The Personalized Approach to Inpatient Management of Decompensated Cirrhosis

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Disclosures

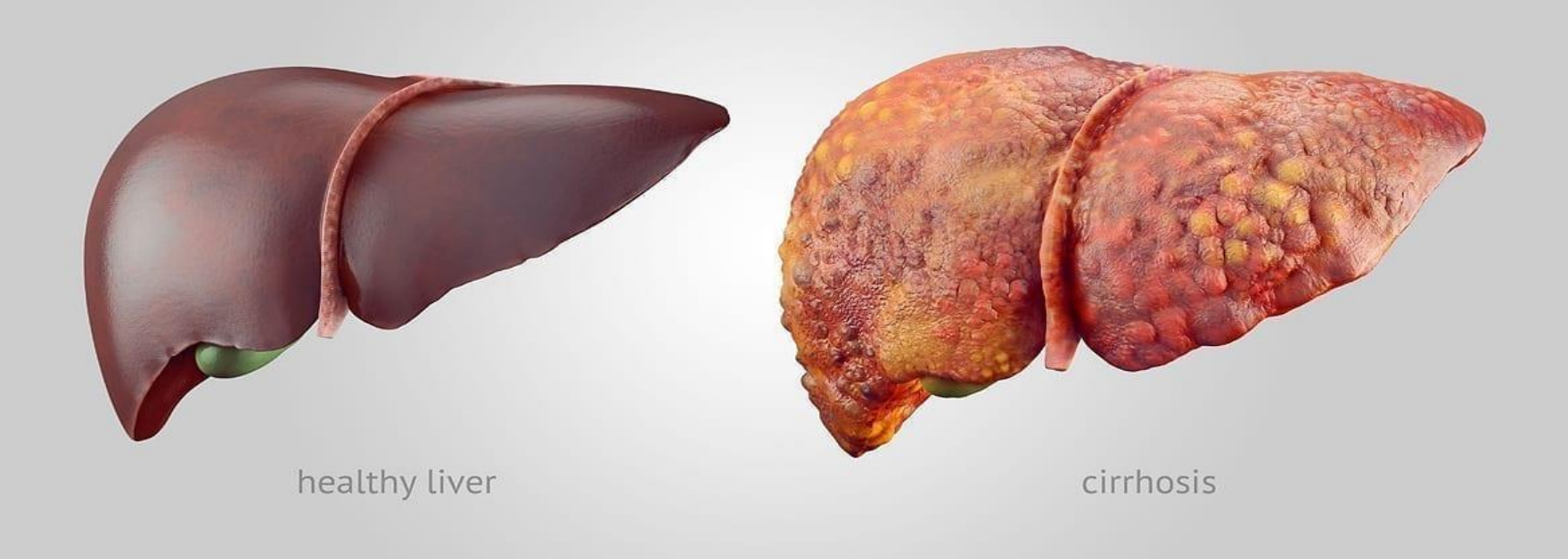
- No relevant commercial relationships to disclose

Objectives

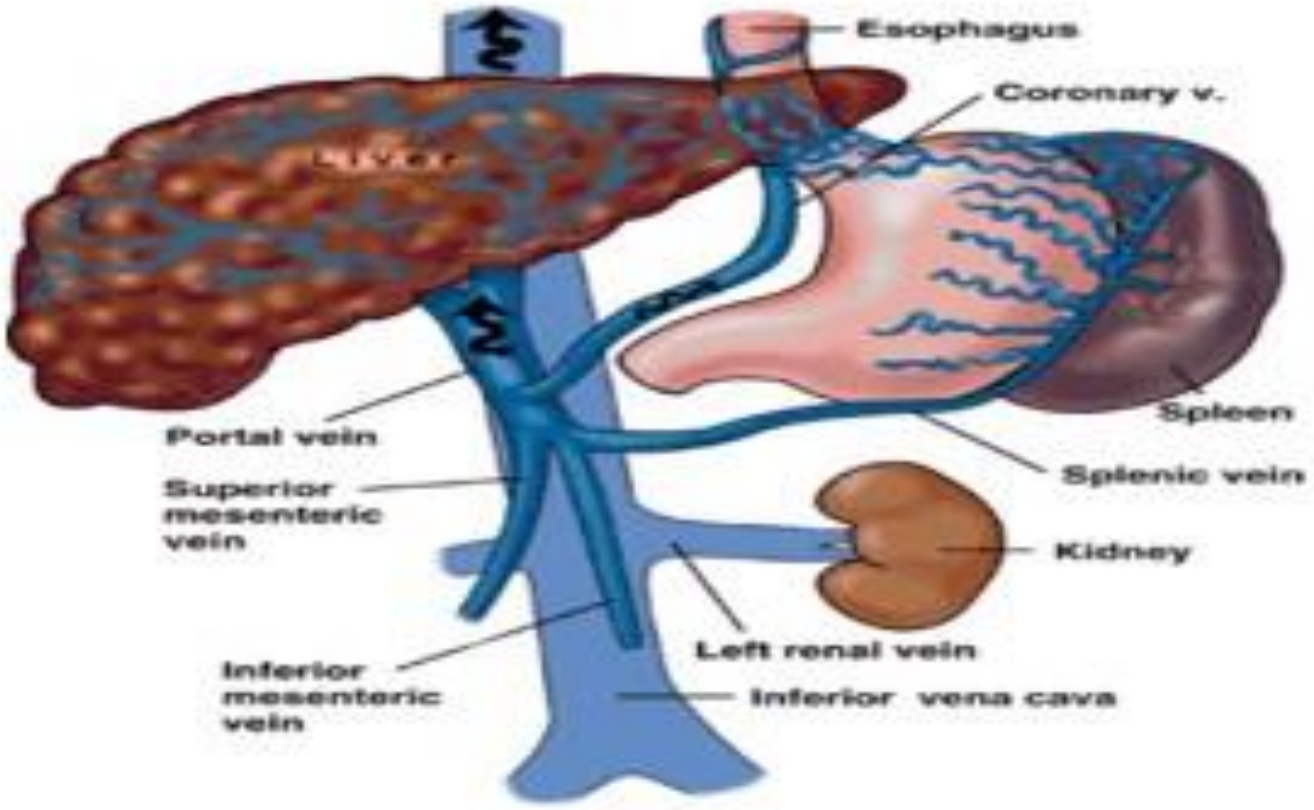
- At the conclusion of this session, participants should be able to:
  - Effectively treat hepatic encephalopathy
  - Manage different types of ascites
  - Identify the approach to acute kidney injury in patients with cirrhosis

Cirrhosis

- Development of regenerative nodules surrounded by fibrous bands in response to chronic liver injury (i.e., significant scarring as a result of chronic injury)



Portal Hypertension



Clinical Complications of Cirrhosis

- Variceal bleeding (esophageal, gastric, ectopic)
- Hepatic Encephalopathy
- Ascites and/or hepatic hydrothorax

❖Cirrhosis with any of these complications is termed **"decompensated"**

- 1-year mortality **> 20%**

Hepatic Encephalopathy

- Brain dysfunction in patients with hepatic dysfunction
- Clinical diagnosis (**Avoid checking ammonia**)

WHC INCLUDING MHE	ISHEN	DESCRIPTION	SUGGESTED OPERATIVE CRITERIA	COMMENT
Unimpaired		No encephalopathy at all, no history of HE	Tested and proved to be normal	
Minimal	Covert	Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change	Abnormal results of established psychometric or neuropsychological tests without clinical manifestations	No universal criteria for diagnosis Local standards and expertise required
Grade I		• Trivial lack of awareness • Euphoria or anxiety • Shortened attention span • Impairment of addition or subtraction • Altered sleep rhythm	Despite oriented in time and space (see below), the patient appears to have some cognitive/behavioral decay with respect to his or her standard on clinical examination or to the caregivers	Clinical findings usually not reproducible
Grade II	Overt	• Lethargy or apathy • Disorientation for time • Obvious personality change • Inappropriate behavior • Dyspraxia • Asterixis	AxOx2	Clinical findings variable, but reproducible to some extent
Grade III		• Somnolence to semistupor • Responsive to stimuli • Confused • Gross disorientation • Bizarre behavior	AxOx1	Clinical findings reproducible to some extent
Grade IV		Coma	Does not respond even to painful stimuli	Comatose state usually reproducible

All conditions are required to be related to liver insufficiency and/or PSS.

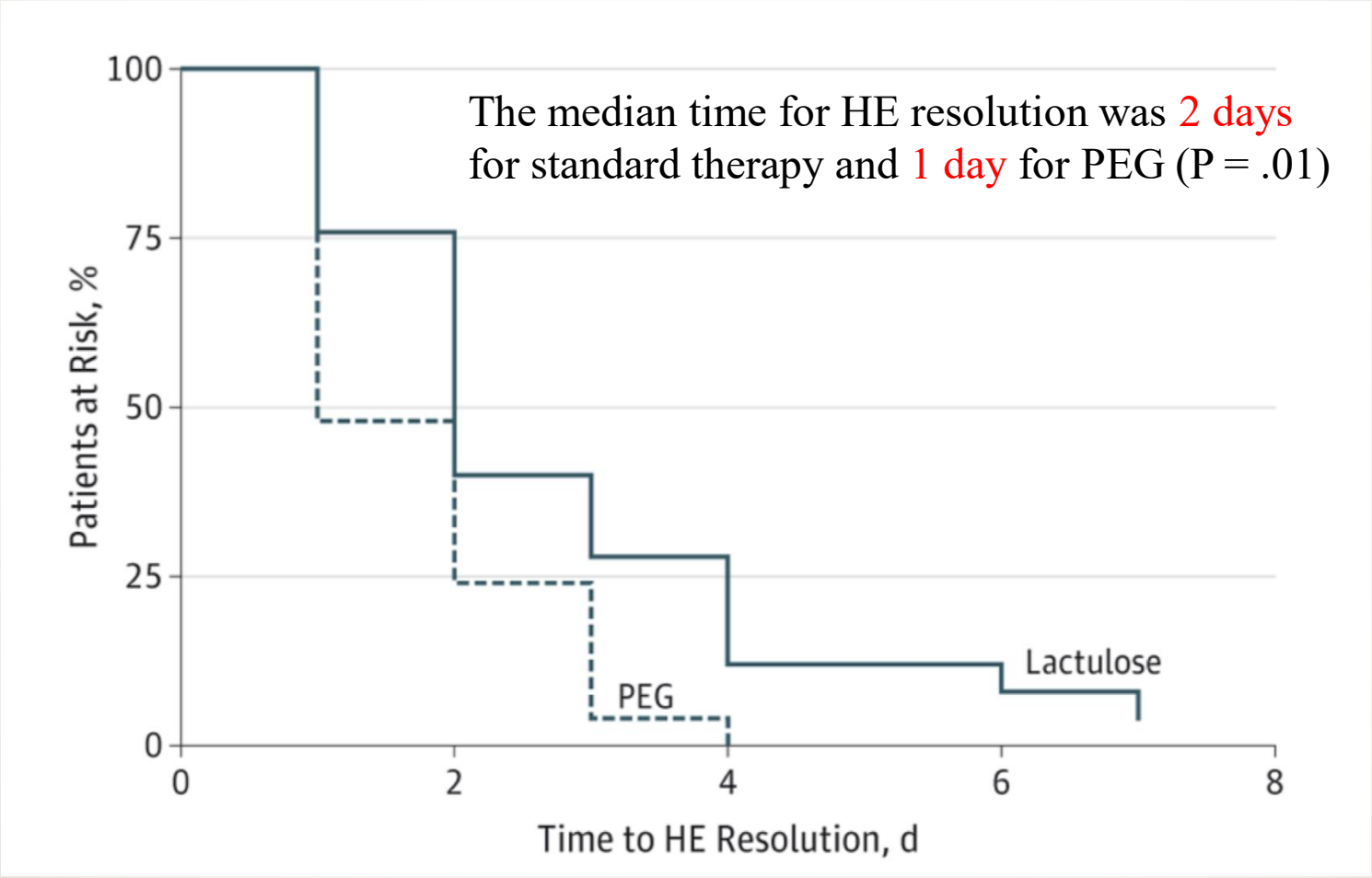
Hepatic Encephalopathy

- Triggers
- Infection (CXR, blood culture, UA +/-cx, and paracentesis even if no signs of infection)
- GI bleeding
- Electrolytes imbalance (e.g., hypokalemia)
- Dehydration/Diuretic overdose
- Suboptimal frequency of BM

Hepatic Encephalopathy

- Treatment (in addition to treating the trigger)

Golytely Can Work Faster Than Lactulose



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Rahimi et al. JAMA IM 2014

Ascites +/- Hepatic Hydrothorax

- Accumulation of fluid in the peritoneum +/- leakage through diaphragmatic defect to the pleura (R>L lung)

Ascites: Diagnosis

- Diagnostic paracentesis should be performed in all patients with new-onset ascites that is accessible for sampling

Fluid Analysis ⇨

- Fluid neutrophil count
- Fluid protein
- Fluid albumin
- Serum albumin
- Fluid culture in blood culture bottles
- Optional: amylase, cytology, or culture for mycobacteria

Ascites Fluid Analysis

	Total Protein < 2.5 g/dL	Total Protein ≥ 2.5 g/dL
SAAG ≥ 1.1 g/dL	Hepatic Portal Hypertension (Cirrhosis)	Cardiogenic Budd Chiari
SAAG < 1.1 g/dL	Kidney Disease	Peritoneal carcinomatosis Tuberculous Pancreatic Kidney Disease

Ascites: Diagnosis

- Diagnostic paracentesis should be performed in all admissions who have hepatic ascites even if no infection symptoms and signs

Fluid neutrophil count

Fluid protein

Fluid culture in blood culture bottles

Ascites +/- Hepatic Hydrothorax

- Management:
- Dietary salt restriction (up to 2 gm a day)➜ Dietician
- Diuretics
- Serial paracentesis
- TIPS
- Avoiding NSAIDs, ARBs, ACEi, and Aminoglycosides

Management of Hepatic Ascites

Grade I

Fluid restriction is not necessary for ascites management unless there is concomitant moderate or severe hyponatremia (<125 mmol/L)

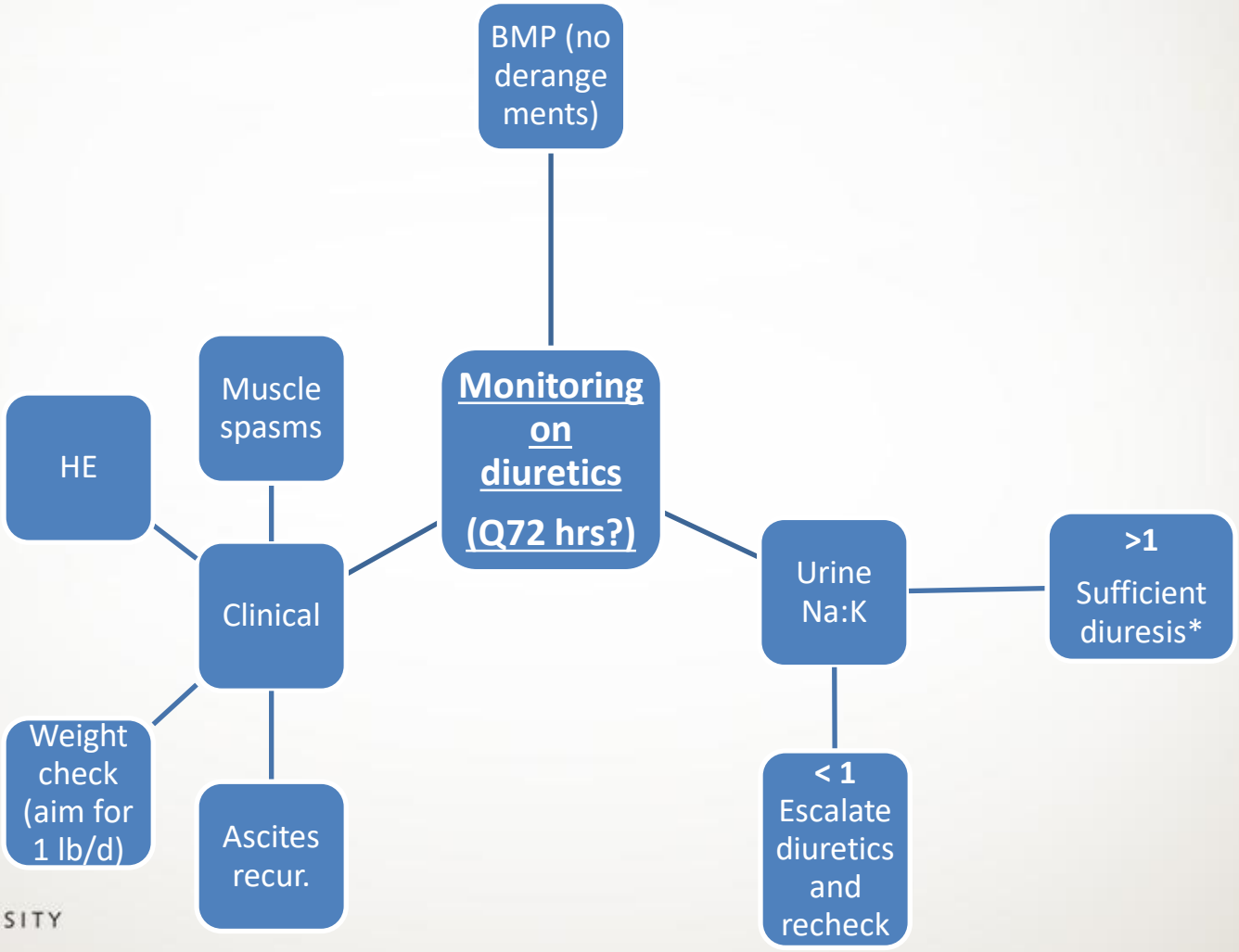
(tense abdomen)

- Diuretics
- Referral for transplant evaluation

Diuretics

- Spironolactone in 100 mg increments (up to 400) OR Amiloride
- Furosemide in 40 mg increments (up to 160) OR Torsemide in 10 mg increments (up to 40)

Ascites: Monitoring Therapy



Diuretics Intractable Ascites

- Hyperkalemia
- Hypokalemia
- Hyponatremia
- Acute kidney injury
- Recurrent hepatic encephalopathy (without an apparent trigger)
- Intractable muscle cramps not responsive to Baclofen

EASL Guidelines. J Hepatology, 2018

Diuretics Intractable Ascites

Hyponatremia

The goal rate of increase of serum Na) = 4-6 (do not exceed 8) mEq/L per 24 hrs

diuretics	gm/d)	saline

Diuretic Resistant Ascites

- Ascites that cannot be mobilized or the early recurrence of which cannot be prevented because of a lack of response to sodium restriction and maximal diuretic treatment.

- Diuretic-intractable and –resistant ascites is treated with LVP, TIPS, and liver transplant

TIPS vs Serial LVP

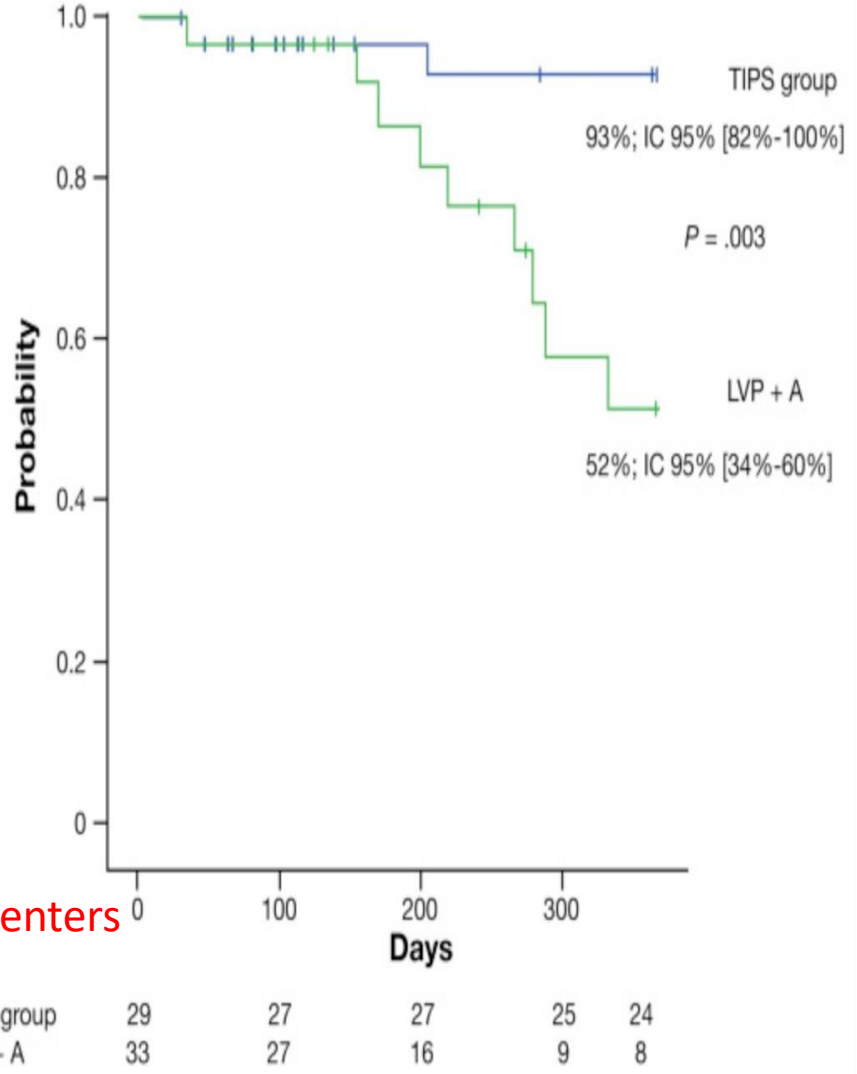
Outcome	TIPS (n = 29)	LVP+A (n = 33)
No. of paracenteses per patient, mean ± SD	1 ± 1	10 ± 7*
Volume extracted, *L/patient*, mean ± SD	6 ± 10	64 ± 47*
Albumin infusion, *g/patient*, mean ± SD	39 ± 70	550 ± 458*
Days in hospital, mean ± SD	17 ± 28	35 ± 40*
Patients with OHE, n	10	11
Episodes of OHE per patient, n, mean ± SD	1.6 ± 0.7	1.7 ± 0.8
Patients with OHE grade >2, n	4	7
Patients with PHT-related bleeding, n	0	6*
Patients with hernia-related complication, n	0	6*
Patients with HRS, n	0	1
Patients with SBP, n	0	2
Patients with sepsis, n	5	9
HCC, n	0	1

View Table in HTML

HCC, hepatocellular carcinoma; HRS, hepatorenal syndrome; SBP, spontaneous bacterial peritonitis.

*$P < .05$; **$P < .01$; ***$P < .001$.

RCT, 62 pts, Multiple French centers



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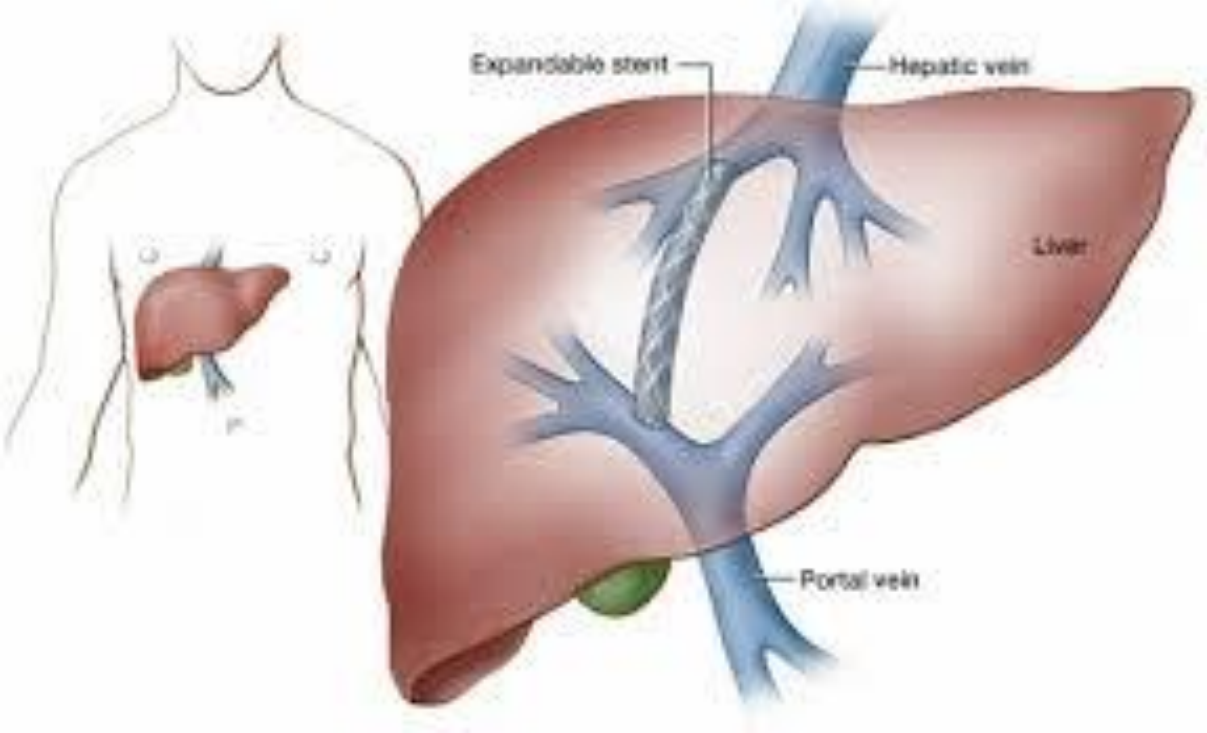
Bureau et al. Gastro, 2017

TIPS



TIPS Precautions

AASLD (2009)

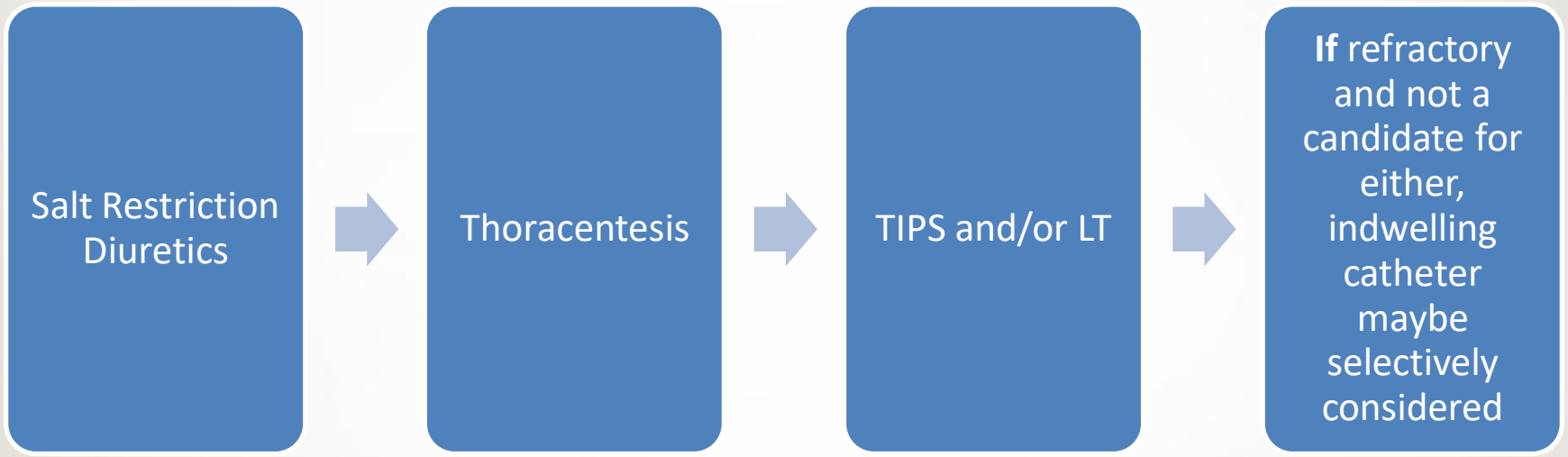
- Patients with MELD > 15-18 or serum bilirubin > 4.0 mg/dL should be informed of their prognosis and TIPS performed only in the absence of other options.
- In high-risk patients, the need for liver trans-plantation should be discussed before the performance of an elective TIPS.

TIPS Contraindications

- TIPS is also not recommended in patients with
- Current hepatic encephalopathy grade ≥2 or chronic hepatic encephalopathy
- Concomitant active infection
- Progressive renal failure
- Severe systolic or diastolic dysfunction
- Pulmonary hypertension

EASL Guidelines. 2018

Hepatic Hydrothorax Management after Making the Diagnosis



Chest tube insertion for HH should be avoided

Ascites-Related Complications

- Hernias

  - Most common is umbilical

  - Emergency surgery if incarceration, strangulation and flood syndrome ☛☛

  - Elective surgery after

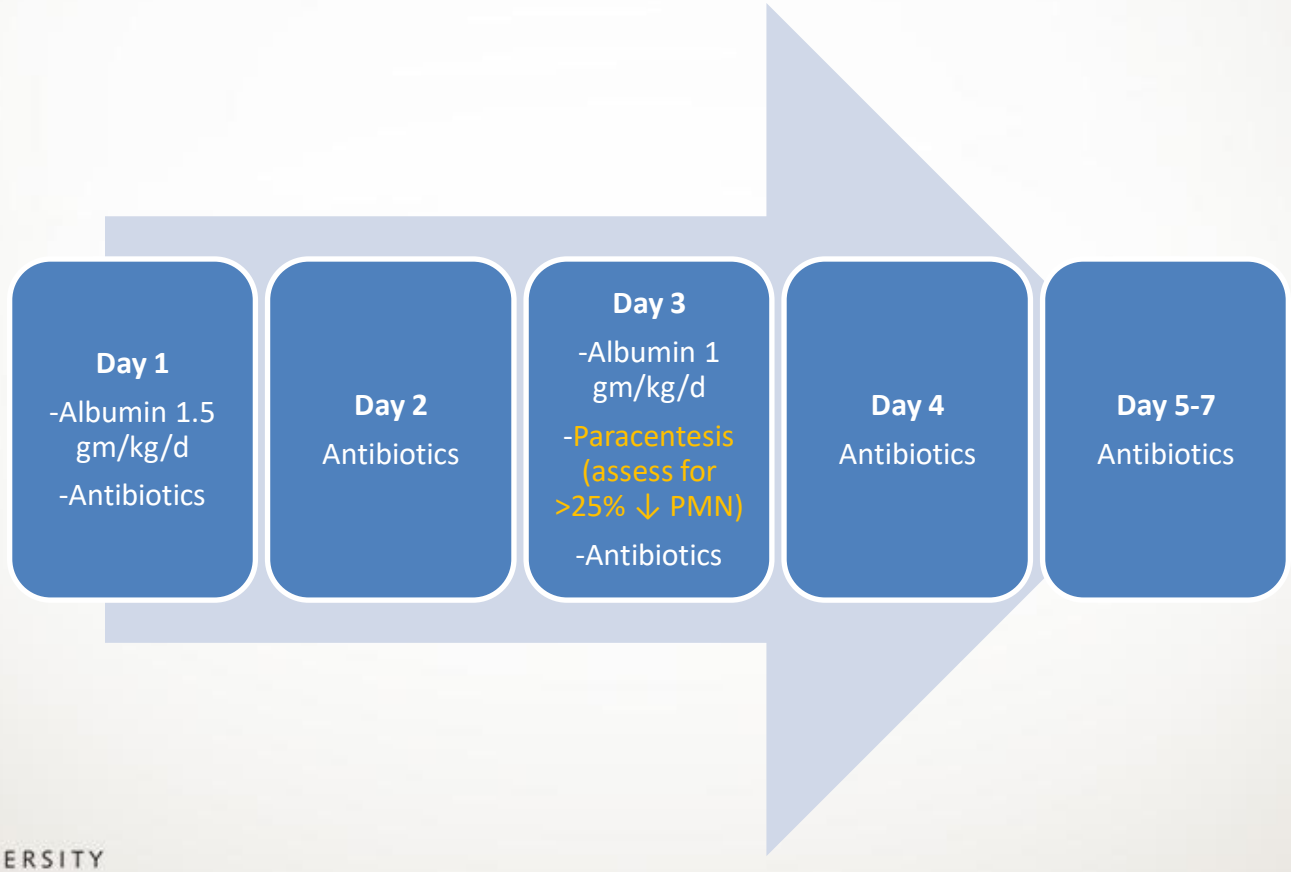
  a) multidisciplinary approach

  b) ascites control

  c) Clinical and nutritional* optimization

Ascites-Related Complications

- Spontaneous Bacterial Peritonitis/Empyema
  - Dx: fluid Polymorphonuclear leukocyte count >250
  - Rx:



Ascites-Related Complications

- Spontaneous Bacterial Peritonitis/Empyema
  - Dx: fluid Polymorphonuclear leukocyte count >250
  - Rx: antibiotics

3rd generation cephalosporine	Broad spectrum antibiotics (e.g., Zosyn or Meropenem)
Community acquired infection	Healthcare-associated infection
	Nosocomial infection
	Sepsis or septic shock
	Recent exposure to broad-spectrum antibiotics

- Secondary prophylaxis (Cipro) should be done following Rx

Ascites-Related Complications

- Spontaneous Bacterial Peritonitis/Empyema Primary Prophylaxis (Ciprofloxacin)

  - Upper GIB: IV ceftriaxone 1 g/24 x 5-7 days

  - Low protein (<1.5 g/L) ascites with one of the following:

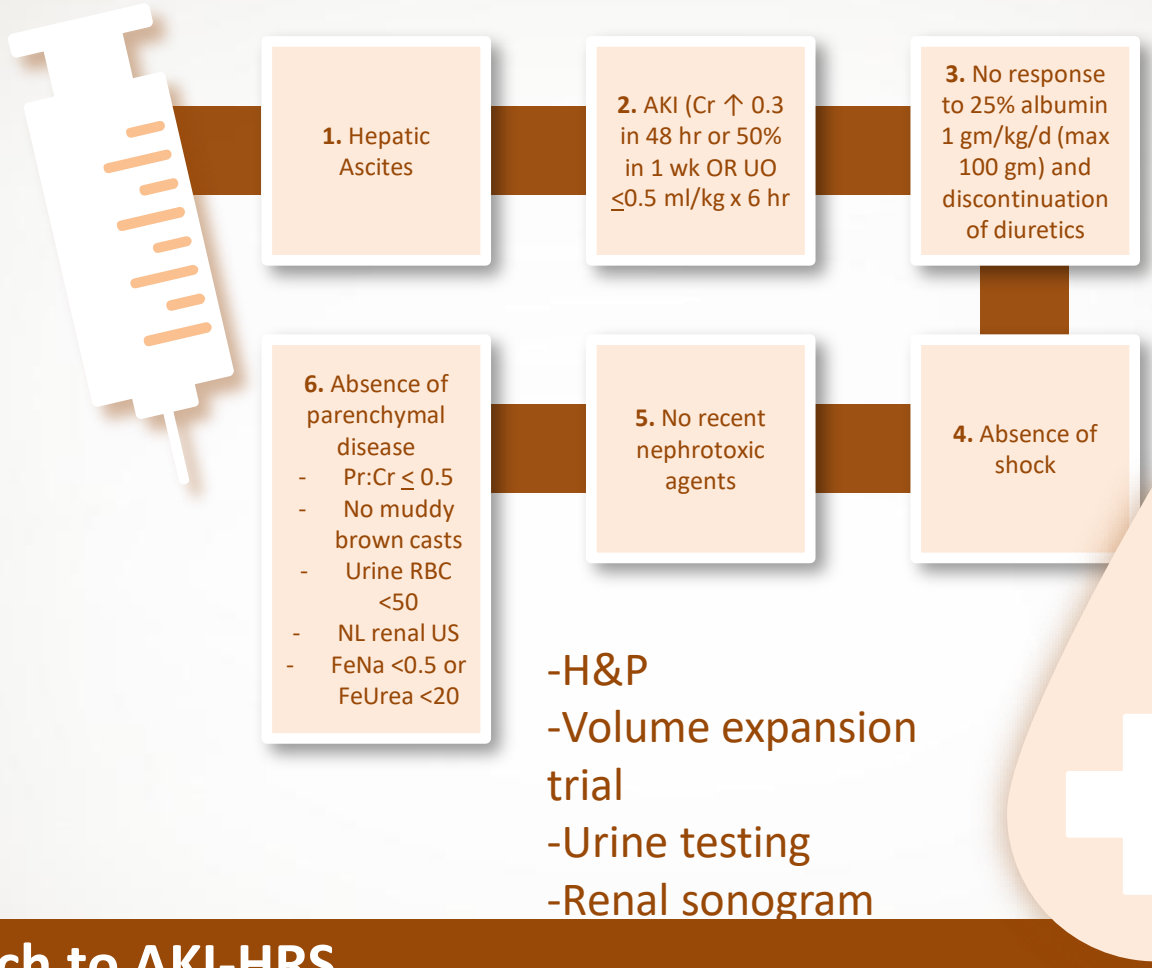
    a) renal dysfunction (serum creatinine level >1.2 mg/dL, blood urea nitrogen level >25 mg/dL, or serum sodium level <130 mEq/L)

    b) liver dysfunction (Child-Pugh-Turcotte score >9 and bilirubin >3 mg/dL)

Acute Kidney Injury In Cirrhosis

- Common pathologies: Acute tubular necrosis (most common), pre-renal azotemia, and hepatorenal syndrome (~20% of AKI)

- Common risk factors: fluid losses, bacterial infections, hemodynamic instability, and nephrotoxic agents (e.g., particularly nonsteroidal anti-inflammatory drugs)



Approach to AKI-HRS

Diagnosis by exclusion

Treatment of HRS-AKI

- First line therapy: Norepinephrine + albumin

  - A/Es: ischemic complications and pulmonary edema

  - Clinical response: Cr ↓ to <1.5 mg/dL or to within 0.3 mg/dL of baseline over a maximum of 14 days

  - If creatinine ≥ the pretreatment level over 4 days with the maximum tolerated doses, therapy may be discontinued

Treatment of HRS-AKI

- Norepinephrine dosing

- Goal(s)

  1) ↑ in MAP of ≥ 10 mmHg

  OR

  2) ↑ in UO >200 mL/4 hrs

- Start at 0.5 mg/hr

- Titrate q 4 hrs by 0.5 mg/hr up to max of 3 mg/hr

Treatment of HRS-AKI

- What about Midodrine and Octreotide?

  - If norepinephrine can't be administered, a trial of these medications may be considered though much less efficient than norepinephrine

- Referral to LT evaluation should be considered

Liver Transplantation and Eligibility

- Medical eligibility
- Surgical eligibility
- Psychosocial eligibility
- Financial eligibility

Medical Eligibility

- Presence of indication

- Standard indication: Cirrhosis with ascites, hepatic encephalopathy, variceal hemorrhage or hepatocellular dysfunction with MELD Score > 15.

- Exception indication

AASLD Guidelines. Hepatology, 2014

Medical Eligibility: Exception Indications

Diagnosis	Criteria
Acute liver failure	Fulminant hepatic failure with onset of hepatic encephalopathy within 8 wk of first symptoms of liver disease, intensive care unit requirement, and one of the following three criteria: (1) ventilator dependence; (2) renal dialysis; or (3) INR >2.0 Primary nonfunction or hepatic artery thrombosis of transplanted liver graft within 7 days of transplant (less priority for those with hepatic artery thrombosis within 14 days of transplant) defined by AST ≥3000 U/L and one of the following: INR ≥2.5 or acidosis (arterial pH ≤7.30, venous pH ≤7.25 or lactate ≥4mmol/L) Wilson disease with acute liver decompensation
Hepatocellular carcinoma	Triple phase CT or MRI showing 1 lesion (2-5 cm) or 2-3 lesions none of which is > 3 cm with NO evidence of spread to vessels, LNs, or other organs. Biopsy is NOT needed in most cases
Cholangiocarcinoma	Neoadjuvant therapy protocol approved by the UNOS committee Unresectable hilar cholangiocarcioma of ≤3 cm documented by cross-sectional imaging and malignant-appearing stricture on cholangiography and one of the following: carbohydrate antigen 19-9 >100 U/mL or biopsy or cytology results demonstrating malignancy or aneuploidy Exclude intrahepatic and extraheptic metastases by cross-sectional imaging of chest and abdomen initially and every 3 mo Exclude regional hepatic and peritoneal metastases by operative staging after neoadjuvant therapy and before liver transplantation Avoid transperitoneal aspiration or biopsy of primary tumor
Hepatopulmonary syndrome	Clinical evidence of portal hypertension, evidence of a right to left extracardiac shunt, $Pa0_2$ <60 mm Hg with the patient breathing room air, and no significant clinical evidence of underlying primary pulmonary disease
Portopulmonary hypertension	Prior MPAP >35mm Hg and elevated transpulmonary gradient >12mm Hg; presently controlled with MPAP <35mm Hg and pulmonary vascular resistance <400 dyn sec/cm^{-5}
Familial amyloid polyneuropathy	Documented amyloidosis, echocardiogram with an ejection fraction of >40%, ambulatory status, identification of gene mutation, and biopsy proven amyloid
Primary hyperoxaluria	Documented primary hyperoxaluria, with AGT deficiency proven by liver biopsy, estimated GFR ≤25 mL/mL for 6 wk or more
Cystic fibrosis	Documented cystic fibrosis, signs of reduced pulmonary function defined by FEV_1 <40%
Metabolic diseases	Urea cycle disorder or organic acidemia

AGT, Alanine-glyoxylate aminotransferase; *AST*, aspartate aminotransferase; *FEV_1*, forced expiratory volume in the first second of expiration; *GFR*, glomerular filtration rate; *INR*, international normalized ratio, *MPAP*, mean pulmonary artery pressure; *UNOS*, United Network for Organ Sharing.

From Organ Procurement and Transplant Network. Policies - OPTN. Available at: https://optn.transplant.hrsa.gov/governance/policies/. Accessed 6 June 2015.

Medical Eligibility

- Absence of contraindication
- Unstable, active cardiopulmonary disease
- Metastatic or incurable non-hepatic primary malignancy
- Severe, irreversible neurologic disease
- Severe malnutrition or frailty
- Advanced age (>70 for many programs)

Surgical Eligibility

- Absence of contraindication

- Morbid Obesity (depending on the center)

- Prohibitive anatomy (e.g., extensive portosystemic venous thrombosis not amenable to recanalization)

Psychosocial Eligibility

- Absence of contraindication

- Recent or active untreated alcohol (and/or other substances) use disorder

- Uncontrolled psychiatric illness

- Insufficient social support (at least two caregivers)

- Non-compliance

- Unstable housing

Liver Transplantation and Eligibility

- All eligibility domains are discussed weekly in the multidisciplinary selection committee
  - Transplant hepatologists
  - Transplant NPs and Pas
  - Transplant surgeons
  - Transplant coordinators (RNs)
  - Transplant social workers
  - Transplant psychiatrists
  - Transplant pharmacists
  - Financial coordinators

Liver Transplantation and Eligibility

Approve

- Case submission to United Network for Organ Sharing (UNOS)
- Waitlisting

Defer

- Further clinical testing
- Fulfillment of psychosocial requirements

Decline

- Can be reconsidered in the future if the reason for decline is addressed

Take Home Points

- Ruling out occult infection (CXR, bl culture, UA, paracentesis on admission) is instrumental in the inpatient care of decompensated cirrhosis
- Ceftriaxone is not a universal recipe for SBP
- Hepatic encephalopathy is a clinical diagnosis and ammonia level is of NO utility in diagnosis & management.
- Start with holding diuretics, weight-dosed concentrated albumin and urine testing in patients with cirrhosis and acute kidney injury
- Always consider referral for transplant evaluation in decompensated cirrhosis without clear C/I

References

- Diagnosis, evaluation, and management of ascites and hepatorenal syndrome. 2021 Practice Guidance From the American Association for the Study of Liver Diseases. https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.31884

- Hepatic Encephalopathy in Chronic Liver Disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. https://www.aasld.org/sites/default/files/2019-06/hepaticencephalopathy82014.pdf

Thank You!

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