ACG Virtual Grand Rounds
Join us for upcoming Virtual Grand Rounds!

Week 17: High-Resolution Manometry: Thinking Beyond the Chicago Classification
John E. Pandolfino, MD, MSCI, FACP
July 16, 2020 at Noon EDT

Week 18: What’s New With Those "Other" Colitides?
Anne G. Tuskey, MD, FACP
July 23, 2020 at Noon EDT

Visit gi.org/ACGVGR to Register

RACISM IN MEDICINE: SHIFTING CULTURE AND PRACTICE
Webinar: Monday, July 13th at 8 pm EDT  Register: gi.org/ACGVGR

Dr. Williams  Dr. Balzora  Dr. Gray
Ms. Abbott  Dr. Conwell  Dr. Oliva-Hemker  Dr. Pochapin
Liver Institute of Virginia
Bon Secours Mercy Health Good Help to Those in Need

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DEADLINE - July 10!

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ACG TELEHEALTH SURVEY 2020

Telehealth Usage in GI: Before, During and After COVID-19

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Your Feedback Will Help Shape the #Future of GI
Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR
ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.

ACG will submit MOC points on the first of each month. Please allow 3-5 business days for your MOC credit to appear on your ABIM account.
MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

Disclosures:

Moderator:
Mark W. Russo, MD, MPH, FACG
Dr. Russo has nothing to disclose.

Speaker:
Mitchell L. Shiffman, MD, FACG
Advisory Board: AbbVie, Gilead, HepQuant, Intercept, Mallinckrodt, Shionogi
Research Grant: Aurora, Celgene, Conatus, CymaBay, Enanta, Exalenz, HepQuant, Gilead, Intercept, Mallinckrodt, NGMBio, Viking
Royalties: Slack
Stock options: Exalenz
Speakers Bureau: AbbVie, Daiichi Sankyo, Eisai, Gilead, Intercept, Shionogi

Off Label Use: Terlipressin for hepatorenal syndrome
MANAGING THE COMPLICATIONS OF CIRRHOSIS

Mitchell L. Shiffman, MD, FACG
Director
Liver Institute of Virginia
Bon Secours Mercy Health
Richmond and Newport News, VA

COMPLICATIONS OF CIRRHOSIS
ALTERATION IN HEPATIC BLOOD FLOW

- Chronic liver injury
- Hepatic fibrosis
- Alters hepatic lobule structure
- Impacts hepatic blood flow
- Portal hypertension
PORTAL HYPERTENSION
ETIOLOGY IN CIRRHOSIS

Hepatocytes

Space of Disse

Stellate cells

Kupffer and endothelial cells

Stellate cells secrete collagen matrix

Kupffer and endothelial cells
PORTAL HYPERTENSION ETIOLOGY IN CIRRHOSIS

Stellate cells secrete collagen
Matrix

Endothelial cells fatten
Fenestrations close

PORTAL HYPERTENSION SEQUENCE OF EVENTS

Sinusoidal fibrosis and loss of endothelial fenestrations
Loss of sinusoidal compliance
Sinusoidal pressure increases
Salt and water retention
ASCITES

Portal hypertension develops when HVPG exceeds 12 mm Hg
Collateral circulation
Shunting portal blood

HEPATIC ENCEPHALOPATHY
VARICES
CIRRHOSIS COMPLICATIONS

- Hepatocellular carcinoma
- Variceal hemorrhage
- Ascites and edema
  - Hyponatremia
  - AKI
  - Hepato-renal syndrome
  - Malnutrition
  - Infections - SBP
- Hepatic encephalopathy

IMPACT OF CURING HCV
HCC, LIVER FAILURE, MORTALITY

**RISK OF HCC PLATELET COUNT**

- **Chronic HCV HALT-C trial**
  - N= 1,005
  - P<0.0001

**Cumulative Risk (%)**

<table>
<thead>
<tr>
<th>Years</th>
<th>Cumulative Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.05</td>
</tr>
<tr>
<td>1</td>
<td>0.10</td>
</tr>
<tr>
<td>2</td>
<td>0.15</td>
</tr>
<tr>
<td>3</td>
<td>0.20</td>
</tr>
<tr>
<td>4</td>
<td>0.25</td>
</tr>
<tr>
<td>5</td>
<td>0.30</td>
</tr>
<tr>
<td>6</td>
<td>0.35</td>
</tr>
</tbody>
</table>

**Platelet Count:**
- <100
- 100-149
- >150


---

**IMPACT OF SURVEILLANCE STAGE OF HCC AT DIAGNOSIS**

- **n = 565**
- **485**
- **591**

**HCC Stage:**
- 4
- 3
- 2
- 1

**% of Patients**

<table>
<thead>
<tr>
<th>Location of Screening</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>LT Center</td>
<td>100</td>
</tr>
<tr>
<td>PCP</td>
<td>90</td>
</tr>
<tr>
<td>None</td>
<td>80</td>
</tr>
</tbody>
</table>

Impact of Surveillance Effect on Survival

Toyoda H, et al.

Esophageal Varices
The Need for Surveillance

Pagliaro L, et al.
In Bosch J and Groszmann RJ, eds.
PREVENTING VARICES FROM FORMING
BETA-BLOCKERS


IDENTIFYING PATIENTS WITH VARICES
PLATELET COUNT AND FIBROSCAN

### PREVENTING FIRST VARICEAL BLEED

**BETA-BLOCKERS**

<table>
<thead>
<tr>
<th></th>
<th>Control (N=600)</th>
<th>Beta Blockers (N=590)</th>
<th>Absolute Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Varices</td>
<td>25%</td>
<td>15%</td>
<td>-10%</td>
</tr>
<tr>
<td>(11 trials)</td>
<td>(N=600)</td>
<td>(N=590)</td>
<td>-16% → -5%</td>
</tr>
<tr>
<td>Large Varices</td>
<td>30%</td>
<td>14%</td>
<td>-16%</td>
</tr>
<tr>
<td>(8 trials)</td>
<td>(N=411)</td>
<td>(N=400)</td>
<td>(-24% → -8%)</td>
</tr>
<tr>
<td>Small Varices</td>
<td>7%</td>
<td>2%</td>
<td>-5%</td>
</tr>
<tr>
<td>(3 trials)</td>
<td>(N=100)</td>
<td>(N=91)</td>
<td>(-11 → 2%)</td>
</tr>
</tbody>
</table>


### PREVENTING FIRST VARICEAL BLEED

**BAND LIGATION vs BETA-BLOCKERS**

<table>
<thead>
<tr>
<th></th>
<th>Beta-blockers</th>
<th>Banding</th>
<th>Delta</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen 1998</td>
<td>1/26 (4%)</td>
<td>2/30 (7%)</td>
<td>3%</td>
</tr>
<tr>
<td>Sarin 1999</td>
<td>4/45 (9%)</td>
<td>12/44 (27%)</td>
<td>18%</td>
</tr>
<tr>
<td>De 1999</td>
<td>2/15 (13%)</td>
<td>1/15 (7%)</td>
<td>-6%</td>
</tr>
<tr>
<td>Jutabha 2000</td>
<td>0/18 (0%)</td>
<td>1/17 (6%)</td>
<td>6%</td>
</tr>
<tr>
<td>De la Mora 2000</td>
<td>1/12 (8%)</td>
<td>2/12 (17%)</td>
<td>9%</td>
</tr>
<tr>
<td>Lui 2002</td>
<td>3/44 (7%)</td>
<td>9/66 (14%)</td>
<td>7%</td>
</tr>
<tr>
<td>Lo 2004</td>
<td>10/50 (20%)</td>
<td>16/50 (32%)</td>
<td>12%</td>
</tr>
<tr>
<td>Schepke 2004</td>
<td>19/75 (25%)</td>
<td>22/77 (29%)</td>
<td>4%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>40/285 (14%)</td>
<td>65/311 (21%)</td>
<td>7%</td>
</tr>
</tbody>
</table>

Khuroo MS, et al.  
ESOPHAGEAL VARICES APPROACH

Cirrhosis

Endoscopy if platelets < 150,000

No Varices

Follow-up EGD Q 2-3 years

Small Varices

Follow-up EGD Q 1-2 years

Medium-Large Varices

Beta-Blockers or Band Ligation


BETA-BLOCKERS IMPACT OF ASCITES

BETA-BLOCKERS
IMPACT OF SBP

Use of beta-blockers significantly increases the risk of AKI and HRS in patients who developed SBP
- RCT, N=602
- Mean age 57 years
- ETOH cirrhosis 55%
- Mean MELD 17
- Child class C 50%
- 90 day mortality with AKI in patients on beta-blockers and h/o SBP = 80%


PORTAL HYPERTENSION
DEVELOPMENT OF ASCITES

- The most common complication of cirrhosis and portal hypertension
- Leads to other complications:
  - Hepatorenal syndrome
  - Hyponatremia

COMPLICATIONS OF ASCITES
MORTALITY

Planas R, et al.
Clin Gastroenterol Hepatol 2006;1385-1394.

ASCITES MANAGEMENT

- Sodium restriction
  - Avoid IV saline when hospitalized
- Diuretics
  - Aldactone 100 200 300 400 mg
  - Lasix 40 80 120 160 mg
  - Paracentesis - Remove as much as possible. IV albumin 8gm/L removed
- Limiting factors:
  - Acute Kidney Injury
  - Hyponatremia
  - Intravenous 25% albumin
  - Tolvaptan
  - TIPS when refractory because of
    - Hyponatremia
    - AKI
**ASCITES COMPLICATIONS AND SURVIVAL**

<table>
<thead>
<tr>
<th></th>
<th>Median Survival (mos)</th>
<th>Median Survival (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td>&gt;80</td>
<td>46</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>&lt;1.2</td>
<td>25</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>&gt;130</td>
<td>27</td>
</tr>
<tr>
<td>Urine Na</td>
<td>&gt;10</td>
<td>46</td>
</tr>
</tbody>
</table>

Cardenas A, et al.  

**RENAL DISEASE IN ESLD ROLE OF IV ALBUMIN**

- Improves vascular oncotic pressure
  - Enhances movement of tissue fluid into vasculature
  - Decreases edema
  - Decreases ascites
- Expands vascular space
  - Improves renal perfusion
  - Enhances urine output
  - Increases serum sodium
  - Lowers Serum Creatinine

- Dose is 25 gm Q 6 H until
  - Anasarca resolved
  - Sodium back to normal
  - Creatinine back to normal or plateaued
  - Start diuretics once Sna > 130
HYPONATREMIA AND AKI
INTRAVENOUS ALBUMIN


SEVERE ASCITES AND EDEMA
IV ALBUMIN

- Start IV albumin 25%, 25 gms Q6 hrs
- Large volume paracentesis
- Role of albumin:
  - Expands vascular space
  - Enhances renal perfusion
  - Increases urine output
- Use for several days until Scr and/or Sna increasing then diuretics
- Continue IV albumin until serum albumin normal/near normal
**IV ALBUMIN IN SBP**

- Occurs in 30% with ascites
- In hospital mortality 20%
- Mortality and AKI reduced significantly with IV albumin
  - RCT, N=126
  - Cefotaxime + IV albumin
  - Mean age 60 years
  - ETOH cirrhosis 30%
  - Mean CTP score 10
  - Culture positive 54%
  - *E. coli* 21%

Sort P, et al.  

**HEPATOrenal SYNDROME TYPE 1 AND TYPE 2**

<table>
<thead>
<tr>
<th>Type 1 – Now called HRS-AKI</th>
<th>Type 2 – Now called HRS-CKD</th>
</tr>
</thead>
</table>
| Previously: Rise in Scr to > 2.5 mg  
Now:  
Increase in Scr by ≥ 0.3 mg within 48 hours  
Increase in SCr by ≥ 50% from baseline within 7 days | Slow rise in Scr over weeks to months  
No precipitating factor |
| Precipitating factors:  
Infection  
SIRS  
Acute on chronic liver injury  
Renal hypoperfusion: Hypotension, sepsis, variceal bleeding |
HEPATOrenal SYNDROME SURVIVAL

![Graph showing survival rates for Type 1, Type 2, and No HRS]


TREATMENT OF HRS MIDODRINE+OCTREOTIDE

![Graph showing survival rates and change in CrCl for HRS Type 1 and Type 2]

TREATMENT OF HRS
TERLIPRESSIN

- Randomized placebo-controlled trial
- N=300
- Randomized 2:1 to Terlipressin
- HRS-AKI
- Failed IV albumin challenge
- All patients remained on IV albumin
- Primary end-point
  - Improvement in Scr
  - No RRT
  - All at day 14

F Wong, et al.
AASLD 2019

CALORIC CONSUMPTION
IMPACT OF ASCITES

<table>
<thead>
<tr>
<th>Accommodation Ratio</th>
<th>Maximal Tolerated Volume (ml)</th>
<th>Caloric Intake (kcal q 3d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>Baseline: 738 (469-1078)</td>
<td>Baseline: 964 (611-1276)</td>
</tr>
<tr>
<td>Ascites</td>
<td>After LVP: 3110* (2160-3860)</td>
<td>After LVP: 3470* (3048-5396)</td>
</tr>
</tbody>
</table>

Aqeel BA, et al.
PROTEIN CALORIE MALNUTRITION PREVALENCE IN CIRRHOSIS

- 50 consecutive patients with cirrhosis
- Patients with HTN or functional GI disorders matched for age, race, sex
- PCM assessed by:
  - Subjective Global Assessment
  - Prognostic Nutrition Index
  - Hand grip


PROTEIN CALORIE MALNUTRITION COMPLICATIONS OF CIRRHOSIS

**TIPS FOR REFRACTORY ASCITES**

**NASTRA STUDY**


**AMMONIA METABOLISM NORMAL**

American College of Gastroenterology
AMMONIA METABOLISM CIRRHOSIS

Cirrhosis → NH3 → Brain

Skeletal Muscle

MALNUTRITION AND MUSCLE WASTING FACTORS IN CIRRHOSIS

Portal hypertension → Ascites

Shunting of hepatic blood → Decreased caloric intake

Inefficient hepatic caloric utilization → Fatigue

Muscle Wasting → Reduced activity
AMMONIA METABOLISM
CIRRHOSIS AND MUSCLE WASTING

Brain
Cirrhosis
NH3
Skeletal Muscle Wasting

DIETARY PROTEIN EFFECT ON HE

Cordoba J, et al.

Dietary protein:
- Low
- Normal
**HIGH CALORIE AND PROTEIN DIET IMPACT ON HE**

![Graph showing percentage of patients improved by stage and initial vs. final serum NH3 levels.](image)


---

**HEPATIC ENCEPHALOPATHY TREATMENT**

- Do not treat the ammonia level
- There is no reason to routinely measure serum ammonia
- If the patient does not have overt HE, they do not need more lactulose
- Treat symptoms of HE
- Do not overdose:
  - Diarrhea
  - Dehydration
  - Electrolyte abnormalities
  - Precipitate HE

![Indication for rifaximin](image)
HEPATIC ENCEPHALOPATHY SECONDARY PROPHYLAXIS

Free of HE (%)

Rifaximin
Placebo

DAYS
0 30 60 90 120 150

Hospitalization (%)
Rifaximin Placebo

90% of patients in both groups on lactulose

Bass N, et al.

SPONTANEOUS SPLENO-RENAL SHUNT
BRTO

Gastric Varices (GOV 1 or 2)
25% of all GOV

SMV

BALLOON OCCLUDED RETROGRADE TRANSVENOUS OBLITERATION
MANAGEMENT OF CIRRHOSIS

SUMMARY

• Screen all patients with cirrhosis for HCC
• Patients with a platelet count below 150,000 and/or FibroScan > 20 kPa need to be screened for esophageal varices
• Band ligation or beta-blockers in patients with medium-large varices to prevent first variceal hemorrhage
• Avoid beta-blockers in patients with Child class B and C cirrhosis and/or ascites
• Treat ascites aggressively to resolution
• Do not restrict protein in patients with HE unless necessary

Questions?

Moderator:
Mark W. Russo, MD, MPH, FACG

Speaker:
Mitchell L. Shiffman, MD, FACG
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