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.
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July 16, 2020 at Noon EDT

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Anne G. Tuskey, MD, FACG
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Dr. Conwell
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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

Stellate cells secrete collagen matrix
Kupffer and endothelial cells

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
- Portal hypertension develops when HVPG exceeds 12 mm Hg
- Collateral circulation shunting portal blood
- Hepatic encephalopathy
- Varices
- Ascites

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

AJ van der Meer et al.
JAMA 2012; 308:2584-2593.
RISK OF HCC
PLATELET COUNT

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

Cumulative Risk (%)
YEARS

0 0.05 0.1 0.15
0 1 2 3 4 5 6

AS Loh, et al.

IMPACT OF SURVEILLANCE
STAGE OF HCC AT DIAGNOSIS

H Toyoda et al.

LOCATION OF SCREENING

LT Center PCP None

% of Patients

HCC Stage:
- 4
- 3
- 2
- 1

n = 565 485 591

IMPACT OF SURVEILLANCE
EFFECT ON SURVIVAL

H Toyoda et al.
ESOPHAGEAL VARICES
THE NEED FOR SURVALENCE

[Graph showing percentage of patients experiencing appearance of new varices and enlargement of varices over years]


PREVENTING VARICES FROM FORMING
BETA-BLOCKERS

[Graph showing percentage of patients free of varices over months with placebo and timolol]


IDENTIFYING PATIENTS WITH VARICES
PLATELET COUNT AND FIBROSCAN

[Graph showing platelet count and liver stiffness with variceal size]

**PREVENTING FIRST VARICEAL BLEED**

**BETA-BLOCKERS**

<table>
<thead>
<tr>
<th></th>
<th>Control (N=600)</th>
<th>Beta Blockers (N=550)</th>
<th>Absolute Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Varices (11 trials)</td>
<td>25% (N=600)</td>
<td>15% (N=550)</td>
<td>-10% (-16% → -5%)</td>
</tr>
<tr>
<td>Large Varices (8 Trials)</td>
<td>30% (N=411)</td>
<td>14% (N=400)</td>
<td>-16% (-24% → -8%)</td>
</tr>
<tr>
<td>Small Varices (3 Trials)</td>
<td>7% (N=100)</td>
<td>2% (N=91)</td>
<td>-5% (-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>4/50 (8%)</td>
<td>12/44 (27%)</td>
<td>18%</td>
</tr>
<tr>
<td>Ok 1999</td>
<td>2/13 (15%)</td>
<td>1/13 (8%)</td>
<td>7%</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>1/2 (5%)</td>
<td>2/12 (17%)</td>
<td>12%</td>
</tr>
<tr>
<td>Lo 2002</td>
<td>3/14 (21%)</td>
<td>9/96 (10%)</td>
<td>7%</td>
</tr>
<tr>
<td>Lo 2004</td>
<td>10/99 (10%)</td>
<td>16/99 (16%)</td>
<td>6%</td>
</tr>
<tr>
<td>Schepke 2004</td>
<td>10/50 (20%)</td>
<td>16/50 (32%)</td>
<td>12%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>40/285 (14%)</td>
<td>65/311 (21%)</td>
<td>7%</td>
</tr>
</tbody>
</table>


**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

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%

M Mandorfer et al
Gastroenterol 2014; 146:1680-1690.
COMPLICATIONS OF ASCITES MORTALITY


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
  - TIPS when refractory because of
  - Hyponatremia
  - AKI

ASCITES COMPLICATIONS AND SURVIVAL

<table>
<thead>
<tr>
<th></th>
<th>Median Survival (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP &gt;80</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Serum creatinine &lt;1.2</td>
<td>25</td>
</tr>
<tr>
<td>Hyponatremia &gt;130</td>
<td>27</td>
</tr>
<tr>
<td>Urine Na &gt;110</td>
<td>46</td>
</tr>
</tbody>
</table>

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

PA McCormick et al.
Gut 1990; 31:204-207.

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
- Continuous 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%

P. Sut et al.,

HEPATORENAL SYNDROME TYPE 1 AND TYPE 2

Type 1 — Now called HRS-AKI
- Previously: Rise in Screat to > 2.5 mg
- Now: Increase in Screat by ≥1.5 mg within 48 hours
- Increase in Scr by ≥30% 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

F. Wong et al.,
Gut 2011; 60:702-709.

HEPATORENAL SYNDROME SURVIVAL

V. Arroyo et al.,
J Hepatol. 2007; 935-946.
TREATMENT OF HRS
MIDODRINE+OCTREOTIDE

<table>
<thead>
<tr>
<th></th>
<th>HRS Type 1</th>
<th>HRS Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>102</td>
<td>60</td>
</tr>
<tr>
<td>SURVIVAL (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0  4  8  12 W</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0  4  8  12 W</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in CrCl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRS1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HRS2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

C. Staggen et al. J COG Gastroenterol 2006; 43:685-688

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 Screat
  - No RRT
  - All at day 14

F. Wong et al. AASLD 2019

CALORIC CONSUMPTION
IMPACT OF ASCITES

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>After LVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal Tolerated Volume (ml)</td>
<td>736 (469-1078)</td>
<td>1110* (2160-3860)</td>
</tr>
<tr>
<td>Caloric Intake (kcal q 3d)</td>
<td>564 (511-1276)</td>
<td>3410* (3048-5396)</td>
</tr>
</tbody>
</table>

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

Gastroenterology Study

PROTEIN CALORIE MALNUTRITION COMPLICATIONS OF CIRRHOSIS

- PCM:
  - Yes
  - No

Complications, Transplantation, Death

Gastroenterology Study

TIPS FOR REFRACTORY ASCITES NASTRA STUDY

- TP
- TIPS

No Ascites (%), Days

- TP
- TIPS

Survival (%), Years

- TP
- TIPS

Gastroenterology Study
AMMONIA METABOLISM
NORMAL

Brain

Skeletal Muscle

NH3

Normal Liver

AMMONIA METABOLISM
CIRRHOSIS

Brain

Skeletal Muscle

NH3

Cirrhosis

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

American College of Gastroenterology
AMMONIA METABOLISM
CIRRHOSIS AND MUSCLE WASTING

Brain

Cirrhosis

Skeletal Muscle Wasting

DIETARY PROTEIN EFFECT ON HE

Dietary protein:
- Low
- Normal

HIGH CALORIE AND PROTEIN DIET IMPACT ON HE

 Improved by:
- 2 Stage
- 1 Stage
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 have they do not need more lactulose
- Treat symptoms of HE
- Do not overdose:
  - Diarrhea
  - Dehydration
  - Electrolyte abnormalities
  - Precipitate HE

Indication for rifaximin

HEPATIC ENCEPHALOPATHY
SECONDARY PROPHYLAXIS

90% of patients in both groups on lactulose

SPONTANEOUS SPLENO-RENAL SHUNT
BRTO

Gastric Varices (GOV 1 or 2)
20% of all GOV

Ballon 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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