

When to Use | Why Use

West Haven Criteria:

Signs/Symptoms

- Changes in behavior with minimal change in level of consciousness +1
- Gross disorientation, drowsiness, possibly asterixis, inappropriate behavior +2
- Marked confusion, incoherent speech, sleeping most of the time but arousable to vocal stimuli +3
- **Comatose, unresponsive to pain; decorticate or decerebrate posturing +4**

4 points

Grade IV Hepatic Encephalopathy

Copy Results | Next Steps

» Next Steps | Evidence | Creator Insights

ADVICE

- Lactulose is a standard treatment for hepatic encephalopathy
- Ammonia testing may be helpful diagnostically or trending levels
- There should always be consideration to other causes of altered mental status in these patients, as they are at high risk for comorbidities including bleeding, infection, drug interactions, and electrolyte disturbances.

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HELP TRIAL PEG VS LACTULOSE

JAMA Network

From: **Lactulose vs Polyethylene Glycol 3350-Electrolyte Solution for Treatment of Overt Hepatic Encephalopathy: The HELP Randomized Clinical Trial**

JAMA Intern Med. 2014;174(11):1727-1733. doi:10.1001/jamainternmed.2014.4746

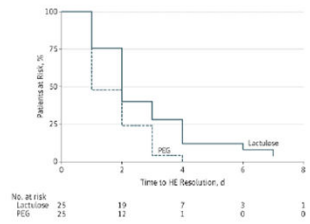

Figure Legend:

Time to Hepatic Encephalopathy (HE) ResolutionShown is a Kaplan-Meier graph depicting the proportion of patients at risk for HE who received either standard-of-care lactulose therapy or polyethylene glycol 3350–electrolyte solution (PEG). Patients receiving PEG had more rapid resolution of HE than those receiving lactulose (P = .01).

Date of download: 5/5/2025

8. Treatment of HE in patients with ACLF/who are critically ill includes lactulose (orally or rectally) or polyethylene glycol if patients are at risk of ileus/abdominal distention. The role of rifaximin as an add-on therapy to lactulose/polyethylene glycol warrants further investigation in ACLF.

Hepatology. 2024;79:1463–1502, AASLD PRACTICE GUIDANCE ONACUTE-ON-CHRONIC LIVER FAILURE

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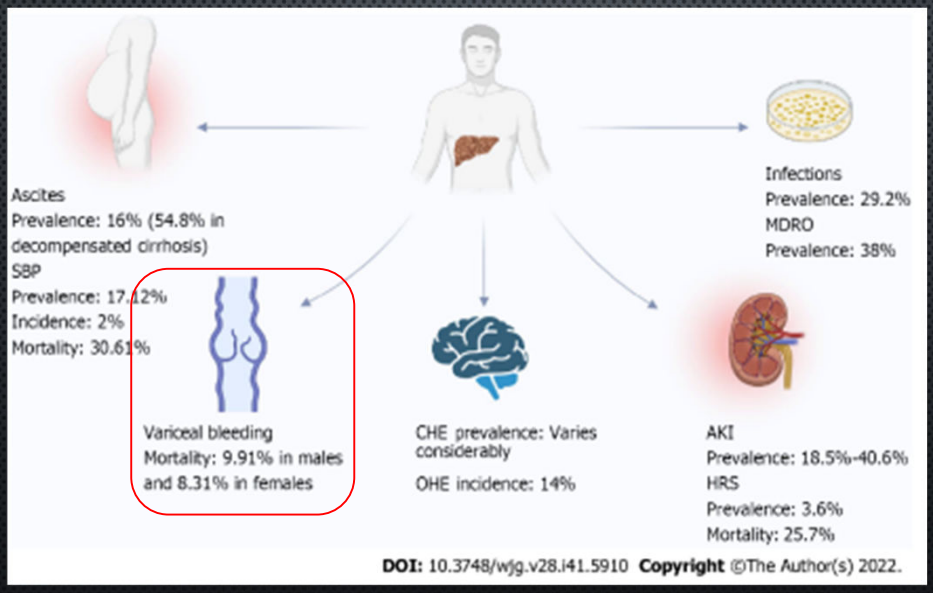
COMMON CAUSES OF DEATH



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VARICEAL BLEEDING

Practice Guidance

AASLD

AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis

"VASOACTIVE THERAPY THAT IS AIMED TO REDUCE PORTAL PRESSURE AND COLLATERAL BLOOD FLOW AS WELL AS ANTIMICROBIAL PROPHYLAXIS SHOULD BE INITIATED IMMEDIATELY ON PRESENTATION AND MAINTAINED FOR 2–5 DAYS."

Hepatology. 2024;79:1180–1211 AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis

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NASOGASTRIC TUBE ?

" BECAUSE ASPIRATION PNEUMONIA IS THE MOST COMMON INFECTION TO DEVELOP IN PATIENTS ADMITTED FOR VARICEAL BLEEDING, CARE SHOULD BE TAKEN AT ENDOSCOPY AND ANY INTERVENTION THAT INVOLVES THE AIRWAY; ROUTINE PRE-ENDOSCOPIC OR PRE-INTUBATION PLACEMENT OF NASOGASTRIC TUBES SHOULD BE DISCOURAGED."

Hepatology. 2024;79:1180–1211 AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis

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WHAT ABOUT FFP ?

- FRESH FROZEN PLASMA FRESH FROZEN PLASMA (APPROXIMATELY 250 ML/U AND DOSED AT 10 ML/KG) IS NOT RECOMMENDED TO CORRECT ANY COAGULATION FACTOR DEFICIENCY. AFTER A HIGH VOLUME IS INFUSED, THERE IS A SUBSTANTIAL INCREASE IN PORTAL PRESSURE.

TABLE 3 Comparison of outcomes in patients who received fresh frozen plasma (FFP) transfusion to those who did not receive FFP transfusion with unadjusted odds ratio and adjusted odds ratio from multivariable analysis

	All patients (n = 244)	Received FFP transfusion (n = 100)	Did not receive FFP transfusion (n = 144)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)[a]
Mortality at 42 d, n (%)	47 (19.3)	37 (37.0)	10 (6.9)	7.87 (3.68-16.83)	9.41 (3.71-23.90)
Failure to control bleeding at 5 d, n (%)	20 (8.2)	14 (14.0)	6 (4.2)	3.74 (1.39-10.11)	3.87 (1.28-11.70)
Length of stay >7 d, n (%)	85 (34.8)	51 (51.0)	34 (23.6)	3.37 (1.94-5.83)	1.88 (1.03-3.42)

[a]Adjusted for age, MELD score and HCC.

Mohanty A, Kapuria D, Canakis A, et al. Fresh frozen plasma transfusion in acute variceal haemorrhage: Results from a multicenter cohort study. Liver Int. 2021;41:1901–1908.

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HEMOSTASIS

29. Fresh frozen plasma and platelet transfusions should not be administered based on international normalized ratio or platelet count targets, respectively, because there is no evidence of benefit of such transfusions in AVH, and in the case of fresh frozen plasma, there is evidence of potential harm.

AGA Clinical Practice Update: Coagulation in Cirrhosis

Hepatology. 2024;79:1180–1211 AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis

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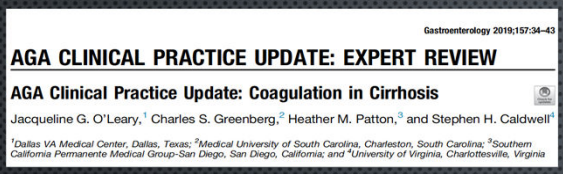
HEMOSTASIS:



Gastroenterology 2019;157:34–43

AGA CLINICAL PRACTICE UPDATE: EXPERT REVIEW

AGA Clinical Practice Update: Coagulation in Cirrhosis

Jacqueline G. O'Leary,[1] Charles S. Greenberg,[2] Heather M. Patton,[3] and Stephen H. Caldwell[4]

[1]Dallas VA Medical Center, Dallas, Texas; [2]Medical University of South Carolina, Charleston, South Carolina; [3]Southern California Permanente Medical Group-San Diego, San Diego, California; and [4]University of Virginia, Charlottesville, Virginia

BEST PRACTICE ADVICE 4: The following transfusion thresholds for management of active bleeding or high-risk procedures may optimize clot formation in advanced liver disease: hematocrit ≥25%, platelet count >50,000, and fibrinogen >120 mg/dL. Commonly utilized thresholds for international normalized ratio correction are not supported by evidence.

Gastroenterology 2019;157:34–43

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HEMOSTASIS:

Gastroenterology 2019;157:34–43

BEST PRACTICE ADVICE 1: Global tests of clot formation, such as rotational thromboelastometry, thromboelastography, sonorheometry, and thrombin generation, may eventually have a role in the evaluation of clotting in patients with cirrhosis, but currently lack validated target levels.

TABLE 9 Future research directions for the management of critically ill patients with cirrhosis and/or ACLF

Coagulopathy	Utilization of viscoelastic testing (TEG/ROTEM) in larger populations of critically ill patients with cirrhosis

Hepatology. 2024;79:1180–1211 AASLD Practice Guidance on risk stratification and management of portal hypertension and varices in cirrhosis

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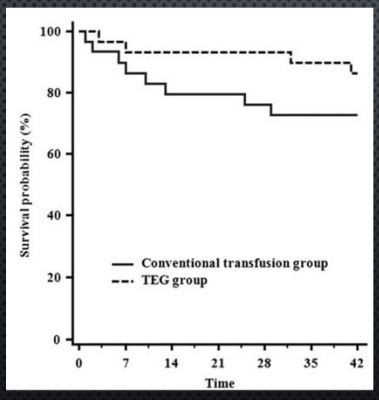
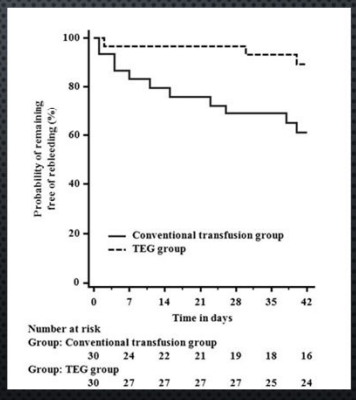
ORIGINAL ARTICLE

Thromboelastography-guided Blood Product Transfusion in Cirrhosis Patients With Variceal Bleeding

A Randomized Controlled Trial

Gyanranjan Rout, MD, Shalimar, DM, Deepak Gunjan, DM, Soumya J. Mahapatra, DM, Saurabh Kedia, DM, Pramod K. Garg, DM, and Baibaswata Nayak, PhD





J Clin Gastroenterol Volume 54, Number 3, March 2020

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GUIDELINES ?

Special Article

Guidelines for the Management of Adult Acute and Acute-on-Chronic Liver Failure in the ICU: Cardiovascular, Endocrine, Hematologic, Pulmonary and Renal Considerations: Executive Summary

9) We suggest using viscoelastic testing (TEG/ROTEM) over measuring INR, platelet, and fibrinogen in critically ill patients with ALF or ACLF	Conditional	Low
13) We recommend viscoelastic testing (TEG/ROTEM), over measuring INR, platelet, fibrinogen, in critically ill patients with ALF or ACLF undergoing procedures	Strong	Moderate

Critical Care Medicine - March 2020 • Volume 48 • Number 3

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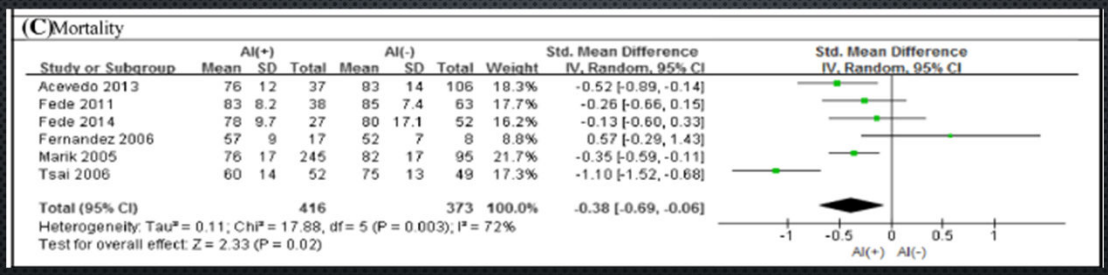
ORIGINAL ARTICLE

Relative Adrenal Insufficiency in Patients with Cirrhosis: A Systematic Review and Meta-Analysis

Gaeun Kim[1] · Ji Hye Huh[2] · Kyong Joo Lee[2] · Moon Young Kim[2,3] · Kwang Yong Shim[2] · Soon Koo Baik[2,3,4]



Dig Dis Sci (2017) 62:1067–1079

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OTHER CRIT CARE RECS:

- Fluids – AASLD: Favor Balanced Solutions
- MAP Goal – AASLD: Individualized MAP Target based on frequent assessments of end-organ perfusion.
- Pressor – AASLD: Norepi 1st line pressor, Vasopressin deficiency has been documented in cirrhotic patients
- Vent - AASLD: With ARDS - "Low PEEP (<10cmH2) strategy is recommended.

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ANALGO-SEDATION APPROACH

Br. J. Anaesth. (1982), **54**, 1267

FENTANYL PHARMACOKINETICS IN ANAESTHETIZED PATIENTS WITH CIRRHOSIS

J. P. HABERER, P. SCHOEFFLER, E. COUDERC AND P. DUVALDESTIN

	Controls	Cirrhosis[b]
$T_{\frac{1}{2}}^{\alpha}$ (min)	9 ± 3	8 ± 4
$T_{\frac{1}{2}}^{\beta}$ (min)	263 ± 49	304 ± 74
V_1 (litre kg^{-1})	0.77 ± 0.29	1.02 ± 0.36
V^{β} (litre kg^{-1})	3.81 ± 67	4.41 ± 72
V^{ss} (litre kg^{-1})	3.44 ± 64	4.27 ± 65
Cl (ml min^{-1} kg^{-1})	10.8 ± 1.2	11.3 ± 1.6
AUC_{total} (ng ml^{-1} min^{-1})	518 ± 53	507 ± 63

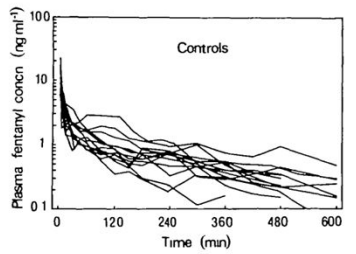

FIG. 1. Fentanyl plasma concentration in 13 surgical patients with normal renal and hepatic function after a single intravenous dose of 5 μg kg^{-1}.

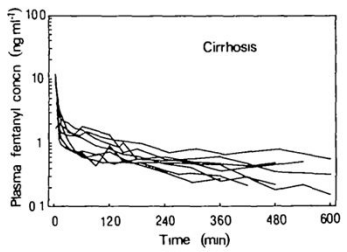

FIG. 2. Fentanyl plasma concentration in 8 cirrhotic patients after a single intravenous dose of 5 μg kg^{-1}.

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RECAP:

- Decompensated Cirrhotic pt's have a high 1-Year mortality
- Infection is one of the most common causes of Death BUT difficult to diagnosis
- SBP is a Cellular Diagnosis – Inoculate a Blood Culture Bottle to increase yield
- Consider Polyethylene Glycol for treatment of Hepatic Encephalopathy
- Don't use FFP to target an Arbitrary INR
- Consider TEG/ROTEM to guide transfusion
- Adrenal Insufficiency may be more common in this population

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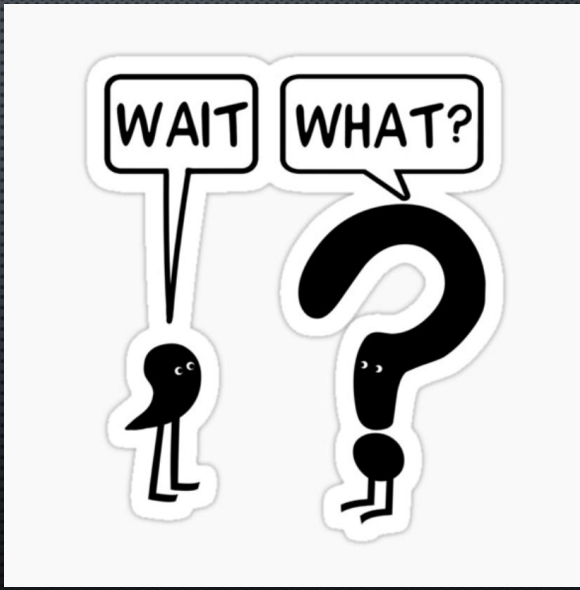
QUESTIONS:



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