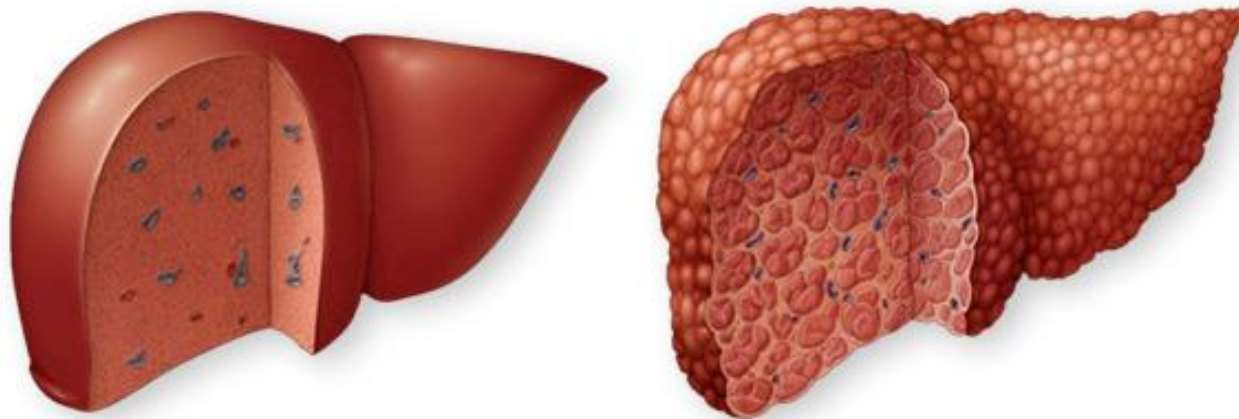


# Cirrhosis Monitoring and Review of the New Guidelines on Frailty and Malnutrition

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**April 2022**

# Disclosure



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**I do not have any relevant financial relationships with  
any commercial interests**

# Learning Objectives

- 1. Describe the long-term complications associated with cirrhosis**
- 2. Review the new AASLD guidelines on malnutrition, frailty, and sarcopenia**
- 3. Discuss how to monitor and address N-stage progression to transplant criteria**

# What is Cirrhosis?

## AASLD-IDSA HCV Guidance Panel Hepatology 2/2020

- Liver biopsy is not required if the the following criteria are met:
  - FIB-4 score  $>3.25$
  - Transient elastography stiffness  $>12.5\text{kPa}^*$
  - Non-invasive serological testing (Fibrosure, Fibrotest, etc.)  $\geq$  F4 cutoff
  - Clinical evidence of cirrhosis (nodular liver, platelet count  $<150,000$ , etc)
  - Prior liver biopsy showing cirrhosis

## Strain Imaging

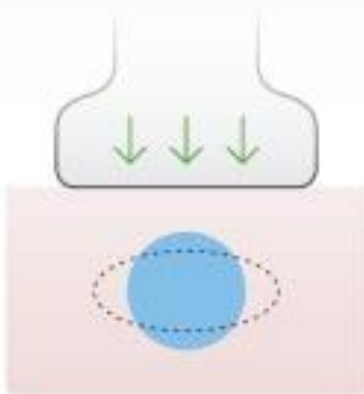
### Strain Elastography (SE)

ElaXto™  
Real-time tissue elastography™  
Elastography

ElaScan™  
eSieTouch™  
Elasticity Imaging

Esaote  
Hitachi  
Aloka

GE, Philips,  
Toshiba,  
Ultrasonix,  
Mindray,  
Samsung,  
Siemens



### Acoustic radiation force impulse (ARFI) Strain Imaging

Virtual Touch™  
Imaging (VTI/ARFI)

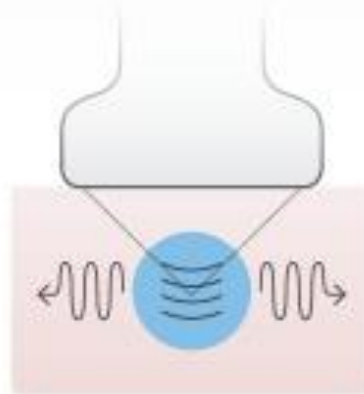
Siemens



### Point Shear Wave Elastography (pSWE/ARFI quantification)

Virtual Touch™  
Quantification (VTQ/ARFI)  
ElastPQ™

Siemens,  
Philips

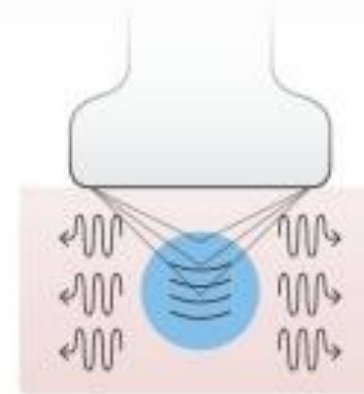


### 2D Shear Wave Elastography (SWE)

Shear Wave Elastography

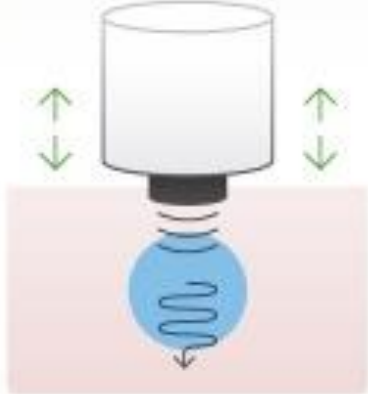
Virtual Touch™  
Quantification (VTIQ/ARFI)

Super  
Sonic  
Imagine,  
Philips,  
Toshiba,  
GE,  
Siemens



### 1D Transient Elastography (TE)

FibroScan™  
Echosens



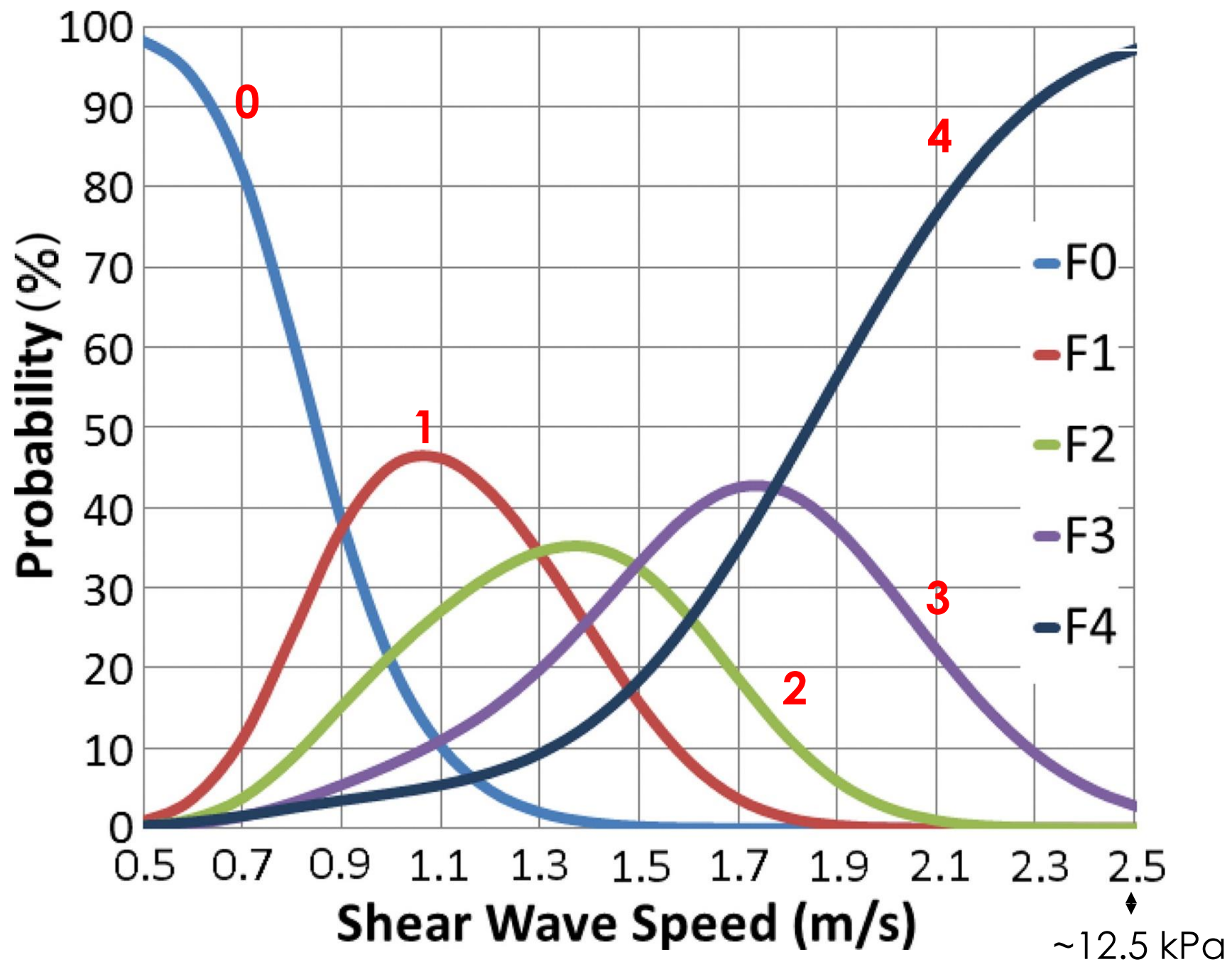


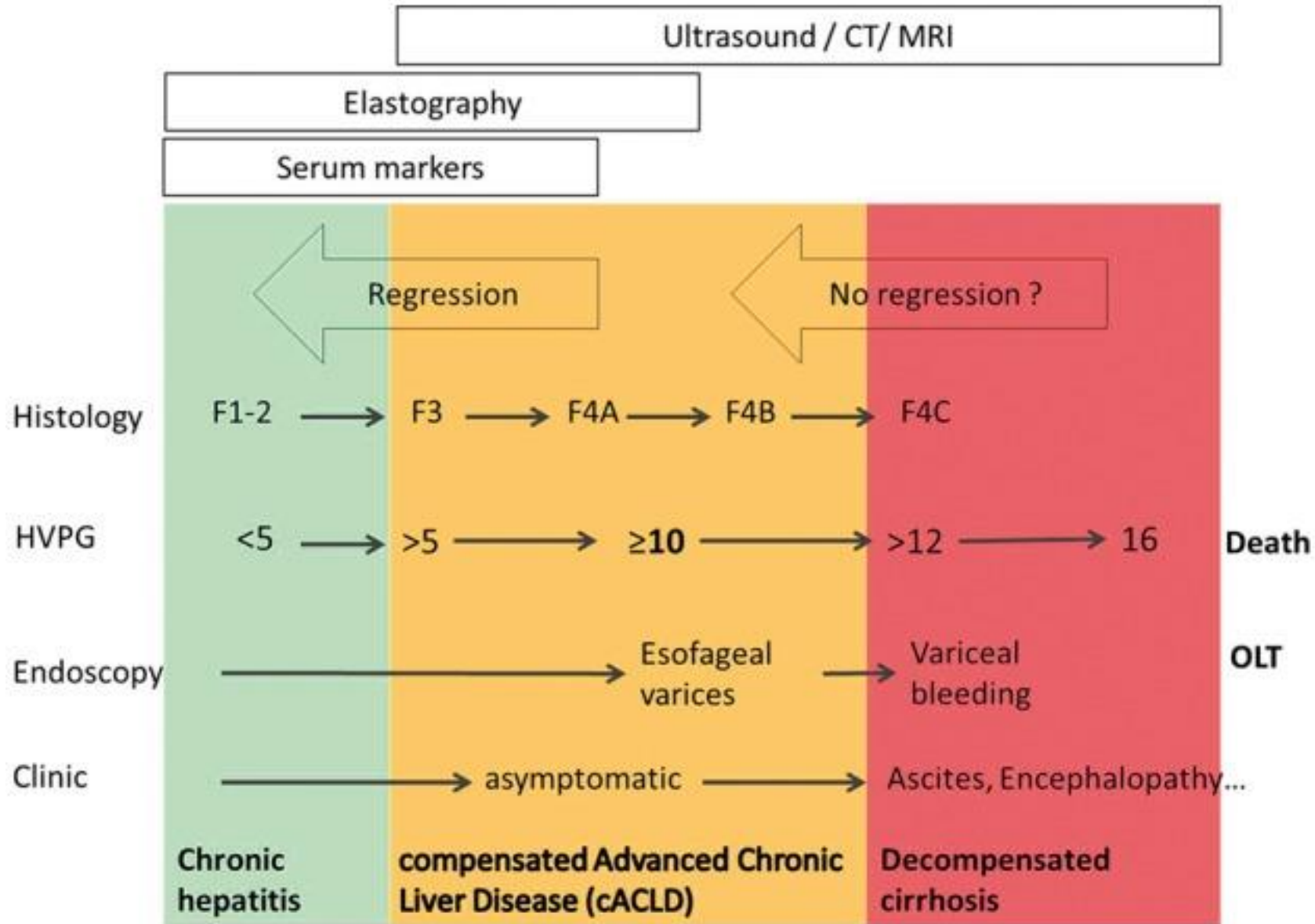
Figure 7: Graph of shear wave stiffness measurements for METAVIR stages based on the meta-analysis (38) in which median and IQR interquartile ratio data were used.

# Prognostic Types of Cirrhosis

- ▶ Compensated: Child-Turcotte-Pugh (CTP) A class (score 5-6)
  - ▶ 12 year average survival
- ▶ Decompensated: History of ascites, variceal hemorrhage, and/or encephalopathy usually CTP-B (7-9) or CTP-C (10-15)
  - ▶ 1.8 year average survival



# Advanced Chronic Liver Disease





# What Is A Liver Test

**Liver Chemistries:** AST, ALT, Alkaline Phosphatase, and Bilirubin  
**Measure inflammation**

**Liver Function Tests:** Albumin, bilirubin, and INR (Prothrombin)  
**Measure hepatocellular Function**

**Platelets\*:** As liver damage increases, the reduced production of thrombopoietin leads to decreased platelet production

**All The Above Can Be Abnormal In Other Non-Hepatic Diseases**  
**ALT is the most specific marker of hepatitis injury**

<http://gi.org/guideline/evaluation-of-abnormal-liver-chemistries/>

# Long-term Cirrhosis Complications

- ▶ Hepatocellular Carcinoma
- ▶ Portal Hypertension
- ▶ Ascites and Associated Conditions
  - ▶ Spontaneous Bacterial Peritonitis (SBP)
  - ▶ Acute Kidney Injury-Hepatorenal Syndrome (HRS)
  - ▶ Hyponatremia
- ▶ Encephalopathy
- ▶ Malnutrition, Frailty, and Sarcopenia

# Main risk factors for primary liver cancer worldwide\*



- ▶ ~90% of HCCs are of known underlying etiology<sup>1</sup>
- ▶ Most frequently HCV, HBV, alcohol and aflatoxin exposure

	Alcohol (%)	HBV (%)	HCV (%)	Others (%)
<b>Europe</b>				
Western	32	13	44	10
Central	46	15	29	10
Eastern	53	15	24	8
<b>North America</b>	<b>37</b>	<b>9</b>	<b>31</b>	<b>23</b>
<b>Andean Latin America</b>	23	45	12	20
<b>Asia</b>				
East Asia	32	41	9	18
Asia-Pacific	18	22	55	6
South-East Asia	31	26	22	21
<b>Africa</b>				
North Africa, Middle East	13	27	44	16
Southern (sub-Saharan)	40	29	20	11
Western (sub-Saharan)	29	45	11	15

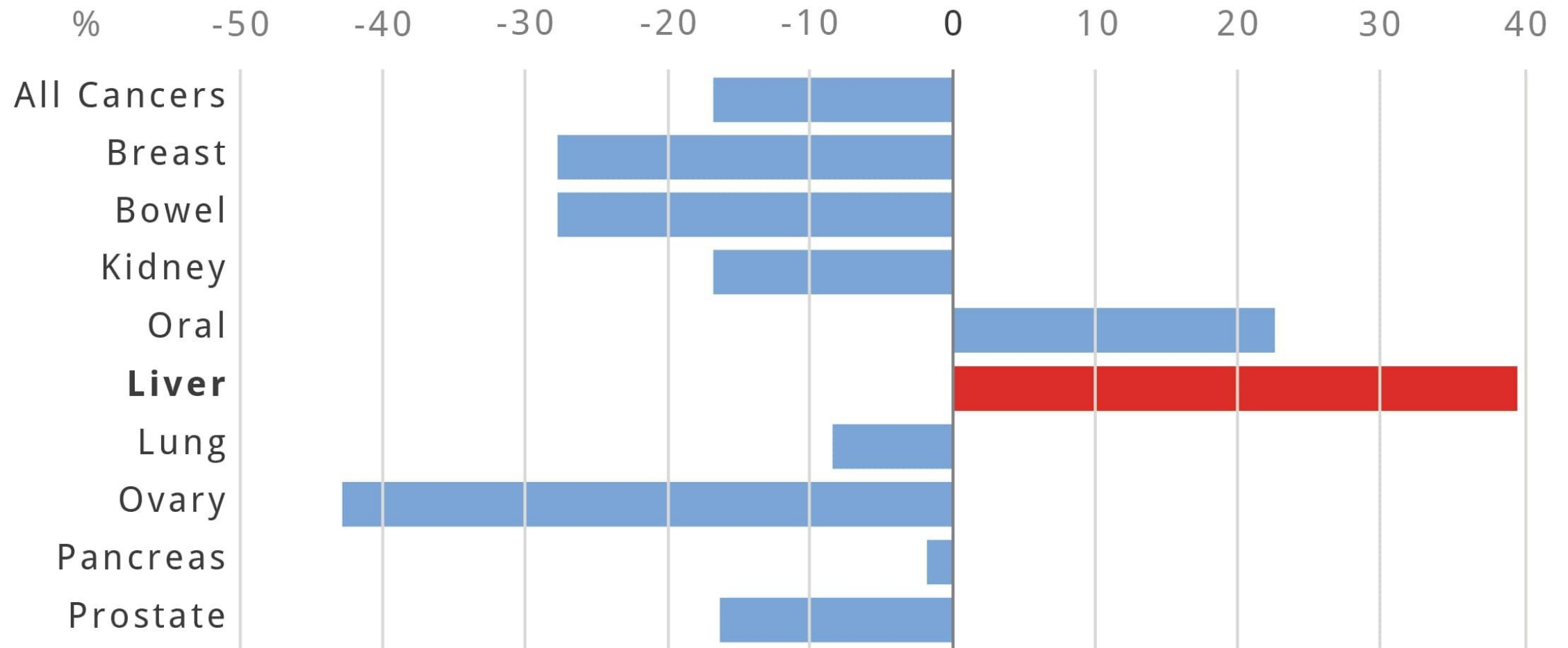
\*Contribution of hepatitis B, C, alcohol and other causes on absolute liver cancer deaths, both sexes, globally and by region 2015. Data refer to all primary liver cancers (HCC, intrahepatic CCA and liver cancer of mixed differentiation)

1. Akinyemiju T, et al. JAMA Oncol 2017;3:1683–91;

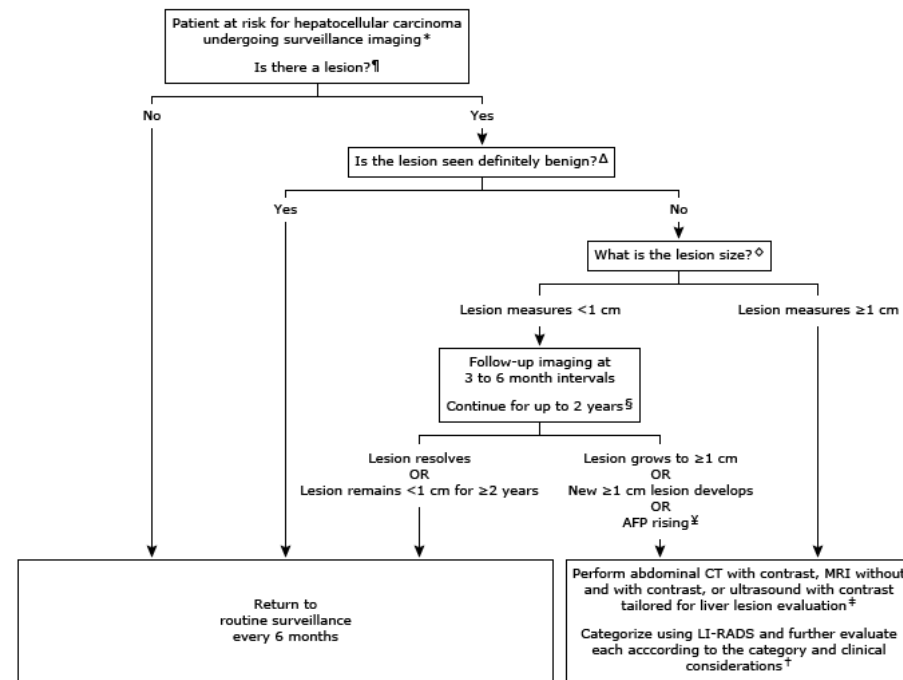
EASL CPG HCC. J Hepatol 2018; doi: 10.1016/j.jhep.2018.03.019

# PROJECTED CANCER MORTALITY RATES

2010 - 2030



## Surveillance imaging in adults at risk for hepatocellular carcinoma



AFP: alpha-fetoprotein; CT: computed tomography; MRI: magnetic resonance imaging; LI-RADS: Liver Imaging Reporting and Data System.

\* Abdominal ultrasound is recommended in most patients. However, surveillance modalities (eg, addition of serum alpha fetal protein, abdominal CT, or MRI with intravenous contrast rather than ultrasound) are sometimes individualized as described elsewhere in UpToDate.

¶ If there are multiple lesions, this algorithm can be applied to each lesion. However, management choice is driven by the lesion that is the most suspicious (eg, largest and not definitely benign, growing).

Δ Examples of definitely benign lesions include simple cysts or those previously characterized on contrast-enhanced liver imaging or biopsy as definitely benign (eg, hemangioma).

◇ Size is defined as the maximum cross-section diameter measured on the image where the lesion is most clearly seen.

§ Same imaging modality should be used for initial follow-up, but subsequent imaging may involve a change in modality. While the two-year follow-up represents our practice, stability over that time does not confirm that a lesion is benign. For these patients, we resume routine surveillance imaging every six months.

¥ Practice varies on whether serum AFP is measured in this setting.

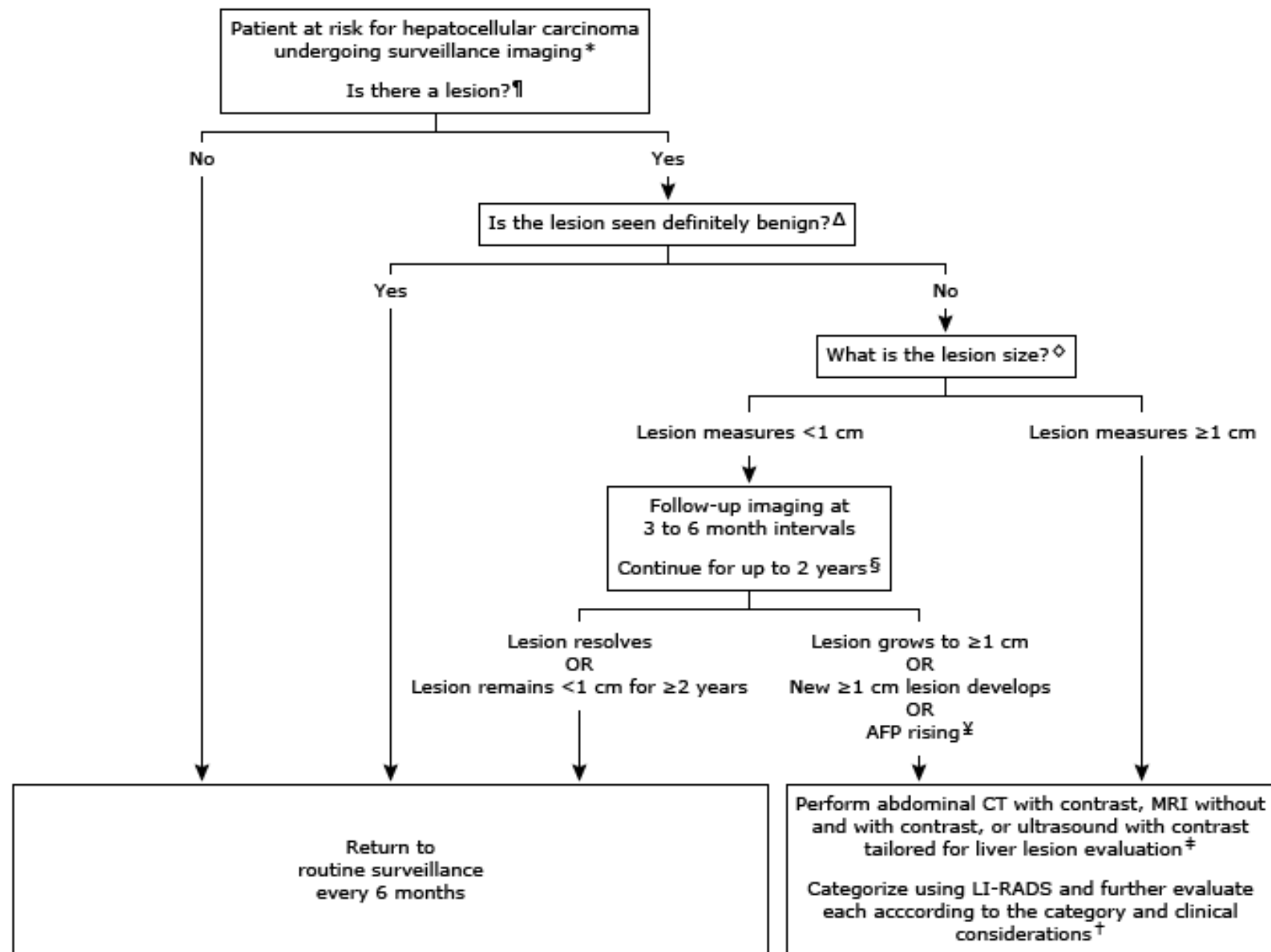
‡ Imaging technology and performance should adhere to standards required for liver lesion characterization which are more stringent than those for routine abdominal imaging and requires multiphase post-contrast imaging<sup>1</sup>. Modality choice depends on available scanner technology, imaging expertise, and patient contraindications. Contrast-enhanced CT and MRI demonstrate comparable accuracy. Contrast-enhanced ultrasound is more limited in availability and its diagnostic performance is not as well characterized.

† Liver Imaging Reporting and Data System (LI-RADS) system to categorize, further evaluate, and diagnose liver lesions is described elsewhere in UpToDate. LI-RADS evaluation can involve biopsy or follow-up imaging with contrast-enhanced CT, MRI, or ultrasound.

### Reference

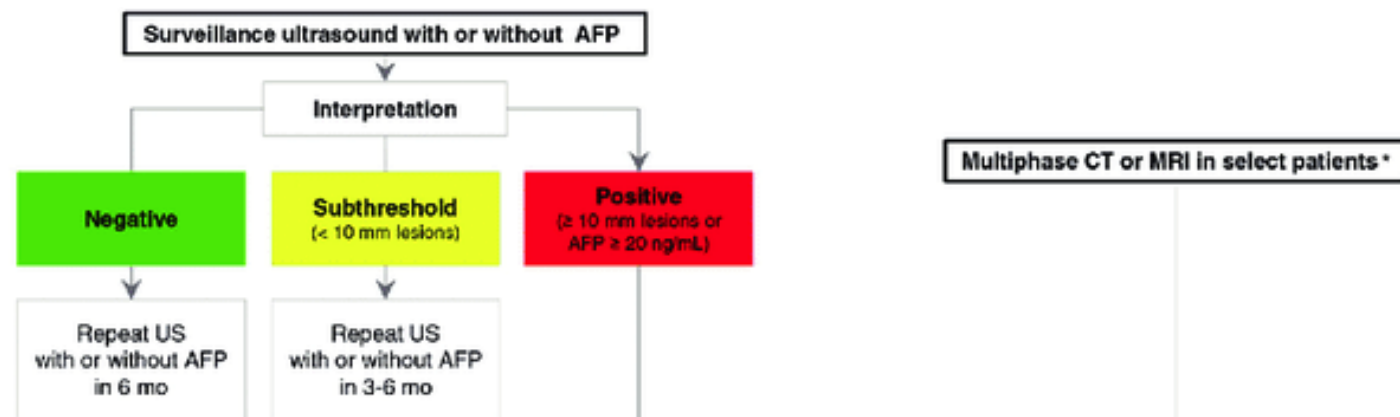
1. American College of Radiology. Liver Reporting & Data System v2017. <https://www.acr.org/Clinical-Resources/Reporting-and-Data-Systems/LI-RADS> (Accessed on December 20, 2017)

## Surveillance imaging in adults at risk for hepatocellular carcinoma

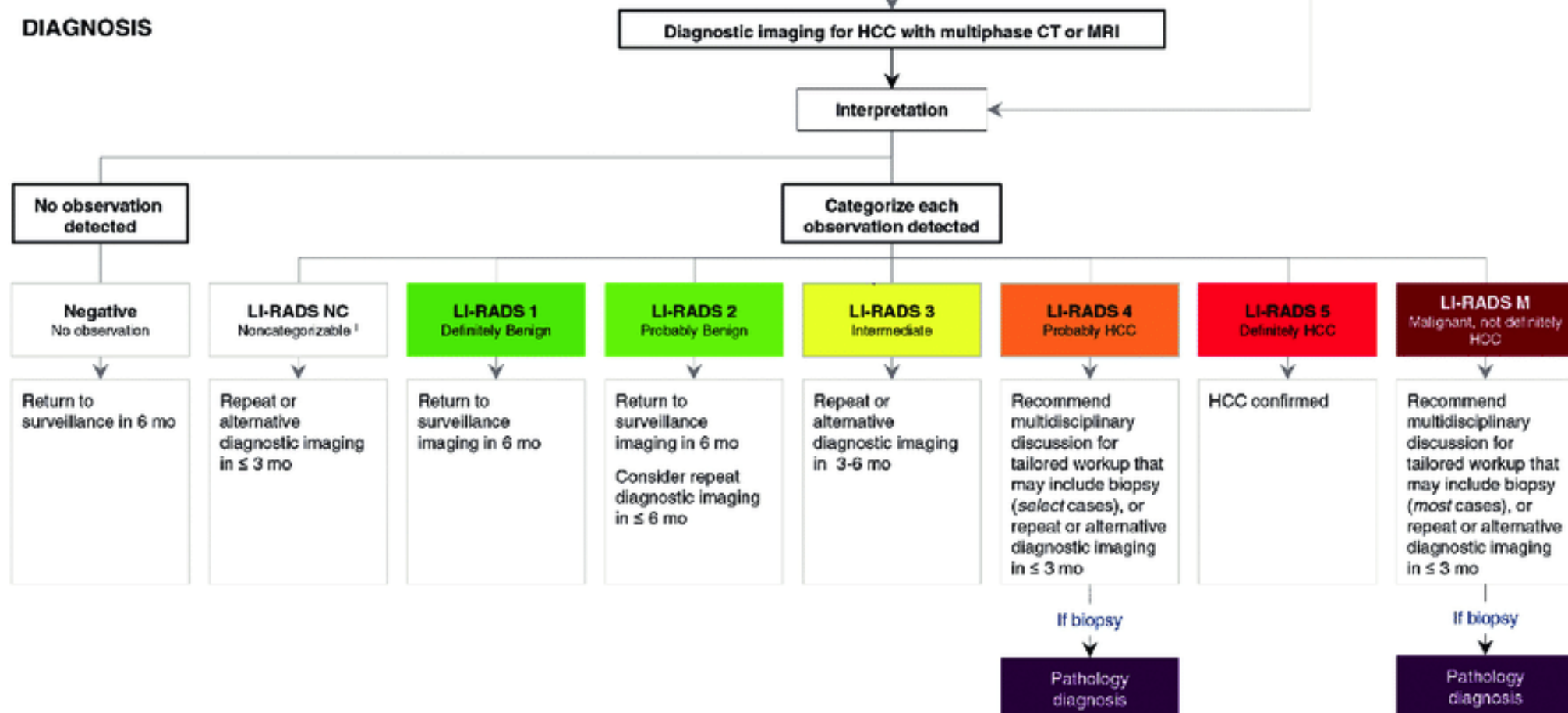




## SURVEILLANCE



## DIAGNOSIS



# AFP in Screening or Not?

- ▶ Test is considered positive if >20 with 60% sensitivity and 90% specificity, but false positive = MRI
- ▶ Meta-analysis 2009, Aliment Pharmacol Ther 2009; 30(1): 37
  - ▶ 6 studies of any stage HCC and 13 early stage only
    - ▶ Overall if US q6 months 94% sensitive overall ,but only 63% for early lesions.
    - ▶ AFP no added benefit
- ▶ Pooled 14 US Studies, Am J Gastr, 2006; 101(3):513
  - ▶ US 60% sensitivity and 97% specificity
  - ▶ AFP sensitivities and specificities varied too widely between studies to attribute values
- ▶ Meta-analysis 2018, Gastroenterology, 2018; 154(6):1706
  - ▶ 32 studies and 13,367 patients
  - ▶ US alone 84% sensitive overall, but only 47% for early lesions
  - ▶ US alone vs US with AFP detected early lesions 45% (30-62% CI) vs 63% (48-75% CI)
  - ▶ MRI 4 studies 83% sensitive

# Portal Hypertension

- ▶ Portal Hypertension (PH) is the initial and main consequence of cirrhosis and responsible for the majority of its complications
- ▶ It is a combination of impaired hepatic flow and increased portal venous inflow.
- ▶ 6 week mortality for a variceal hemorrhage is 15-25%
- ▶ Compensated cirrhotics should be separated into those with mild PH or clinically significant PH (CSPH) defined as a hepatic venous pressure gradient (HVPG)  $\geq 10$  mm Hg
- ▶ HVPG measurements have been routine in Europe for years and now increasingly also in the United States

# Portal Hypertension

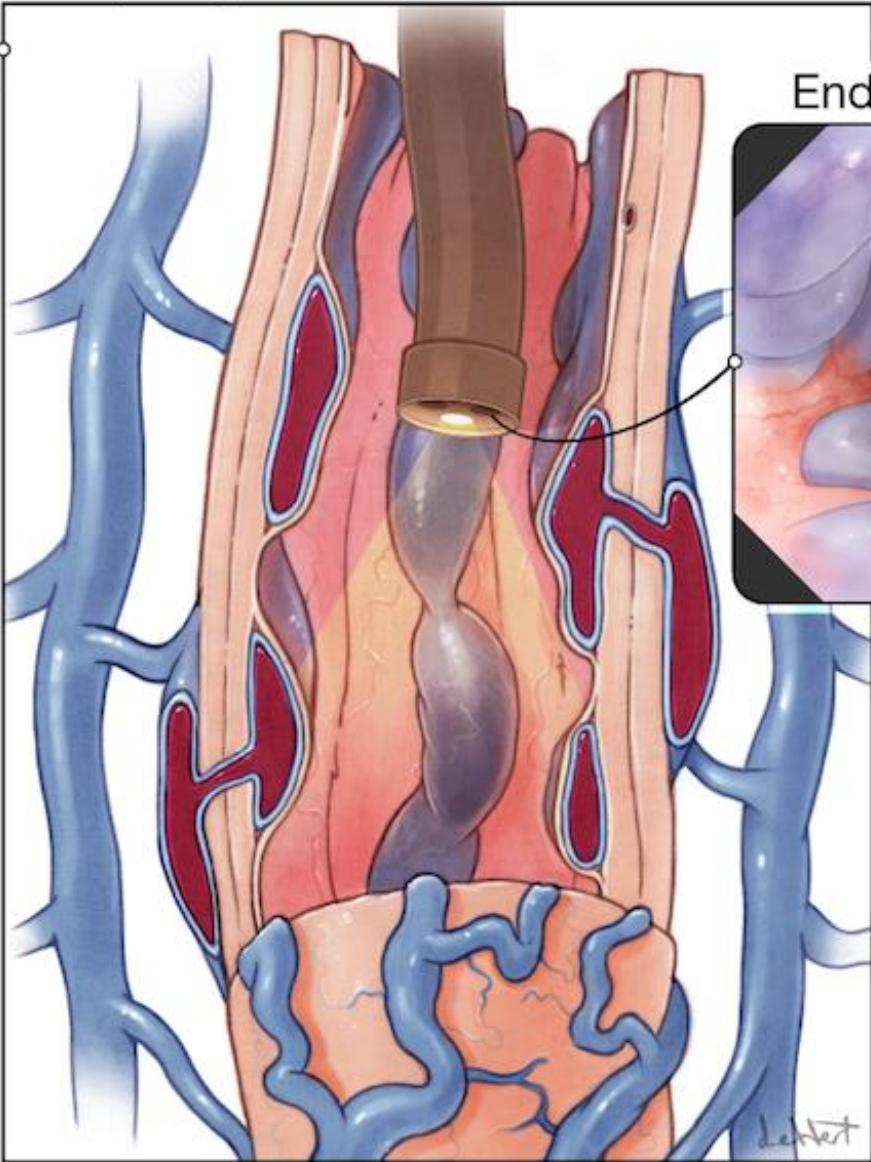
- ▶ Clinically Significant Portal Hypertension (CSPH) is present in 50-60% of patient's with compensated cirrhosis and no varices
- ▶ 30-40% of Compensated cirrhotics (CC's) have gastroesophageal varices (GEV)
- ▶ 60-85% of decompensated cirrhotics have GEV's
- ▶ Varices develop in CC's at 10-15% per year

# Prognostic Value of HVPG in Patients with Chronic Liver Disease

Measurement	Significance
1-5 mm Hg	Normal
$\geq 6$ mm Hg	Risk of disease progression in persons with HCV recurrence after liver transplantation
$\geq 10$ mm Hg	Clinically significant portal hypertension
$\geq 12$ mm Hg	Increased risk for rupture of varices
$\geq 16$ mm Hg	Increased risk of mortality
$\geq 20$ mm Hg	Treatment failure and mortality in acute variceal bleeding



End



Endplate



# Portal Hypertension Non-Invasive Diagnosis

- ▶ US provides an inexpensive way to obtain PH information
  - ▶ Portosystemic collaterals or reversal of portal flow 100% sensitive for CSPH
  - ▶ Spleen size and low platelets correlate, but with poor sensitivity
- ▶ Liver elastography at  $>20\text{-}25$  kPa 90% accurate for CSPH
- ▶ Spleen elastography is a newer method with greater accuracy
- ▶ Protocols combining liver stiffness, spleen size, and platelet counts are being evaluated

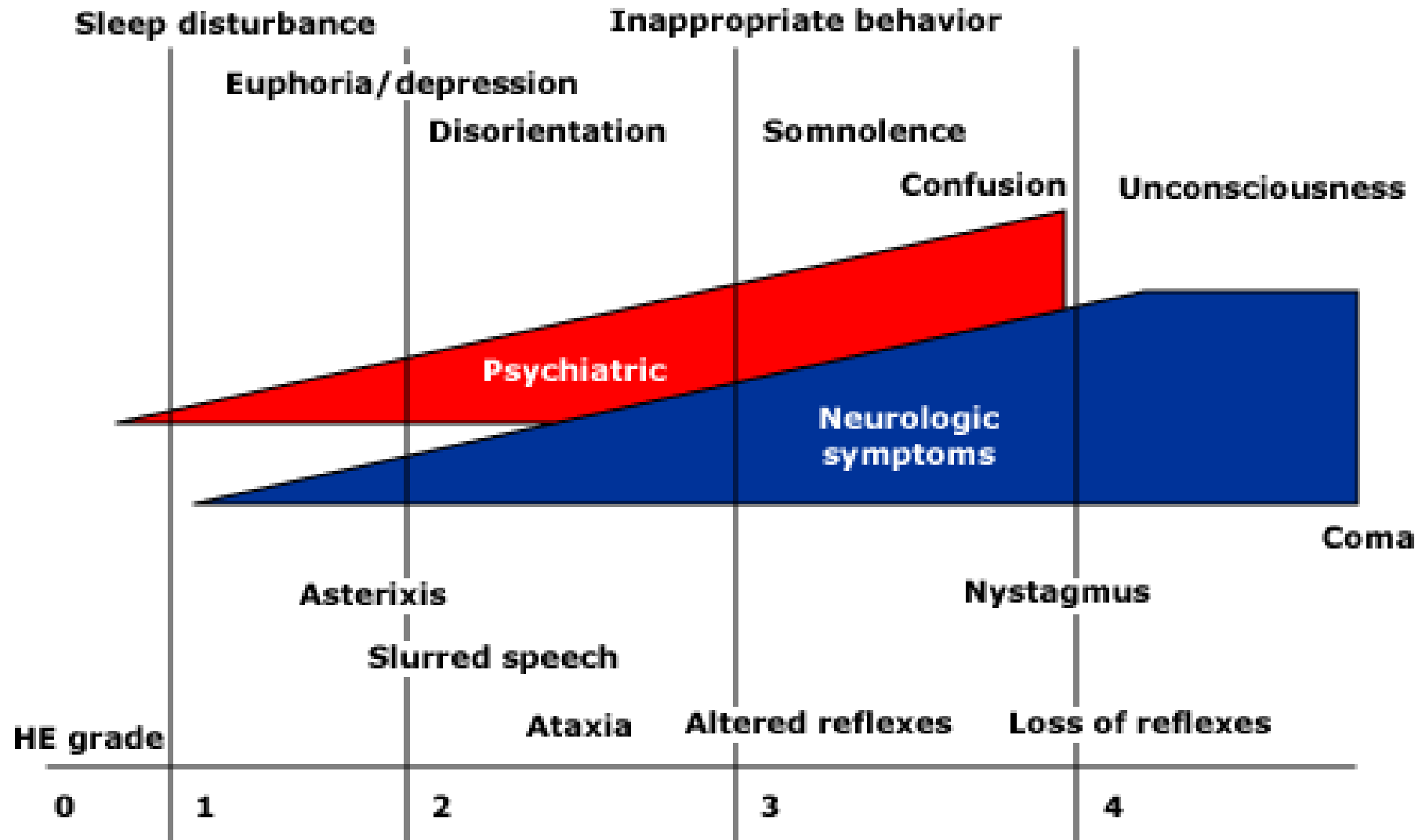
# Diagnosing Clinically Relevant Varices

- ▶ Patient's with TE scores <20 kPa **and** platelets >150,000 are very unlikely to have high risk varices and can avoid EGD monitoring (excludes 20-25%)
- ▶ Platelet to spleen size ratio 95% accurate in excluding varices if >1000 (past guideline criteria)
- ▶ EGD recommended when the diagnosis is made in those not meeting low risk criteria
  - ▶ CC patients without varices should have EGD's every 2 years if active hepatitis on going (HCV, EtOH, etc) or every 3 years if hepatitis quiescent.
  - ▶ CC patients found to have small varices should have EGD's every year if active hepatitis on going (HCV, EtOH, etc) or every 2 years if hepatitis quiescent if not placed on primary prophylaxis
  - ▶ EGD's should be done with any evidence of worsening such as spleen size increase, collaterals, or clinical signs of decompensation

# Hepatic Encephalopathy

- ▶ Broad range of neuropsychiatric abnormalities caused by advanced hepatic insufficiency or portosystemic shunting
  - ▶ Pathogenesis not clearly understood yet nor a single clinical entity identified
  - ▶ Defines being decompensated
  - ▶ Risk of 1<sup>st</sup> episode is 5-25% within 5 years of cirrhosis diagnosis
  - ▶ Minimal hepatic encephalopathy (HE) will develop in 80% of cirrhosis patients
  - ▶ Overt HE will develop in 30-40% of cirrhosis patients
  - ▶ Those with an OHE bout have a 40% 1 year reoccurrence rate

# Evolution of hepatic encephalopathy



# Hepatic Encephalopathy

## Diagnosis and Severity

- ▶ Diagnosis is by clinical findings and excluding other causes of altered mental status
- ▶ Ammonia levels are **not** diagnostic and **not** encouraged by experts.
  - ▶ Ammonia levels must be drawn without a tourniquet, transported on ice, and run in <20 minutes as well

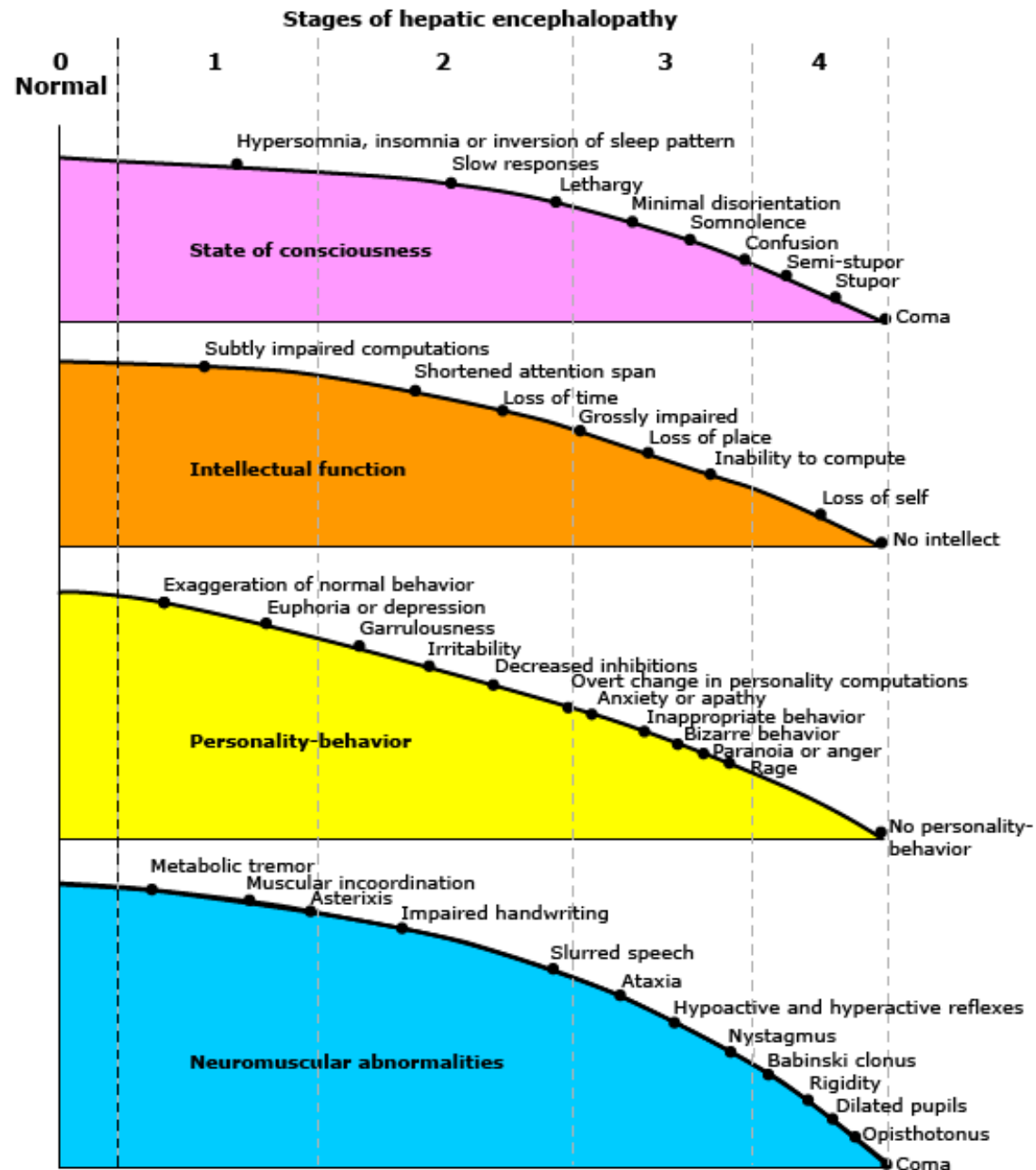
## Differential diagnosis of hyperammonemia

Reye syndrome
Gastrointestinal bleeding
Renal disease
Urinary tract infection with a urease-producing organism (eg, <i>Proteus mirabilis</i> )
Ureterosigmoidostomy
Shock
Severe muscle exertion/heavy exercise
Cigarette smoking
Transient hyperammonemia in newborns
Certain inborn errors of metabolism (urea cycle defects and organic acidemia)
Any cause of portosystemic shunting of blood
Parenteral nutrition
After high-dose chemotherapy
Drugs such as:
Valproic acid
Barbiturates
Narcotics
Diuretics
Alcohol
Salicylate intoxication
Systemic <i>Mycoplasma hominis</i> or <i>Ureaplasma</i> spp infection in lung transplant recipients

[https://www.uptodate.com/contents/hepatic-encephalopathy-in-adults-clinical-manifestations-and-diagnosis?search=hepatic%20encephalopathy&source=search\\_result&selectedTitle=2~150&usage\\_type=default&display\\_rank=2#H335422231](https://www.uptodate.com/contents/hepatic-encephalopathy-in-adults-clinical-manifestations-and-diagnosis?search=hepatic%20encephalopathy&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H335422231)



# Clinical features of hepatic encephalopathy in adults



UpToDate diagram depicting the grade of hepatic Encephalopathy in adults and the clinical features associated with advancing stages

## Precipitants of hepatic encephalopathy in patients with cirrhosis

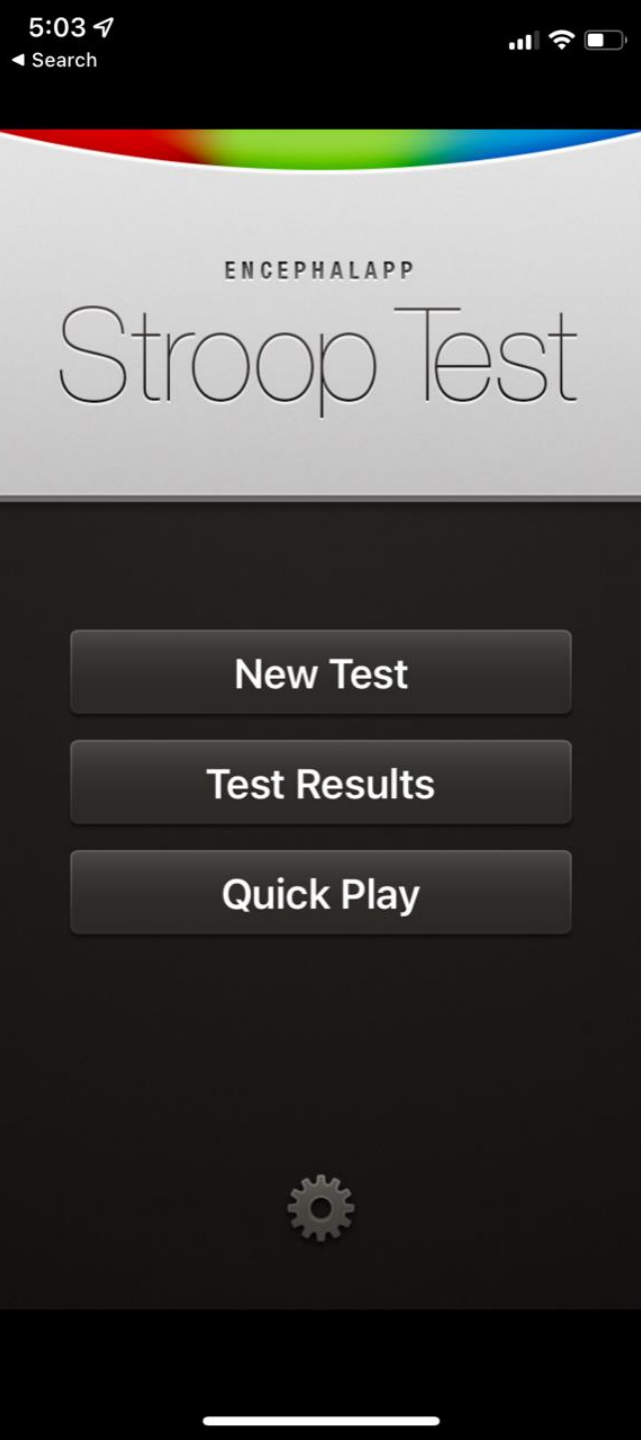
Drugs
Benzodiazepines
Nonbenzodiazepine hypnotics (eg, zolpidem)
Narcotics
Alcohol
Increased ammonia production, absorption or entry into the brain
Excess dietary intake of protein
Gastrointestinal bleeding
Infection
Electrolyte disturbances such as hypokalemia
Constipation
Metabolic alkalosis
Dehydration
Vomiting
Diarrhea
Hemorrhage
Diuretics
Large volume paracentesis
Portosystemic shunting
Radiographic or surgically placed shunts
Spontaneous shunts
Vascular occlusion
Hepatic vein thrombosis
Portal vein thrombosis
Primary hepatocellular carcinoma

[https://www.uptodate.com/contents/hepatic-encephalopathy-in-adults-clinical-manifestations-and-diagnosis?search=hepatic%20encephalopathy&source=search\\_result&selectedTitle=2~150&usage\\_type=default&display\\_rank=2#H2](https://www.uptodate.com/contents/hepatic-encephalopathy-in-adults-clinical-manifestations-and-diagnosis?search=hepatic%20encephalopathy&source=search_result&selectedTitle=2~150&usage_type=default&display_rank=2#H2)

## Asterixis (Flap Tremor)



WHC including MHE	ISHEN	Description	Suggested operative criteria	Comment
Unimpaired		<ul style="list-style-type: none"> <li>No encephalopathy at all, no history of HE</li> </ul>	Tested and proved to be normal	
Minimal	Covert	<ul style="list-style-type: none"> <li>Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change</li> </ul>	Abnormal results of established psychometric or neuropsychological tests without clinical manifestations	<p>No universal criteria for diagnosis</p> <p>Local standards and expertise required</p>
Grade I		<ul style="list-style-type: none"> <li>Trivial lack of awareness</li> <li>Euphoria or anxiety</li> <li>Shortened attention span</li> <li>Impairment of addition or subtraction</li> <li>Altered sleep rhythm</li> </ul>	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	<ul style="list-style-type: none"> <li>Lethargy or apathy</li> <li>Disorientation for time</li> <li>Obvious personality change</li> <li>Inappropriate behavior</li> <li>Dyspraxia</li> <li>Asterixis</li> </ul>	Disoriented for time (at least three of the following are wrong: day of the month, day of the week, month, season, or year) $\pm$ the other mentioned symptoms	Clinical findings variable, but reproducible to some extent
Grade III		<ul style="list-style-type: none"> <li>Somnolence to semistupor</li> <li>Responsive to stimuli</li> <li>Confused</li> <li>Gross disorientation</li> <li>Bizarre behavior</li> </ul>	Disoriented also for space (at least three of the following wrongly reported: country, state [or region], city, or place) $\pm$ the other mentioned symptoms	Clinical findings reproducible to some extent
Grade IV		<ul style="list-style-type: none"> <li>Coma</li> </ul>	Does not respond even to painful stimuli	Comatose state usually reproducible



Blue

Green

Red

Blue

×

1.276



## Proposed Nomenclature of Hepatic Encephalopathy

Type	Encephalopathy Associated With	Subcategory	Subdivisions
<b>A</b>	<b><u>A</u></b> cute liver failure		
<b>B</b>	Portal-systemic <b><u>b</u></b> ypass and no intrinsic hepatocellular disease		
<b>C</b>	<b><u>C</u></b> irrhosis and portal hypertension and/or portal-systemic shunts	Episodic	Precipitated Spontaneous <sup>+</sup> Recurrent <sup>*</sup>
		Persistent <sup>**</sup>	Mild (grade 1) Severe (grades 2 to 4) Treatment-dependent
		Minimal	

<sup>+</sup>Without recognized precipitating factors

<sup>\*</sup>Recurrent = two episodes within one year

<sup>\*\*</sup>Persistent = cognitive deficits that impact negatively on social and occupational functioning

## Hepatic encephalopathy descriptors

Type	Grade		Time course	Spontaneous or precipitated
A	MHE	Covert	Episodic	Spontaneous
	1		Recurrent	
B	2	Overt		Recurrent
	3		Persistent	
C	4			

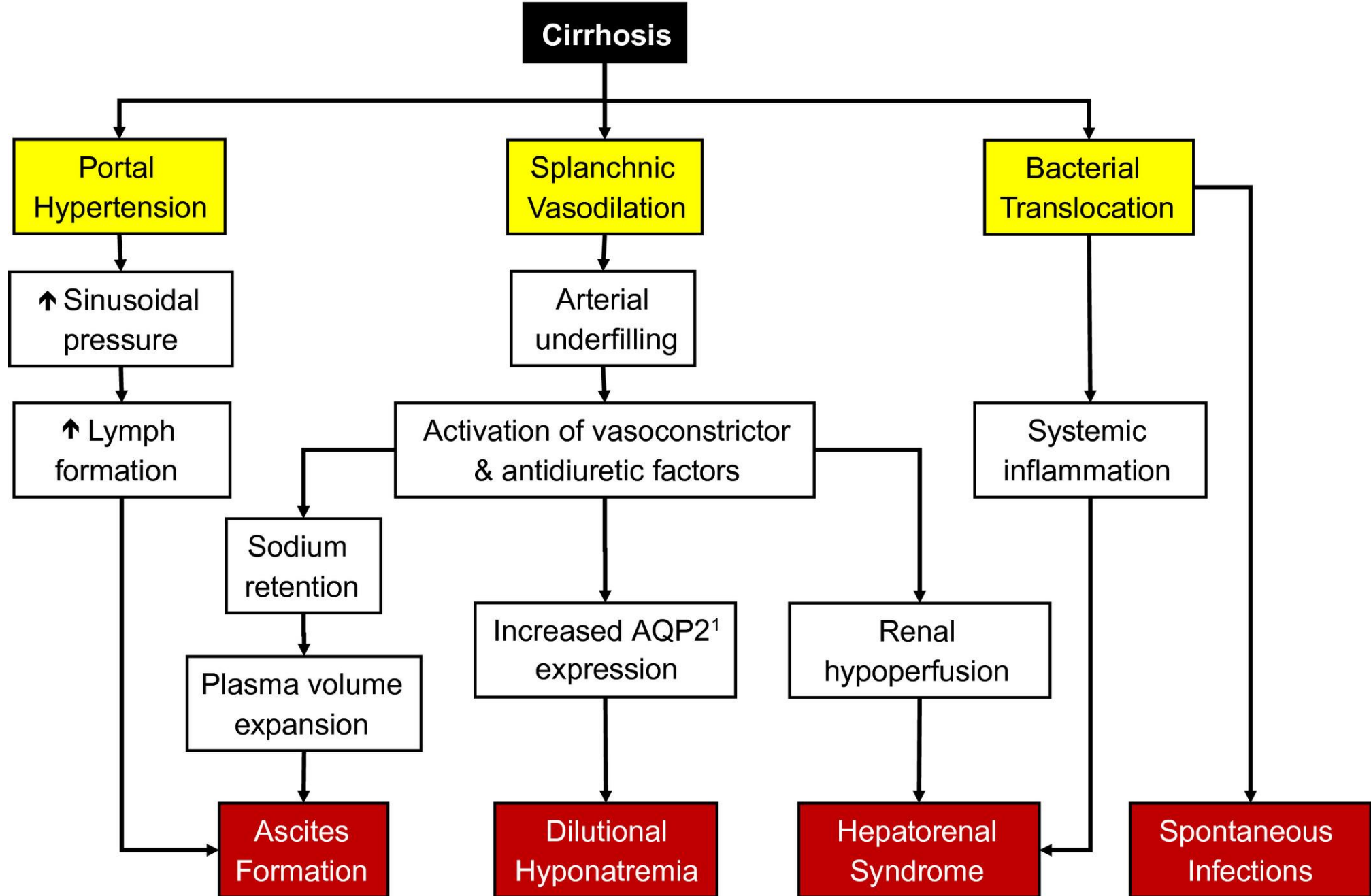
The patient with hepatic encephalopathy (HE) should be characterized by one component from each of the four columns. Example of a recommended description of a patient with HE: "The patient has HE, Type C, Grade 3, Recurrent, Precipitated (by urinary tract infection)." The description may be supplemented with operative classifications (eg, the Glasgow Coma Score or psychometric performance).

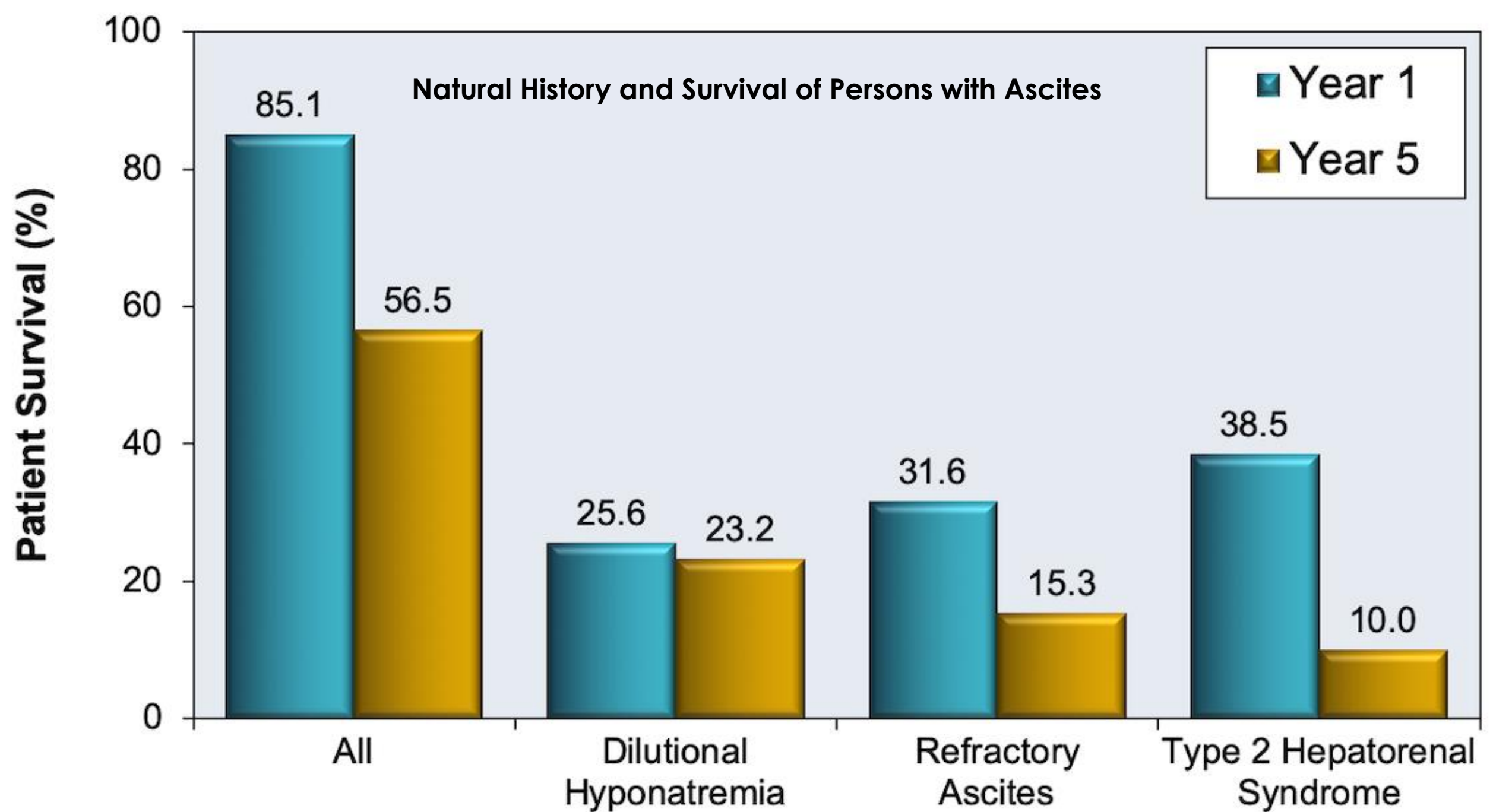
MHE: minimal hepatic encephalopathy.

*From: Vilstrup H, Amodio P, Bajaj J, et al. 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. Hepatology 2014; 60:715. <http://onlinelibrary.wiley.com/doi/10.1002/hep.27210/abstract>. Copyright © 2014 American Association for the Study of Liver Diseases. Reproduced with permission of John Wiley & Sons Inc. This image has been provided by or is owned by Wiley. Further permission is needed before it can be downloaded to PowerPoint, printed, shared or emailed. Please contact Wiley's permissions department either via email: [permissions@wiley.com](mailto:permissions@wiley.com) or use the RightsLink service by clicking on the 'Request Permission' link accompanying this article on Wiley Online Library (<http://onlinelibrary.wiley.com>).*

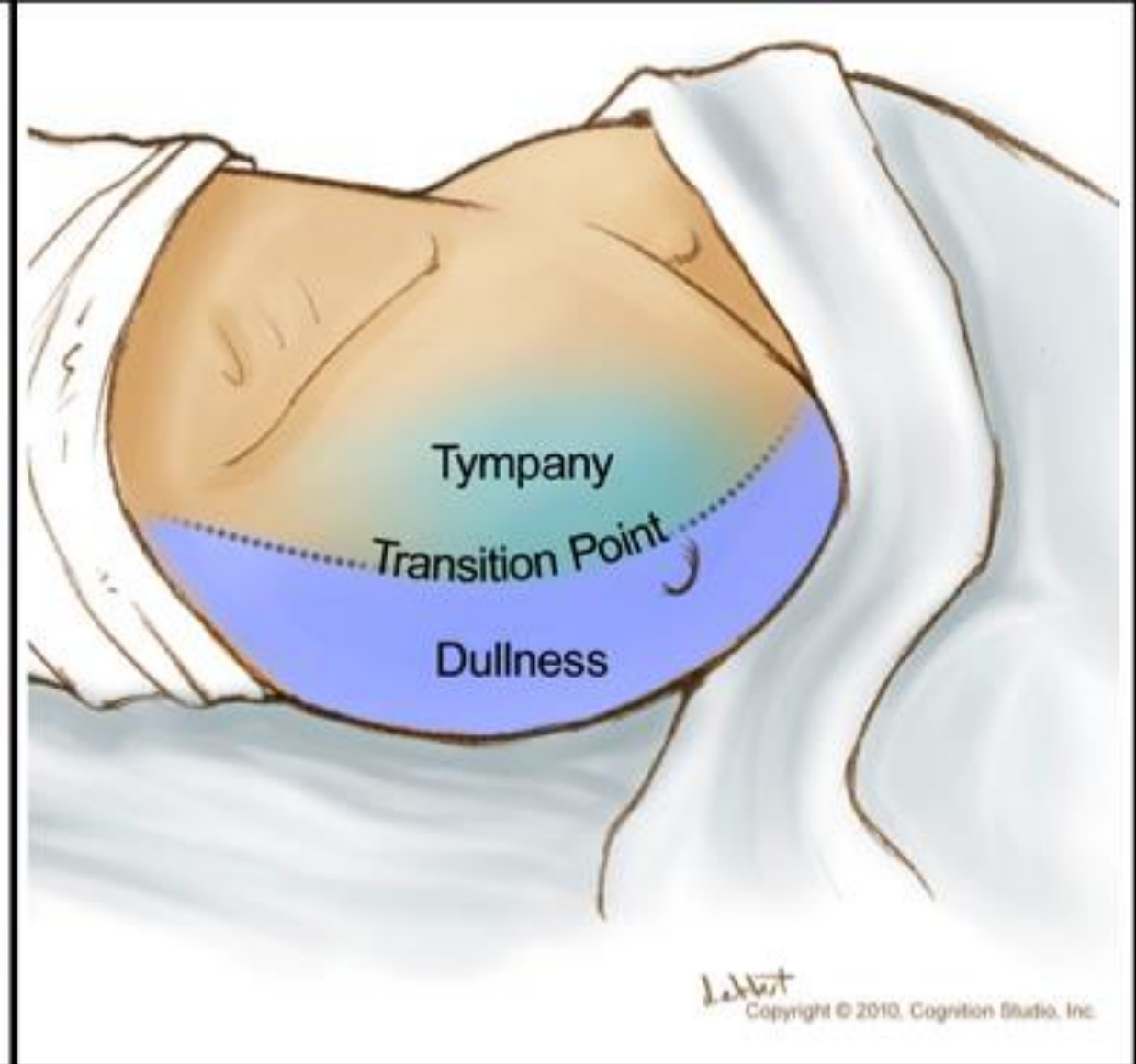
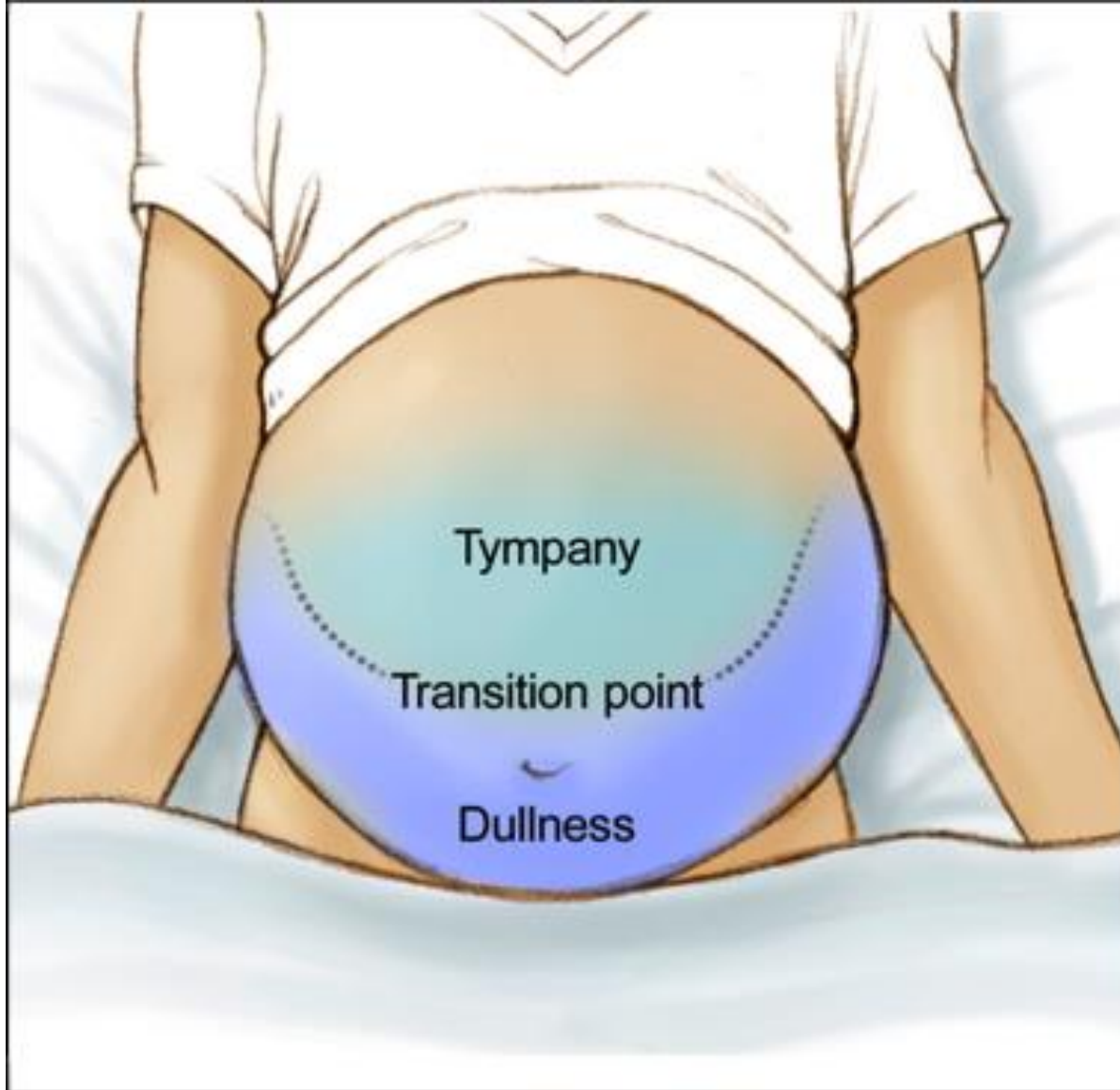
# Ascites

- ▶ Ascites is defined as an abnormal accumulation of fluid in the abdomen
- ▶ It is the most common complication of cirrhosis
- ▶ About 50% of cirrhosis patients will develop it over 10 years
- ▶ If hospitalization required mortality is 15% at 1 year and 50% at 5 years
- ▶ Major complications include:
  - ▶ Spontaneous bacterial peritonitis (SBP)
  - ▶ Dilutional hyponatremia
  - ▶ Acute Kidney Injury-Hepatorenal syndrome (AKI-HRS)
- ▶ New AASLD guidelines were released 8/21 on the diagnosis, evaluation, and management of ascites, SBP, and AKI-HRS









**Figure 4 - Shifting Dullness in Person with Ascites**

To perform the shifting dullness test, have the individual move to a supine position, then percuss the entire abdominal region and mark the dullness-tympany transition point (left figure). Then place the person in the right lateral decubitus position, wait 30 to 60 seconds, repeat the percussion, and again mark the dullness-tympany transition point (right figure). A positive shifting dullness test is indicated by a shifting of the transition point.

# Paracentesis

## Cirrhosis Indications

- ▶ On new ascites diagnosis
- ▶ On hospitalization
- ▶ Signs of Spontaneous Bacterial Peritonitis
  - ▶ New fever >37.8
  - ▶ Abdominal pain
  - ▶ Hepatic encephalopathy
  - ▶ Metabolic acidosis
  - ▶ Renal failure
  - ▶ Hypotension
  - ▶ Diarrhea
  - ▶ Paralytic ileus
  - ▶ Hypothermia
  - ▶ Signs of bacterial infection

Disorder	SAAG		Additional Diagnostic Tests
	≥ 1.1 g/dL	< 1.1 g/dL	
Liver related			
Cirrhosis	X		Ascitic fluid cell count and differential for SBP, total protein
Alcoholic hepatitis	X		
Acute liver failure	X		
Budd-Chiari Syndrome	X		Imaging
Sinusoidal Obstruction Syndrome	X		
Sarcoidosis, hepatic granulomas	X		Liver biopsy
Polycystic liver disease	X		Imaging
Nodular regenerative hyperplasia	X		Liver biopsy
Cardiac			
CHF, constrictive pericarditis, pulmonary hypertension	X		Echocardiogram, right heart catheterization
Neoplasm			
Hepatocellular carcinoma	X		Imaging
Liver metastases	X		Imaging
Peritoneal carcinomatosis		X	Imaging, cytology
Malignant chylous ascites		X	Ascitic fluid triglyceride, imaging
Infection			
Tuberculous peritonitis		X	Mycobacterial culture on directed peritoneal biopsy and ascitic fluid
Secondary bacterial peritonitis		X	Ascitic fluid glucose, LDH, Gram's stain, CEA, alkaline phosphatase
Other			
Nephrotic syndrome		X	24-hour urine protein
Pancreatic ascites		X	Ascitic fluid amylase
Thyroid myxedema	X		Serum thyroid tests
Postoperative lymphatic leak		X	Ascitic fluid triglyceride

# Spontaneous Bacterial Peritonitis

- ▶ Defined as ascitic fluid having  $> 250$  leukocyte cells/ml with a positive culture or without when no other explanation can be found
- ▶ Occurs in 10-30% of those with ascites followed for a year
- ▶ 13% of patient's with it have no symptoms
- ▶ Putting 10cc of the ascitic fluid directly into a culture bottle improves culture yields.
- ▶ Risks include:
  - ▶ Ascitic fluid protein  $< 1$  g/dl
  - ▶ Total serum bilirubin  $> 2.5$
  - ▶ Variceal hemorrhage
  - ▶ Prior SBP
- ▶ Use of PPI's increase risk slightly so should have clear indications for chronic use
- ▶ Antibiotic prophylaxis long-term after 1<sup>st</sup> SBP episode and for 7 days after a VH is standard



# AKI and HRS

## New 8/21 AASLD Changes

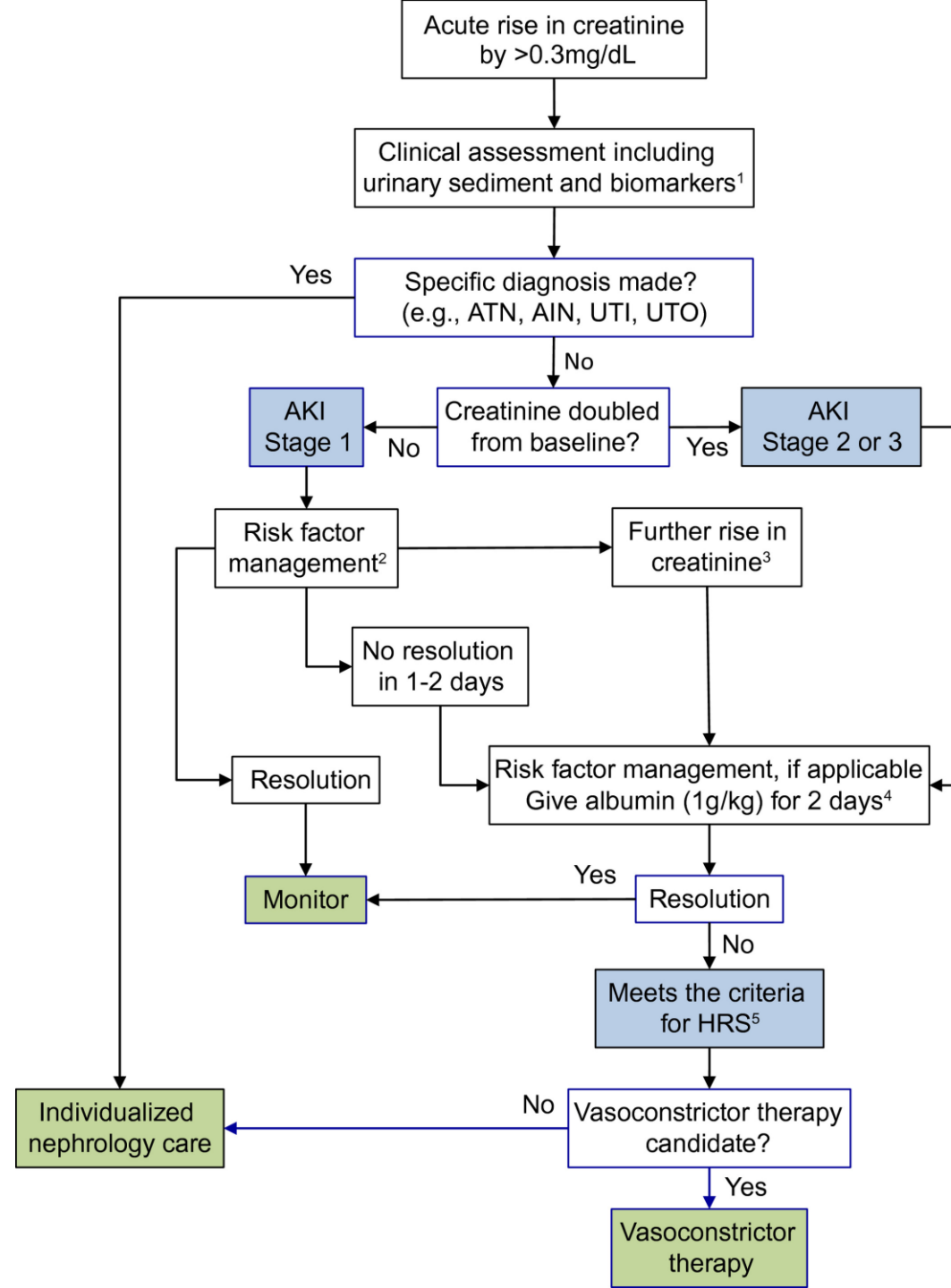
- ▶ Acute Kidney Injury (AKI) occurs in 27-53% of hospitalized cirrhosis patients and is associated with 29-44% 30 days mortality
- ▶ AKI is defined as serum Cr increase  $\geq 0.3$  mg/dl in 48 hours or  $\geq 50\%$  increase over 7 days
- ▶ AKI Stages are:
  - ▶ Stage 1:  $\geq 0.3$  mg/dL Cr increase to 2 fold baseline
  - ▶ Stage 2: 2 fold to 3 fold mg/dL Cr increase
  - ▶ Stage 3:  $>3$  fold mg/dL Cr increase or Cr  $> 4$  mg/dL
- ▶ Main causes for AKI in cirrhosis is prerenal AKI (hypovolemia and HRS) and Acute Tubular Necrosis (ATN)
- ▶ Hepatorenal Syndrome (HRS) is a type of AKI

# AKI and HRS

## New 8/21 AASLD Changes

### Diagnosis of HRS-AKI

- ▶ No response after 2 days of diuretic withdrawal and volume expansion with albumin
- ▶ Absence of shock
- ▶ No current or recent use of nephrotoxic drugs
- ▶ No signs of structural kidney injury as indicated by proteinuria >500 mg/day, microhematuria with >50 RBC's per high power field, or abnormal renal US



# Hyponatremia

## AASLD Guidance Statements

- ▶ Hyponatremia as defined as serum Na <135 mEq/L is present in 49% of cirrhotics with ascites and 22% will have serum Na's < 130 mEq/L
- ▶ Mild hyponatremia (126-135 mEq/L) without symptoms requires only monitoring and free water restriction
- ▶ Water restriction to 1000 mL/day and cessation of diuretics and/or laxatives is recommended for moderate hyponatremia (120-125 mEq/L) due to hypovolemia and fluid resuscitation
- ▶ Goal range for raising serum Na is 4-8 mEq/L per day

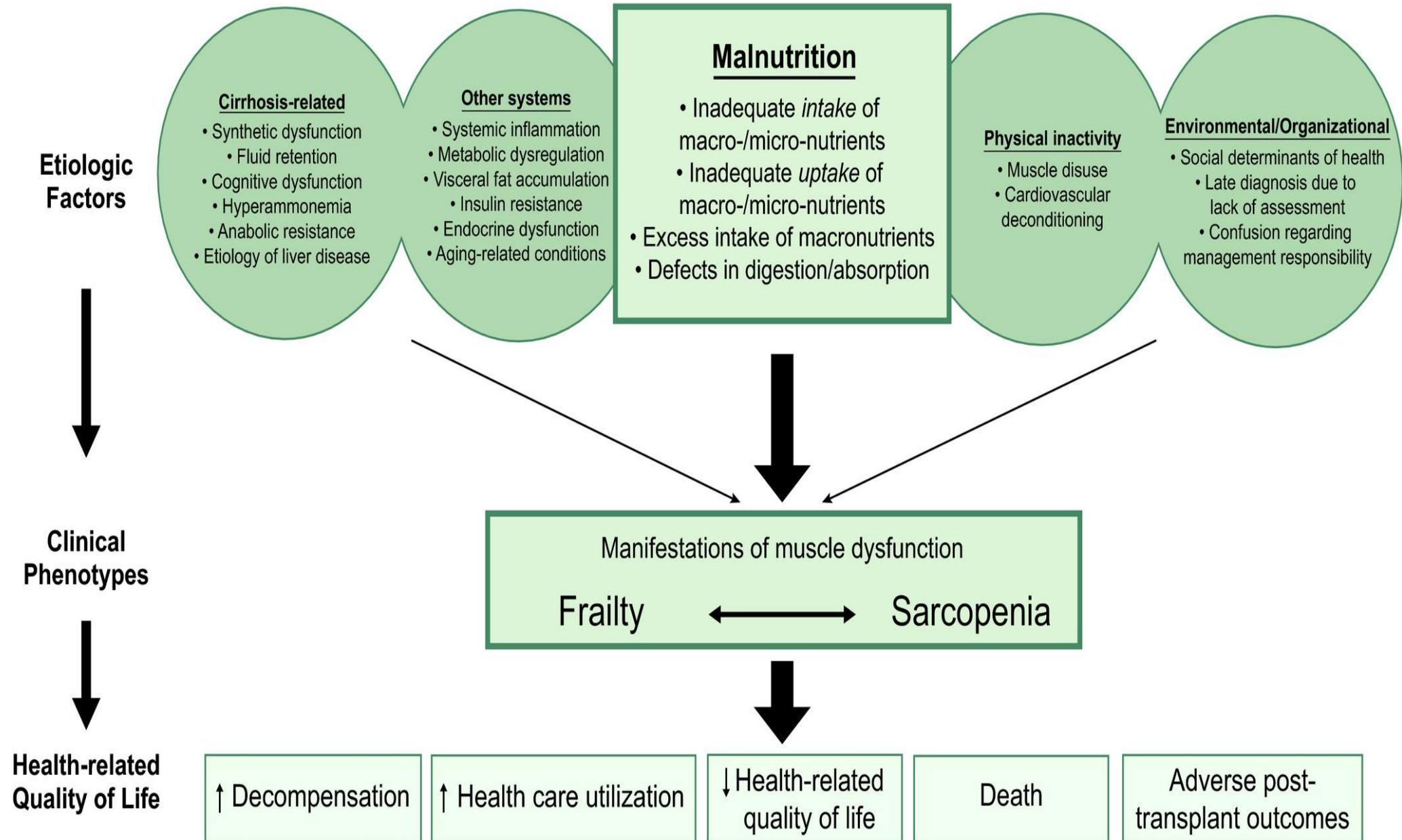
# Malnutrition, Frailty, and Sarcopenia in Patient's With Cirrhosis

## AASLD 2021 Guidance Statements

### Definitions

- ▶ Malnutrition: A clinical syndrome that results from an imbalance that causes measurable adverse effects on tissue/body form or function, and/or clinical outcome
- ▶ Frailty: A clinical state of decreased physiologic reserve and increased vulnerability to health stressors. AASLD as opposed to geriatrics focused more solely on decreased physical functioning, functional performance, and disability due the weight of evidence in cirrhosis research
- ▶ Sarcopenia: A progressive and generalized skeletal muscle disorder associated with an increased likelihood of adverse outcomes including falls, fractures, disability, and mortality combining muscle mass, strength, and performance in it's definition

# Factors Contributing to Malnutrition, Frailty, Sarcopenia And Relationships



# Frailty

- ▶ Frailty associated increased 90 day mortality has a RR of 1.8 when  $\geq 3$  ADL assistances are needed
- ▶ Frailty is strongly associated with hospitalizations, falls, depression, disability, and global QOL
- ▶ 1. All patients should be assessed for frailty with a standardized tool at least annually and q3-6 months if decompensated
  - ▶ Tools include:
    - ▶ Clinical Frailty Scale: <https://gmrtoolkit.ca/app2/>
    - ▶ ADL's: Numerous scales including Katz Index of Independence <https://www.alz.org/careplanning/downloads/katz-adl.pdf>
    - ▶ Other more objective tests taking more time and some equipment and training
- ▶ 2. All patients with cirrhosis should be counseled on the risks and adverse clinical consequences regardless of their baseline frailty status



# Sarcopenia

- ▶ Present in 30-70% of end-stage patients with 21% women and 70% of men awaiting transplant meeting criteria in a large study
- ▶ Sarcopenic obesity
  - ▶ 20-35% prevalence and NAFLD a strong risk factor
  - ▶ Independent risk factor for mortality
  - ▶ Likely to increase as NAFLD increases
- ▶ CT is the gold standard for the assessment of muscle mass in cirrhosis
  - ▶ Cost and radiation prohibitive as sole indication, but can be added when being done for other indications
- ▶ DEXA and anthropometrics (midarm muscle circumference and tricep muscle skin thickness) other methods and may be limited by fluid retention

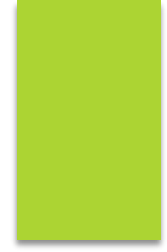
# New Guideline Statements Most Relevant to Corrections

- ▶ Recommended daily protein intake for adults with cirrhosis is 1.2-1.5 g/kg ideal body weight
- ▶ Critically ill adults with cirrhosis should get 1.2-2.0 g/Kg ideal body weight protein intake
- ▶ Protein should not be restricted in those with hepatic encephalopathy
- ▶ A late night snack of 149-710 kcal has been shown to increase total protein and fat free mass.
- ▶ Fasting should be minimized and ideally small meals be eaten every 3-4 hours while awake

# New Guideline Statements Most Relevant to Corrections

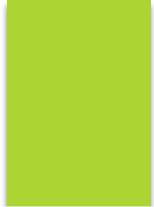
- ▶ Vitamin and mineral deficiencies are common in cirrhosis so micronutrients should be checked annually including:
  - ▶ Fat soluble vitamins A, D, E, and K
  - ▶ Water soluble vitamins B1, B3, B6, B9, B12, and C
  - ▶ Trace elements Zinc, selenium (rare), and copper
- ▶ Bariatric surgery patient's commonly have deficiencies independently of:
  - ▶ Commonly Vitamins B12, B9, D, A, K, and E and rarely B1
  - ▶ Minerals iron and calcium common and rarely copper, magnesium, and zinc
  - ▶ Impaired protein digestion and absorption

# Fat-soluble Vitamins



	Symptoms of Deficiency	Repletion	Comments
<b>Vitamin A</b>	Ocular and skin changes, growth retardation	2,000-200,000 IU/d based on severity for 4-8 weeks	Risk of toxicity if level >120 ug/dL, If not responding consider zinc deficiency
<b>Vitamin D</b>	Bone pain, muscle weakness, osteomalacia, anorexia, hair loss, poor wound healing, hypocalcemia, and hypophosphatemia	50,000 IU/week of D2 or D3 for 8 weeks followed by 1500-2000 IU/d	Target 25-OH level > 30ng/mL and give with calcium to those with low bone density
<b>Vitamin E</b>	Hemolytic anemia, neuro deficits (like ataxia, periheral neuropathy), and muscle pain	Tocopherol acetate 400-800 IU/d po	Much less common, high doses antagonize vitamin A and have cardiac concerns
<b>Vitamin K</b>	Bleeding, petechiae, purpura, ecchymosis, and INR prolongation	Phytonadione 1-10 mg po, SC, or IV	Not stored so deficiencies occur rapidly

# Water-soluble Vitamins



	Symptoms of Deficiency	Repletion	Comments
<b>Thiamine B1</b>	Dry/wet beriberi, Wernicke/Korsakoff, and muscle weakness	Asymptomatic patients 100 mg/d, Suspected Wernicke encephalopathy full IV replacement	Measurements not widely available
<b>Niacin B3</b>	Pellagra, GI sx's, apathy, fatigue, headache, memory loss, and abnormal behavior	300-1,000 mg/d for deficiency states	Blood levels unreliable and hepatic toxicity possible with excess dosing
<b>Pyridoxine B6</b>	Paresthesias, seizures, glossitis, and oral lesions	100 mg/d	Isolated deficiency uncommon, may reduce zinc, and B12 cotreatment recommended
<b>Folic acid B9</b>	Muscle weakness, glossitis, oral lesions, and macrocytic anemia	1-5 mg/d	High doses may block Zinc absorption
<b>Cobalamin B12</b>	Oral changes, muscle weakness, neuropathy, gait, cognition, hyperpigmentation, and anemia	1,000-2,000 ug/d	High doses may be required
<b>Ascorbic Acid C</b>	Perifollicular petechiae, keratosis, ecchymosis, impaired wound healing, oral changes, and anemia	500-1,000 mg/d	Requirements are increased in critical illnesses

# Trace Elements

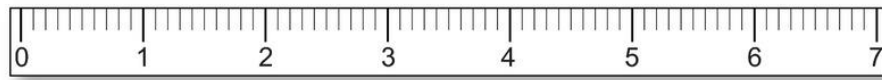
	Symptoms of Deficiency	Repletion	Comments
<b>Zinc</b>	Rash, alopecia, poor healing, myopathy, altered taste/smell, and it may aggravate HE	30-50 mg elemental zinc per day	Replacing zinc may help normalize Vitamin A metabolism, High doses may cause copper deficiency
<b>Selenium</b>	Cardiomyopathy, myositis, cramping, alopecia, dry skin, and skin erythema	50-100 ug/day	Deficiency is relatively rare
<b>Copper</b>	Bone marrow suppression, microcytic anemia, leukopenia, pancytopenia, hypercholesterolemia, delayed wound healing, neuropathies, and ataxia	2-4 mg IV for 6 days followed by 3-8 mg po daily until symptoms resolve or levels normalize	Blood copper level for screening deficiency and ceruloplasmin to guide when inflammation present

# Physical Activity Related Interventions

## 3 General Principles



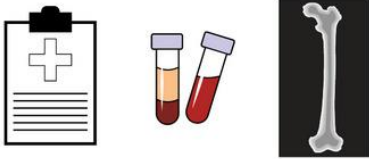
- ▶ Assess frailty and/or sarcopenia with a standardized tool
- ▶ Recommend a combination of aerobic and resistance exercises
- ▶ Tailor recommendations based on reassessments





## Diagnostic Toolbox

Select tools based on the clinical scenario

	 Clinician questions	 Physical exam findings	 Objective measures
<div>Screen for Malnutrition &amp; Assess for frailty and/or sarcopenia</div>	<ul style="list-style-type: none"> <li>• <b>Karnofsky Performance Scale</b></li> <li>• <b>Clinical Frailty Scale</b></li> <li>• <b>Activities of Daily Living</b></li> <li>• <b>Pediatric populations</b> <ul style="list-style-type: none"> <li>• Royal Free Hospital-Nutrition Prioritizing Tool</li> <li>• Lansky play performance scale</li> <li>• Fried-exhaustion, shrinkage, Pediatric Quality of Life Inventory</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Muscle wasting</b> – wasting at the temples, clavicle, shoulder, scapula/ribs, quadriceps, interosseous muscle between the thumb and forefinger</li> <li>• <b>Use of a walking aid</b></li> <li>• <b>Inability to stand up from the chair independently or getting off the exam table independently, slowness</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>CT scan L3 skeletal muscle index</b></li> <li>• <b>Liver frailty index</b></li> <li>• <b>Handgrip strength</b></li> <li>• <b>6 minute walk test</b></li> <li>• <b>4 meter gait speed</b></li> <li>• <b>Triceps skin-fold thickness (pediatrics)</b></li> </ul>
<div>Identify factors contributing to malnutrition, frailty, and sarcopenia</div>	<ul style="list-style-type: none"> <li>• <b>Hunger Vital Sign</b> (<i>abnormal if either or both are true</i>)             <ul style="list-style-type: none"> <li>• Within the past 12 months, we worried whether our food would run out before we got money to buy more.</li> <li>• Within the past 12 months, the food we bought just didn't last and we didn't have money to get more.</li> </ul> </li> <li>• <b>Physical inactivity</b> <ul style="list-style-type: none"> <li>• In the past week, on how many days have you done a total of 30 min or more of physical activity, which was enough to raise your breathing rate?</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Ascites</b></li> <li>• <b>Hepatic encephalopathy</b></li> <li>• <b>Poor dentition</b></li> <li>• <b>Dysgeusia</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>MELD-Na</b></li> <li>• <b>Child Pugh score</b></li> <li>• <b>Testosterone level (men)</b></li> <li>• <b>Data from patient's fitness tracker (e.g., daily steps, average heart rate)</b></li> </ul>

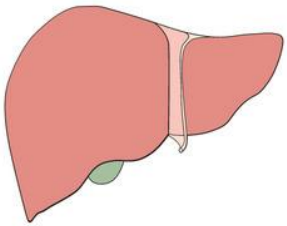
# Mechanisms resulting in sarcopenia and failure to respond to standard supplementation



- ▶ Anabolic resistance and dysregulated proteostasis result in failure to respond to standard supplementation
- ▶ These mechanisms represent potential therapeutic targets



## Management Toolbox

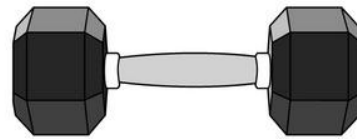


### Liver specific

Management of disease etiology

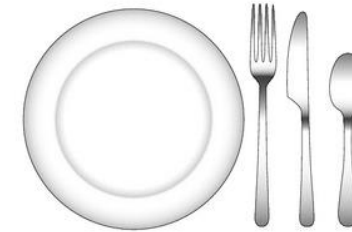
Management of ascites

Management of hepatic encephalopathy



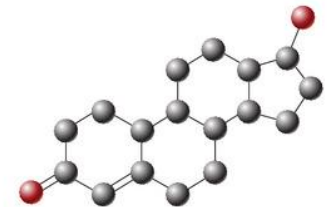
### Physical activity

- **Personalized activity prescription (guided by FITT):**
  - **Frequency** – Aerobic (4-7 d/week); Resistance (2-3 d/week)
  - **Intensity** – Use the talk test (be short of breath but can still speak a full sentence); 3 sets of 10-15 repetitions at a time
  - **Time** – Start slow and build up
    - Aerobic: 150 min per week
    - Resistance:  $\geq 1$  days per week
  - **Type** – aerobic, resistance, flexibility and balance
- **Consult a certified exercise physiologist or physical therapist**



### Intake/Uptake

- **Calorie intake of at least 35 kcal/kg (non-obese)**
- **Protein intake of 1.2 to 1.5 g/kg body weight/d**
- **Micronutrient repletion**
- **Frequent, small meals and minimize fasting (e.g. late evening snack)**
- **Address barriers to intake (e.g. liberalize sodium restrictions as needed)**
- **Consult a registered dietitian**



### Other systems

- **Testosterone replacement (men)**
- **Refer to health behavior specialist**
- **Diabetes control**

# Monitoring Progression to N-Stage

- ▶ United Network for Organ Sharing, the organization that coordinates available organs with recipients, does not factor a patient's prison status when determining suitability for a transplant.
- ▶ An organ transplant and follow-up care can cost the prison system up to one million dollars.
- ▶ If a prisoner qualifies, a state may allow compassionate early release to avoid high costs associated with organ transplants

# Prison inmate awaits organ transplant

08:45 PM PDT on Friday, April 8, 2005

By CHRIS INGALLS / KING 5 News

SEATTLE - For the first time in Washington state, a prison inmate is on the organ transplant waiting list and taxpayers will pay for the expensive operation.

The state prisoner is in dire need of a liver and an operation that could cost up to \$500,000.

KING 5 Investigators have learned that the inmate is housed at the Monroe Correctional Facility.

The operation will be performed at the University of Washington Medical Center, where the inmate is now on a liver transplant waiting list.

The Department of Corrections medical director, Dr. Marc Stern, is bracing for criticism that a prisoner will receive such a costly operation.

"I would understand that, however we're bound to execute the 8th Amendment as we interpret it and provide basic medical care, and as we see it, this is basic medical care," Stern said.

The operation will cost between \$250,000 to \$500,000. Taxpayers will foot the bill through the prison system's \$80-million health care budget.



**CTP Calculator**

APRI Calculator

BMI Calculator

CrCl Calculator

FIB-4 Calculator

Glasgow Coma Scale

GFR Calculator

MELD Calculator

SAAG Calculator

## Substance Use Screening Tools

Alcohol: AUDIT-C

Alcohol: CAGE

Opioid: Risk Tool

**Child-Turcotte-Pugh (CTP) Calculator**

Share

Use the Child-Turcotte-Pugh Classification for Severity of Cirrhosis calculator to estimate the cirrhosis severity. Select the applicable Clinical and Lab Criteria, then check the classification at the bottom.

## Clinical and Lab Criteria

Points

## Encephalopathy

- |                       |                                 |    |
|-----------------------|---------------------------------|----|
| <input type="radio"/> | None                            | +1 |
| <input type="radio"/> | Mild to moderate (grade 1 or 2) | +2 |
| <input type="radio"/> | Severe (grade 3 or 4)           | +3 |

## Ascites

- |                       |  |    |
|-----------------------|--|----|
| <input type="radio"/> | None                                   | +1 |
| <input type="radio"/> | Mild to moderate (diuretic responsive) | +2 |
| <input type="radio"/> | Severe (diuretic refractory)           | +3 |

## Bilirubin (mg/dL)

- |                       |     |    |
|-----------------------|-----|----|
| <input type="radio"/> | < 2 | +1 |
| <input type="radio"/> | 2-3 | +2 |
| <input type="radio"/> | > 3 | +3 |

## Albumin (g/dL)

- |                       |         |    |
|-----------------------|---------|----|
| <input type="radio"/> | > 3.5   | +1 |
| <input type="radio"/> | 2.8-3.5 | +2 |
| <input type="radio"/> | < 2.8   | +3 |

## International normalized ratio

- |                       |         |    |
|-----------------------|---------|----|
| <input type="radio"/> | < 1.7   | +1 |
| <input type="radio"/> | 1.7-2.3 | +2 |
| <input type="radio"/> | > 2.3   | +3 |

Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)



## Clinical Calculators

CTP Calculator

APRI Calculator

BMI Calculator

CrCl Calculator

FIB-4 Calculator

Glasgow Coma Scale

GFR Calculator

**MELD Calculator**

SAAG Calculator

## Substance Use Screening Tools

Alcohol: AUDIT-C

Alcohol: CAGE

Opioid: Risk Tool

# Model for End-Stage Liver Disease (MELD) for ages 12 and older

Share

The Model for Liver Disease (MELD) predicts survival for persons with advanced liver disease.

The United Network for Organ Sharing (UNOS) made a policy change regarding a revision in the MELD scoring system on January 11, 2016 that is related to transplant listing. The new MELD scores are calculated first by determining the traditional MELD score as an initial score (MELD<sub>01</sub>). If the initial MELD<sub>01</sub> score is 12 or greater, the score is adjusted by incorporating the serum sodium value.

## MELD

Serum Bilirubin (mg/dL):

INR (International Normalized Ratio):

Serum Creatinine (mg/dL):

Did the patient have dialysis at least twice in the past week, or receive 24 hours of CVHD within the prior week?

☐ No

☐ Yes

Serum Sodium (mmol/L):

MELD<sub>01</sub> scores less than 12 do not require Serum Sodium correction.

MELD<sub>01</sub> score:

**MELD Score:**

<https://www.hepatitisc.uw.edu/page/clinical-calculators/ctp>



**The End**



**Questions**