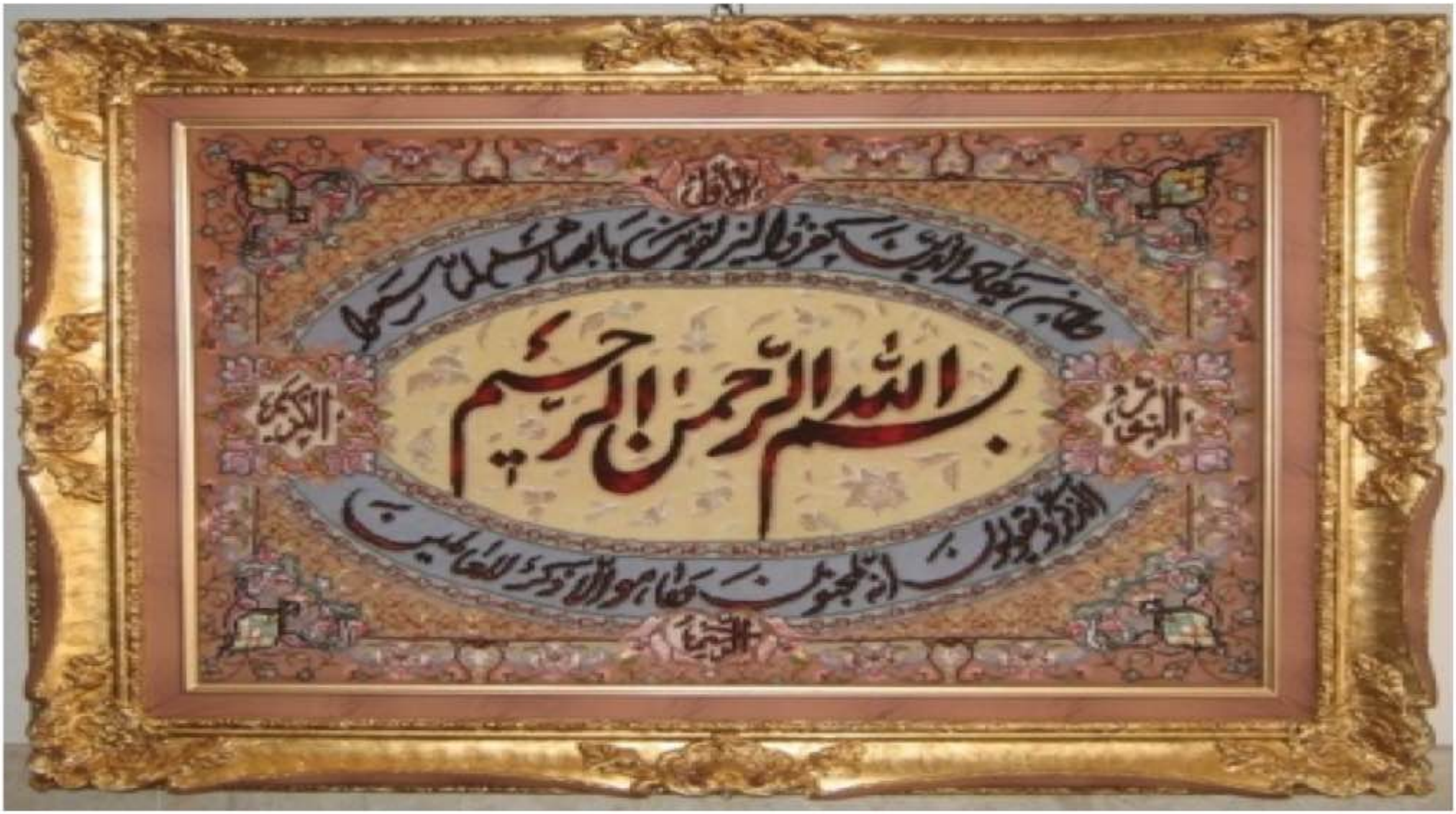

بسم الله الرحمن الرحيم

Updates in Management of Patients with Cirrhosis

Mohammad Taher
Associate Professor of Medicine
TUMS, IKHC

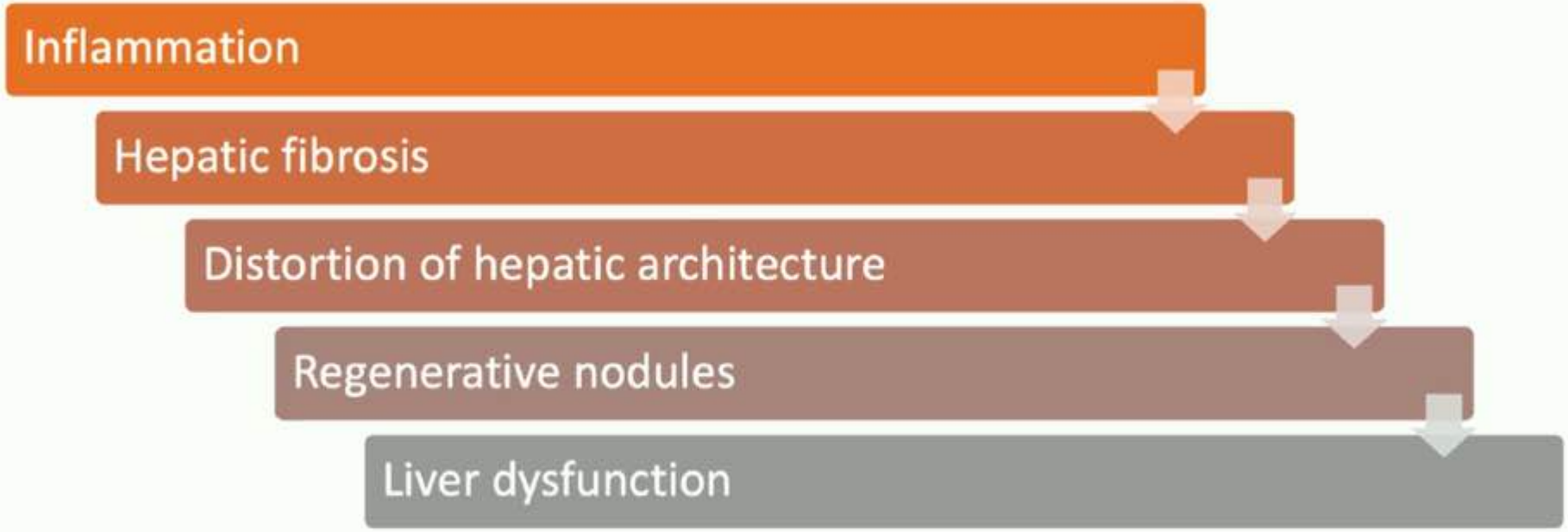
Goals and Objectives

Prevalence

Pathophysiology

Management

Definition of Cirrhosis



What is the current most common cause of cirrhosis?

A. Hepatitis C
B. Metabolic Dysfunction Associated Steatotic Liver Disease
C. Primary Biliary Cirrhosis
D. Alcohol Use Disorder

Prevalence of Cirrhosis

1 million deaths worldwide annually

11th most common cause of death globally

3rd leading cause of death in ages 45-64

Asrani et al. J Hepatology 2019

Prevalence **doubled** in US over 6 years

MASLD is disproportionately **increasing**

Common causes:

- Alcohol – 26-45%
- MASLD – 21-25%
- Hepatitis C – 20-41%

Ladner et al. PLoS One 2024

What is the current most common cause of cirrhosis?

A. Hepatitis C
B. Metabolic Dysfunction Associated Steatotic Liver Disease
C. Primary Biliary Cirrhosis
D. Alcohol Use Disorder

Causes of Cirrhosis

- **Metabolic (alcohol/ALD, obesity/MASLD)**
- **Infectious (Hepatitis B and C)**
- Genetics (Hemochromatosis, Wilson's disease)
- Host and Environmental Triggers (Autoimmune hepatitis, PBC, PSC)

More than one risk factor → rapid progression

Clinical Features

Palmar erythema

Scleral icterus

Jaundice

Gynecomastia

Spider angiomas

Caput Medusa

Asterixis

Fatigue

Weight loss

Bruising

Cramping

Pruritus

Lab abnormalities

+/- AST/ALT

Elevated alkaline phosphatase

Elevated gamma-glutamyl transpeptidase

Thrombocytopenia

Leukopenia

Anemia

Hypoalbuminemia

Elevated INR

Hyperbilirubinemia

Hyponatremia

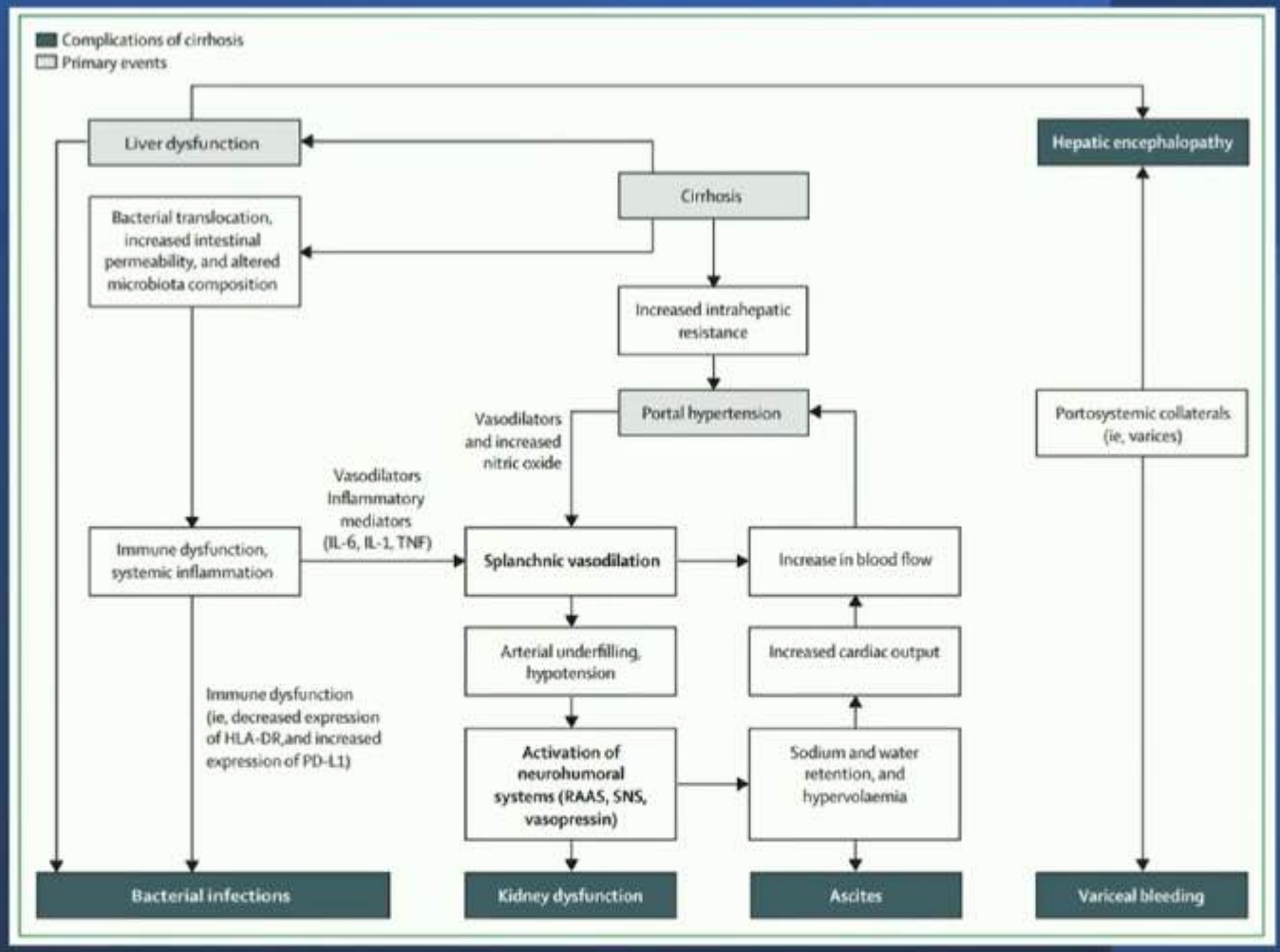
Elevated Cr

Diagnostic Criteria for Cirrhosis

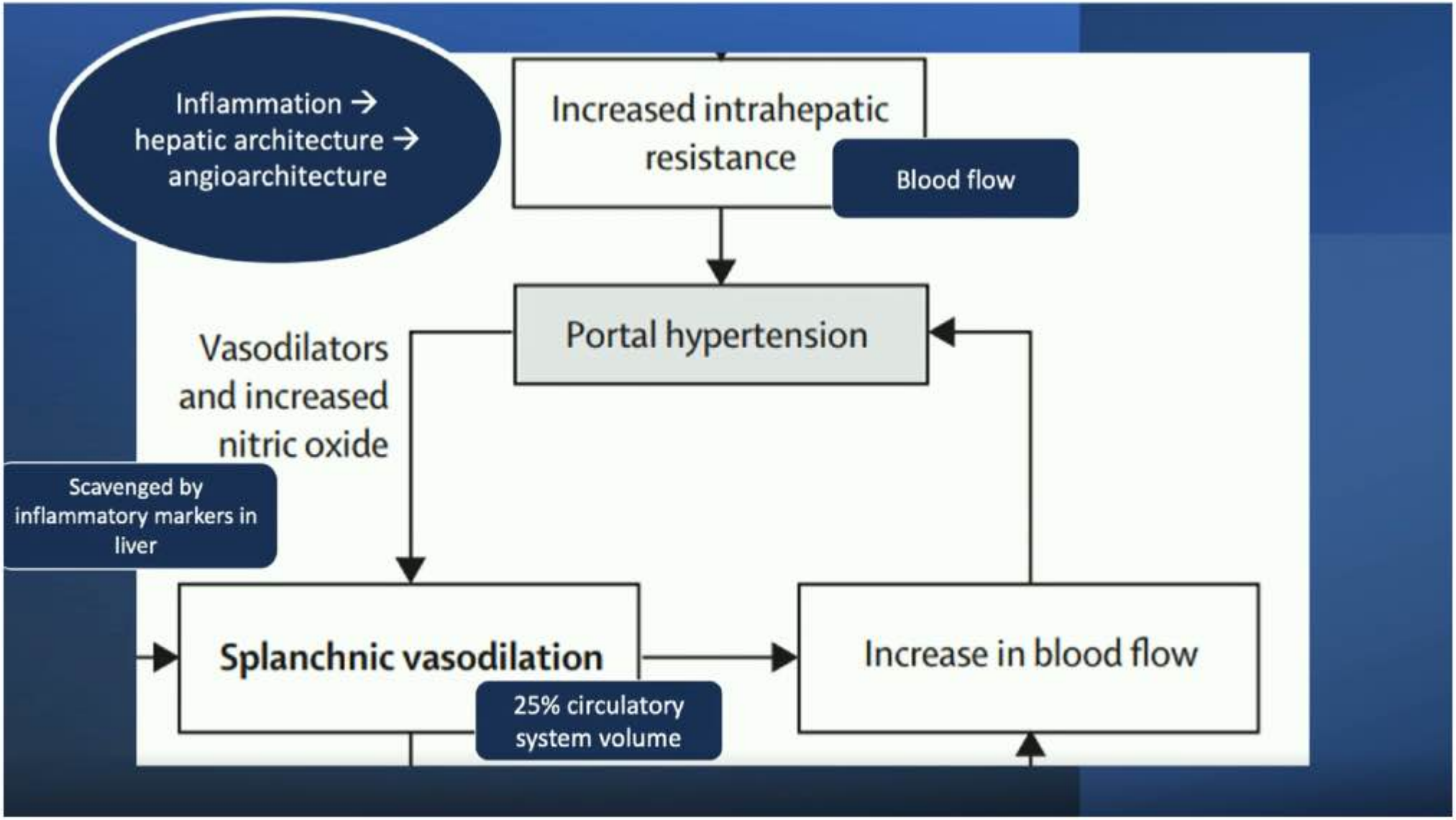
Quantify the degree of hepatic **fibrosis**
- Risk factors
- Liver Function Panels/Fibrosis-4 Index
- Elastography
- Liver biopsy

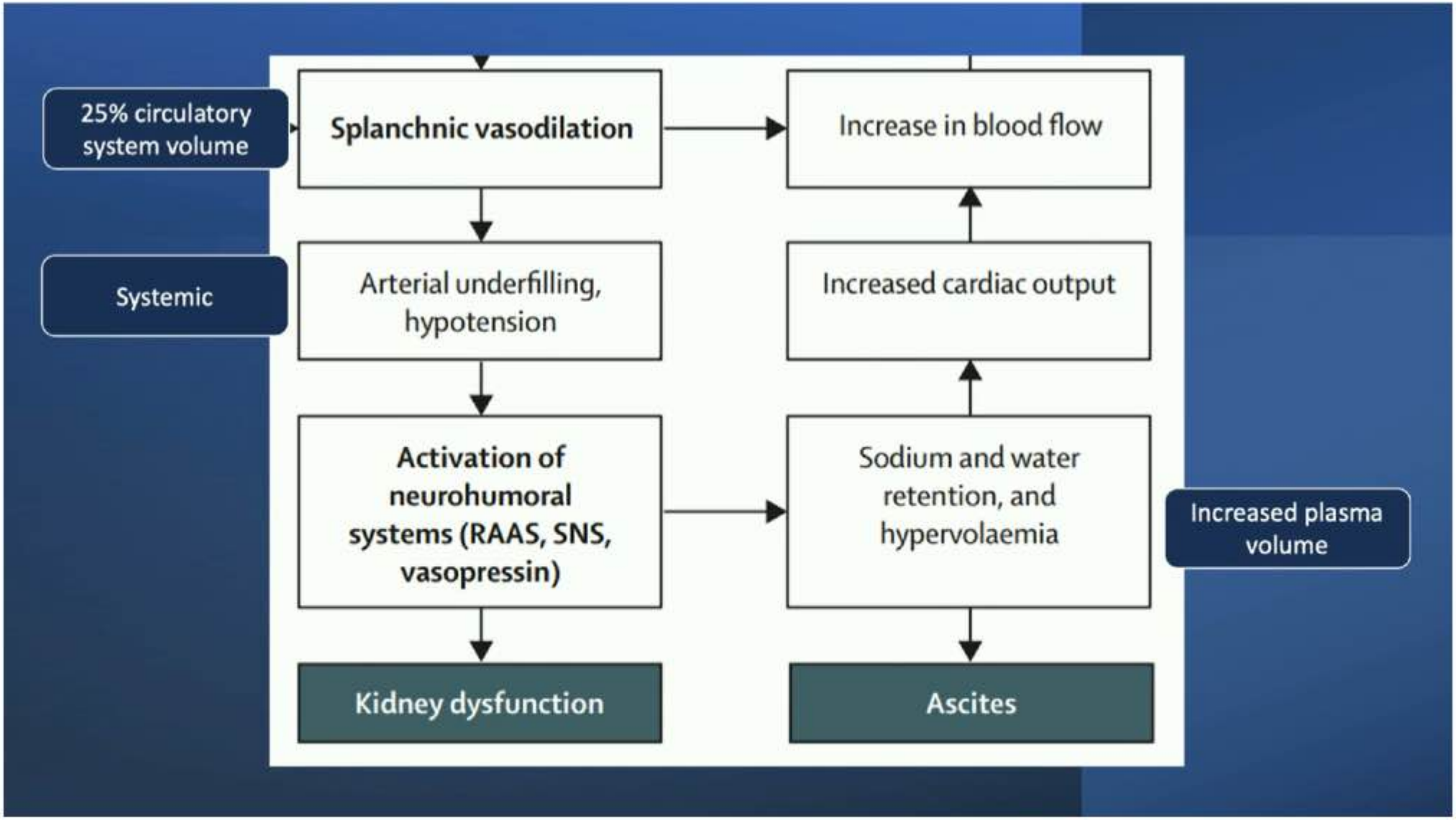
Assess for **portal hypertension**

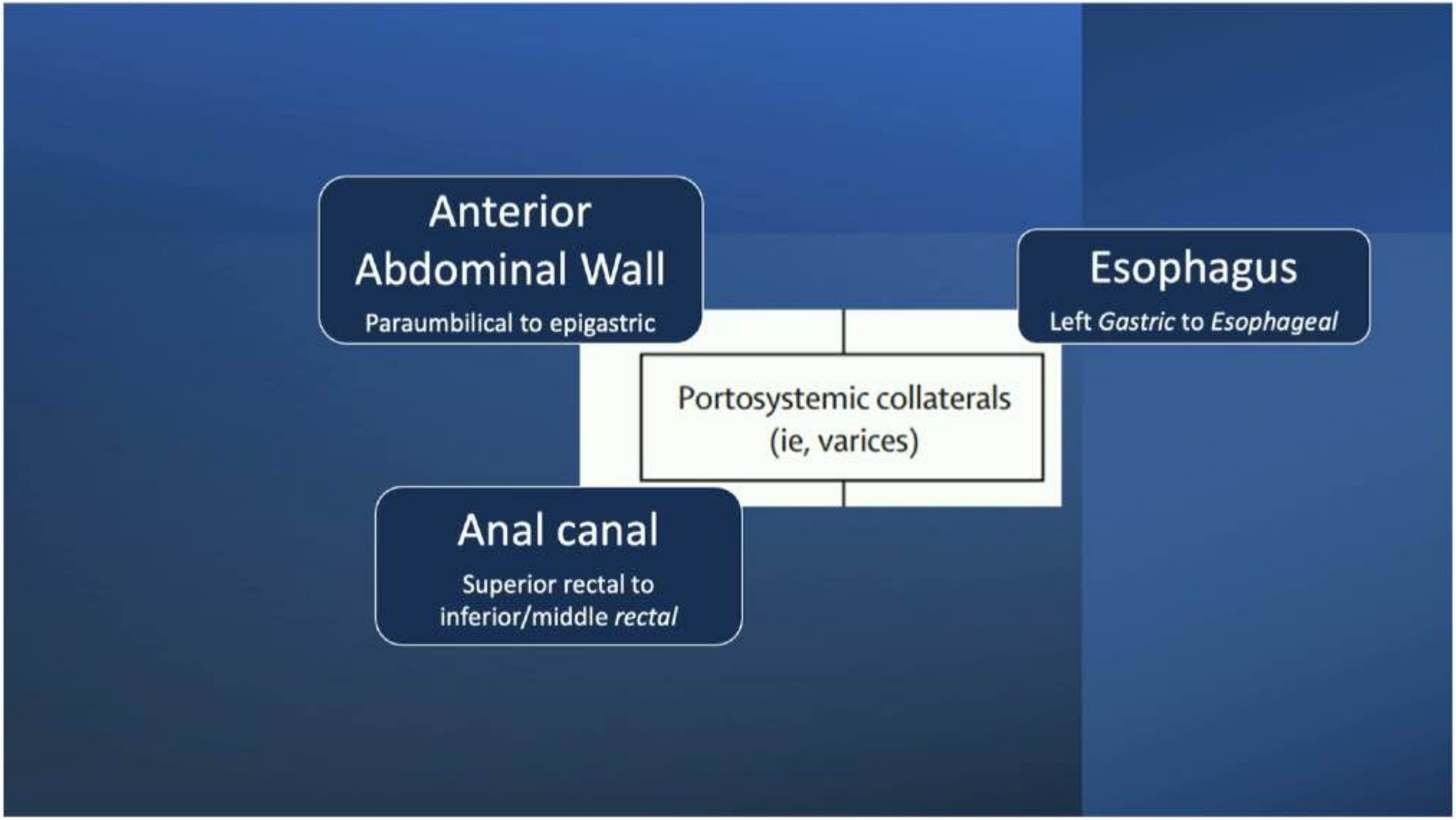
Determine the **cause**(s) of cirrhosis



Ginès et al, Lancet 2021


Inflammation → hepatic architecture → angioarchitecture
Increased intrahepatic resistance
Blood flow
Portal hypertension
Vasodilators and increased nitric oxide
Scavenged by inflammatory markers in liver
Splanchnic vasodilation
25% circulatory system volume
Increase in blood flow


25% circulatory system volume
Splanchnic vasodilation
Increase in blood flow
Systemic
Arterial underfilling, hypotension
Increased cardiac output
Activation of neurohumoral systems (RAAS, SNS, vasopressin)
Sodium and water retention, and hypervolaemia
Increased plasma volume
Kidney dysfunction
Ascites


Anterior Abdominal Wall
Paraumbilical to epigastric
Esophagus
Left *Gastric* to *Esophageal*
Portosystemic collaterals (ie, varices)
Anal canal
Superior rectal to inferior/middle *rectal*

What is the first-line treatment for ascites not controlled by diet?

(A) Furosemide

(B) Spironolactone

(C) Serial paracentesis

(D) Transjugular intrahepatic portosystemic shunt

Ascites

Accumulation of fluid within the peritoneal cavity ranging from mild to a distended abdomen

Uncomplicated/Recurrent: controlled with diet, diuretics, occasional paracentesis with albumin

Complicated/Refractory: paracentesis or transjugular intrahepatic portosystemic shunt (TIPS)

Ascites

Sodium and
Water
Restriction

Moore & Aithal, Gut 2006

Ascites

Sodium and Water Restriction

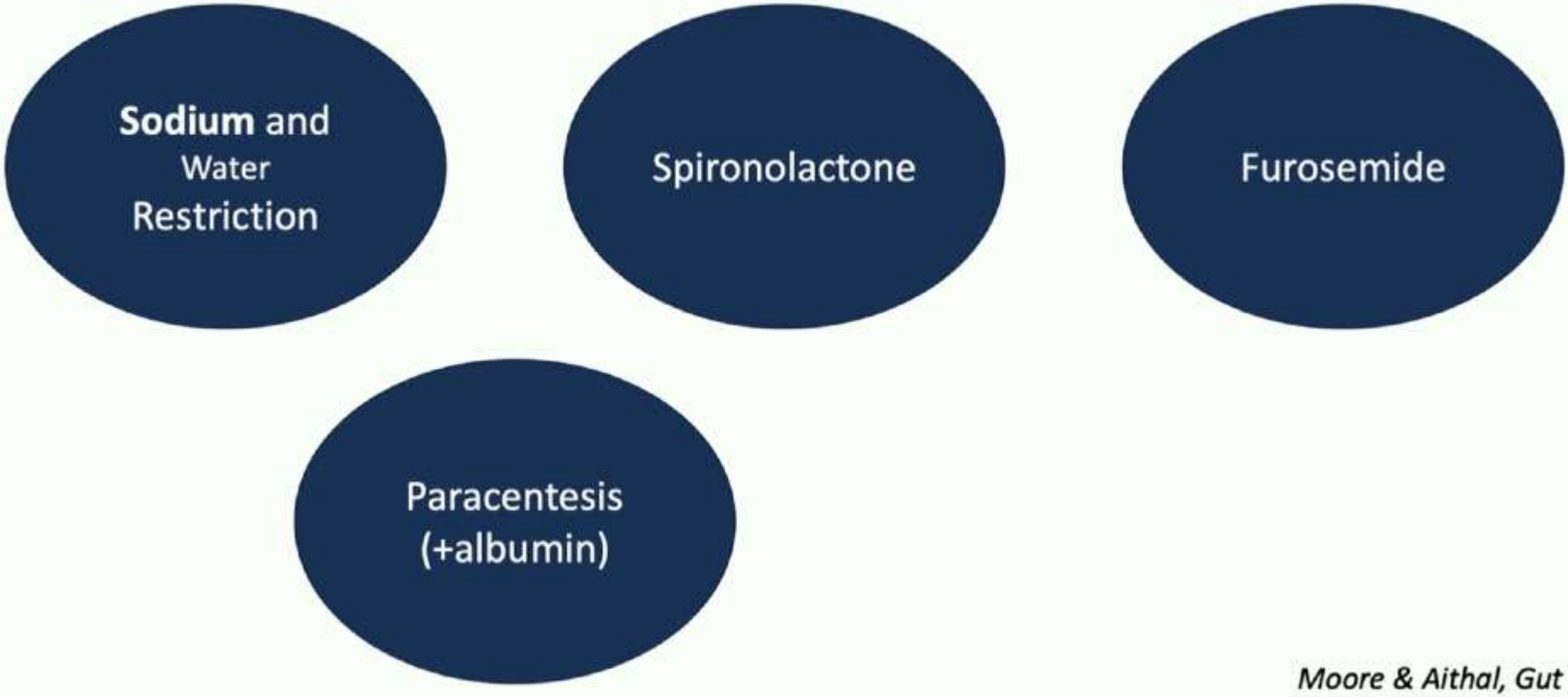
Spironolactone

Moore & Aithal, Gut 2006

Ascites

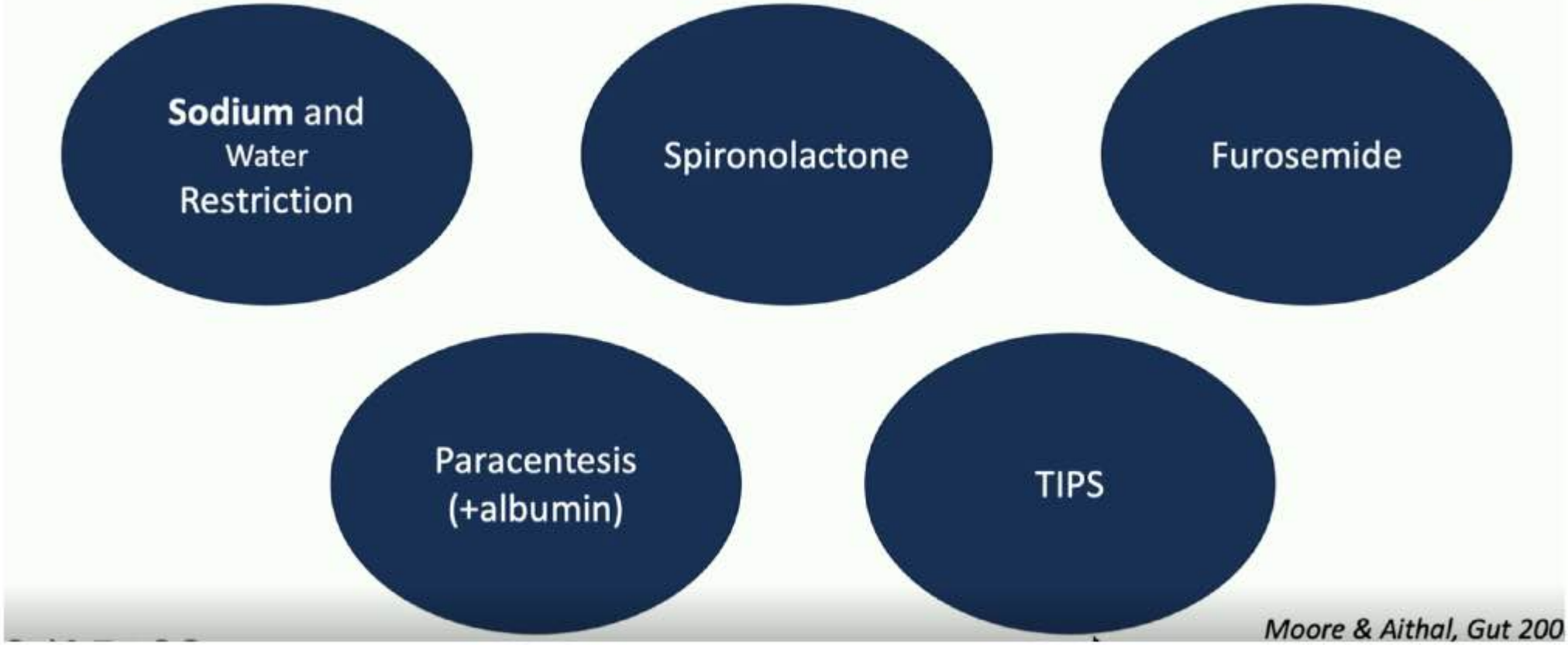
Moore & Aithal, Gut 2006

Ascites



Moore & Aithal, Gut 2006

Ascites


Sodium and Water Restriction
Spironolactone
Furosemide
Paracentesis (+albumin)
TIPS
Moore & Aithal, Gut 200

What is the first-line treatment for ascites not controlled by diet?

(A) Furosemide

(B) Spironolactone

(C) Serial paracentesis

(D) Transjugular intrahepatic portosystemic shunt

What is the first-line therapy to prevent recurrent hepatic encephalopathy?

(A) Rifaximin

(B) Zinc

(C) Lactulose

(D) Probiotics

Hepatic Encephalopathy

Reversible, fluctuating neuropsychiatric abnormalities that range from very subtle abnormalities to asterixis to coma.

NO gold standard test, but caregivers may report:

- Changes in sleep
- Lethargy
- Personality changes
- Confusion

Can be precipitated by sepsis, medications, or post-TIPS

Note: Ammonia level NOT NEEDED!

Hepatic Encephalopathy

Rudler et al, Clinical Liver Disease 2021

Hepatic Encephalopathy

Diagnose and Treat Precipitating factors

Lactulose (Prophylaxis and Treatment)

Rudler et al, Clinical Liver Disease 2021

Hepatic Encephalopathy

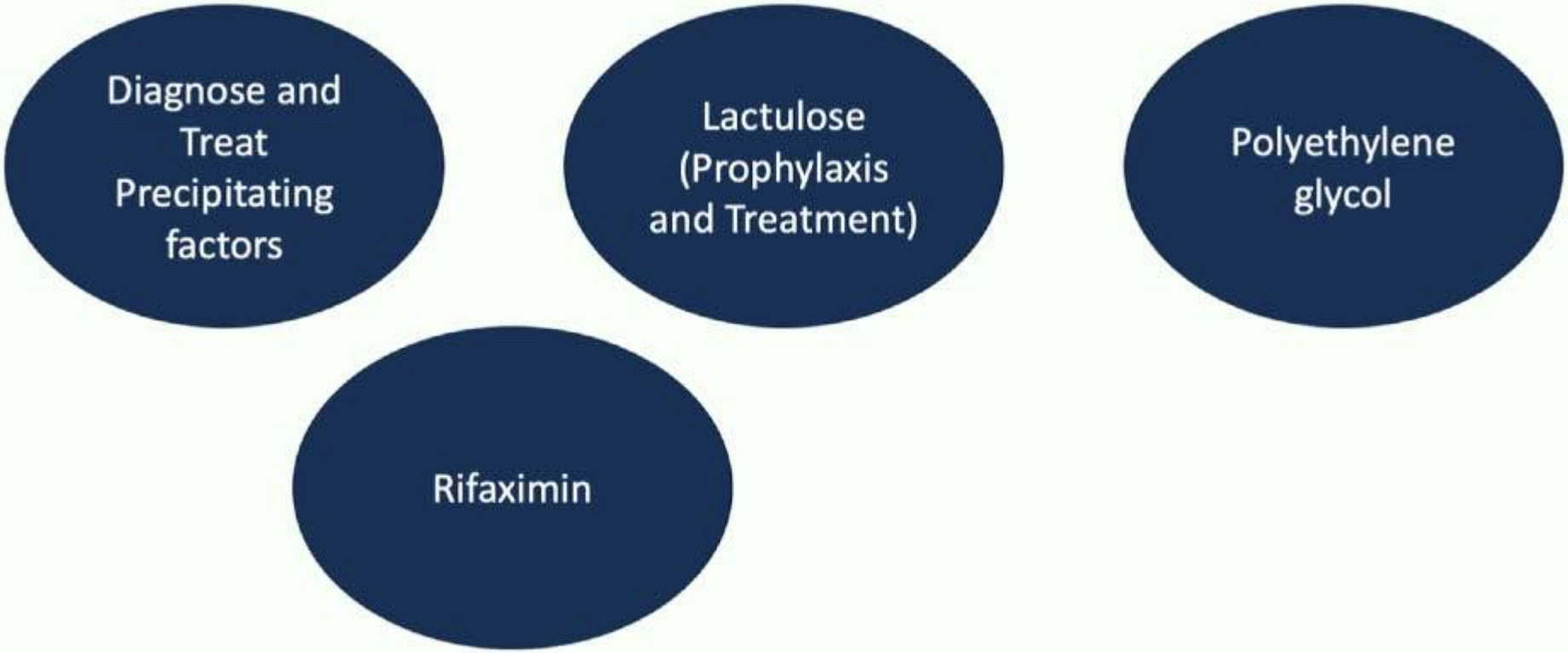
Diagnose and Treat Precipitating factors

Lactulose (Prophylaxis and Treatment)

Polyethylene glycol

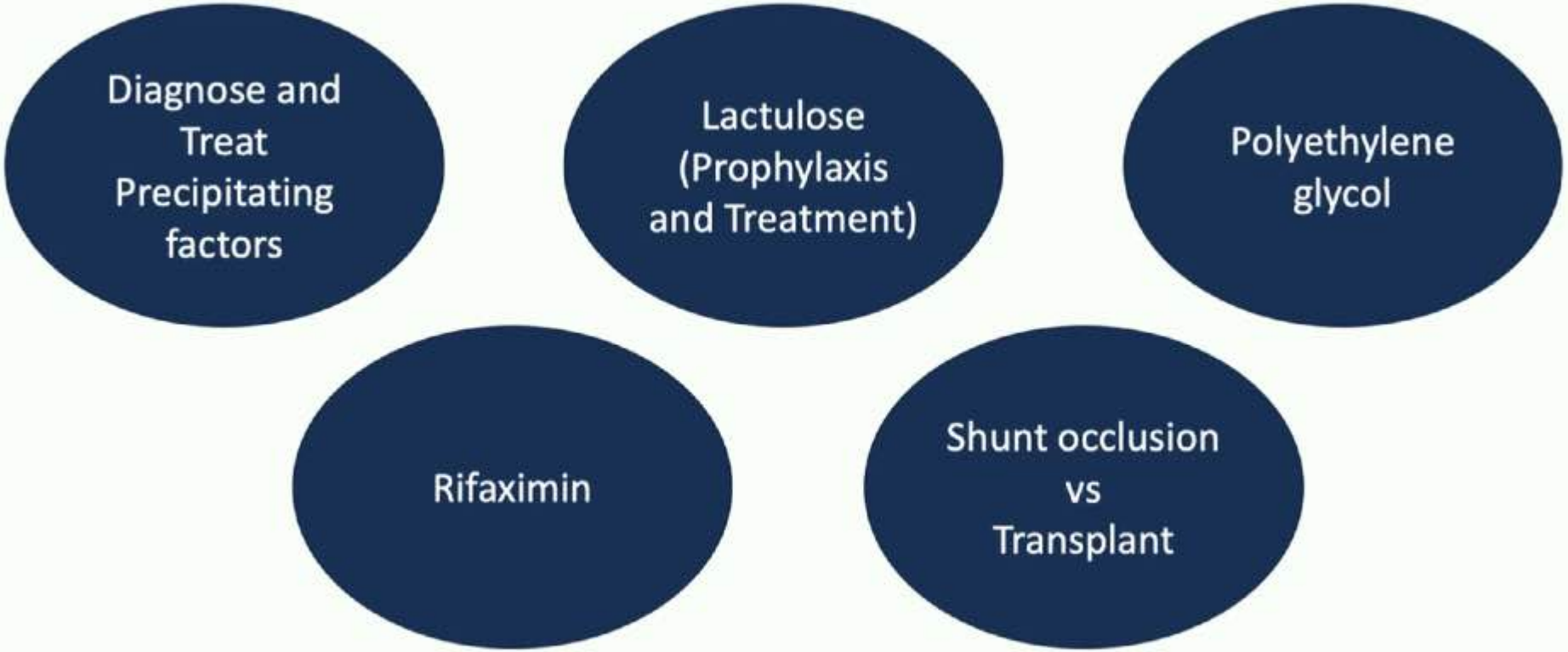
Rudler et al, Clinical Liver Disease 2021

Hepatic Encephalopathy



Rudler et al, Clinical Liver Disease 2021

Hepatic Encephalopathy



Rudler et al, Clinical Liver Disease 2021

What is the first-line therapy to prevent recurrent hepatic encephalopathy?

(A) Rifaximin

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(C) Lactulose

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Note: Rifaximin CAN BE first line if patient is lactulose intolerant OR can be used as an adjunct to lactulose

Which treatments are indicated in a variceal bleed?

(A) Transfusion to Hgb >7
(B) Colloid resuscitation
(C) Crystalloid resuscitation
(D) FFP
(E) Transfusion to platelets to > 50
(F) Ceftriaxone
(G) Octreotide/Terlipressin
(H) Nadolol

Portal Hypertension Related Bleeding

Varices: Life threatening emergency with 20% Risk of Mortality

Increased pressure through portosystemic collaterals causing varices (abnormally dilated submucosal veins)

Excess blood flow can result in increased intravariceal pressure and rupture

Also: gastropathy, enteropathy, colopathy

Portal Hypertension Related Bleeding

Resuscitation
Crystalloids
Hgb 7-8

Vashishtha & Sarin,
Clinics in Liver Disease, 2024

Portal Hypertension Related Bleeding

Resuscitation
Crystalloids
Hgb 7-8

Antibiotic prophylaxis

Vashishtha & Sarin,
Clinics in Liver Disease, 2024

Portal Hypertension Related Bleeding

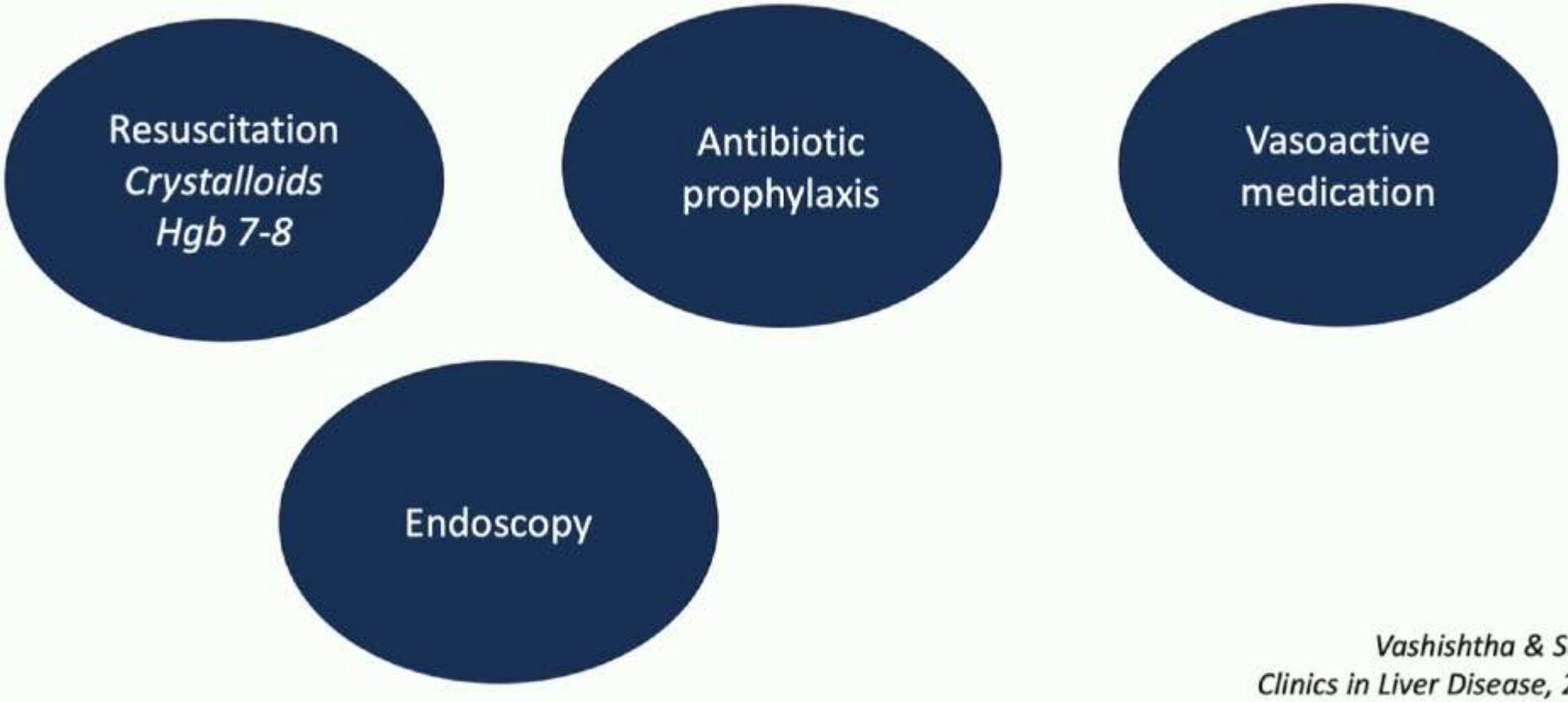
Resuscitation
Crystalloids
Hgb 7-8

Antibiotic prophylaxis

Vasoactive medication

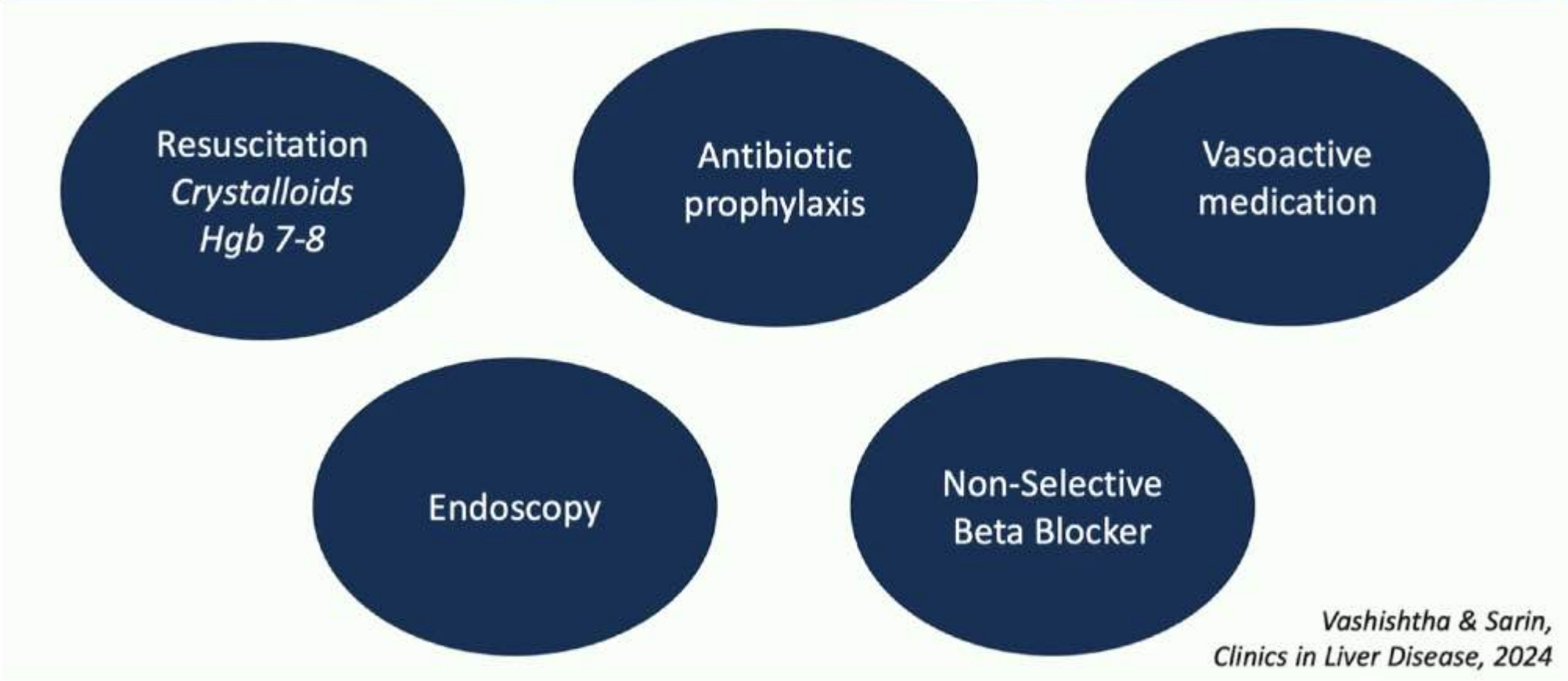
Vashishtha & Sarin,
Clinics in Liver Disease, 2024

Portal Hypertension Related Bleeding



Vashishtha & Sarin,
Clinics in Liver Disease, 2024

Portal Hypertension Related Bleeding



Vashishtha & Sarin,
Clinics in Liver Disease, 2024

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What is the best first-line therapy for hepatorenal syndrome-acute kidney injury?

(A) Renal replacement therapy/dialysis
(B) Albumin
(C) Terlipressin
(D) Midodrine
(E) Octreotide

Hepatorenal Syndrome-Acute Kidney Injury

Abrupt impairment of kidney function in **decompensated** cirrhosis due to hemodynamic changes.

Bacterial infections are the most common risk factor due to the systemic inflammatory response.

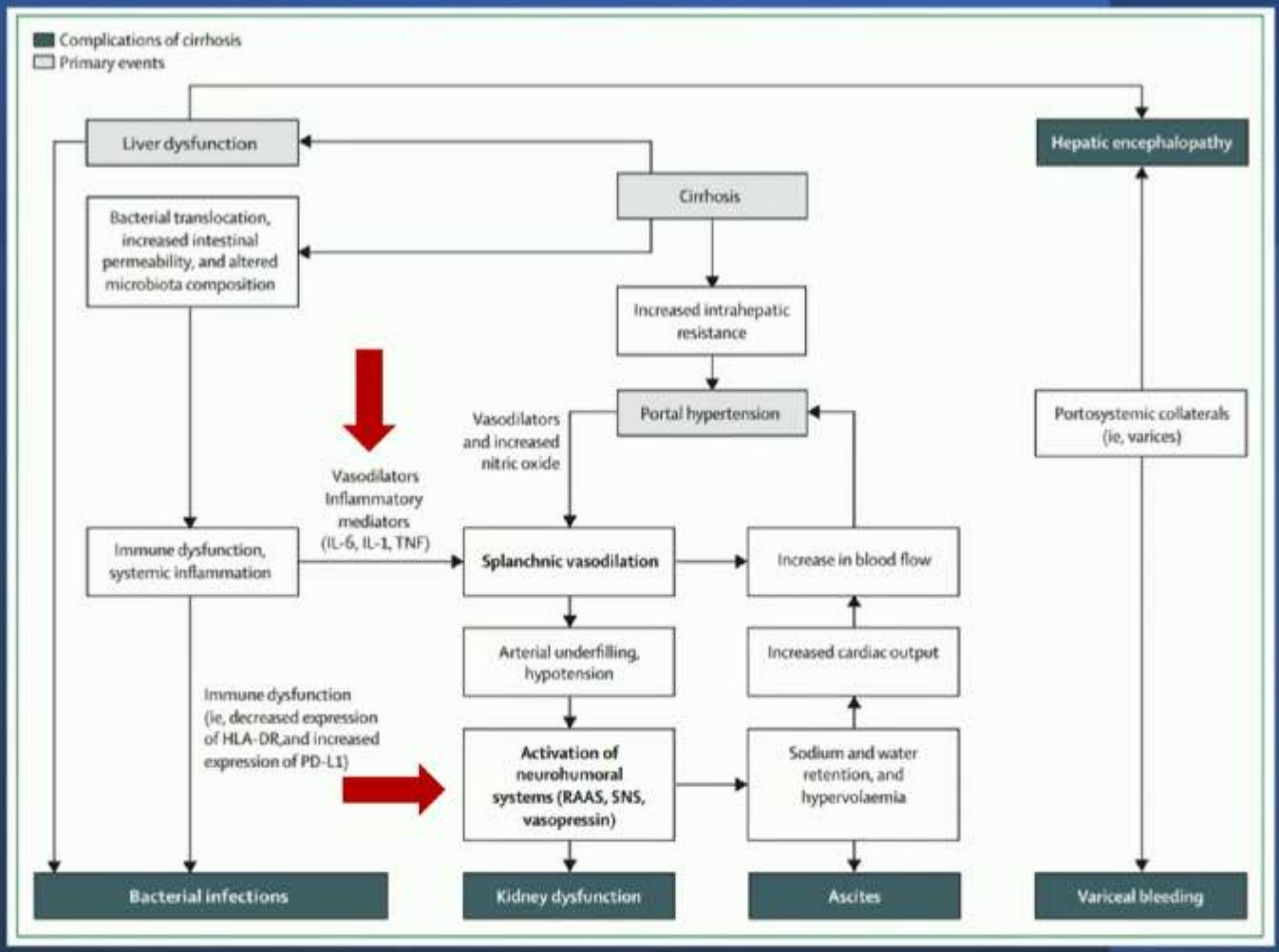
Portal hypertension and splanchnic vasodilation lead to RAAS/SNS activation → severe vasoconstriction of the kidneys

Pose et al, Gastroenterology, 2024

Table 2. HRS-AKI Diagnostic Criteria

Cirrhosis with ascites
Diagnosis of AKI according to ICA-AKI criteria: acute increase in sCr ≥0.3 mg/dL (≥26.5 μmol/L) within 48 h; or, a percentage increase in sCr ≥50% from baseline that is known, or presumed, to have occurred within the prior 7 d[a]
No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin (1 g/kg of body weight, with a maximum of 100 g/d)
Absence of shock
No current or recent use of nephrotoxic drugs (NSAIDs, aminoglycosides, iodinated contrast media, etc)
No macroscopic signs of structural kidney injury, defined as: Absence of proteinuria (>500 mg/d) Absence of microhaematuria (>50 RBCs per high-power field) Normal findings on renal ultrasonography

NSAIDs, nonsteroidal anti-inflammatory drugs; RBCs, red blood cells.
[a]The definition of classical type 1 HRS requires an increase of sCr >100% from baseline within 2 weeks to a final value > 2.5 mg/dL.



Ginès et al, Lancet 2021

Hepatorenal Syndrome-Acute Kidney Injury

Pose et al
Gastroenterology, 2024

Hepatorenal Syndrome-Acute Kidney Injury

Rule Out Hypovolemic Acute Kidney Injury

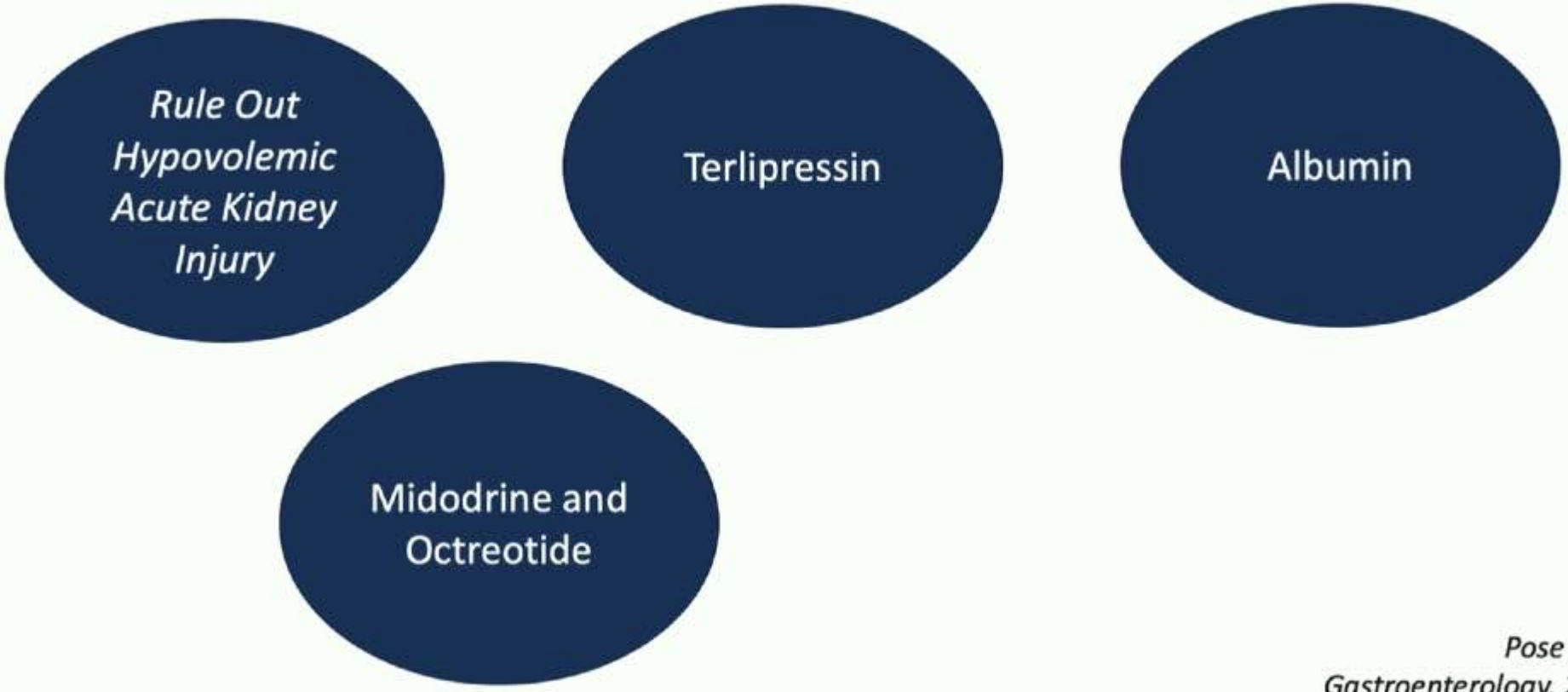
Terlipressin

Pose et al
Gastroenterology, 2024

Hepatorenal Syndrome-Acute Kidney Injury

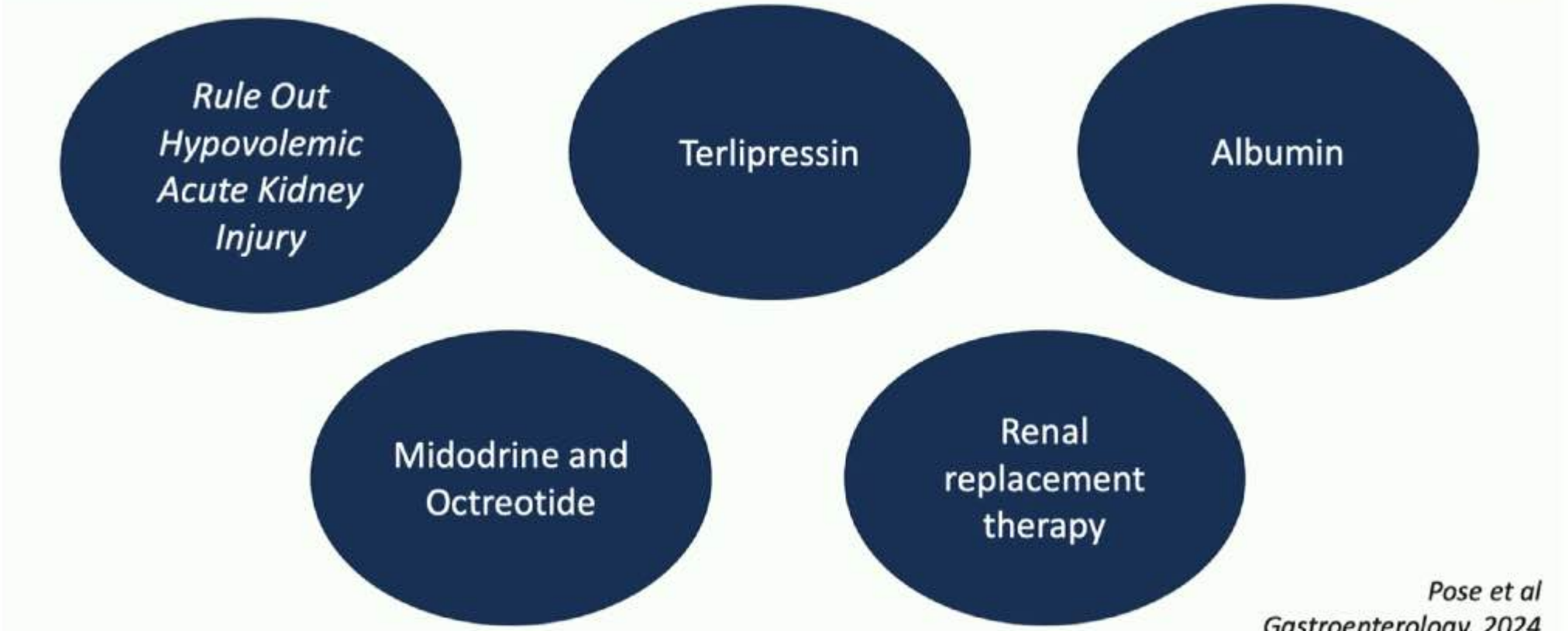
Pose et al
Gastroenterology, 2024

Hepatorenal Syndrome-Acute Kidney Injury



Pose et al
Gastroenterology, 2024

Hepatorenal Syndrome-Acute Kidney Injury



Pose et al
Gastroenterology, 2024

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(E) Octreotide

A patient with ascites presents with decompensated cirrhosis. Select all indications for diagnostic paracentesis.

(A) Acute kidney injury
(B) Hepatic encephalopathy
(C) Fever
(D) Abdominal pain

Spontaneous Bacterial Peritonitis

Infection of ascites in the absence of an apparent intra-abdominal focus with an ascitic neutrophil count >250 cells/microliter or positive ascitic culture

Typically a monomicrobial infection with common agents being *Escherichia coli* and gram positive cocci, with increasing multidrug resistant organisms

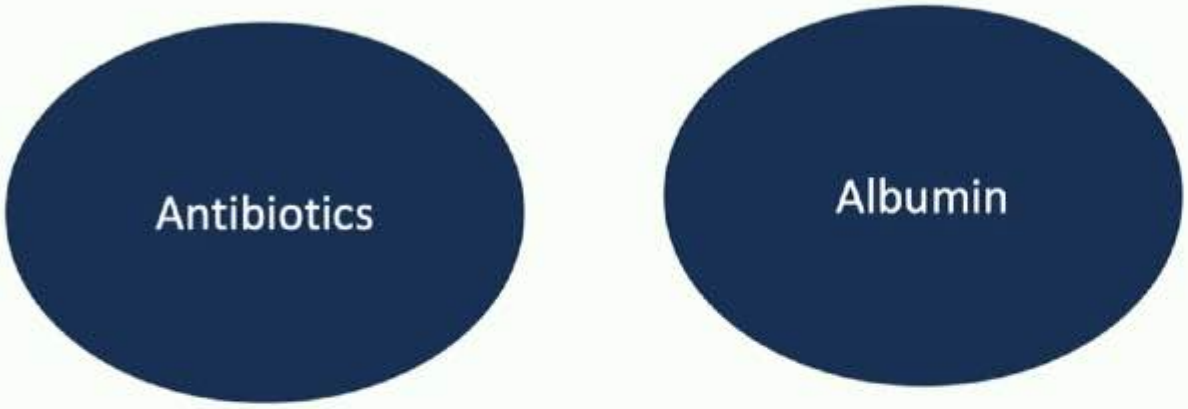
Patients can present in a variety of ways: encephalopathy, kidney injury, fever, abdominal pain

→ Some patients have *no abdominal symptoms*

Spontaneous Bacterial Peritonitis

Mattos et al
Annals of Hepatology, 2020

Spontaneous Bacterial Peritonitis



Mattos et al
Annals of Hepatology, 2020

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Mattos et al
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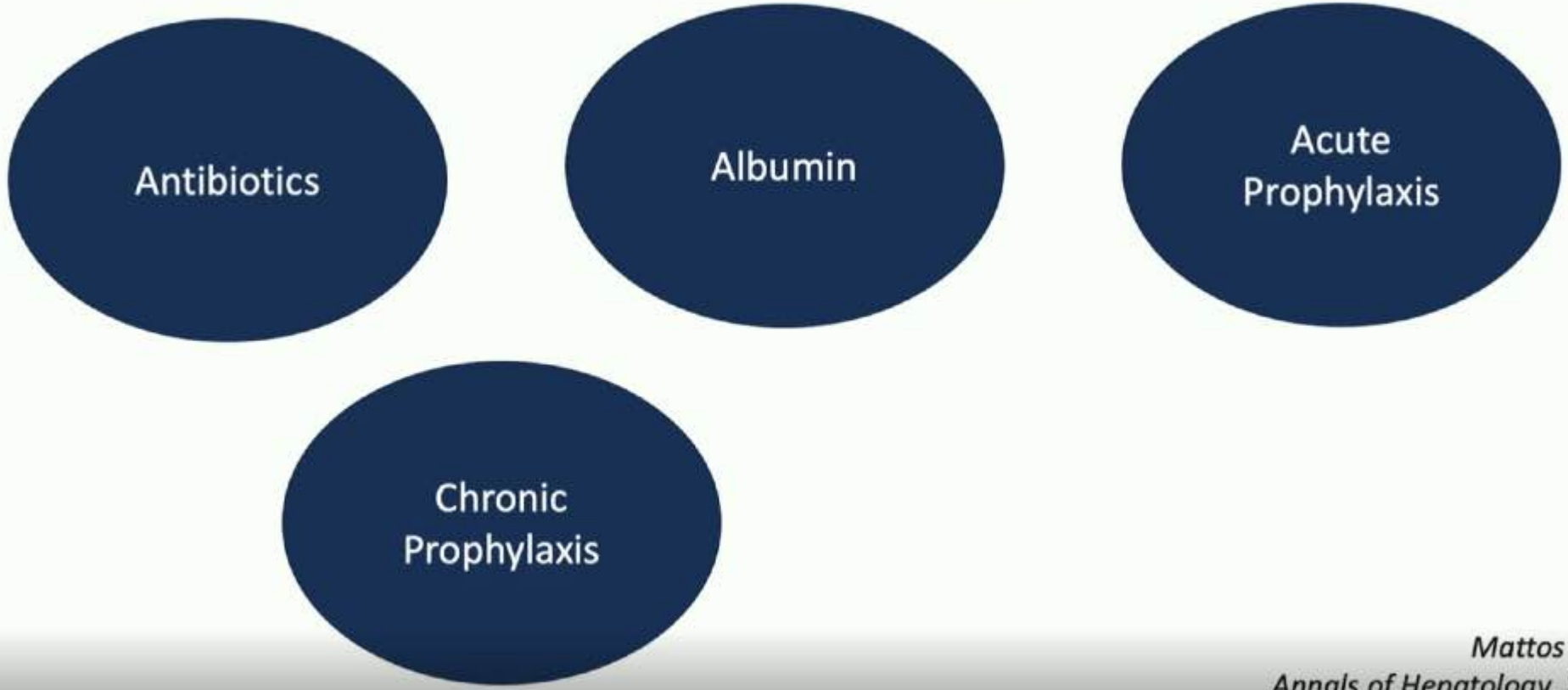

Mattos et al
Annals of Hepatology, 2020

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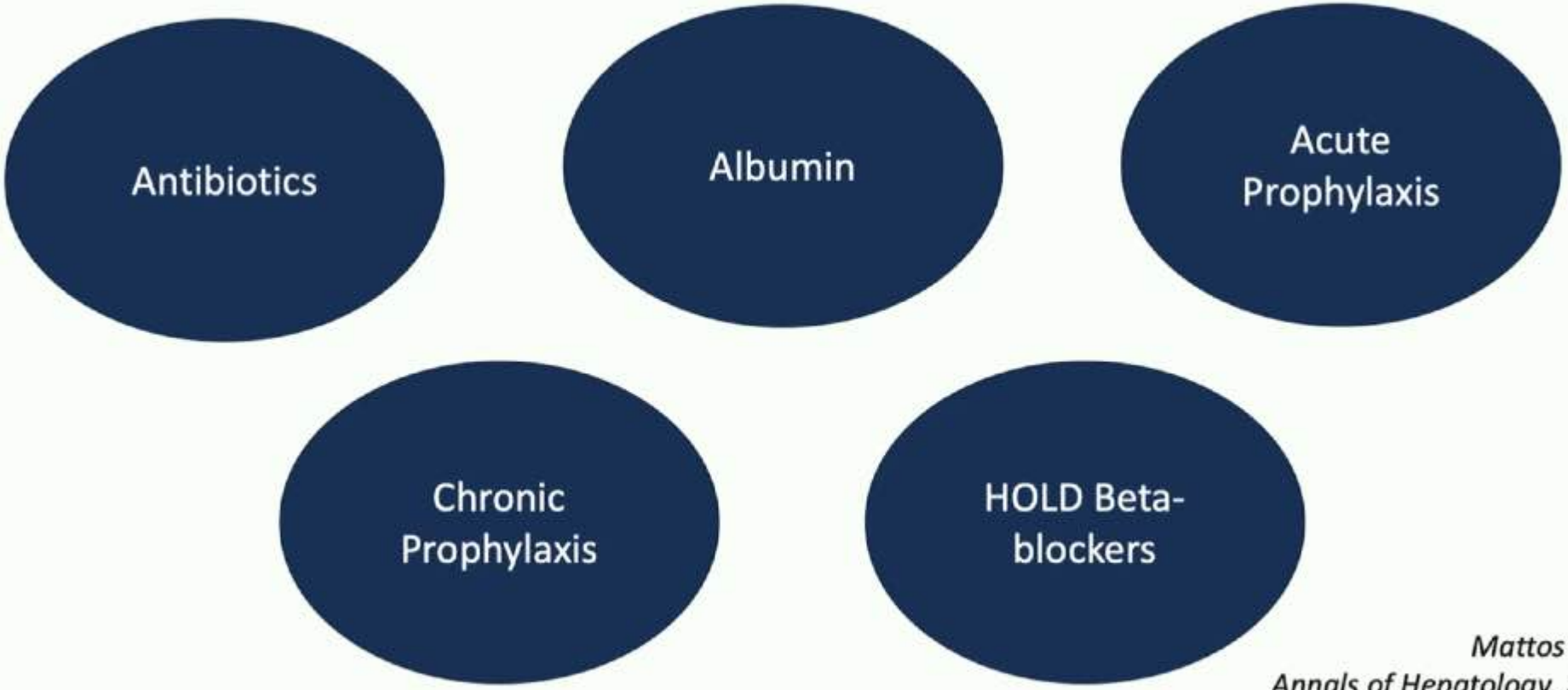

Mattos et al
Annals of Hepatology, 2020

Other Bacterial Infections

>25% at or during hospital admission w/**2.6x** risk of sepsis

- Respiratory tract infections
- SSTI
- UTI

Table 1
Basic diagnostic workup to assess for bacterial infections in patients with cirrhosis.

(a) General blood tests: WBC, liver and renal tests, serum electrolytes
(b) Diagnostic paracentesis (if ascites is present)
(c) Cultures: blood, urine, ascites, sputum (if suspicion of respiratory tract infection)
(d) Imaging: chest X-ray and abdominal ultrasound
(e) Consider biomarkers for acute inflammatory response (CRP or PCT)

WBC – white blood cell count; CRP – C reactive protein; PCT – procalcitonin.

Mattos et al
Annals of Hepatology, 2020

A patient with ascites presents with decompensated cirrhosis. Select all indications for diagnostic paracentesis.

(A) Acute kidney injury
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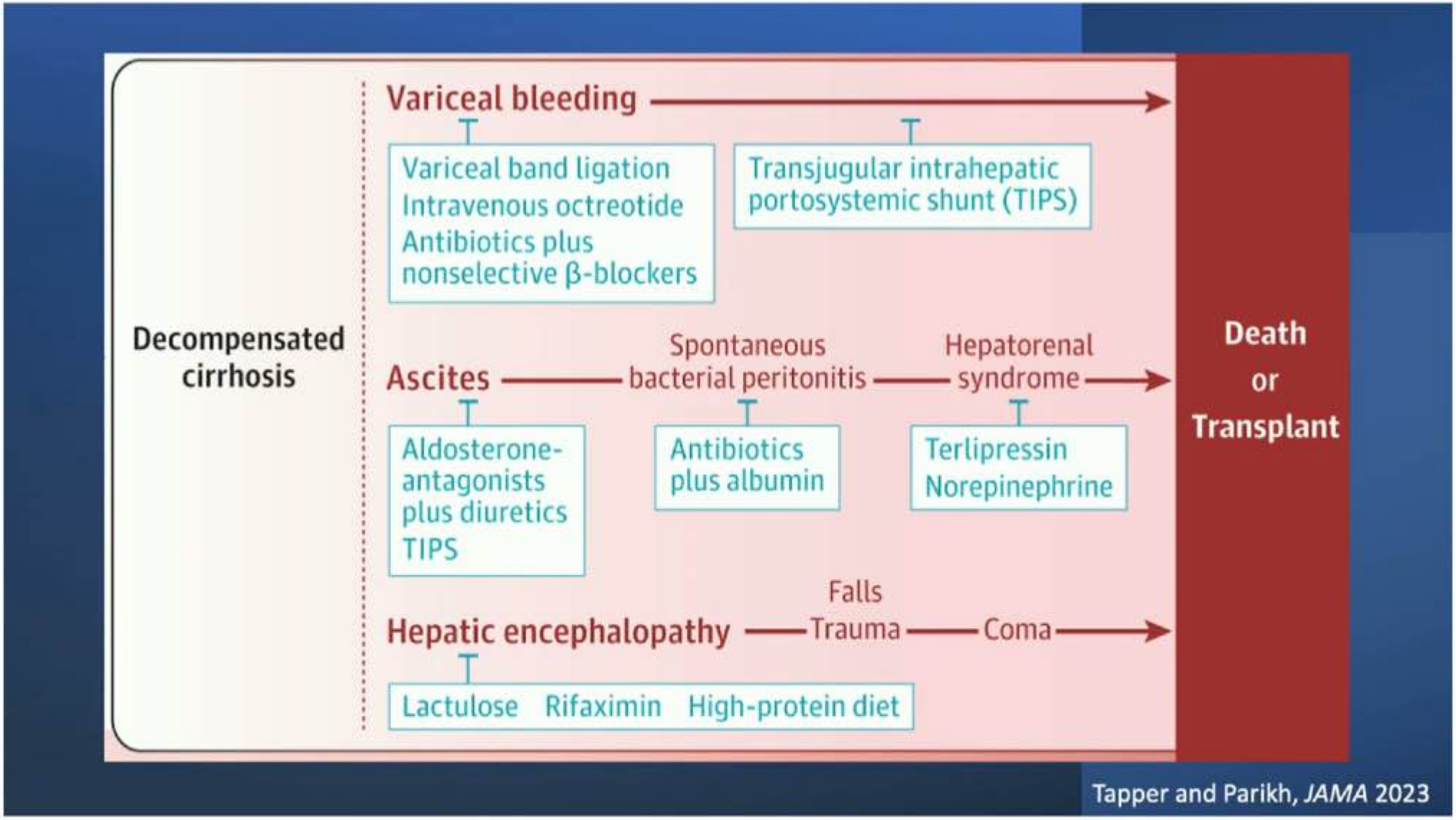

Decompensated cirrhosis
Variceal bleeding
Variceal band ligation
Intravenous octreotide
Antibiotics plus nonselective β-blockers
Transjugular intrahepatic portosystemic shunt (TIPS)
Ascites
Spontaneous bacterial peritonitis
Hepatorenal syndrome
Aldosterone-antagonists plus diuretics
TIPS
Antibiotics plus albumin
Terlipressin
Norepinephrine
Hepatic encephalopathy
Falls
Trauma
Coma
Lactulose
Rifaximin
High-protein diet
Death or Transplant
Tapper and Parikh, JAMA 2023

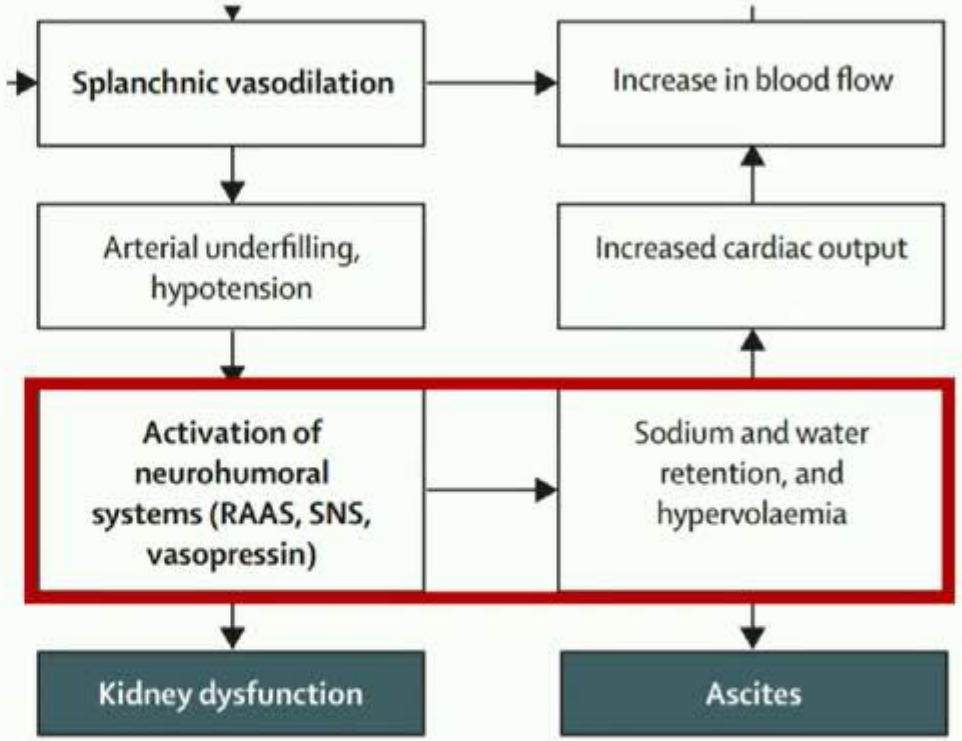
Hyponatremia

Multiple categories:

- Na < 135
- Na < 130
- **Na <125**
- **Na <120**

Multiple causes:

- RAAS/SNS/Vasopressin
- Hypervolemia
- Hypovolemia



Hyponatremia

STOP beta-blockers, diuretics

Ryu et al
Clinical and Molecular Hepatology, 2024

Hyponatremia

STOP beta-blockers, diuretics

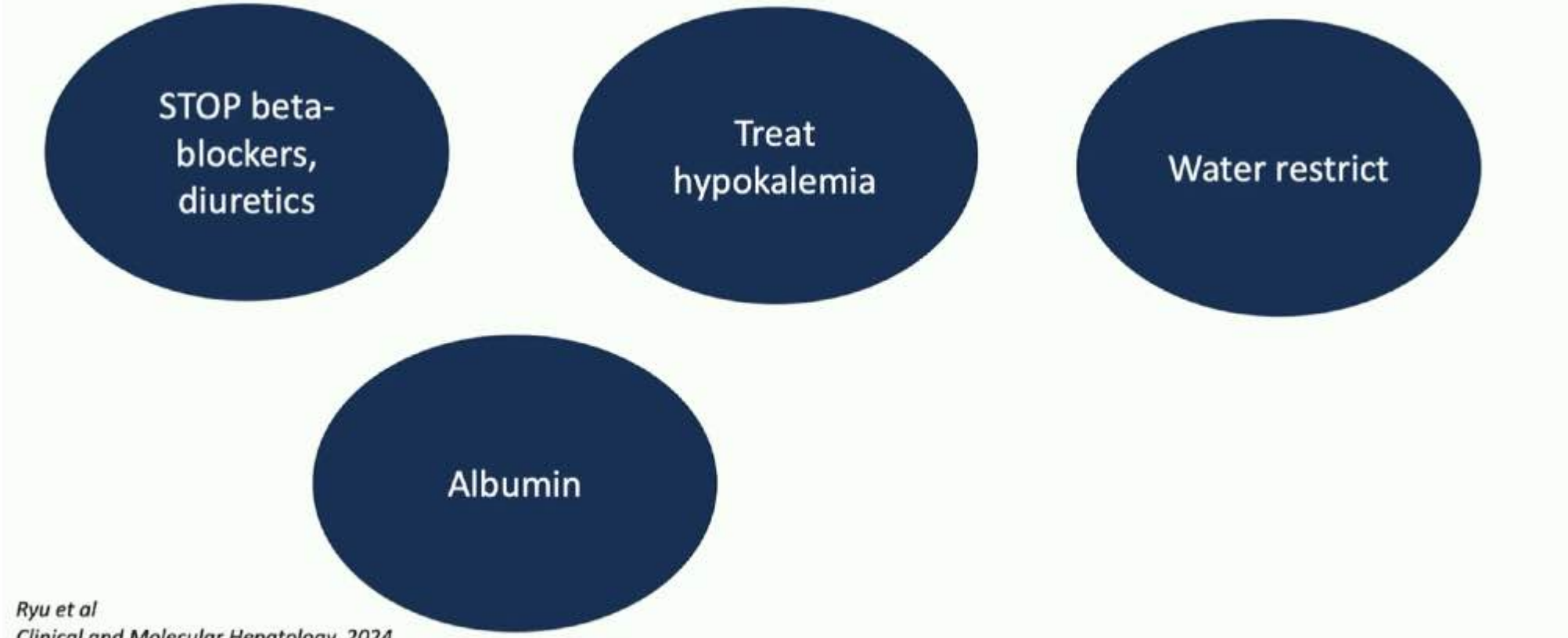
Treat hypokalemia

Ryu et al
Clinical and Molecular Hepatology, 2024

Hyponatremia

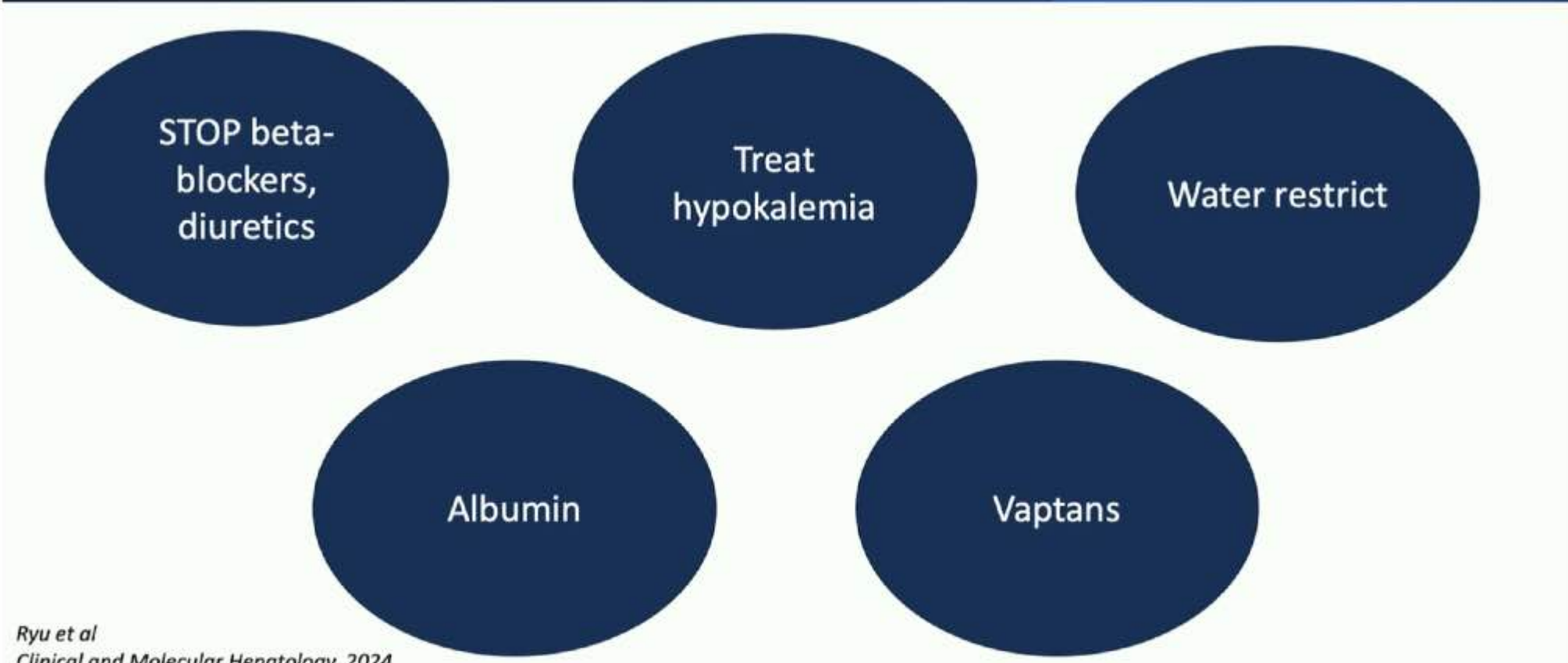
Ryu et al
Clinical and Molecular Hepatology, 2024

Hyponatremia



Ryu et al
Clinical and Molecular Hepatology, 2024

Hyponatremia



Ryu et al
Clinical and Molecular Hepatology, 2024

Key Points

- Cirrhosis is increasing in prevalence and is primarily due to alcohol use disorder right now, but over time may be primarily due to factors such as obesity and type 2 diabetes
- There variety of complications of cirrhosis are linked to portal hypertension, including ascites, hepatic encephalopathy, kidney injury, and bacterial infections
- Treatment of complications is often nuanced and may require expert consultation, recognizing decompensation is a harbinger of mortality

Questions?