# End-Stage Liver Disease (ESLD): A Guide for HIV Physicians

**Marion G. Peters, MD**
John V. Carbone, MD, Endowed Chair
Professor of Medicine
Chief of Hepatology Research
University of California San Francisco

IAS–USA

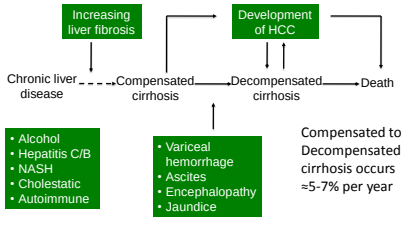
## Learning Objectives

After attending this presentation, learners will be able to:

- Diagnose cirrhosis
- Assess for liver fibrosis
- Identify the complications of cirrhosis
- Manage the complications of cirrhosis

Slide 3 of 43

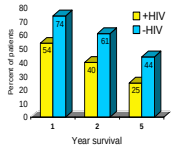
## Natural History of ESLD




*HCC, hepatocellular carcinoma; NASH, nonalcoholic steacohepatitis*
Garcia Tsao CCO Hepatitis.com 2008

Slide 4 of 43

## Survival Time from First Liver Decompensation to Death in HCV




- Death during study
  - 366/1037 HCV
  - 100/180 HIV/HCV
- Risk factors for death:
  - HIV
  - Baseline CTP
  - MELD >13
  - Age

Decompensation with Ascites
Encephalopathy
Variceal bleed
Synthetic dysfunction (INR, Bili, Alb)

*Pineda, Hepatology 2005*

Slide 5 of 43

## Manage ESLD

- Need to know if your patient has cirrhosis
- Need to know if compensated or decompensated
- Then need to manage complications

Slide 6 of 43

## ARS Question #1

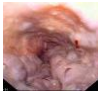
Which of the following statements is/are not true? (May be more than one)

1. Cirrhosis can be diagnosed by LFTs.
2. Cirrhosis can be diagnosed by transient elastography.
3. Cirrhosis can be diagnosed by MELD.
4. Cirrhosis can be diagnosed by CPT.

Slide 7 of 43

## Diagnosing Cirrhosis – Physical Exam






Slide 8 of 43

## Diagnosing Cirrhosis – Labs

**EXAM:**
Spider nevi, splenomegaly

**Most labs not helpful**
- 50% Child's A normal
- AST:ALT often >1

**Synthetic dysfunction**
- Hypoalbuminemia
- Prolonged PT/ INR
- Hyperbilirubinemia

**Portal Hypertension**
- Thrombocytopenia
- Leukopenia
- Anemia

**Renal dysfunction**
- Elevated creatinine remember depends on muscle mass

**Hyponatremia** with ascites

Slide 9 of 43

## Diagnosing Cirrhosis – Imaging

- **Ultrasound poorly diagnoses cirrhosis**
  - In absence of portal hypertension
  - Only ≈50% confirmed by Biopsy
  - Increased echogenicity (ultrasound)= disease not F4
  - Surface nodularity
  - Small nodular liver
- **"Hidden" clues from radiology report of Portal HTN**
  - Ascites
  - Portal/splenic/superior mesenteric vein thrombosis
  - Portosystemic collaterals
  - Splenomegaly



Slide 10 of 43

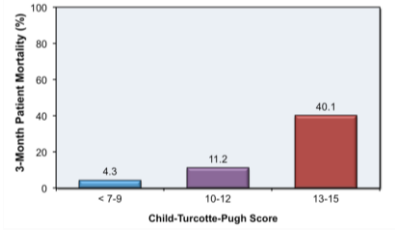
## Prognosticating Decompensated Cirrhosis

| Child-Turcotte-Pugh Classification for Severity of Cirrhosis | | | |
|---|---|---|---|
| Clinical and Lab Criteria | Points* | | |
| | 1 | 2 | 3 |
| Encephalopathy | None | Grade 1 or 2 | Grade 3 or 4 |
| Ascites | None | Mild to moderate (diuretic responsive) | Severe (diuretic refractory) |
| Bilirubin (mg/dL) | < 2 | 2-3 | >3 |
| Albumin (g/dL) | > 3.5 | 2.8-3.5 | <2.8 |
| Prothrombin time<br>Seconds prolonged<br>or<br>International normalized ratio | <4<br><br><1.7 | 4-6<br><br>1.7-2.3 | >6<br><br>>2.3 |
| *Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points) | | | |
| **Class A** = 5 to 6 points | | | |
| **Class B** = 7 to 9 points | | | |
| **Class C** = 10 to 15 points | | | |

http://hepatitisc.uw.edu/go/management-cirrhosis-related-complications/liver-transplantation-referral/core-concept/all

Slide 11 of 43

## 3-Month Mortality Based on CTP




Wiesner R, Edwards E, Freeman R, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. Gastroenterology. 2003;124:91-6.

Slide 12 of 43

## MELD and Liver Transplantation

- MELD
  - Prioritization on liver transplant list
  - Most IMPORTANT single value in prognostication
  - Easy to calculate prior to referral
- MELD = 15 or greater
  - Benefit from OLT
- Important predictor of liver-related outcomes

Slide 13 of 43

## MELD

INR
Bilirubin
Creatinine




***MELD Formula***

The MELD score is calculated using the following formula:

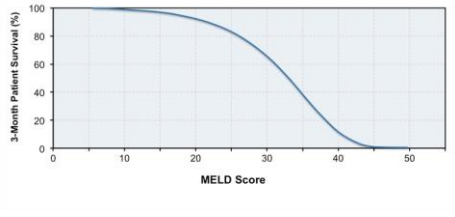
MELD Score = 0.957 x $Log_e$(creatinine mg/dL)
+ 0.378 x $Log_e$(bilirubin mg/dL)
+ 1.120 x $Log_e$(INR)
+ 0.643[1]

Multiply the score by 10 and round to the nearest whole number.

Laboratory values less than 1.0 are set to 1.0 for the purposes of the MELD score calculation.

Slide 14 of 43

## 3-Month Survival Based on MELD




http://hepatitisc.uw.edu/go/management-cirrhosis-related-complications/liver-transplantation-referral/core-concept/all

Slide 15 of 43

## Steps in Assessing Cirrhosis

1. **Clinical evidence of cirrhosis**
   - Labs (elevated INR, low albumin, bilirubin)
   - Radiology evidence of portal HTN
   - Exam (ascites, varices, encephalopathy)
2. **Transient elastography**
3. **Noninvasive markers**
   - E.g. APRI Fib 4- uses AST, platelets, ALT
4. **If further delineation is needed→ Liver biopsy with measurement of portal pressure**
   - Not needed in many/ most situations with HCV

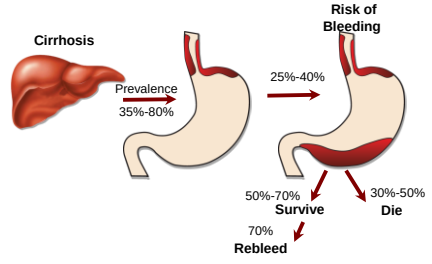
Slide 16 of 43

## Which statement is true?

1. The prevalence of esophageal varices is low in cirrhotics.
2. Cirrhosis is the commonest cause of Ascites in hospitalized patients.
3. Spontaneous bacterial peritonitis is usually symptomatic.
4. Patients with hepatic encephalopathy should restrict protein intake.

Slide 17 of 43

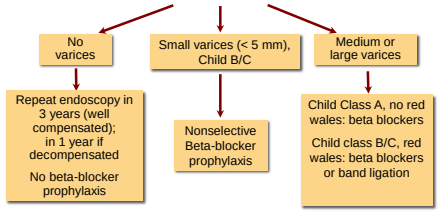
## Risk of Bleeding from Esophageal Varices




Slide 18 of 43

## Variceal Surveillance

All cirrhotics require esophagogastroduodenoscopy.

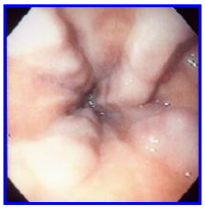



Slide 19 of 43

Garcia-Tsao G, et al. Hepatology. 2007;46:932-938.

## Varices

Esophageal

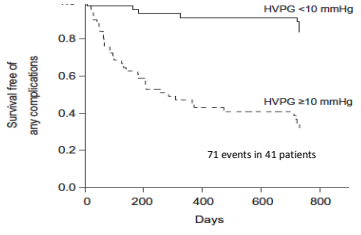


Gastric



Slide 20 of 43

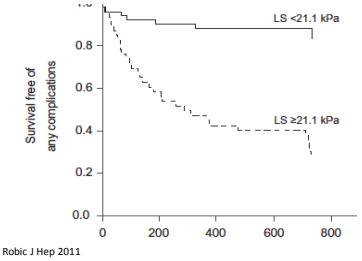
## Hepatic Venous Pressure to Predict Portal Hypertension




Robic J Hep 2011: 100 pts followed for 2y: ETOH 38; v hep 28: 75 F3-4

Slide 21 of 43

## Liver Stiffness to Predict Portal Hypertension




Robic J Hep 2011

Slide 22 of 43

## Ascites

- Most common complication of cirrhosis
  - Most common indication for hospitalization
- 15% with ascites die in 1 year
- 44% with ascites die in 5 years
- 85% of hospitalized patients with ascites have cirrhosis as cause of ascites

AASLD guidelines 2012

Slide 23 of 43

## Stages of Ascites

- Diuretic-responsive ascites
- Refractory ascites
- Hyponatremia
- Hepatorenal syndrome (HRS)

Each stage reflects a more deranged circulatory state.

Slide 24 of 43

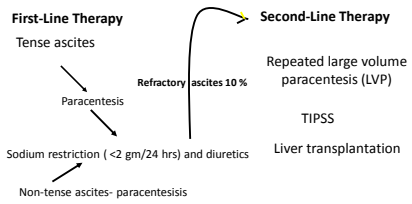
## When to Tap Ascites

- Diagnostic paracentesis with ALL new onset ascites (either inpatient or outpatient)
- FFP and/or platelets are NOT needed prior to the procedure
  - 1% reported rate of abdominal wall hematoma with 71% having abnormal prothrombin time

*Runyon Hepatology 2012*

Slide 25 of 43

## Management of Ascites




**Diuretics: Spironolactone 50-75 mg/day, furosemide 20-40 mg/day or bumetanide 1 mg. Titrate stepwise to spironolactone 400 mg/day, furosemide 160 mg/day or bumetanide 4 mg/day as long as it is tolerated AT 2-WEEK INTERVALS (electrolytes)**

Slide 26 of 43

## Spontaneous Bacterial Peritonitis (SBP)

- Most common type of bacterial infection in hospitalized cirrhotic patients
- Clinical suspicion:
  - <50%: fever, abdominal pain or tenderness, and leukocytosis
  - Unexplained encephalopathy, jaundice
  - Worsening renal failure
- Diagnose: tap ascites: WCC>500, **PMN > 250 cells/**$mm^3$
  - Place ascites in blood culture bottles
- Start treatment immediately before culture results

Slide 27 of 43

## SBP Treatment

- Cephalosporins 3rd gen ie cefotaxime 2g q8
- Renal dysfunction is main cause of death
  - Prevented by the use of intravenous albumin (1.5g/kg day 1 and 1.0 g/kg day 3) if
    - Serum bilirubin > 4 mg/dL
    - Serum creatinine > 1 g/dL
    - Or blood urea nitrogen level > 30 mg/dL
- Prevent recurrence: ciprofloxacin, TMP/SMX, norfloxacin
- Primary prophylaxis: ciprofloxacin weekly if MELD >12 all subjects, >9 with HIV

*Runyon Hepatology 2012*

Slide 28 of 43

## Hepatorenal Syndrome (HRS)

- Acute renal failure occurs in 14% to 25% of hospitalized patients with cirrhosis
- Most commonly prerenal failure (accounting for 60% to 80% of the cases)
  - HRS is a form of prerenal failure
- Results from vasodilatation and marked reduction in effective arterial blood volume leading to renal vasoconstriction
- Occurs in patients with refractory ascites and/or hyponatremia.

Slide 29 of 43

## Hepatorenal Syndrome

- Type 1 HRS: rapidly progressive renal failure in 2 weeks
  - With doubling serum creatinine to > 2.5 mg/dL
  - Or halving creatinine clearance to < 20 mL/min
  - Prognosis: < 50% survival at 1 month
- Type 2 HRS: slowly progressive
  - Increase in serum creatinine > 1.5 mg/dL
  - Creatinine clearance of < 40 mL/mi
  - Or a urine sodium < 10 mEq/d
  - Associated with ascites that is unresponsive to diuretic medications
  - Median survival: ~ 6 months

Slide 30 of 43

## HRS Treatment

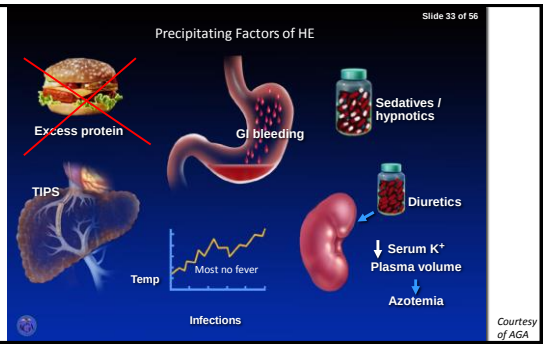
- OLT
- Midodrine and octreotide
  - HRS due to extreme splanchnic and systemic vasodilatation
  - Drugs → vasoconstriction
- Albumin to increase intravascular volume

Slide 31 of 43

## Hepatic Encephalopathy

- Results from a combination of
  - Portosystemic shunting and failure to metabolize neurotoxic substances
  - Ammonia remains the most important neurotoxic substance but poorly correlates with stage

Slide 32 of 43

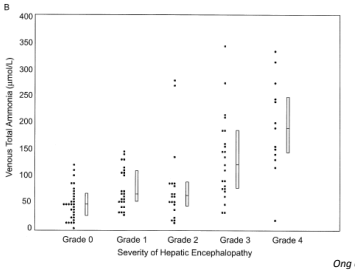



## Hepatic Encephalopathy

- Treatment aims to reduce production of NH3 from the colon through
  - Nonabsorbable disaccharides
    - Lactulose, lactitol, and lactose: 3-4 BM per day
  - Nonabsorbable antibiotics
    - Rifaximin 550 mg bid, neomycin rarely used
  - Protein restriction promotes protein degradation and, if maintained for long periods, worsens nutritional status and decreases muscle mass
    - No longer recommended

Slide 34 of 43

## Correlation Between Ammonia and Encephalopathy




*Ong et al, Am J Medicine, 2003*



## Hepatocellular Carcinoma (HCC)

- Late complication of end-stage liver disease
  - Exceptions: HBV seen in non cirrhotics
- Diagnosis by US, CT scan, MRI
  - Histology is not essential
- Alpha-fetoprotein level may be elevated
  - 20-40% with HCC have normal AFP
  - 20-30% without HCC have abnormal AFP
  - The higher the AFP, the more likely the diagnosis of HCC

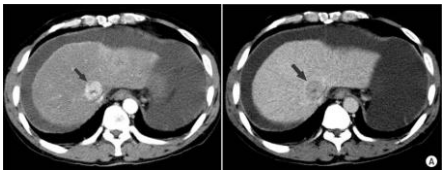


## Hepatocellular Carcinoma (HCC)

- Surveillance
  - Screen *all patients with cirrhosis* for HCC
    - Up to 8% risk of HCC/year
  - Also HBV: male>40y and female HBV >50y (even if they don't have cirrhosis)
    - Up to 0.6% risk of HCC/year
- Screen with ultrasound q 6 months
  - No benefit to shortening interval
  - ??No benefit to screening with AFP
  - In practice many still use cross-sectional imaging and AFP to screen as well

*Bruix et al Hepatology 2010*

## Quad Phase CT Appearance of HCC



Arterial Phase Portal venous Phase washout

Hypervascular lesion that washes out on portal venous phase

Slide 38 of 43

## Treatment of HCC

- Resection
- Local-regional therapy
  - TACE: transarterial chemoembolization
  - RFA: radiofrequency ablation
  - Ethanol ablation
- Liver transplantation
- Systemic
  - Sorafenib

Slide 39 of 43

## Local Regional Therapies for HCC

CHEMOEMBOLIZATION
- Conventional and Drug-eluting beads

ABLATION
- CHEMICAL
  - Percutaneous ethanol injection (PEI)
- THERMAL
  - Radiofrequency ablation (RFA) (Laparoscopic, percutaneous or open)
  - Microwave/ Cryoablation

RADIOEMBOLIZATION (YITTRIUM - 90)

Slide 40 of 43

## Take Home: HCC

- Screen ALL patients with u/s q6 months if they have cirrhosis
- Usually radiographic diagnosis
  - Biopsy rarely needed if classic imaging
  - Cross-sectional imaging look for "arterial enhancement" and "washout"
- Treatment:
  - Possibly "curative": ablation, resection, transplant
  - Palliative: TACE, sorafenib

Slide 41 of 43

## End Stage Liver Disease

- 5% to 7% of Child's A cirrhotics decompensate per year
- Diagnosis of Child's A, even B cirrhosis may be subtle
- Screen for HCC
- Perform EGD
- Monitor closely on therapy
- HCV with Child's B can be treated- OLT back up plan

Slide 42 of 43

## Question-and-Answer

Slide 43 of 43