Management of Ascites

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I have no disclosures to make relative to my presentation.

Cirrhosis is the Most Common Cause of Ascites

Source of the main 3 causes of ascites

<table>
<thead>
<tr>
<th>Entity</th>
<th>Source</th>
<th>Pathophysiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>Hepatic sinusoid</td>
<td>Patients with cirrhotic ascites have an HVPG of at least 12 mmHg (nl 3-5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Morali et al. J Hepatol 2002</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Hepatic sinusoid</td>
<td>Congestion of liver due to right heart failure (post-hepatic block)</td>
</tr>
<tr>
<td>Peritoneal malignancy/TB</td>
<td>Peritoneum</td>
<td>Inflammation or infiltration of the peritoneum</td>
</tr>
</tbody>
</table>
The Serum-Ascites Albumin Gradient (SAAG) Correlates With Sinusoidal Pressure

The rationale behind the Serum-Ascites Albumin Gradient (SAAG)

Serum – ascites albumin gradient (g/dL)

SAAG (g/dL) vs. HVPG (mmHg) for Cirrhotic ascites, Cardiac ascites, Peritoneal malignancy

SAAG is an indicator of sinusoidal pressure. If > 1.1 ascites is coming from the sinusoid.

Serum-Ascites Albumin Gradient and Ascites Protein Levels in the Most Common Causes of Ascites

<table>
<thead>
<tr>
<th>CAUSE</th>
<th>Serum-Ascites Albumin Gradient (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhotic ascites</td>
<td>1.1-4.0</td>
</tr>
<tr>
<td>Cardiac ascites</td>
<td>0.8-2.0</td>
</tr>
<tr>
<td>Peritoneal malignancy</td>
<td>0.6-2.8</td>
</tr>
</tbody>
</table>

SIN = Sinusoidal + PER = Portal

SAAG = Serum – Ascites albumin
The permeability of the hepatic sinusoid varies in health and disease.

In cirrhosis, the hepatic sinusoid is less leaky.

Hepatocytes

The normal sinusoid is "leaky".

Sinusoid

Fibrous tissue deposition

Cirrhotic ascites

Cardiac ascites

Peritoneal malignancy

1.1

3.0

2.0

1.0

0

Serum – ascites albumin gradient (g/dL)

Ascitic fluid total protein (g/dL)

SAAG is an indicator of sinusoidal pressure. If >1.1 ascites is coming from the sinusoid.

Ascites protein is an indicator of leakiness of sinusoid, >2.5 the sinusoid is leaky (i.e. normal).

CONDITION

SAAG

ASCITES PROTEIN

Cirrhosis

high

low

Peritoneal malignancy

low

high

Heart failure

high

high

Cutoff

1.1 g/dL

2.5 g/dL
Serum BNP has a higher diagnostic accuracy for cardiac ascites than SAAG/ascites protein

Patients with new onset ascites

Farias et al. Hepatology 2014; 59:1043-51

<table>
<thead>
<tr>
<th>Test</th>
<th>LR (+) (rules in)</th>
<th>LR(-) (rules out)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAAG &gt;1.1; prot &gt;2.5</td>
<td>9.63</td>
<td>1.272</td>
</tr>
<tr>
<td>Serum BNP &gt;364 pg/mL</td>
<td>168.09</td>
<td></td>
</tr>
<tr>
<td>SAAG &lt;1.1; prot &lt; 2.5</td>
<td>1.272</td>
<td>0.000</td>
</tr>
<tr>
<td>Serum BNP &lt; 182 pg/mL</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Natural History of Chronic Liver Disease

Chronic liver disease → Compensated cirrhosis → Decompensated cirrhosis → Death

VH = variceal hemorrhage

In a cohort of patients with compensated cirrhosis, ascites was the most common decompensating event

D'Amico G. Gastroenterology 2001; 120: A2
Intrahepatic resistance

Portal (sinusoidal) hypertension

Splanchnic / systemic vasodilatation

Effective arterial blood volume

Activation of neurohumoral systems

Cirrhosis

Ascites

Spironolactone is More Effective Than Furosemide in Uncomplicated Ascites

<table>
<thead>
<tr>
<th>Response</th>
<th>No response</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone (150-300 mg/d)</td>
<td>18</td>
<td>1</td>
</tr>
<tr>
<td>Furosemide (80-160 mg/d)</td>
<td>11</td>
<td>10</td>
</tr>
</tbody>
</table>

Perez-Ayuso et al. Gastroenterology 1983; 84:961

Treatment of ascites

- Not an emergency, treat ascites in a stepwise unhurried manner
- Other complications (GI bleed AKI, infection) are absent or have resolved
- If patient uncomfortable → large volume paracentesis
- Treatment aimed at achieving a negative sodium balance
Less frequent dose reductions are needed when spironolactone is started alone

<table>
<thead>
<tr>
<th></th>
<th>Spironolactone alone*</th>
<th>Spironolactone + Furosemide</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=50)</td>
<td>(n=50)</td>
<td></td>
</tr>
<tr>
<td>Response Rate</td>
<td>94%</td>
<td>98%</td>
</tr>
<tr>
<td>Time to Response</td>
<td>12.8 days</td>
<td>12.3 days</td>
</tr>
<tr>
<td>Dose reduction needed</td>
<td>34%</td>
<td>68%</td>
</tr>
</tbody>
</table>

Santos et al., J Hepatol 2003; 39:187
* Followed by furosemide if necessary

In addition to spironolactone-based diuretics....

- Salt restriction (2g/day = ~90mEq/day)
  - Do not compromise nutritional status
- Avoid non-steroidal anti-inflammatory drugs
- No water restriction unless serum Na <130 mEq/L
- Low threshold to perform a diagnostic paracentesis to investigate SBP

Management of Ascites

- Follow weight and labs (BUN, creatinine, lytes)
- Weight loss goals
  - 2-3 lb a week; no more than 1 lb / day
- If no weight loss
  - Make sure patient is not on NSAIDs
  - Check urine Na. If any of the following, patient is eating too much salt:
    - > 50 mEq/L or greater than daily Na intake
    - Spot UNa >UK (correlates with a 24-hour sodium excretion >78 mEq/L)
Hepatic Hydrothorax

- Occurs in ~6% of patients with cirrhosis

- Due to trans-diaphragmatic movement of fluid from the peritoneum to the pleural space through diaphragmatic defects

- Management same as for cirrhotic ascites

Krok KL, Cardenas A. Semin Respir Crit Care Med 2012; 33: 3-10.

Cirrhosis

- Intrahepatic resistance
- Portal (sinusoidal) hypertension
  - Splanchnic / systemic vasodilatation
  - Effective arterial blood volume
  - Activation of neurohumoral systems

- Sodium retention
- Ascites
- Refractory Ascites

Large volume-paracentesis (LVP):
- Local therapy
- Recurrence of ascites is the rule
- May be associated with post-paracentesis circulatory dysfunction
LVP Without Albumin Leads to Increases in Renin, Renal Failure and Hyponatremia

Gines et al., Gastroenterology 1988; 94:1493

Consequences of post-paracentesis circulatory dysfunction (PCD)

- Shorter time to ascites recurrence
- Higher incidence of hyponatremia and renal dysfunction
- Higher mortality

Gines et al., Gastroenterology 1988; 94:1493; Gines et al., Gastroenterology 1996; 111:1002; Ruiz del Arbol et al., Gastroenterology 1997; 113:579

Post-paracentesis circulatory dysfunction (PCD) is lowest in patients receiving albumin after LVP

Gines et al., Gastroenterology 1988; 94:1493; Gines et al., Gastroenterology 1996; 111:1002; Sola-Vera et al., Hepatology 2003; 37:1147

*6-8 g per liter of ascites removed
Intrahepatic resistance
Portal (sinusoidal) hypertension
Cirrhosis

Ascites

Splanchnic / systemic vasodilatation

Effective arterial blood volume

Renal vasoconstriction

Water retention

Sodium retention

Refractory Ascites

Hyponatremia

Hepatorenal syndrome

Activation of neurohumoral systems

Other volume expanders? Vasoconstrictors?

LVP

Compared to alternative treatment, albumin reduces the rate of PCD

Recurrence of ascites is no different in patients treated with LVP + albumin vs. octreotide/midodrine


Bari et al. Accepted Clin Gastroenterol Hepatol.
In refractory ascites, TIPS is more effective than LVP in preventing ascites recurrence

<table>
<thead>
<tr>
<th>Event</th>
<th>Better TIPS</th>
<th>Better LVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrence of ascites</td>
<td>0.14 (0.08-0.28)</td>
<td></td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>2.34 (1.41-3.87)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0.90 (0.44-1.81)</td>
<td></td>
</tr>
<tr>
<td>Death (excluding Lebrec)</td>
<td>0.74 (0.40-1.37)</td>
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In a meta-analysis of individual patient data, survival was better with TIPS than LVP

Greater survival benefit in patients treated with TIPS who had a MELD score <15

Greater survival benefit in patients treated with TIPS who had a MELD score <15

TIPS= transjugular intrahepatic portosystemic shunt
LVP= large-volume paracentesis

*individual data meta-analysis
Refractory hepatic hydrothorax

- A trial of in-hospital diuretic therapy should be attempted
- Serial thoracenteses – may be required too frequently
- Chest tube or indwelling catheter should not be placed (→ infection, AKI)
- TIPS may need to be considered earlier
  - Clinical response (67%) and survival are also associated with pre-TIPS MELD <15

In patients with large varices that have not bled, a decrease in HVPG >10% leads to less ascites, RA and HRS.

**Cirrhotic ascites**

- The most common decompensating event in cirrhosis
- It is not an emergency unless complicated by infection or hepatorenal syndrome
- Ideal treatment strategies should be based on its pathophysiology
  - Increase sodium excretion
  - Decrease sinusoidal pressure
  - Remove fluid while replenishing intravascular volume