The Liver for the Nonhepatologist

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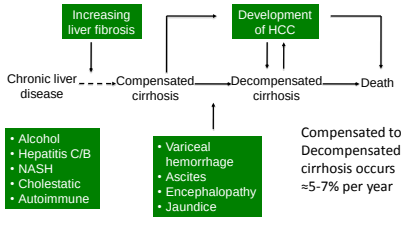
Learning Objectives

After attending this presentation, learners will be able to:

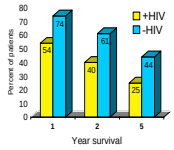
- Diagnose cirrhosis
- Assess for liver fibrosis
- Identify the complications of cirrhosis
- Manage the complications of cirrhosis

Natural History of ESLD



HCC, hepatocellular carcinoma; NASH, nonalcoholic steacohepatitis

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

Manage ESLD

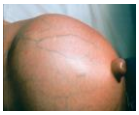
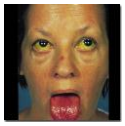
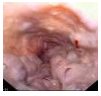
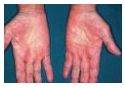
- Need to know if your patient has cirrhosis
- Need to know if compensated or decompensated
- Then need to manage complications

ARS Question #1

Which of the following statements is true?

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.

Diagnosing Cirrhosis – Physical Exam

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

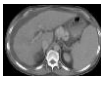
Portal Hypertension
- Thrombocytopenia
- Leukopenia
- Anemia

Renal dysfunction
- Elevated creatinine remember depends on muscle mass

Hyponatremia with ascites

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

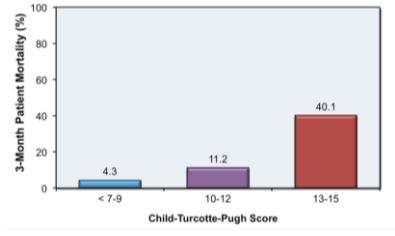


Prognosticating Decompensated Cirrhosis

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 Seconds prolonged or International normalized ratio	<4 <1.7	4-6 1.7-2.3	>6 >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-

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.

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

MELD

INR
Bilirubin
Creatinine

MELD Formula

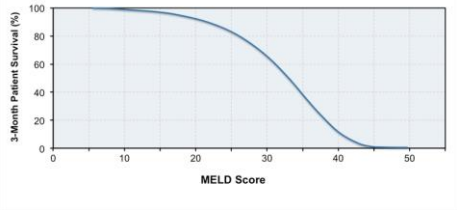
The MELD score is calculated using the following formula:

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.

3-Month Survival Based on MELD



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

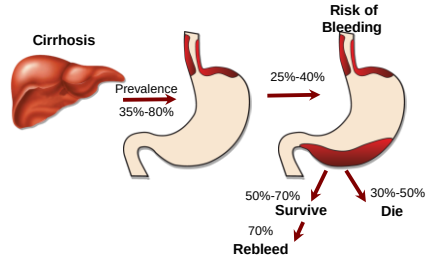
Steps in Assessing Cirrhosis

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

Which statement is true?

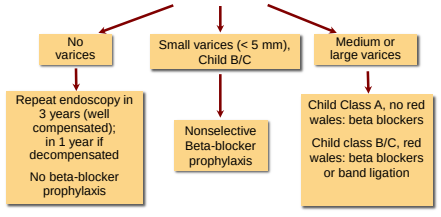
1. The prevalence of esophageal varices is low in cirrhotics.
2. Cirrhosis is the commonest cause of Ascites in hospitalized patients.
3. Spontaneous bacterial peritonitis is usually symptomatic.
4. Patients with hepatic encephalopathy should restrict protein intake.

Risk of Bleeding from Esophageal Varices



Variceal Surveillance

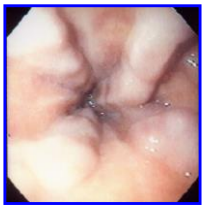
All cirrhotics require esophagogastroduodenoscopy.



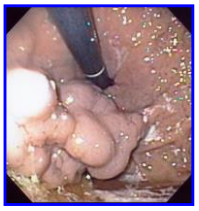
Garcia-Tsao G, et al. Hepatology. 2007;46:932-938.

Varices

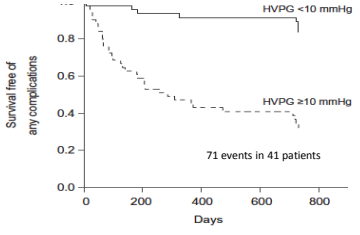
Esophageal



Gastric

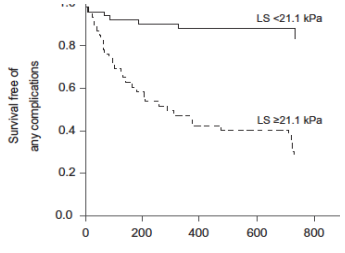


Hepatic Venous Pressure to Predict Portal Hypertension



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

Liver Stiffness to Predict Portal Hypertension



Robic J Hep 2011

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

Stages of Ascites

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

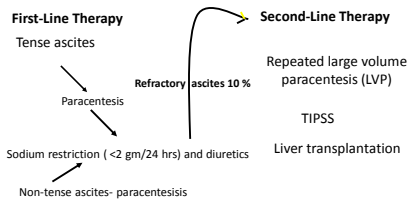
Each stage reflects a more deranged circulatory state.

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

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)

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

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

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.

Hepatorenal Syndrome

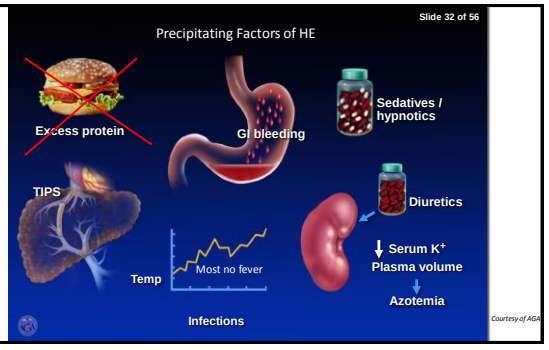
- Type 1 HRS: rapidly progressive renal failure in 2 weeks
  - With doubling serum creatinine to > 2.5 mg/dL
  - Or halving creatinine clearance to < 20 mL/min
  - Prognosis: < 50% survival at 1 month
- Type 2 HRS: slowly progressive
  - Increase in serum creatinine > 1.5 mg/dL
  - Creatinine clearance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

HRS Treatment

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

Hepatic Encephalopathy

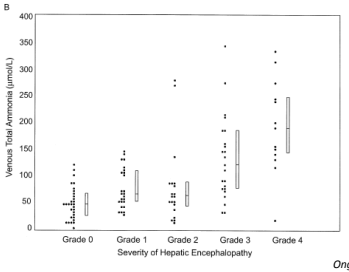
- Results from a combination of
  - Portosystemic shunting and failure to metabolize neurotoxic substances
  - Ammonia remains the most important neurotoxic substance but poorly correlates with stage



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

Correlation Between Ammonia and Encephalopathy



Ong et al, Am J Medicine, 2003

Hepatocellular Carcinoma (HCC)

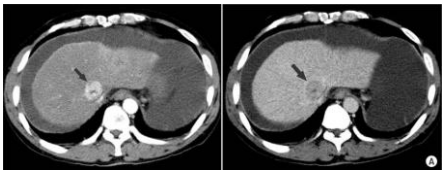
- Late complication of end-stage liver disease
  - Exceptions: HBV seen in non cirrhotics
- Diagnosis by US, CT scan, MRI
  - Histology is not essential
- Alpha-fetoprotein level may be elevated
  - 20-40% with HCC have normal AFP
  - 20-30% without HCC have abnormal AFP
  - The higher the AFP, the more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

Treatment of HCC

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

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)

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

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

Question-and-Answer

Remember to raise your hand and wait until you have the microphone before you ask your question—we are recording!

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