TIPS on Managing Decompensated Liver Disease

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Disclosures

- Gilead Speakers Bureau
- Abbvie Speakers Bureau
- Janssen Pharmaceuticals Consultant
Goals

- Definitions of Different States of Decompensated Liver Disease
- Primary Therapies
- Preventive Therapeutics
- Surveillance Guidelines
Question?

- From what origin does the word **cirrhosis** stem?
Cirrhosis

- Greek: kirrhos=yellow, -osis=condition of
- Late stage of scarring of the liver
- Stage 4 of the Metavir scoring system
Liver Biopsy Scoring System: Metavir

F = fibrosis

- F0 = no fibrosis
- F1 = portal fibrosis without septa
- F2 = portal fibrosis with rare septa
- F3 = numerous septa, not cirrhosis
- F4 = cirrhosis
Progression to Cirrhosis
## Four-Stage Cirrhosis Classification System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Compensated Cirrhosis</th>
<th>Decompenated Cirrhosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stage 1</td>
<td>Stage 2</td>
</tr>
<tr>
<td>Clinical</td>
<td>No Varices No Ascites</td>
<td>Varices No Ascites</td>
</tr>
<tr>
<td>Death (at 1 Year)</td>
<td>1%</td>
<td>3%</td>
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Survival in Patients with Compensated versus Decompensated Cirrhosis

Signs Associated With Diagnosis of Cirrhosis
Clubbing

- Heart, Lung and Endocrine disease
- GI diseases
  - Crohn’s and UC
  - Malabsorption
  - Cirrhosis (especially PBC)
  - Hepatopulmonary syndrome
- Caused from overproduction of hepatocyte growth factor/platelet derived growth factor and/or dysfunctional prostaglandin metabolism
Spider Angiomas

- 33% of cirrhotics have these
- Due to high levels of estrogen
- Seen in distribution of superior vena cava
- Fill from the center outwardly
- Due to failure of the sphincteric muscle surrounding cutaneous arteriole
- Can also see during pregnancy
Gynecomastia

- Due to decreased metabolism of estrogen
- Alcohol decreases production of testosterone

- What medication could also cause this?
Caput medusae (head of Medusa)

- “Palm tree sign”
- Due to porto-systemic collateral circulation via the umbilical vein
- Can also see in pregnancy—not cirrhotic!
Leukonychia

- “totalis”
  - Liver failure, kidney failure, malabsorption syndromes, sulfonamides

- “partialis”

- “striata”
  - Mees’ lines
    - Trauma, heavy metal poisoning (arsenic, lead), chemotherapy, severe illness with high fevers such as measles, malaria, herpes and leprosy
  - Cirrhosis
Signs Associated with Etiology

- Parotidomegally (EtOH)
- Peripheral Neuropathy (EtOH and some drugs)
- Cerebellar Signs (EtOH and Wilson’s disease)
- Kayser-Fleisher Rings (Wilson’s)
- Hepatomegaly (EtOH, NAFLD, Hemochromatosis)
- Increased skin pigmentation (Hemochromatosis)
- Diabetes (Hemochromatosis)
Dupuytren’s Contracture

- Fibrosis with shortening and thickening of the palmar aponeurosis
- Flexion contracture of the “ring and pinky” fingers into the palm of the hand
- Typically seen with alcoholic cirrhosis
- No real therapy
Other Signs/Labs of Cirrhosis

- Palmar erythema
- Testicular atrophy
- Anemia
- Bruising/bleeding dysfunction
- Jaundice (Bilirubin ~3.0)
- Wasting
- **Thrombocytopenia**, elevated PT/INR
- Hypoalbuminemia
- Hyponatremia
- Elevated ALT/AST
- Elevated GGT (seen mostly in EtOH liver disease)
Compensated vs. Decompensated Disease

- Compensated cirrhotics:
  - Do not have symptoms related to their cirrhosis, but may have non-bleeding esophageal or gastric varices

- Decompensated cirrhotics:
  - Have symptomatic complications related to cirrhosis, including those related to hepatic insufficiency (jaundice), and those related to portal hypertension (ascites, variceal hemorrhage, or hepatic encephalopathy)
Signs Associated with **Decompensated** Liver Disease

- Drowsiness (HE)
- Hyperventilation (HE)
- **Metabolic Flap/Asterixis** (HE)
- **Jaundice** (Excretory dysfunction), Scleral icterus
- Peripheral Edema (Hypoalbuminemia)
- Bruising (Coagulopathy)
- **Ascites** (Hypoalbuminemia)
- Variceal Hemorrhage
Decompensated Liver Disease

- Hepatic Encephalopathy
- Jaundice
- Variceal Hemorrhage
- Ascites
A new patient presents to your office and has a hx of never treated, “stable,” HCV cirrhosis. Hx of variceal hemorrhage s/p multiple bandings, old but not active jaundice, poorly controlled ascites, and active yet controlled hepatic encephalopathy. What should be your next, most important referral?

- A. GI/Hep for HCV therapy
- B. GI/Hep for banding
- C. GI/Hep for diuretic management
- D. GI/Hep for transplant evaluation
- E. IR for TIPS evaluation
Question?

- If a new patient presents to your office for evaluation and has a hx of never treated, “stable,” HCV cirrhosis and hx of variceal hemorrhage s/p multiple bandings, old but not active jaundice, poorly controlled ascites, and active yet controlled hepatic encephalopathy. What should be your next, most important referral?

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- D. **GI/Hep for transplant evaluation**
- E. IR for TIPS evaluation
Question?

You draw labs and see: WBC 3.6, Hgb 8.9, Plts 85, Na 130, K 3.6, BUN 45, Cr 1.2, Glucose 125, ALT 46, AST 54, Bili 1.4, PT 4.8, INR 1.7

What labs are used to calculate the MELD score?
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MELD Score

\[ 10 \times (0.957 \times \ln(\text{Creatinine})) + (0.378 \times \ln(\text{Bilirubin})) + (1.12 \times \ln(\text{INR})) + 6.43 \]

\[ \text{MELD} = 15 \]

3 month mortality is \(~6\%\)

Refer to Transplant Center if MELD >10
MELD Score

- The Model for End-Stage Liver Disease (MELD) system was implemented February 27, 2002 to prioritize patients waiting for a liver transplant.

- MELD is a numerical scale used for adult liver transplant candidates.

- The range is from 6 (less ill) to 40 (gravely ill).

- The score determines how urgently a patient needs a liver transplant within the next three months.

**FOLLOW THE MELD IN YOUR CHRONIC LIVER PATIENTS!**

- Use smartphone calculators/apps.
CAUTION
This Truck May Be Hauling
POLITICAL PROMISES!
49 y/o Asian, cirrhotic female with longstanding HBV (on therapy) presents with her husband for routine check-up. He is complaining that she is irritable, moody (more than normal) and is now sleeping all day and watches TV (can’t sleep) at night, which is interfering with his sleep. What is the next best step?

A. Refer to Gyn for hormonal therapy
B. Check ammonia level
C. Check ammonia level and treat only if it is elevated
D. Start Xifaxin
E. Send her to live with her mother
Question?

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- **E.** Send her to live with her mother
Hepatic Encephalopathy

- HE is a brain dysfunction caused by liver insufficiency and/or PSS; it is a wide spectrum of neurological or psychiatric abnormalities ranging from subclinical alterations to coma.

- Minimal, Covert, and Overt


Hepatic Encephalopathy

- Lactulose is first line therapy
- Rifaximin is “add-on” therapy after second recurrence
- Branched-chain amino acids
- Neomycin
- Metronidazole
- Zinc replacement, 220mg BID
Hepatic Encephalopathy

- Your patient with overt HE with continued asterixis on therapy follows up every few months but never seems to have any family with him at his visits.

- What are 2 important issues about this patient?
Hepatic Encephalopathy

- 1. Is he taking his medication appropriately?
- 2. How did he get to his office visit?

Free rectal photography with every Eye Test.
Gastroesophageal Varices

- 50% with cirrhosis
  - Childs Pugh A = 40%
  - Childs Pugh C = 85%

- If cirrhotic and no varices, will develop at ~8% per year
- If has varices, will bleed at ~5-15% per year
- Greatest predictor is size (large = 15% per year)
- Bleeding stops spontaneously ~40% of the time
- If bleed, mortality ~20% at 6 weeks
- Late rebleeding 60% of time if no intervention
Variceal Bleeding

- Esophageal
- Gastric
- Duodenal
- Rectal
Esophageal Varices

- No Varices $\rightarrow$ EGD in 3 years or if/when decompensates

- Small Varices
  - High Risk Stigmata $\rightarrow$ Prophylaxis
    - Never bled $\rightarrow$ beta blockers or banding
  - No Stigmata $\rightarrow$ Surveillance in 1 year

- Medium/Large Varices $\rightarrow$ Prophylaxis
  - Banding

- Still bleeding after 2 endoscopic interventions
  - Emergent TIPS
Variceal Bleeding

- **DO NOT FORGET ANTIBIOTICS WITH VARICEAL BLEEDING!**

- Intravenous ceftriaxone for 7 days or twice daily norfloxacin for 7 days should be given to prevent bacterial infections in patients with cirrhosis and gastrointestinal hemorrhage

- **DO NOT USE** beta blockers for variceal prophylaxis if the patient has ASCITES!
Ascites

- Once develops, 1-year survival is ~50%
- Increased BP in splanchnic bed
- Decreased albumin (oncotic pressure)
- Treatment does NOT enhance survival
  - (Tx improves QOL)
Ascites

- Paracenteses on **ALL** in/outpatients with **new ascites** or if ascites noted on **admitted** patients

- No FFP or platelets

- Cell count/diff, total protein, ascites albumin, cultures, AFP if bloody tap (draw serum albumin at same time!)

- SAAG > 1 is **CIRRHOSIS**, right heart failure, Budd-Chiari

- SAAG < 1 is ascites not associated with increased portal pressure, i.e., tuberculosis, pancreatitis, infection, serositis, peritoneal carcinomatosis


Ascites Treatment

- Spironolactone with/without Lasix
  - What ratio to start diuretic?
  - What doses are considered diuretic failure?
- Vaptans not recommended
- Repeat paracenteses (Albumin 6-8gm/liter if >5 liters removed)
- TIPS
- Peritoneovenous shunt
- Transplant
- Caution with beta blockers!!!
- Caution with NSAIDS, ACEs/ARBs!!!
Question?

- At what doses of Spironolactone and Lasix do you consider “diuretic failure”?
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- At what doses of Spironolactone and Lasix do you consider “diuretic failure”?

- 400mg Spironolactone and 160mg Lasix
Ascites/SBP Treatment

- If PMN count in fluid $\geq 250$ cells/mm$^3$ give Cefotaxime 2gm IV q 8 hours

- Oral ofloxacin (400 mg twice per day) can be considered a substitute for intravenous cefotaxime in inpatients without prior exposure to quinolones, vomiting, shock, grade II (or higher) hepatic encephalopathy, or serum creatinine greater than 3 mg/dL

- Clinical suspicion of SBP, who also have a serum creatinine $>1$ mg/dL, blood urea nitrogen $>30$ mg/dL, or total bilirubin $>4$ mg/dL should receive 1.5 g albumin per kg body weight within 6 hours of detection and 1.0 g/kg on day 3

Ascites/SBP Treatment

- Patients who have survived an episode of spontaneous bacterial peritonitis (SBP) should receive long-term prophylaxis with daily norfloxacin (or trimethoprim/sulfamethoxazole)

- Recurrence of SBP has been reported to be 69% in 1 year

- Norfloxacin 400 mg per day orally has been reported to successfully prevent SBP in (1) patients with low-protein ascites and (2) patients with prior SBP


Ascites/SBP Treatment

- Intravenous ceftriaxone for 7 days or twice daily norfloxacin for 7 days should be given to prevent bacterial infections in patients with cirrhosis and gastrointestinal hemorrhage. (Class I, Level A). Perhaps parenteral antibiotic, while the patient is bleeding and oral antibiotic after oral intake is resumed, for a total of 7 days, is a practical treatment regimen.

- A group in France reported a reduction in hospitalization mortality for patients with variceal hemorrhage from 43% to 15%.

- 5 trials in patients with cirrhosis and gastrointestinal bleeding has shown a survival advantage of 9.1%.


Ascites and PEG Tubes

- Percutaneous endoscopic gastrostomy **should be avoided** in patients with cirrhosis and ascites

- One study showed a 38.5%, 30-day mortality; 9 of 10 patients who died within 30 days had ascites at the time of tube placement

65 y/o cirrhotic female with longstanding autoimmune hepatitis now presents with increasing SOB over the past few weeks. Not tachycardic or hypotensive but SaO2 is 91% on room air. (No hx of tobacco use or lung disease.) You perform a CXR and see this. What is the most likely diagnosis?
Question?

- How would you **acutely** treat this condition?
  
  - A. Talc pleurodesis
  - B. Emergent chest tube
  - C. Therapeutic/diagnostic thoracentesis
  - D. Maximize diuretic therapy
  - E. CT chest to look for lung mass and/or infectious process
Hepatic Hydrothorax

• First line therapy is
  • Sodium restriction
  • Diuretics (Spironolactone and Lasix)

• DO NOT PLACE CHEST TUBES! CONTRAINDIANTED!

• Repeat thoracenteses

• TIPS for refractory hepatic hydrothorax
Hepatorenal Syndrome

1) cirrhosis with ascites
2) creatinine greater than 1.5 mg/dL
3) no improvement of serum creatinine (decrease to a level of 1.5 mg/dL or less) after at least two days with diuretic withdrawal and volume expansion with albumin
4) absence of shock
5) no current or recent treatment with nephrotoxic drugs
6) absence of parenchymal kidney disease, no proteinuria, >500 mg/day/microhematuria, >50 red blood cells per high power field, and no abnormal renal US

Hepatorenal Syndrome

- **Type I HRS**
  - **Rapidly progressive** reduction in renal function
  - A doubling of the initial serum creatinine to a level greater than 2.5 mg/dL or a 50% reduction of the initial 24-hour creatinine clearance to a level lower that 20 mL per minute in less than 2 weeks

- **Type II HRS**
  - **Slowly progressive** course
  - Commonly associated with death in patients who do not die of other complications of cirrhosis

HRS Treatment

- Albumin plus vasoactive drugs such as octreotide and midodrine should be considered in the treatment of type I HRS.
- Albumin plus norepinephrine should also be considered in the treatment of type I HRS, when the patient is in the intensive care unit.
- Patients with cirrhosis, ascites, and type I or type II HRS should have an expedited referral for liver transplantation.


Runyon BA, Hoefs JC, Morgan TR. Ascitic fluid analysis in malignancy-related ascites. Hepatology 1988; 8:1104-1109
Question?

- 52 y/o male with HCV cirrhosis develops a new, 2 cm liver lesion in the R hepatic lobe seen on a q 6 month screening US. What is the next best test?

- A. Repeat US in 3 months
- B. Repeat US in 6 months
- C. Dual phase CT of liver
- D. Triple phase CT of liver
- E. Contrast enhanced US with AFP
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Hepatocellular Carcinoma

- Hepatocellular carcinoma (HCC) is worldwide the 5th most common cancer in men and the 7th in women
- HCC represents the 3rd most frequent cause of cancer death worldwide
- In the US, the prevalence has increased from 2003-2012

Bruix J, Sherman M. Management of Hepatocellular Carcinoma, AASLD Guidelines. Hepatology 2010

Hepatocellular Carcinoma

- HBV and HCV infections account for ~78% of global HCC cases
- Eleven states had significant increases in incidence rates, with the highest APC (annual percent change in rate) reported for Oklahoma (11.7), Iowa (9.0), and Georgia (7.4)
- HCC is no longer a universal death sentence. HCC can now be prevented, detected early, and can be cured with appreciable frequency given early detection

Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. J Hepatol 2006;45:529--38
Liver nodule

< 1 cm

- Repeat US at 3 months
  - Growing/changing character
    - Investigate according to size
  - Stable

> 1 cm

- 4-phase MDCT/ dynamic contrast enhanced MRI

  - Arterial hypervascularity AND venous or delayed phase washout
    - Other contrast enhanced study (CT or MRI)
      - Yes
        - HCC
      - No
        - Biopsy
    - No
Hepatocellular Carcinoma

- Pathognomonic Finding on TRIPLE PHASE CT/MRI is:
  - Arterial (hepatic artery) phase hyperdense lesion with portal venous phase “washout”

HCC and Milan Criteria

- Can only pursue liver transplant if HCC lesions:
  - Single lesion <5 cm or,
  - No more than 3 lesions all less than 3 cm in size
    - (The 3 lesions cannot measure more than 9 cm cumulatively)
  - (Barcelona Clinic Liver Cancer Group, BCLC)
    - Single lesion < 2 cm or,
    - 3 lesions, <3 cm
Preventative Measures

- Vaccinate
  - Hepatitis A and B
  - Yearly Influenza
  - Pneumococcal
  - Shingles Vaccine?

- Avoid NSAIDs and Tylenol/tylenol containing products

- Absolutely NO ALCOHOL! No smoking/THC/drug use

- Dental referral if needed

- Refer for transplant evaluation EARLY!
  - Childs Pugh >7 or MELD >10
Cancer Screening

- Colon
- Breast
- Gynecologic
- Prostate
- Skin
- ENT?
Surveillance Measures

• Ultrasound q 6 months
• AFP with q 6 month lab work
• Follow MELD with clinic visits
• Variceal screening if indicated
• Vaccines if indicated
Goals

- Definitions of Different States of Decompensated Liver Disease
- Primary Therapies
- Preventive Therapeutics
- Surveillance Guidelines
GI References

- ASGE
- ACG
- Hepatitis C Online
  - [http://www.hepatitisc.uw.edu](http://www.hepatitisc.uw.edu)
- huntstefanie@hotmail.com
The “End”