Managing the Patient with Cirrhosis: New Guidelines

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Cirrhosis is a growing problem

• Prevalence exceeds > 1 million persons in the United States

• Hospitalizations for cirrhosis have increased by 90% and their rate now exceeds that for heart failure

• Mortality from cirrhosis has risen by 65% since 2008.

HCV, EtOH and NAFLD are the predominant causes of cirrhosis
What exam findings will be most helpful in diagnosing underlying cirrhosis?

Imaging is specific, but not sensitive for cirrhosis

There are several ways to diagnose cirrhosis
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- FIB-4 ≥ 2.67
- FibroTest ≥ 0.58 for ALD/viral
- FibroTest ≥ 0.48 for NAFLD

VCTE (Fibroscan)

- < 10 - <1% 3-year risk of decompensation and liver related death
- 10-15 – suggestive of advanced LD
- >15 – highly suggestive of advanced LD

The key factor in prognosis is whether the cirrhosis is compensated or not
What is Clinically Significant Portal HTN?

- LSM < 15 and PLT > 150 rules out CSPH
- In virus and/or alcohol related LD and non-obese (BMI <30 kg/m²) NASH - LSM ≥25 rules in CSPH
- In patients with virus and/or alcohol related and non-obese NASH with LSM <25:
  
  - LSM 20-25 and platelet count <150 or
  - LSM 15-20 kPa and platelet count < 110 (NAFLD) have a CSPH risk of at least 60%
We now recommend NSBB for the prevention of decompensation in CSPH!

- **Carvedilol** is preferred:
  - more effective in reducing HVPG
  - better tolerance than traditional NSBBs
  - shows improvement in survival compared to no active therapy

- Patients who are on NSBB for the prevention of decompensation do not need a screening endoscopy for the detection of varices

PREDESCI Trial – Lancet 2019

- Evaluated the role of NSBBs in patients with CSPH with no or small varices.
- Patients were randomized to propranolol (or carvedilol in cases where HVPG did not decline by 10% on propranolol) or placebo.
- Primary outcome - composite of decompensation (ascites, variceal hemorrhage, or encephalopathy) or death.
- The cumulative incidence of decompensation or death was significantly lower in the NSBB group compared with placebo (hazard ratio, 0.51; 95% confidence interval, 0.26–0.97). NNT = 9.
- Major complication prevented was ascites.

Decompensation of Cirrhosis

- **Ascites**
- **Varices**
- **Encephalopathy**
Ascites

Typically the first decompensating event

5-year survival falls from 80% to 30%

Paracentesis is safe in cirrhosis

• No need for routine FFP or PLT transfusions

1% complication risk = abdominal wall hematoma

Despite elevated INR in 70% of pts.

Runyon BA. Arch Intern Med 1986;146:2259-2261.

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Despite elevated INR in 70% of pts.
Hemoperitoneum or bowel perforation < 1/1000
Study of 1100 therapeutic taps – no complications
Many with low plts and high INR
Study of 4700 pts – 9 bleeds, 8 in AKI

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What tests should you order on ascites?

A simple set of ascites values gives the most information

- Always perform paracentesis in new ascites
- Obtain albumin, TP and cell count
- Cultures if possible

<table>
<thead>
<tr>
<th>SAAG &gt; 1.1</th>
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<tr>
<td>TP &lt; 2.5</td>
<td>Malignancy</td>
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<tr>
<td>TP &gt; 2.5</td>
<td>Infection</td>
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Sodium restriction is crucial, but fluid restriction is not

Treat ascites with: Na restriction (2000 mg/day) and diuretics

- Max doses: 400 spironolactone
  160 furosemide

- Dose spironolactone QD, furosemide QD or BID

- No fluid restriction unless NA < 125

Spironolactone may be associated with painful gynecomastia

Alternatives:

- Eplerenone (50 mg = 100 mg spironolactone)
- Amiloride (10mg = 100 spironolactone)
Refractory ascites can be treated in a number of ways

Repeated LVP with albumin support
6-8 gm albumin/liter if >5 liters removed

TIPS in selected patients
Child score <12 and bilirubin <5.8 g/dl with preserved cardiac function
Consider liver transplant evaluation
PV shunt if not a candidate for transplant, TIPS

Review the med list in patients with ascites

• No NSAIDs
• ACE and ARB should be used with caution
• Refractory ascites
  B-blockers may be risky
  No ACE/ARB
The Beta-Blocker Controversy

In refractory ascites, one study showed increased mortality

Subsequent studies did not

Guidelines – avoid higher doses (propranolol 160, nadolol 80)

Avoid if SBP < 90, Na < 130, or worsening renal function

SBP is best treated with 3rd generation cephalosporin or quinolone

• SBP → 250 PMN
  • 3rd gen cephalosporin– cefotaxime 2 gm q 8 hrs
  • Oral ciprofloxacin in mild cases
  • Borderline cell count and signs of infection = treat

Albumin if: Cr > 1, BUN > 30, bilirubin > 4
  Give 1.5g/kg on day 1 → 1 gm/kg on day
  EASL recommends albumin in all SBP, HRS risk is 30%
Prophylactic antibiotics prevent recurrent SBP

• Secondary prophylaxis with daily quinolone, rifaximin, or TMP/SMX – intermittent Rx is less effective

• May use primary prophylaxis if ascites TP < 1.5 with Cr > 1.2, Na < 130, bili > 3.

What is a “normal” creatinine in cirrhotic patients?

Serum creatinine in cirrhotics should be < 1.0

Cr > 1.5 = GFR of 30-40

Cr > 1.0 = GFR of 60
Hepatorenal Syndrome is often difficult to diagnose

- Cirrhosis with ascites
- Serum creatinine > 1.5 mg/dl
- Absence of hypovolemia → no improvement after 2 days of diuretic withdrawal, albumin 1 g/kg/day up to a maximum of 100 g/day

Hepatorenal Syndrome is often difficult to diagnose

- Absence of shock
- No current or recent treatment with nephrotoxic drugs
- Absence of parenchymal renal disease
  - Proteinuria < 0.5 g/day
  - Microhaematuria < 50 red cells/HPF
  - Normal renal U/S

General approach to HRS

- Look for infection
- Paracentesis for comfort – limited data
  - Some choose to tap only 3-5 liters
- Stop diuretics
  - May use furosemide to stimulate U/O once diagnosis is established
  - Avoid spironolactone
Medical therapies for HRS
• Albumin, midodrine, octreotide
• Albumin, norepinephrine
• Liver txp referral
• Terlipressin/albumin – not yet available in US

CONFIRM trial – NEJM 2021
300 patients with HRS
Terlipressin 1 gm IV q 6 hrs
HRS reversal higher in terlipressin group – 32% vs. 17%, but no improved survival
Increased resp. failure in terlipressin group
Caveats – Cr > 2.25 is very high
Albumin given in 83%

ATTIRE trial – NEJM 2021
777 patient with decompensated cirrhosis
Daily albumin infusion to maintain serum ALB > 3.0
Primary end point = infection, renal failure, or death
No difference b/n groups
Albumin group had more severe or life-threatening serious adverse events, especially pulmonary edema or fluid overload.
Hepatic Encephalopathy is usually triggered by a clinical change

• Look for a reason!

• Ammonia level is not usually helpful

• Overt HE – Lactulose is first line

• Rifaximin is an add-on or a prophylactic therapy

Dietary Recommendations for Hepatic Encephalopathy

• Muscle is critical for the metabolism of ammonia - recommend 1 gram dietary protein per kilogram actual bodyweight

• Patients with cirrhosis have inadequate gluconeogenesis:
  - Avoid fasting
  - Have high-calorie/high-protein night-time or early-morning snack

• Branched-chain amino acids are frequently supplemented but may not be required if adequate protein intake

Variceal Hemorrhage requires medical and endoscopic therapy

Transfusion – to Hgb of 8, avoid overdoing fluids

Octreotide for 3-5 days (3 is OK)

IV CTX or ciprofloxacin for 5 days – may give IV in house and switch to oral at D/C
Antibiotics for GI Bleeding Improve Outcomes in Cirrhosis

12 trials (1241 pts)

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<th>Condition</th>
<th>RR</th>
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<tr>
<td>SBP</td>
<td>0.29</td>
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<tr>
<td>Bacterial infection</td>
<td>0.43</td>
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<tr>
<td>PNA</td>
<td>0.45</td>
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<tr>
<td>Rebleeding</td>
<td>0.53</td>
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<tr>
<td>Mortality</td>
<td>0.79</td>
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Cochrane Systematic Review 2010

Variceal Hemorrhage requires medical and endoscopic therapy

EGD within 12 hours

TIPS if not controlled

Embolization of varices via IR
Muscle cramps are common in patients with cirrhosis
- Seen in up to 1/3 of patients with cirrhosis
- Therapies:
  - Electrolyte repletion
  - Baclofen 10 TID
  - Taurine
  - Zinc

Patients with cirrhosis are at risk for sarcopenia
- Results from malnutrition, hyperammonemia, negative energy balance (particularly due to ascites or fasting)
- Potent predictor of falls, HE and mortality.
- Nutritional management of sarcopenia and frailty:
  - late-night snacks
  - avoiding fasting
  - high (1g/kg/day) protein and calorie (~30 kcal/kg/day) consumption,
  - increasing physical activity.

Pruritus is common in patients with hyperbilirubinemia or Primary Biliary Cholangitis

Therapeutic options:
- Cholestyramine
- Gabapentin
- Rifampin
- Naltrexone
References


• Wong F et al. Terlipressin plus Albumin for the Treatment of Type 1 Hepatorenal Syndrome. NEJM 2021 Mar;4;384(9):818-826


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