

# Challenging cases of hospitalized patients with cirrhosis

Danielle Brandman, MD, MAS  
Associate Professor of Clinical Medicine  
Program Director, Transplant Hepatology Fellowship  
Inpatient Chief of Service, Hepatology

October 17, 2019

# Disclosure

- Grant/research support: Grifols





# Case 1

- 63M with HCV cirrhosis is hospitalized due to worsened fluid retention, with ascites and lower extremity edema



# Case 1

- 63M with HCV cirrhosis is hospitalized due to worsened fluid retention, with ascites and lower extremity edema
- He denies fever or frank abdominal pain, though is uncomfortable from abdominal distension.

# Case 1

- 63M with HCV cirrhosis is hospitalized due to worsened fluid retention, with ascites and lower extremity edema
- He denies fever or frank abdominal pain, though is uncomfortable from abdominal distension.
- He finds it difficult to walk as a result of severe leg edema

# Case 1

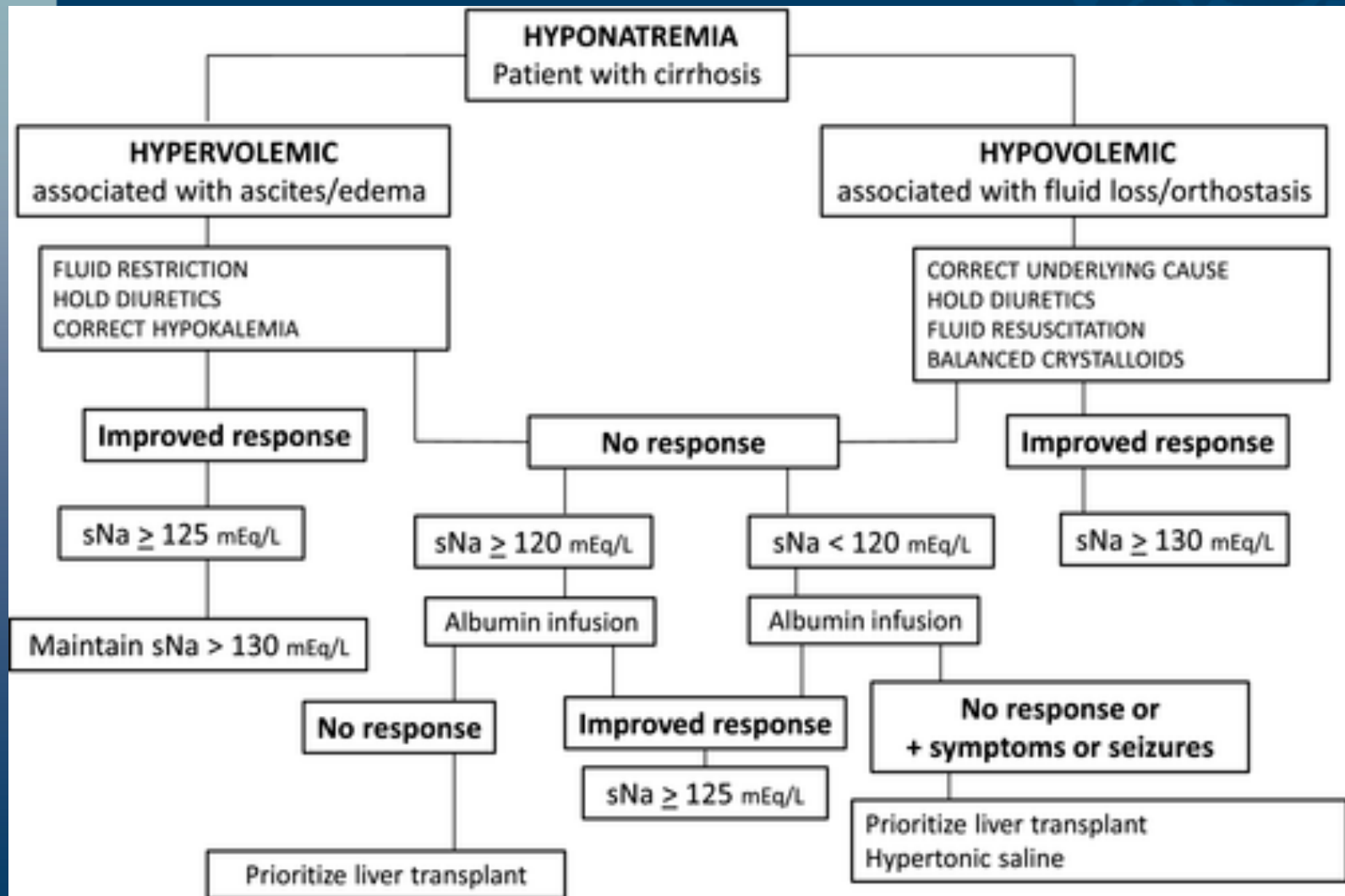
- VS: T37 HR 65 BP 110/70 RR 20 SpO2 98%
- Gen: chronically ill
- CV: 3+ BLE edema, anasarca
- Resp: normal other than decreased BS at bases
- GI: distended abdomen with dullness to percussion, nontender
  
- Labs: WBC 4, hct 32, plt 60, INR 1.9, Na 122, Cr 2.5, total bili 6, albumin 2.8

# Case 1

- What is your strategy for management of this patient's volume overload?
- How would you handle his hyponatremia?



# Approach to hyponatremia in cirrhosis





# IV albumin leads to resolution of hyponatremia

	<b>Albumin – (n= 349)</b>	<b>Albumin+ (n= 777)</b>	<b>p-value</b>
NACSELD-ACLF	5% (16/349)	16% (121/776)	<0.0001
Length of stay (days)	9.11 (9.67)	16.80 (18.60)	<0.0001
In-hospital mortality	4% (14/349)	8% (64/777)	0.01
30-day mortality	8% (27/349)	16% (126/777)	0.0001
Resolution of hyponatremia	61% (213/347)	69% (537/774)	0.0085

NACSELD-ACLF score [13] is defined as the occurrence of two of the following: brain failure defined by grade 3 or 4 hepatic encephalopathy, circulatory failure defined by shock requiring vasopressors, renal failure defined by need for renal replacement therapy, and respiratory failure defined by use of BiPAP or mechanical ventilation

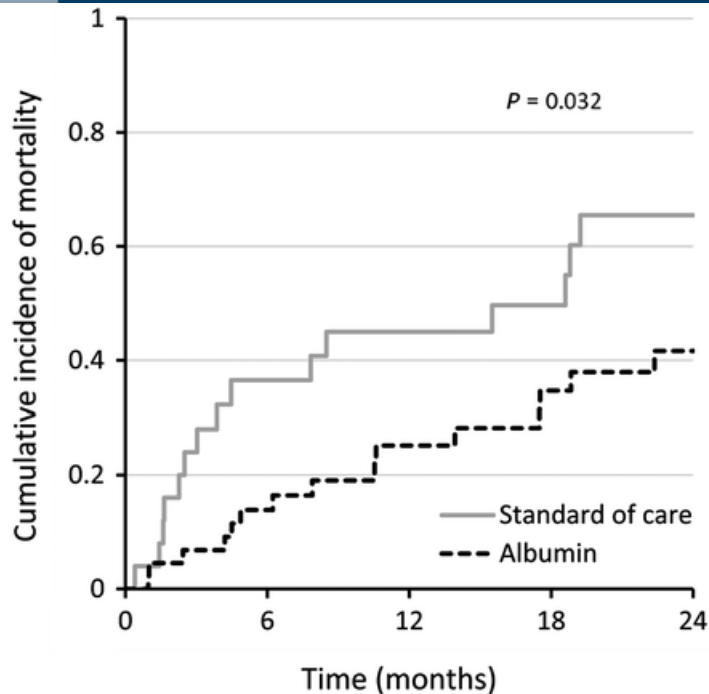
AMERICAN JOURNAL OF GASTROENTEROLOGY

# IV albumin and ascites

	Treatments	Study sample	Outcomes
ANSWER	Albumin 40g BIW x 2 weeks then 40g/wk + SMT vs SMT alone	n = 431 On diuretics, ascites	IRR for death 0.61 favoring albumin
MACHT	Albumin 40g q 15d + midodrine vs placebo	n = 196 (only 173 analyzed) Listed for LT, ascites	No difference in survival or liver complications More LT in albumin group (68% vs 55%; p=0.08)

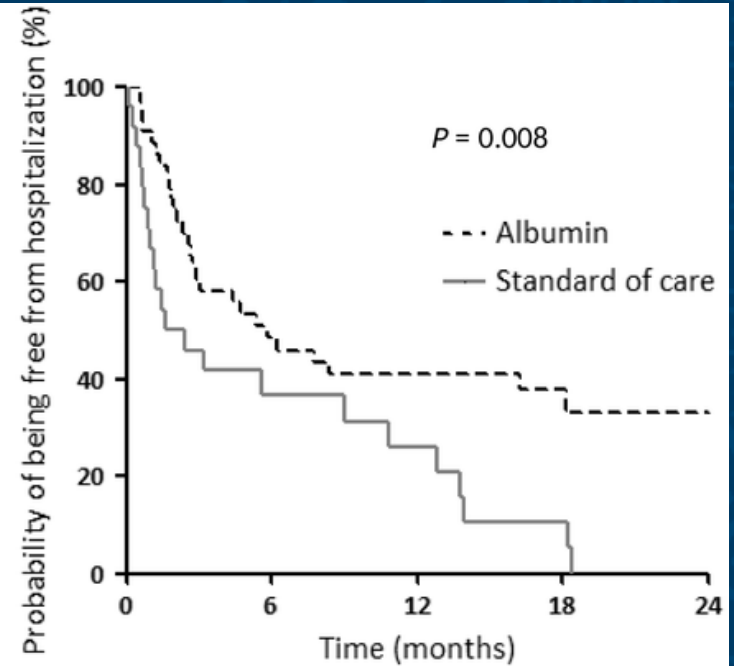
# Outpatient IV albumin use may improve survival and hospitalization

## Mortality



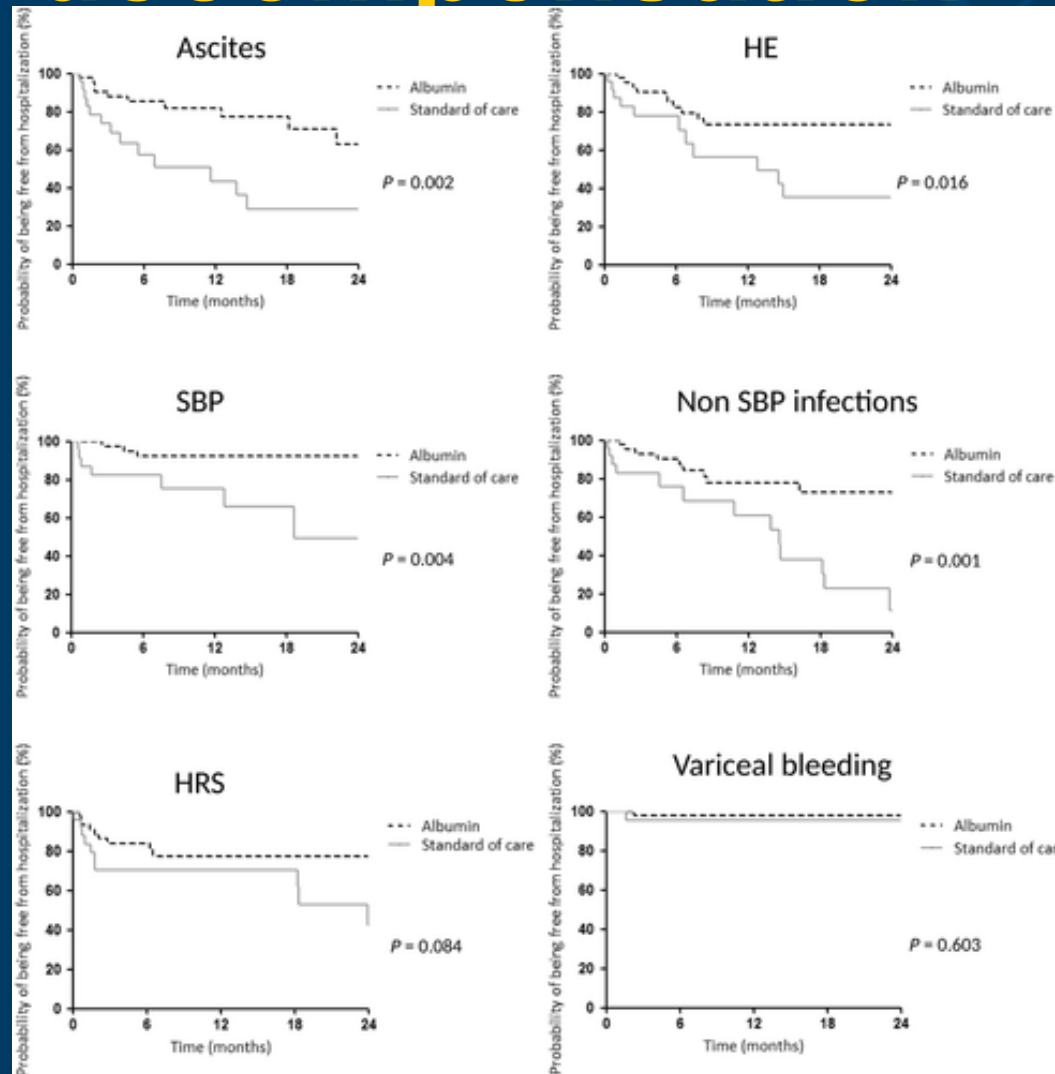
PTS at risk	0	6	12	18	24
SOC	25	13	10	8	5
Albumin	45	34	21	16	12

## Hospitalization

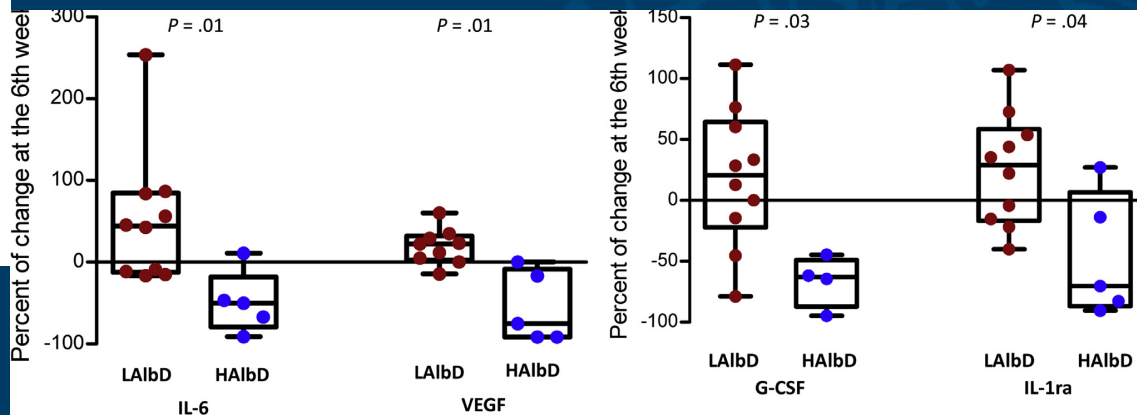
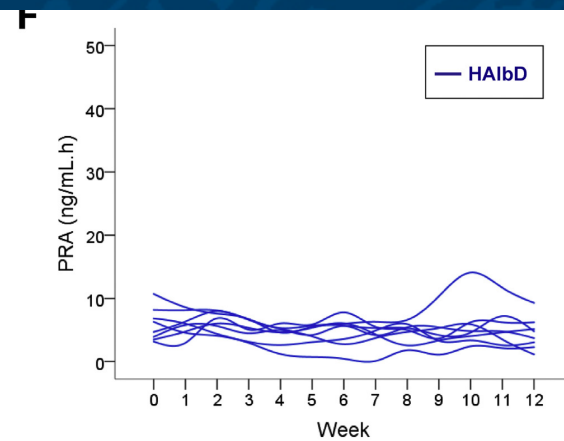
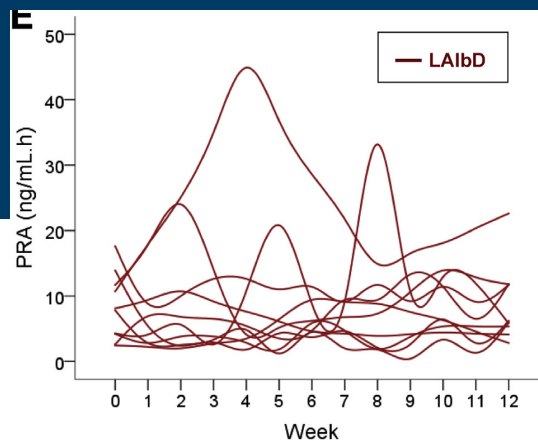
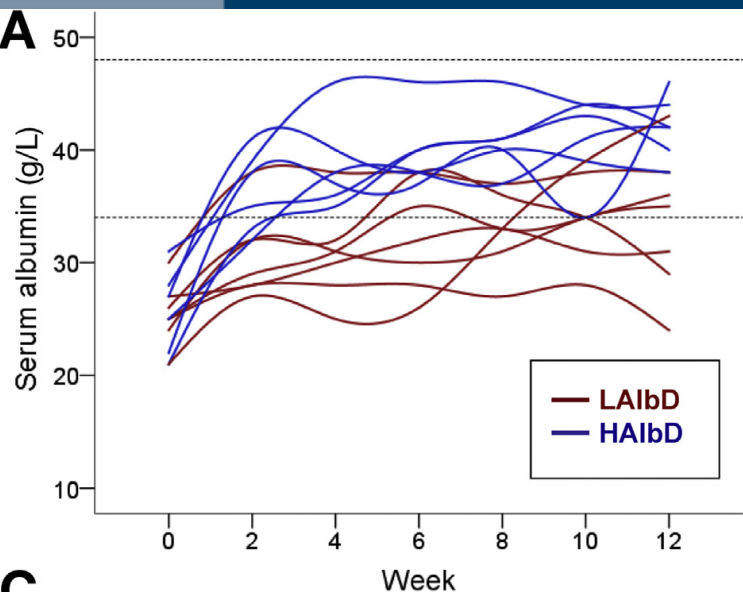


PTS at risk	0	6	12	18	24
SOC	25	7	5	2	0
Albumin	45	20	14	8	5

# Outpatient IV albumin use may decrease incidence of decompensation



# IV albumin reduces plasma renin activity and inflammatory markers



# Tolvaptan is not recommended

- May increase sodium in hypervolemic hyponatremia in cirrhosis when used in short-term
- FDA issued a black box warning for this drug due to drug-induced liver injury observed in patients with polycystic kidney disease



# My approach to hyponatremia

- Use history and physical exam findings to do your best to determine intravascular volume status
- Almost always hold diuretics
- Almost always IV albumin challenge unless signs of respiratory compromise
- If ascites present, diagnostic paracentesis to rule out SBP
- Free water restrict
- Understand what the baseline serum Na is so you know what target you're trying to hit
- If refractory to above, consider other causes or under-resuscitation



# Case 2

- 57F with NASH cirrhosis is hospitalized for the 4<sup>th</sup> time in 2 months with shortness of breath

# Case 2

- 57F with NASH cirrhosis is hospitalized for the 4<sup>th</sup> time in 2 months with shortness of breath
- She has a history of hepatic hydrothorax that has gotten progressively worse over time

# Case 2

- 57F with NASH cirrhosis is hospitalized for the 4<sup>th</sup> time in 2 months with shortness of breath
- She has a history of hepatic hydrothorax that has gotten progressively worse over time
- She undergoes therapeutic thoracentesis now twice weekly, with 1-2L fluid removed each time

# Case 2

- 57F with NASH cirrhosis is hospitalized for the 4<sup>th</sup> time in 2 months with shortness of breath
- She has a history of hepatic hydrothorax that has gotten progressively worse over time
- She undergoes therapeutic thoracentesis now twice weekly, with 1-2L fluid removed each time
- She is frustrated with her frequent hospitalizations and poor quality of life



# Case 2

- 57F with NASH cirrhosis is hospitalized for the 4<sup>th</sup> time in 2 months with shortness of breath
- She has a history of hepatic hydrothorax that has gotten progressively worse over time
- She undergoes therapeutic thoracentesis now twice weekly, with 1-2L fluid removed each time
- She is frustrated with her frequent hospitalizations and poor quality of life
- Diuretic doses have been increased to the highest tolerable dose, with higher doses associated with AKI, hyponatremia, and/or hyperkalemia in the past

# Case 2

- VS: T36.4 HR 73 BP 109/53 RR 24 SpO2 95% 2LNC
- Gen: chronically ill
- Resp: Decreased breath sounds throughout all lung fields on the right
- Labs: WBC 6, hct 28, plt 51, INR 1.6, Na 130, Cr 1.02, total bili 2, albumin 2.7

# Case 2

- What treatment options are available to this patient?

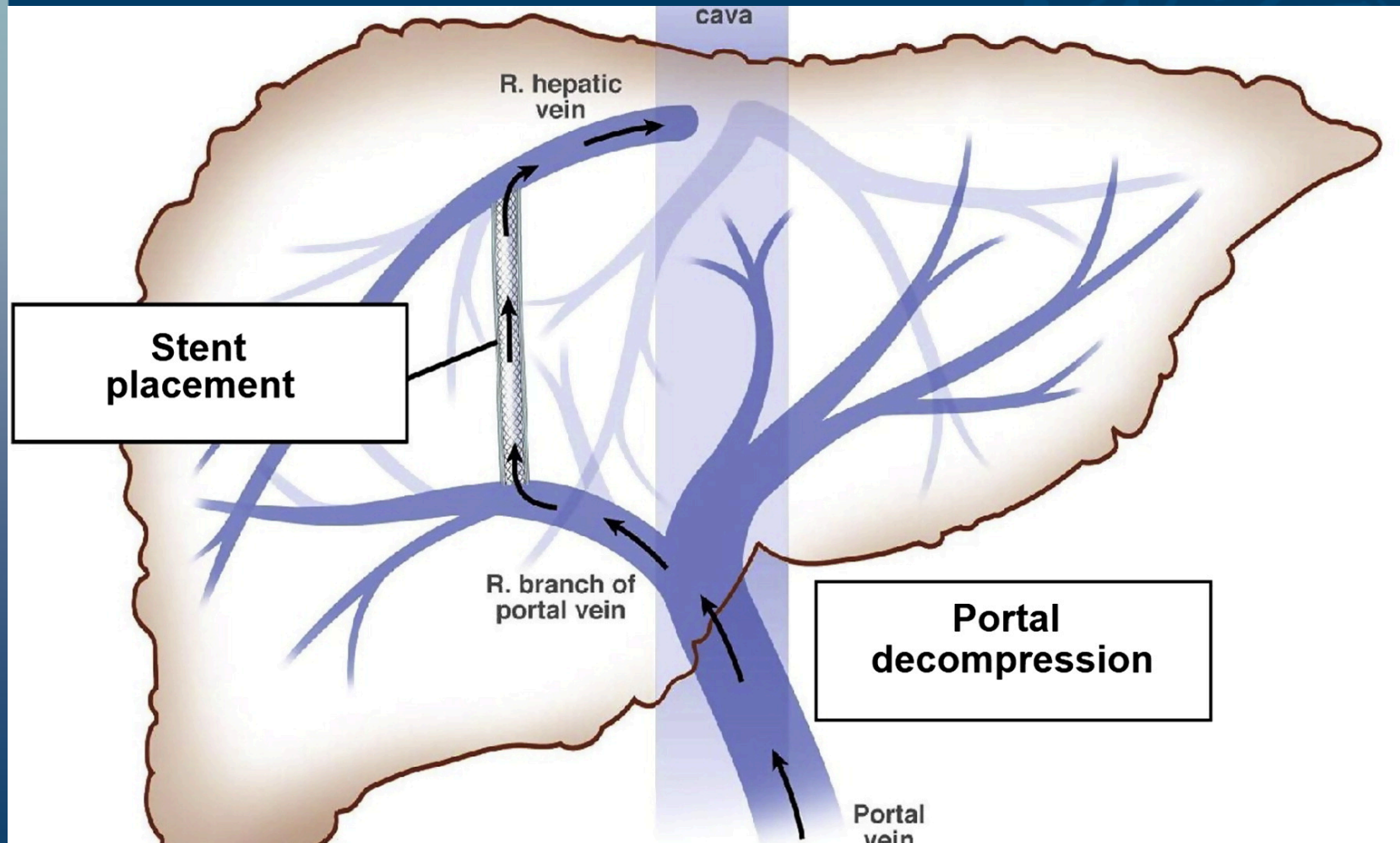
# Evaluation and management of hepatic hydrothorax (HH)

- Confirm transudative, particularly if not right-sided (15%)
  - ◆ 30% of pleural effusions in cirrhosis were not HH
  - ◆ 35% of left-sided effusions in cirrhosis were HH
- Medical management same as ascites:
  - ◆ Salt restriction
  - ◆ Diuretics: furosemide: spironolactone 5:2
- Therapeutic thoracentesis
- TIPS
- Pigtail catheter

# Maintain high level of suspicion for SBE

- Present in 13-16% of patients with hepatic hydrothorax
- Mortality: 20-38%
- Diagnostic criteria
  - ◆ Positive fluid culture and PMN >250 or
  - ◆ Negative fluid culture and PMN >500
  - ◆ No evidence of pneumonia or parapneumonic effusion
- Can be present even if SBP not present

# Transjugular intrahepatic portosystemic shunt (TIPS)



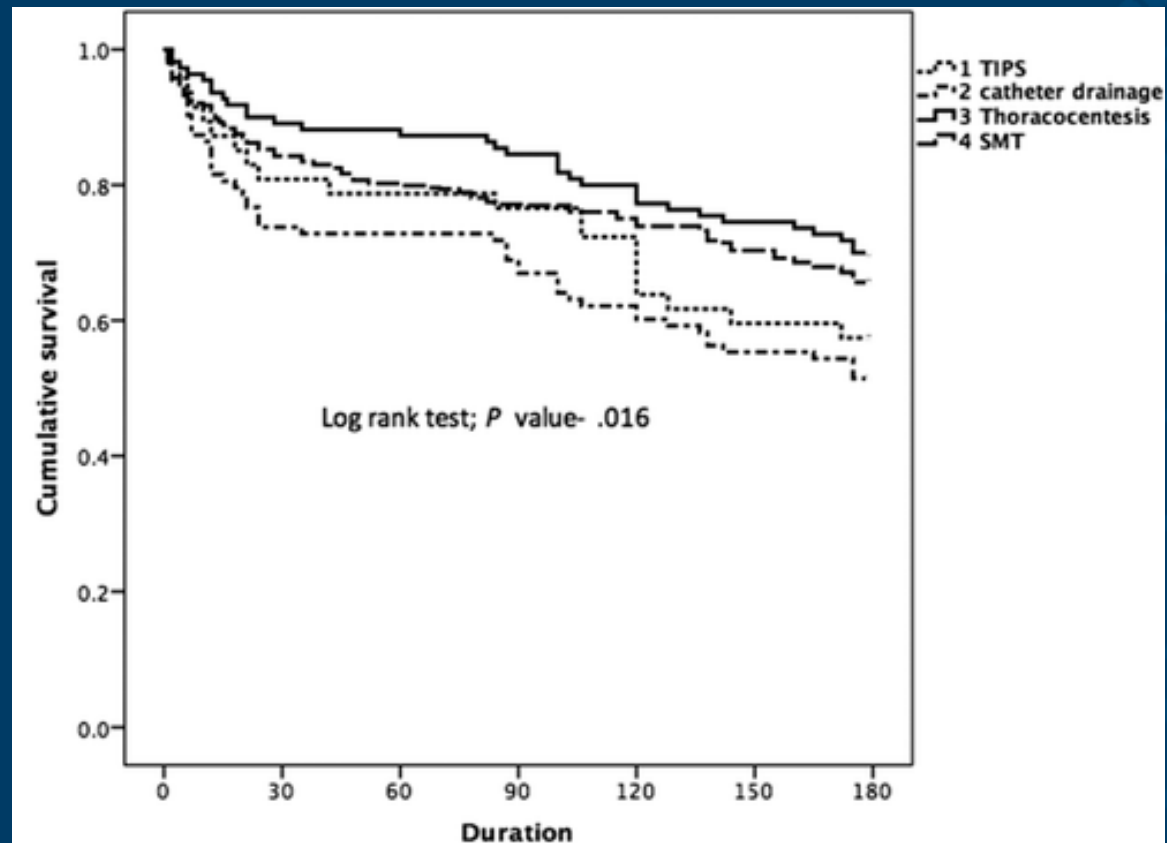


# TIPS and hepatic hydrothorax

- Response rates: 59-82%
- Mortality
  - ◆ 30-day: 5-25%
  - ◆ 1-year: 36-52%



# Management of hepatic hydrothorax



	Day 0	Day 30	Day 90	Day 180
TIPS	47	38	36	27
Catheter drainage	103	76	69	53
Thoracocentesis	110	98	93	77
SMT	617	520	476	405

# Contraindications to TIPS

## Box 1

### Contraindications for TIPS

#### Relative

Hepatocellular carcinoma, especially centrally located  
Obstruction of all HVs  
PV thrombosis  
Moderate pulmonary hypertension  
Severe coagulopathy (international normalized ratio >5)  
Thrombocytopenia of  $<20,000$  cells/cm<sup>3</sup>  
Hepatic encephalopathy

#### Absolute

Primary prevention of variceal bleeding  
Congestive heart failure  
Severe tricuspid regurgitation  
Severe pulmonary hypertension  
Multiple hepatic cysts  
Uncontrolled systemic infection or sepsis  
Unrelieved biliary obstruction

# Case 2

- What treatment options are available to this patient?
- What if her labs looked like this:
  - ◆ INR 2.7, Na 130, Cr 1.02, total bili 7

# Pleural catheter for HH

- Attractive option for patients who need frequent thoracentesis or who are at higher risk of bleeding
- May result in spontaneous pleurodesis in 33%
- Risk of complications: 36%
  - ◆ 10-16% SBE
  - ◆ Deaths typically due to sepsis
- If used as a bridge to transplant, plan should be made in conjunction with transplant team



# Case 3

- 47M with alcohol related cirrhosis is brought into the ED with altered mental status



# Case 3

- 47M with alcohol related cirrhosis is brought into the ED with altered mental status
- He had been taking lactulose as prescribed, but his family notes that he has not had a bowel movement in the past 24 hours

# Case 3

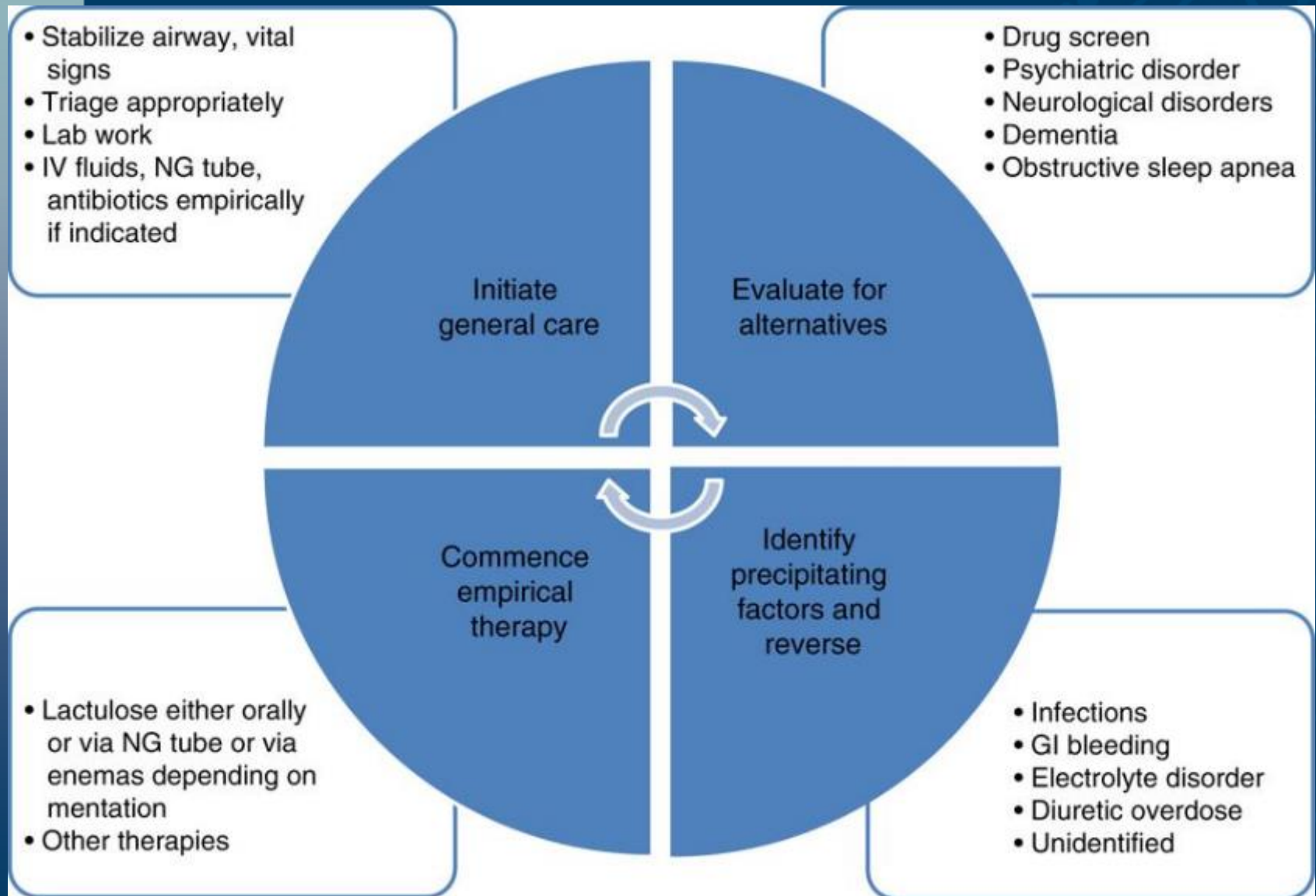
- VS: T36.7 HR 80 BP 117/62 RR 12 SpO2 99%
- Gen: chronically ill, muscle wasting
- Neuro: lethargic, only briefly wakes up with verbal stimuli. Oriented x 0. +clonus
- Labs: WBC 5, hct 33, plt 95, INR 1.9, Na 136, Cr 0.97, total bili 4.7, albumin 2.6

# Case 3

- What are your initial steps for management?



# Management of hepatic encephalopathy



# Case 3

- The patient is intubated for airway protection given concerns for airway protection. An NGT is placed for administration of lactulose. He initially passed a small amount of stool. After aggressively dosing lactulose q2 hours, the patient develops abdominal distension and has not passed any stool

# Case 3

- The patient is intubated for airway protection given concerns for airway protection. An NGT is placed for administration of lactulose and rifaximin. He initially passed a small amount of stool. After aggressively dosing lactulose q2 hours, the patient develops abdominal distension and has not passed any stool

???



# Case 3

- The patient is intubated for airway protection given concerns for airway protection. An NGT is placed for administration of lactulose and rifaximin. He initially passed a small amount of stool. After aggressively dosing lactulose q2 hours, the patient develops abdominal distension and has not passed any stool



# Case 3

- What are your next steps in management?



# Ileus and HE

- Confirm you are dealing with an ileus and not small bowel obstruction. KUB as first line, CT if unsure
- If in fact ileus, key is “afterload reduction”
  - ◆ Lactulose enema until bowels start to move





# Case 4

- 63F with cirrhosis due to primary biliary cholangitis presents with hematemesis and melena



# Case 4

- 63F with cirrhosis due to primary biliary cholangitis presents with hematemesis and melena
- She had 2 prior episodes of bleeding due to esophageal varices within the past 3 months

# Case 3

- VS: T37 HR 115 BP 90/54 RR 12 SpO2 99%
- Gen: alert, mildly uncomfortable
- GI: soft, NT, ND, no detectable ascites. Rectal with melena
  
- Labs: WBC 7, hct 20 (baseline 31), plt 48, INR 2.8, Na 137, Cr 0.65, total bili 2.5, albumin 3.1

# Case 4

- What are your next steps in management?



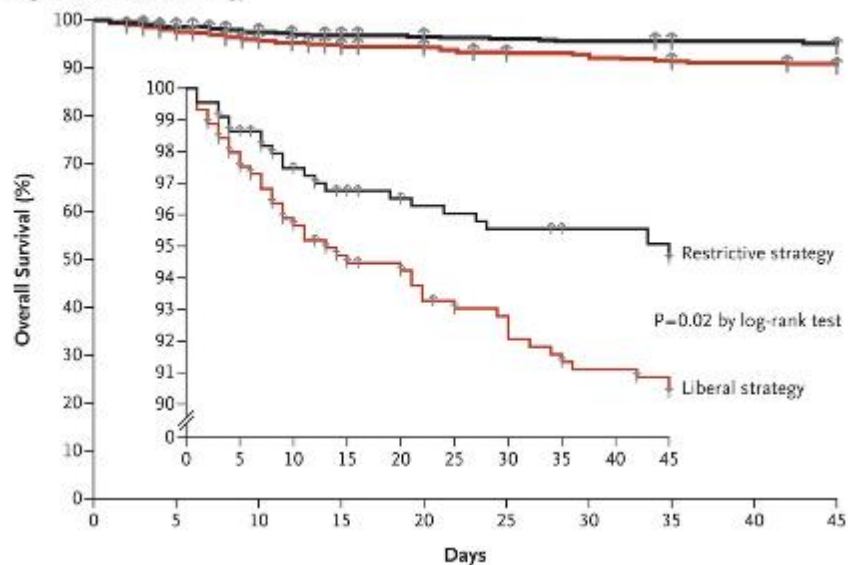


# Management of GI bleeding in cirrhosis

- ABCs
- Type and cross pRBCs +/- FFP and platelets
- Octreotide
- PPI IV

# Transfuse to a goal Hb 7-9g/dL

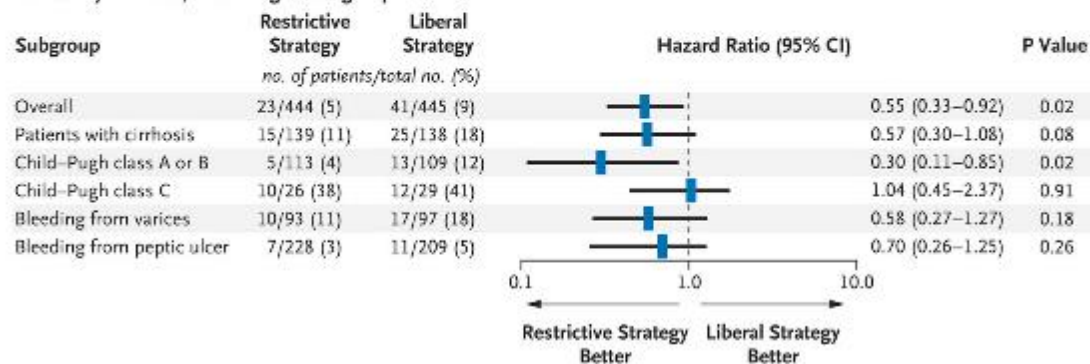
**A Survival, According to Transfusion Strategy**



**No. at Risk**

Restrictive strategy	444	429	412	404	401	399	397	395	394	392
Liberal strategy	445	428	407	397	393	386	383	378	375	372

**B Death by 6 Weeks, According to Subgroup**



# No definitive data on INR or platelet goals

- INR is a poor predictor of bleeding (or clotting) risk in cirrhosis
- Recombinant factor VIIa not clearly beneficial
- No guidance available on platelet goal



# Octreotide reduces mortality and need for transfusion

- Octreotide dosing
  - ◆ Initial bolus of 50 µg (repeat in first hour if ongoing bleeding)
  - ◆ Continuous IV infusion of 50 µg/hr for up to 5 days
- Use of vasoactive agents reduces 7-day mortality by 36%
- 32% decreased risk of rebleeding
- Blood transfusion requirement 0.7 units lower in patients receiving vasoactive agents

# Antibiotics improve outcomes in GI bleeding in cirrhosis

- Risk of infection after GI bleeding may be as high as 35-66% within 2 weeks
- Meta-analysis demonstrated reduced risk of infection compared with placebo
  - ◆ Any infection: 14% vs 45%
  - ◆ SBP or bacteremia: 8% vs 27%
- First line antibiotic choice: ceftriaxone

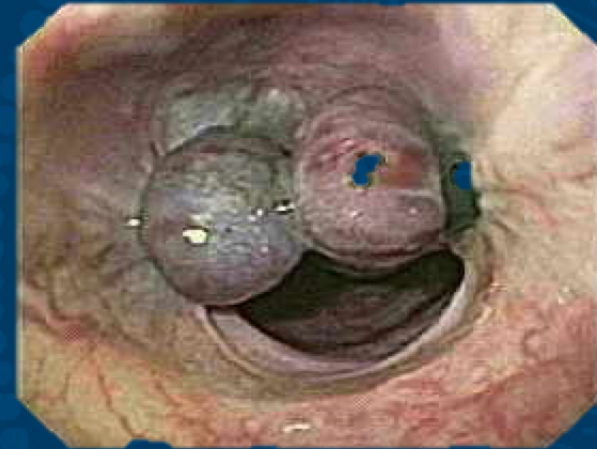
# Predictors of poor outcome after variceal bleeding

- Child-Pugh class
- AST
- Shock on admission
- Portal vein thrombosis
- HCC
- Active bleeding at endoscopy
- Hepatic venous pressure gradient >20
- MELD

10-15% of patients with  
have persistent and/or  
early rebleeding

# Endoscopic therapy in variceal bleeding

- Band ligation within 12 hours considered standard of care for esophageal varices
- Other modalities
  - ◆ Hemostatic powder/spray
  - ◆ Esophageal stent
  - ◆ (Sclerosants)
- Treatment for gastric varices: cyanoacrylate injection +/- coil



# Case 4

- Upper endoscopy is performed and shows 3 columns of large esophageal varices with high risk stigmata

# Case 4

- Upper endoscopy is performed and shows 3 columns of large esophageal varices with high risk stigmata
- The gastroenterologist is unable to successfully place bands due to scarring from prior band ligation. Active bleeding begins at the end of the case.

# Case 4

- Upper endoscopy is performed and shows 3 columns of large esophageal varices with high risk stigmata
- The gastroenterologist is unable to successfully place bands due to scarring from prior band ligation. Active bleeding begins at the end of the case.
- What options for treatment are available?





# Gastroesophageal balloon tamponade

- Temporizing measure to bridge to TIPS

# Gastroesophageal balloon tamponade

- Temporizing measure to bridge to TIPS

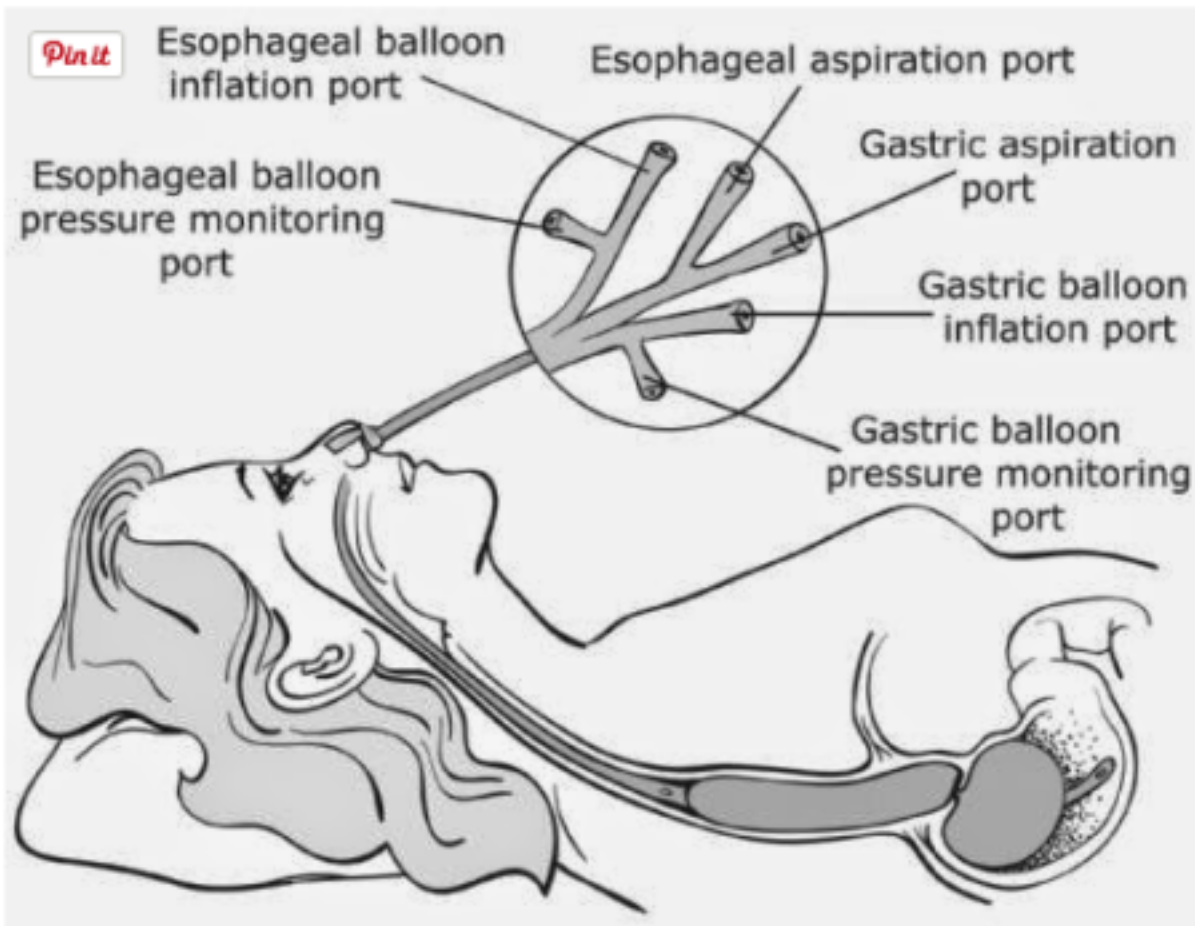
	Balloon types	Ports
Minnesota		
Sengstaken-Blakemore		
Linton		

# Gastroesophageal balloon tamponade

- Temporizing measure to bridge to TIPS

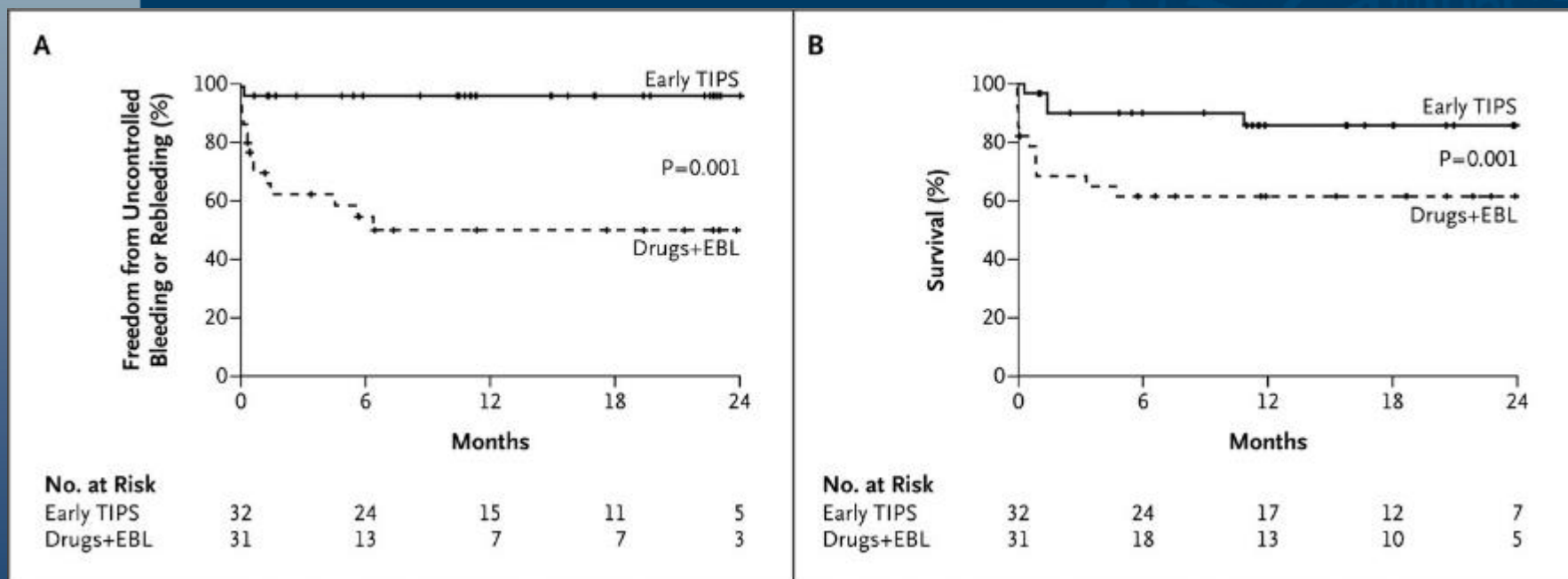
	<b>Balloon types</b>	<b>Ports</b>
Minnesota	Gastric Esophageal	2 balloon 2 aspiration
Sengstaken- Blakemore	Gastric Esophageal	2 balloon 1 aspiration (gastric)
Linton	Gastric	1 balloon 2 aspiration

# Gastroesophageal balloon tamponade



The Minnesota Tube

# Early TIPS in variceal bleeding



Careful patient selection is critical





# Case 5

- 60F with NASH cirrhosis presents with jaundice and worsened fluid retention

# Case 5

- 60F with NASH cirrhosis presents with jaundice and worsened fluid retention
- Exam:
  - ◆ VS: T 38, HR 110, BP 95/50, RR 20, 97%RA
  - ◆ Jaundiced
  - ◆ Abdominal distension with dullness to percussion
  - ◆ Confused, slow to respond

# Case 5 (cont'd)

## Labs

	6 weeks ago	Current presentation
INR	1.3	2.5
Na	140	134
Cr	0.6	2.3
Total bilirubin	1.0	5.2
Albumin	4.0	3.3
MELD-Na	9	32

# Case 5

**How could you classify this patient's presentation?**



# Acute on Chronic Failure



# Acute on Chronic Failure: Consensus Definition

“A syndrome in patients with chronic liver disease with or without previously diagnosed cirrhosis which is characterized by acute hepatic decompensation resulting in:

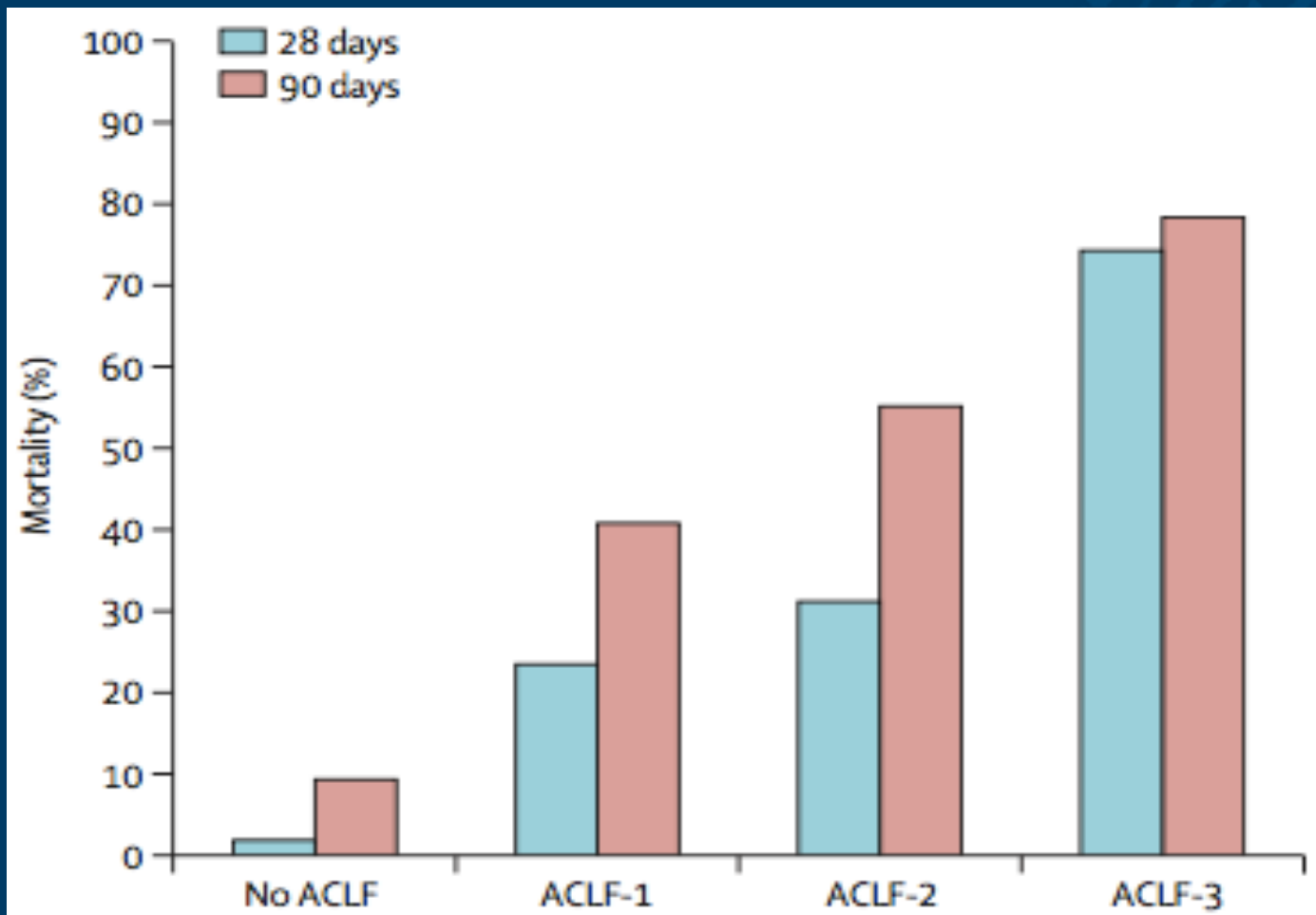
- 1) liver failure (jaundice and elevated INR) *and*
- 2) one or more extrahepatic organ failures that is associated with increased mortality within a period of 28 days and up to 3 months from onset”



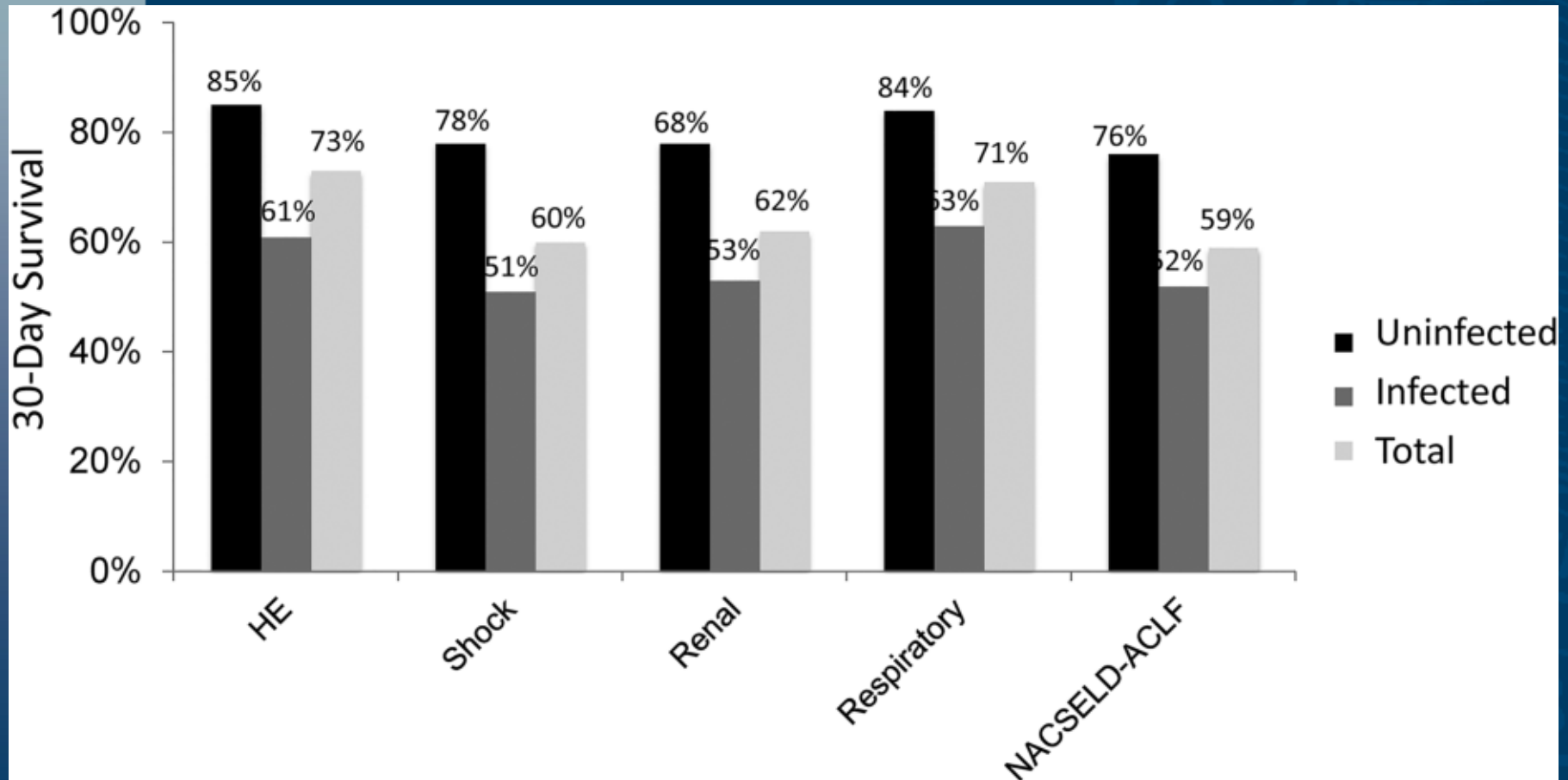
# Acute on Chronic Liver Failure (ACLF)

- 32,335 hospitalizations for ACLF per year
- Mortality 50% (previously 65%)
- Mean length of stay: 16 days
- Indicates need for liver transplantation
  - ◆ Presence may increase risk of post-transplant morbidity and mortality

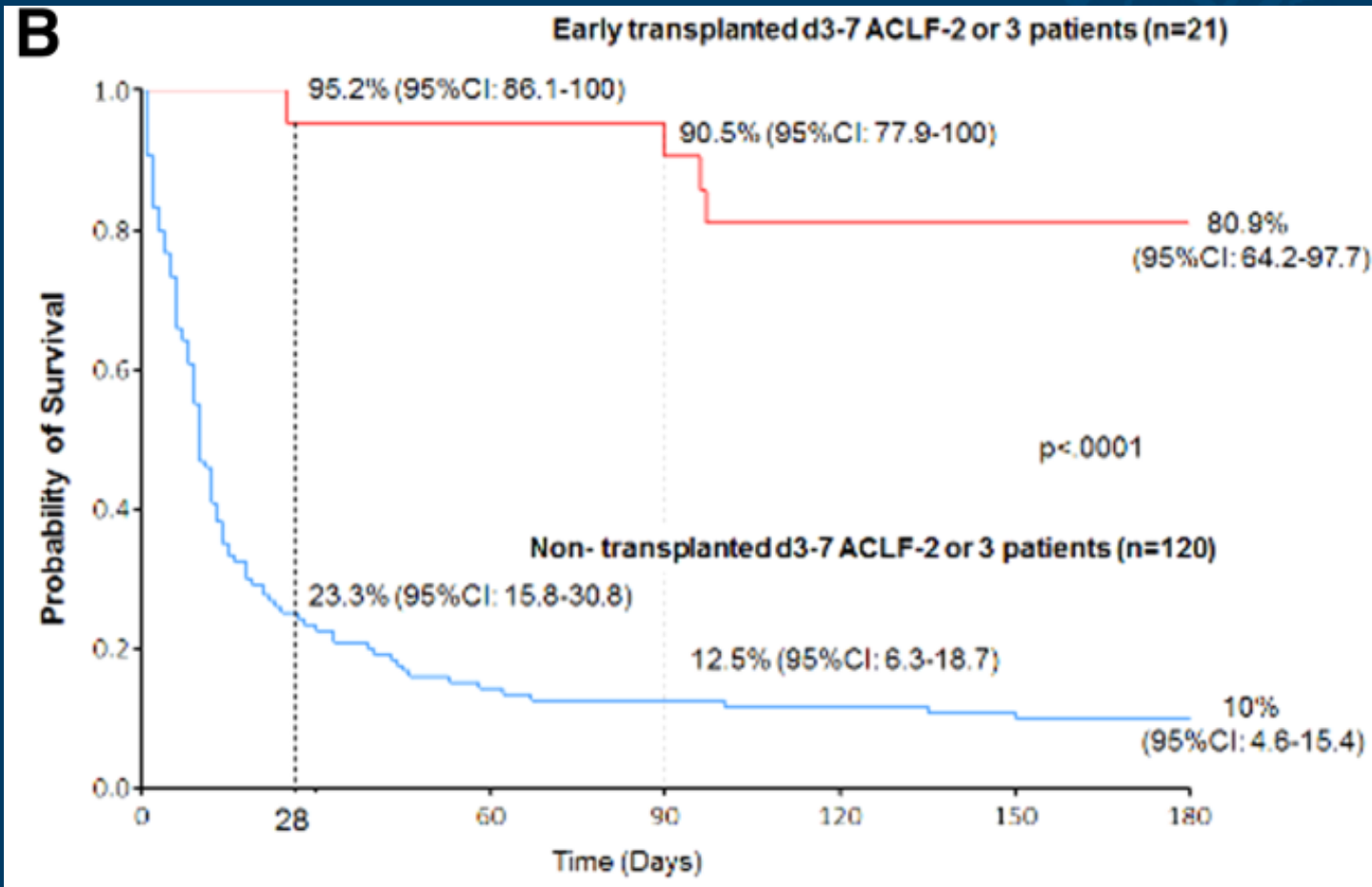
# ACLF strongly predicts 28- and 90-day mortality



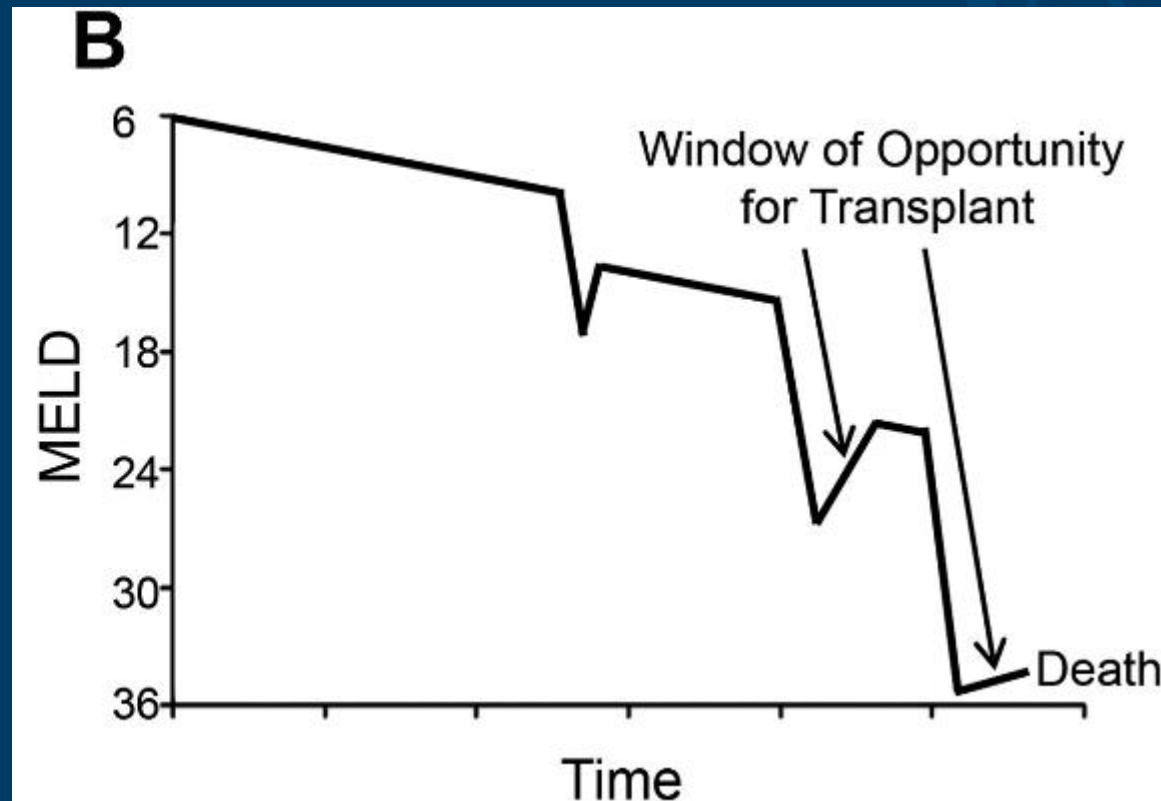
# Infection is associated with increased risk of 30-day mortality



# LT improves survival in ACLF



# Narrow window for LT in ACLF



# When should you consult hepatology for a patient with cirrhosis?

# When should you consult hepatology for a patient with cirrhosis?

- Decompensated cirrhosis or ACLF
  - ◆ Assistance in management
  - ◆ Liver transplant evaluation
- When TIPS is being considered
- Evaluation of a liver mass
- Variceal bleeding (center variability)



# Cases or questions from the audience

# Thank you!

[Danielle.Brandman@ucsf.edu](mailto:Danielle.Brandman@ucsf.edu)