Complications of Portal Hypertension: What to Do?

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Medical Director of Liver Transplantation
Director of Hepatology
Lahey Hospital and Medical Center
Associate Professor of Medicine
Tufts University School of Medicine

Agenda

• Pathophysiology of portal hypertension

• Portal hypertensive bleeding
  – Endoscopic
  – Radiologic
  – Surgical

• Ascites
  – Radiologic
 ALTERATIONS IN MICROVASCULATURE IN CIRRHOSIS

- Activation of stellate cells
- Collagen deposition in space of Disse
- Constriction of sinusoids
- Defenestration of sinusoids
Poiseuille’s Law

\[ R = \frac{8 \eta l}{\pi r^4} \]

**Increased Resistance in Cirrhosis is Due to a Reduction in the Sinusoidal Radius**

**Normal**

- Hepatocytes
- Sinusoid

**Cirrhosis**

- Fibrous tissue deposition
- Increased resistance

\[ \Delta R = 16x \]
\[ \Delta R = 256x \]
Mechanisms of Portal Hypertension

- Pressure ($P$) results from the interaction of resistance ($R$) and flow ($Q$):
  
  \[ P = Q \times R \]

- Portal hypertension can result from:
  - increase in resistance to portal flow and/or
  - increase in portal venous inflow

In Cirrhosis:

- Increased intrahepatic resistance is the initial mechanism leading to portal hypertension
NORMALLY, INCREASES IN PORTAL FLOW CAUSES NO INCREASE IN PORTAL PRESSURE

Fasting  \[ P = Q \times R \]  Post-prandial

Portal flow = 700 ml/min  Portal flow = 1500 ml/min

IN CIRRHOSIS, SMALL INCREASES IN PORTAL FLOW PRODUCE LARGE INCREASES IN PORTAL PRESSURE

Fasting  \[ P = Q \times R \]  Post-prandial

Portal flow = 700 ml/min  Portal flow = 1500 ml/min
Portal-Systemic Collaterals

In Cirrhosis:

Increased intrahepatic resistance is the initial mechanism leading to portal hypertension but is also influenced by increased portal inflow.
Variceal Bleeding

Treatment of Acute Variceal Bleeding

- Pharmacologic therapy
  - Goal: Reduction of portal pressure
  - Octreotide
  - Non-specific beta-blockers
- Sengstaken-Blakemore tube
- Endoscopic therapy
  - Goal: Obstruction of blood flow
  - Sclerotherapy
  - Band Ligation
- TIPS
  - Goal: Reduction of portal pressure
Covered Stents Are More Likely to Remain Functional Than Uncovered Stents

Bureau et al. Gastroenterology 2004; 126:469
Band Ligation vs. Early TIPS

- 63 pts with acute variceal bleeding
  - CTP 7-13
  - 82% had exclusion criteria
  - Bleeding controlled with pharmacotherapy and endoscopy within 12 hours

- Randomized to:
  - Pharmacotherapy + EBL
  - Covered TIPS within 72 hours

### Primary Prophylaxis

#### Banding vs. Beta-blockers (Mortality)

<table>
<thead>
<tr>
<th>Study</th>
<th>Banding (n/N)</th>
<th>Beta-Blockers (n/N)</th>
<th>Risk Ratio, M-H, Random, 95% CI</th>
<th>Risk Ratio</th>
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Gluud, Krag, Cochran Collab, 2012

\[ p = 0.08 \]

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<td>16/50</td>
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<td>11/15</td>
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<td>1.88</td>
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<tr>
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<td>5/31</td>
<td>4/31</td>
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</table>

Gluud, Krag, Cochran Collab, 2012

\[ p = 0.13 \]
“Nonselective” Shunts for Variceal Bleeding

- End to Side
- Side to Side

- Meso-caval
- Porto-renal

Distal Splenorenal Shunt
**Distal Splenorenal Shunt**

- **Advantages**
  - preservation of portal flow (early)
  - decompression of gastric & esophageal varices
  - avoidance of hepatic hilum
  - relief of hypersplenism
  - refractory encephalopathy rare
- **Disadvantages**
  - late reduction in portal perfusion
  - technically demanding
  - aggravation of ascites
  - potential for complications:
    - portal vein thrombosis
    - pancreatic pseudocyst

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**The Role of the Distal Splenorenal Shunt (DSRS) In The Modern Era of Liver Transplantation**

- Determine the clinical outcome of cirrhotic patients after DSRS for recurrent variceal bleeding (failed medical therapy) or those with gastric varices or portal HTN gastropathy

- 41 Consecutive patients with well-compensated cirrhosis who underwent DSRS between 9/1999-12/2011 at the Lahey Clinic

### Pre-operative clinical features

<table>
<thead>
<tr>
<th>Feature</th>
<th>Count</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Alcoholic liver disease</td>
<td>15</td>
<td>36.6%</td>
</tr>
<tr>
<td>Child-Turcotte-Pugh classification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Class A</td>
<td>29</td>
<td>70.7%</td>
</tr>
<tr>
<td>- Class B</td>
<td>12</td>
<td>29.3%</td>
</tr>
<tr>
<td>Ascites (medically-controlled)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>29.3%</td>
</tr>
<tr>
<td>Encephalopathy grade I-II</td>
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<td></td>
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<tr>
<td></td>
<td>7</td>
<td>17.1%</td>
</tr>
<tr>
<td>Thrombosed TIPS</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>6</td>
<td>14.6%</td>
</tr>
</tbody>
</table>

### Post-operative complications after DSRS

<table>
<thead>
<tr>
<th>Complication</th>
<th>Count</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Overall Morbidity</td>
<td>17</td>
<td>41.5%</td>
</tr>
<tr>
<td>- Progressive ascites</td>
<td>6</td>
<td>14.6%</td>
</tr>
<tr>
<td>- Wound complication (wound infection, dehiscence, incisional hernia)</td>
<td>6</td>
<td>14.6%</td>
</tr>
<tr>
<td>- Non surgical site infection</td>
<td>6</td>
<td>14.6%</td>
</tr>
<tr>
<td>- Hepatic encephalopathy</td>
<td>3</td>
<td>7.3%</td>
</tr>
<tr>
<td>- Intra-abdominal collection</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>- Atelectasis</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>- Recurrent variceal bleeding</td>
<td>1</td>
<td>2.4%</td>
</tr>
<tr>
<td>- Myocardial infarction</td>
<td>1</td>
<td>2.4%</td>
</tr>
</tbody>
</table>
Multivariate logistic regression analysis: Overall mortality rate

<table>
<thead>
<tr>
<th>Factors</th>
<th>Odds ratio (95% CI)</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Age &gt; 60</td>
<td>4.05 (0.32-51.15)</td>
<td>0.28</td>
</tr>
<tr>
<td>Male gender</td>
<td>8.28 (0.51-134.89)</td>
<td>0.14</td>
</tr>
<tr>
<td>Non-alcoholic, non-cholestatic disease†</td>
<td>0.38 (0.06-2.37)</td>
<td>0.30</td>
</tr>
<tr>
<td>Previously-performed TIPS</td>
<td>1.74 (0.15-20.36)</td>
<td>0.66</td>
</tr>
<tr>
<td>Ascites</td>
<td>13.09 (1.24-137.95)</td>
<td>0.03 *</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>2.44 (0.21-28.63)</td>
<td>0.48</td>
</tr>
<tr>
<td>Total bilirubin &gt; 2</td>
<td>0.99 (0.09-11.23)</td>
<td>0.99</td>
</tr>
<tr>
<td>Albumin &lt; 3.5</td>
<td>0.81 (0.12-5.52)</td>
<td>0.83</td>
</tr>
<tr>
<td>INR &gt; 1.2</td>
<td>9.11 (0.33-249.25)</td>
<td>0.19</td>
</tr>
<tr>
<td>Platelet &lt; 100</td>
<td>0.37 (0.04-3.88)</td>
<td>0.41</td>
</tr>
<tr>
<td>Creatinine &gt; 1</td>
<td>0.47 (0.05-4.45)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

† cause of portal hypertension: “non-alcoholic, non-cholestatic disease” (viral hepatitis, NASH, PV thrombosis, cryptogenic) compared to reference group (alcoholic, cholestatic cause such as PBC, PSC)
Acute Variceal Bleed

Endoscopic/Pharmacologic control

if bleeding recurs

Endoscopic/Pharmacologic control

Child's A

DSRS

Child's B/C

TIPS ± OLTx

Portal Hypertensive Gastropathy

- Associated with portal HTN
- Fundus most frequently affected

Carpinelli et al. Ital J Gastroenterol Hepatol 1997; 29:533
Management of Acute Bleeding from Portal Hypertensive Gastropathy

- Similar principles to esophageal variceal bleeding
- Portal pressure lowering drug (i.e. octreotide)
- Endoscopy
- Temporizing measures
  - Focal coagulation
  - Band ligation

Ripoll C, Garcia-Tsao G. Dig Liver Dis 2011;345-351

Management of Chronic Bleeding from Portal Hypertensive Gastropathy

**Initial medical management**
(Non-Cardioselective beta-blockers and iron supplement)
Management of Chronic Bleeding from Portal Hypertensive Gastropathy

Initial medical management (Non-Cardioselective beta-blockers and iron supplement)

Bleeding controlled?

YES

Continue medical therapy

Bleeding controlled?

NO

Transfusion dependent?

NO

Blood transfusion as needed

YES

Continue medical therapy
Management of Chronic Bleeding from Portal Hypertensive Gastropathy

**Initial medical management**
(Non-Cardioselective beta-blockers and iron supplement)

- **Bleeding controlled?**
  - YES
  - NO

- **Transfusion dependent?**
  - YES
  - NO

- **Continue medical therapy**

- **Blood transfusion as needed**

---

**Management of Chronic Bleeding from Portal Hypertensive Gastropathy: Is There a Role for Endoscopy?**

- Historically, PHG does not respond to argon plasma coagulation (APC)
  - 11 pts with PHG acute and chronic bleeding
  - Treatment: APC q2-4wks until obliteration
  - Success = fewer transfusions, Hct ≥ 30% or Hct ≥ baseline + 10%
  - Mean sessions per pt: 2.2 ± 2.0
  - 81% success
Gastric Antral Vascular Ectasia (GAVE)

- Endoscopic findings:
  - Red spots without background mosaic pattern
  - Linear aggregates in antrum: “watermelon stomach”
  - Diffuse lesions in proximal and distal stomach

- Often occurs in absence of portal hypertension

- May be difficult to differentiate from portal hypertensive gastropathy (PHG)

- Ideal therapy not known

Typical Gastric Antral Vascular Ectasia
Severe PHG May be Difficult to Distinguish from Diffuse GAVE

Endoscopy and Biopsy Distinguish Between Portal Hypertensive Gastropathy (PHG) and Gastric Antral Vascular Ectasia (GAVE)

<table>
<thead>
<tr>
<th></th>
<th>PHG</th>
<th>GAVE</th>
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<tbody>
<tr>
<td>Distribution in stomach</td>
<td>Proximal</td>
<td>Distal</td>
</tr>
<tr>
<td>Mosaic pattern</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Red signs</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Biopsy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombi</td>
<td>-</td>
<td>+ ++</td>
</tr>
<tr>
<td>Spindle cell proliferation</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Fibrohyalinosis</td>
<td>+</td>
<td>+ + +</td>
</tr>
<tr>
<td>Treatment:</td>
<td>Beta blockers ? Transplant</td>
<td>TIPS</td>
</tr>
</tbody>
</table>
Management of Chronic Bleeding from GAVE: Is There a Role for Endoscopy?

- Primary treatment is endoscopic
  - APC
    - Lower risk of perforation
    - Focal and “paint brush”
    - Repeat q2-6 weeks
  - Nd:YAG laser
    - Higher risk of perforation
    - Rapid response
    - Repeat q2-4 weeks

- Surgery for treatment failure
  - Antrectomy
  - Liver transplantation, if cirrhotic

Ripoll C, Garcia-Tsao G. Dig Dis 2011;345-351

Ascites
**The Development of Ascites**

**The Revised Underfill Theory**

- Peripheral vasodilation occurs as the result of decreased hepatic clearance of vasodilators such as glucagon and NO.
- The body compensates for the perceived drop in circulating blood volume in two ways:
  - increased cardiac output (Q)
  - activation of the renin-angiotensin system resulting in increased renal retention of sodium and free water.

---

**Initial Workup of Ascites**

**Diagnostic Paracentesis**

- Glucose, LDH
- Optional: Protein/Albumin, Amylase, Cytology
- PMN count, Culture
- ? secondary infection
- ? cirrhotic ascites
- ? pancreatic ascites
- ? SBP
- ? malignant ascites

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ACG Regional Postgraduate Course - Los Angeles, CA
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Serum Ascites Albumin Gradient (SAAG)

Best test for classifying ascites into portal hypertensive (SAAG >1.1 g/dL) and non–portal hypertensive (SAAG <1.1 g/dL) causes.

<table>
<thead>
<tr>
<th>≥1.1 g/dL</th>
<th>&lt;1.1 g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>Peritoneal carcinomatosis</td>
</tr>
<tr>
<td>Alcoholic hepatitis</td>
<td>Peritoneal TB</td>
</tr>
<tr>
<td>CHF</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Vascular occlusion</td>
<td>Serositis</td>
</tr>
<tr>
<td>Fatty liver of pregnancy</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Massive hepatic mets</td>
<td>Bowel perf/obstruct/infarct</td>
</tr>
<tr>
<td>Myxedema</td>
<td></td>
</tr>
</tbody>
</table>

The Management of Ascites

- Dietary measures
  - Sodium
  - Fluid
- Diuretics
  - Spironolactone
- Large volume paracentesis
- TIPS
- Peritoneovenous shunt
- Liver transplantation
**TIPS for Ascites**

**Reaccumulation, 12 months**

<table>
<thead>
<tr>
<th>Study</th>
<th>TIPS (n/N)</th>
<th>Paracentesis (n/N)</th>
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<td>Lebrec 1996</td>
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<td>11/12</td>
<td>0.30</td>
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<td>19/33</td>
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<td>Total</td>
<td>133</td>
<td>137</td>
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Favors TIPS Favors Paracentesis

**TIPS for Ascites**

**Hepatic Encephalopathy**

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<td>2.37</td>
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<tr>
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<td>137</td>
<td>2.24</td>
<td></td>
</tr>
</tbody>
</table>

Favors TIPS Favors Paracentesis
Hepatic Hydrothorax

Reasonable options
- Diuretics
- Fluid management
- VATS
  - 48% success
  - 40% 40-day mortality
- TIPS
  - 70% success
  - 20% 30-day mortality

Ineffective options
- Thoracentesis
- Chest tube
- Pleurodesis
- Surgical repair of diaphragm
- Peritoneovenous shunt

Conclusion
- Portal hypertension is a result of increased intrahepatic vascular resistance and portal inflow
- Management of upper GI bleeding related to portal hypertension
- Role of surgery
- Management of ascites