Complications of Portal Hypertension – A Practical Management Approach

Advances in Liver Disease 2018: A Year in Review
12/8/18
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Einstein Healthcare Network
Outline

• Ascites
• Hepatorenal syndrome
• Varices
• Hepatopulmonary Syndrome
• Portopulmonary Hypertension
• Hepatic Encephalopathy
• Acute on Chronic Liver Failure
For Your Listening Pleasure

BEDSIDE
Hosted by Adam Rodman, MD

GI PEARLS
Gastroenterology Literature Review
PART II.

Hepatitis.


Hepatic Cirrhosis. — See also, Ascites.

Acid, Nitric. Acid, Nitrohydrochloric.

Ammonium Chloride. Anisatin.

Gold and Sodium Carbonate. Iodides. Iodoform. Iodoform.

Iodole. Mercurialis. Sodium Phosphate.

Hepatic Diseases. — See also, Blenorrhagia, Cancer, Jaundice, Jaundice. Hepatic Con Phagia, Hepatic Cirrhosis, Hepatitis, Jaundice.


Herpetic.


Herpes.


Herpes Zoster.

Acid, Carbolic. Aloe. Aonite and Opium: locally.
Cirrhosis and Portal Hypertension

Median Survival > 12 years

Median Survival < 2 years

1 year Mortality 57%

Cirrhosis and Portal Hypertension

Cirrhosis and Portal Hypertension

Ascites

• The most common complication of cirrhosis
• 50% of cirrhotics develop ascites ≤ 10 years
  – 15% 1 year mortality risk
  – 44% 5 year mortality risk
• Most common cause of hospital admission

Albumin with Paracentesis

- Albumin shown to decrease risk of complications after paracentesis
  - hypotension, hyponatremia and HRS
- RCT of 105 patients with LVP vs LVP + albumin showed
  - less change in BUN, RAAS, and Na
- Reduced AKI, but no change in mortality
- Advise albumin if more than 4 L removed
- Paracentesis induced circulatory dysfunction (PICD) is seen in 18-25% of patients receiving albumin during large volume paracentesis
  - Terlipressin may reduce incidence but has side effects
    - Ischemia, bradycardia, hypertension

Gines P. Gastroenterol. 1988;94:1493-1502
Midodrine and Albumin with Paracentesis

• Cirrhotics randomized to Albumin alone (40g), Terlipressin (1mg q8h x 1d) with Albumin or Midodrine (7.5 mg q8h x 3d) with Albumin
  – Excluded sepsis, cardiac dysfunction, kidney injury
• Primary outcome – Assess occurrence of PICD
  – Defined PICD rise in plasma renin activity 50% or 4ng/ml/hr on day 6
  – Secondary outcomes included AKI, hyponatremia, bleeding, frequency of paracentesis and hospitalization within 28 days

Kulkarn A et al. AASLD 2018, San Francisco #114
Midodrine and Albumin with Paracentesis

• Results: n=150
  – PICD –
    • Albumin 28%
    • Albumin + Terlipressin 30%
    • Albumin + Midodrine 18% (p=0.33)
  – Complications higher in Albumin (56%) and Albumin + Terlipressin (50%) than Albumin + Midodrine (24%) (p< 0.001)
  – Most frequent complication were hyponatremia followed by AKI
  – Need for paracentesis over next 28 days highest in Group 1 and 2 (1.76 +/- 1.27 and 1.56 +/- 1.03) vs Group 3 (1.02 +/- 0.93 p < 0.001)
  – MAP and UOP better maintained in Albumin + Midodrine
  – No difference in mortality

Kulkarni A et al. AASLD 2018, San Francisco #114
Vaptans

• Vasopressin receptor antagonists
  – Tolvaptan - approved for edema in the setting of cirrhosis
  – Selective vasopressin type 2 receptor antagonist
• Counteracts ADH driven water reabsorption
• Problems
  – Questionable efficacy
  – May lead to hypernatremia
  – May be associated with increased mortality
Tolvaptan Improves Survival

- 260 patients hospitalized for refractory ascites
  - 57 treated with diuretics and albumin (2010-2013)
  - 149 treated with this + Tolvaptan (2013-2017)
- Primary outcome – renal function at 1 year

<table>
<thead>
<tr>
<th></th>
<th>Tolvaptan</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN at 1 year</td>
<td>25</td>
<td>32.1</td>
</tr>
<tr>
<td>Cr at 1 year</td>
<td>1.25</td>
<td>1.98</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Tolvaptan with low dose Furosemide</th>
<th>High dose Furosemide (&gt;40mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year survival</td>
<td>67.8%</td>
<td>24.4%</td>
</tr>
<tr>
<td>3 year survival</td>
<td>45.3%</td>
<td>3.1%</td>
</tr>
</tbody>
</table>

Hosui A et al. AASLD 2018, San Francisco #969
Tolvaptan Improves Survival

• Prognostic factors for survival Tolvaptan group
  • Male (OR 1.59, p = 0.049)
  • High BUN (>20 mg/dl: OR 1.67, p = 0.03)
  • High Bilirubin (>2.0 mg/dl: OR 1.89 , p =0.009)
  • High dose Furosemide at start of treatment (> 40 mg : OR 2.63, p < 0.0001)

• Conclusion: Tolvaptan may improve survival when started prior to high dose furosemide administration

Hosui A et al. AASLD 2018, San Francisco #969
Liver Injury

- Resistance to portal flow
- Portal hypertension
  - Portal-systemic shunting
  - Splanchnic & peripheral vasodilation
    - Increased plasma volume
      - Ascites
- Impaired synthesis
  - Hypoalbuminemia
  - Coagulopathy
  - Cachexia
- Ascites
- Salt and Water retention
  - Salt and Water retention
- Varices
  - Encephalopathy
- Renal Vasoconstriction
- Renal Insufficiency
Survival and HRS

Prevention of HRS

• Albumin + antibiotics for SBP
  – 1.5 g/kg albumin at diagnosis
  – 1.0 g/kg albumin at 48 hours

• Prophylactic antibiotics for patients at risk for SBP
  – Ascitic protein < 1.5 gm and
  – Severe liver or kidney dysfunction
    • Bilirubin > 3
    • CPT > 10
    • Serum sodium < 130
    • Creatinine > 1.2

• Drug therapy
  – Judicious use of diuretics
  – Avoidance of NSAIDs
Hepatorenal Syndrome

• HRS treatment
  – Octreotide: somatostatin analogue
  – Midodrine: alpha 1 adrenergic agonist
  – Albumin: colloid volume expander
  – Norepinephrine: vasoconstrictor
  – Terlipressin: vasopressin derivative (also vasoconstrictor)
    • Acts as a systemic vasoconstrictor via vascular vasopressin V1 receptors
    • Approved for treatment of HRS-1 in multiple countries but not in the United States or Canada
    • International treatment guidelines recommend use of terlipressin plus albumin as first-line therapy for HRS-1

Terlipressin Improves Lower ACLF Grade HRS

• Acute on chronic liver failure (ACLF) is increasingly being recognized as an entity clinicians should be aware of
  – Acute liver decompensation + other organ malfunction(s) + severe inflammation
  – High short term mortality

• Retrospective analysis 4 cohorts Type 1 HRS
  – n=298, 2007-2016
  – ACLF graded as 1 (HRS alone), 2 (HRS + 1 organ failure), 3, (HRS + 2 or more more organ failures)
Terlipressin Improves Lower ACLF Grade HRS

- 53% response to treatment
- 60% response Grade 1 ACLF
- Multivariate analysis – Baseline Cr and ACLF grade were independently associated with treatment response
- ACLF grade largest determinant of response

Esophageal Varices

- Transfuse for Hg 7-8
- Hold Beta Blockers in acute setting
- Antibiotics
  - 3rd Generation Cephalosporin or Quinolone (7 days)
  - Reduce risk of SBP and other infections (decrease mortality)
- EGD within 12 hrs and Octreotide drip for 2-5 d
- Combination of EVL and beta blockers for secondary prophylaxis
- TIPS if rebleeding, high risk of failure, or can’t control with EGD
  - HVPG > 20 mmHg, CPT C, or B with active bleeding
  - Meta-analysis shows early TIPS associated with reduced bleeding at 1 year (OR 0.08, 95% CI 0.04-0.17, p < 0.001)

Transjugular Intrahepatic Portosystemic Shunt

- Liver failure
- Infections
- Bleeding
- Heart failure
- Encephalopathy
Low Dose Terlipressin Safe in Variceal Bleeding

- Low dose continuous infusion Terlipressin better tolerated than bolus dosing in HRS
  - No data in variceal bleeding
- RCT 180 variceal bleeds
  - No prior CAD, PVD or HTN
- Assigned to Bolus 2 mg QID or 4 mg/24 hr infusion x 72 hours
- Primary outcome – HVPG at 24 hours
  - Less than 20 mmHg or > 10% decline from baseline

Choudhury SP et al. AASLD 2018, San Francisco #151
Low Dose Terlipressin Safe in Variceal Bleeding

• Significantly more responders in continuous infusion
  – 74.4% vs 37.8% (p < 0.001)
• Overall required less medication
• AEs less in infusion group
  – 35.6% vs 14.4% (p = 0.004)
  – Hypertension and Bradycardia most common
• No difference in rebleeding or survival
  – Larger sample may be needed to show these benefits

Choudhury SP et al. AASLD 2018, San Francisco #151
Variceal Screening

Diagnosis of Cirrhosis

Endoscopy

No Varices

Follow-up EGD in 2-3 years*

Follow-up EGD in 1-2 years*

Small Varices

Medium/Large Varices

Beta-blocker therapy*

*EGD every year in decompensated cirrhosis

• Step-wise increase until maximally tolerated dose
• Continue beta-blocker indefinitely

No Contraindications
Variceal Screening

- If decompensate, should have EGD immediately (regardless of prior variceal status)
- No indication to start NSBB if no varices or small-low risk varices
- Carvedilol may be preferred in advanced cirrhotics
- EGD can be avoided if LS < 20 Kpa on Fibroscan and Plt > 150

Low Risk Variceal Bleeding with Low Liver and Spleen Stiffness

- Liver (LS) and Spleen (SS) stiffness can predict presence of portal htn
  - LS 20 kpa and SS 55 kpa
  - Some data that SS superior to LS
  - SS can’t be measured by TE
- RCT compensated cirrhosis (n=548)
- Randomized to LSSM screening or conventional
- Primary outcome: variceal bleed
- 127 of 274 patients in LSSM needed EGD
- Avoided EGD in 53% of LSSM arm
- Variceal bleeding 4.4% vs 4% (p=0.711)

Wong GLH et al. AASLD 2018, San Francisco #152
The Changing Role of Beta Blockers

Early cirrhosis
- Beta-blockers have no effect on survival, may increase adverse events
- May use beta-blocker for cardiovascular indications
- Cardiac reserve intact
- SNS and RAAS activity at baseline
- Low risk of gut bacterial translocation
- Low risk of mortality

Decompensated cirrhosis (medium-large varices)
- Beta-blockers improve survival by reducing variceal bleeding and gut bacterial translocation
- Cardiac reserve intact but steadily declining
- SNS and RAAS activity increased but not maximal
- Increased risk of gut bacterial translocation
- Increased risk of mortality

End-stage cirrhosis (refractory ascites)
- Beta-blockers reduce survival due to negative impact on cardiac reserve, resulting in decreased perfusion to vital organs during periods of stress and precipitation of hepatorenal syndrome
- Cardiac compensatory reserve critically impaired, with baseline hypotension
- SNS and RAAS maximally stimulated, can no longer maintain adequate blood pressure
- High risk of gut bacterial translocation
- High risk of mortality

# Two Distinct Pulmonary Vascular Complications of Liver Disease

<table>
<thead>
<tr>
<th>Hepatopulmonary Syndrome</th>
<th>Portopulmonary Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary vasodilatation</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Intrapulmonary shunt</td>
<td>Normal PCWP</td>
</tr>
<tr>
<td>Increased alveolar-arterial oxygen gradient</td>
<td>No other etiology of pulmonary hypertension</td>
</tr>
</tbody>
</table>
Hepatopulmonary Syndrome

- Up to 30% of patients undergoing liver transplant evaluation have HPS
- Present with dyspnea, spider nevi, clubbing, hyperdynamic circulation
- Hyperventilation → respiratory alkalosis on ABG
- Hyperoxia testing as noninvasive approach
Diagnosis

- Intrapulmonary vasodilatation
- Diffusion impairment
  - $A-a$ gradient $\geq 15$ mm Hg
  - $A-a \geq 20$ mm Hg if age $> 64$ years
  - $P_{aO_2} < 80$ mm Hg when breathing room air
- Hepatic dysfunction or portal hypertension
Dilated Capillaries in HPS Lead to Shunting Pathophysiology

Increase in nitric oxide production (by endothelin B receptors)

Kinane TB et al. NEJM. 2004;351:1667-75
Evaluation - HPS

- History and Physical Examination
  - Platypnea
    - Dyspnea when upright which is relieved when supine
  - Orthodeoxia
    - Decrease in PaO2 > 4 mmHg, supine to upright
    - Decrease in PaO2 of > 5%, supine to upright
- Chest radiograph
- Pulmonary function testing
- Arterial blood gas
- Echocardiography with contrast
Management

• Supplemental oxygen
  – No data to support improved outcomes
• No approved medical treatment
• Staging
  – Mild PaO2 > 80 mmHg
  – Moderate PaO2 60-80 mmHg
  – Severe 50-60 mmHg
  – Very Severe < 50 mmHg
• Liver transplant curative
  – Exception points granted on wait list
Severity of HPS Linked to Post OLT Survival

Goldberg DS et al. Gastroenterology. 2014;146:1256-65
Sorafenib for HPS

- Sorafenib potent multikinase inhibitor
  - Blocks VEGF and PDGFR receptors
  - Potent anti-angiogenesis effect
- Mouse models suggest improved intrapulmonary shunting and intrapulmonary angiogenesis
- Clinical trial comparing sorafenib to placebo completed enrollment
  - ClinicalTrials.gov Identifier: NCT02021929

Portopulmonary Hypertension (PoPH)

• Prevalence 5% in patients with ESLD

• Presence of portal hypertension
• Absence of other pulmonary disease
• mPAP > 25 mm Hg
• PCWP < 15 mm Hg
• PVR > 3 WU , 240 dynes-sec/cm5

PVR is calculated NOT measured

\[
PVR = \frac{mPAP - PCWP}{CO}
\]

Normal PVR 20-120 dynes-sec/cm5 or 0.25-1.7 WU

Normal Cardiac Output 4-8 L /min
Risk Factors – PoPH

• Female sex
  – OR 2.9 (1.2 – 7.0)

• Autoimmune hepatitis
  – OR 4.0 (1.1 – 14.2)

• Hepatitis C
  – OR 0.2 (0.1 – 0.7)

Evaluation

• 2D echocardiogram
  – PASP < 30 mm Hg has a negative predictive value of 100%
  – PASP > 30 mm Hg has a positive predictive value of 59%

• Right heart catheterization
Treatment - PoPH

• Now a total of 14 drugs for PoPH!
• Prostacyclin analogs
  – Vasodilatory, anti-thrombotic, anti-inflammatory properties
  – IV epoprostenol/IV treprostinil/ Inhaled iloprost
• PDE5 inhibitors
  – Interferes with cGMP metabolism (mediating NO)
  – Sildenafil (improves mPAP and PVR in PoPH)
• Endothelin receptor antagonists
  – Bosentan, Macitentan
Macitentan Safety in PoPH

- Minimal data in cirrhosis
- 12 week double blind RCT
- PVR > 320 dynes and MAP > 25
  - No CPT C or MELD > 19
- Most common AE edema and headache
  - 4 patients d/cd macitentan (all unrelated to liver)
- One patient experienced increase in liver chemistries > 3 ULN
- No hepatic safety profile concerns

<table>
<thead>
<tr>
<th>Primary endpoint</th>
<th>Baseline</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macitentan N=43</td>
<td>Placebo N=42</td>
<td>Macitentan N=43</td>
</tr>
<tr>
<td>PVR, dyn·sec/cm²</td>
<td>552±193</td>
<td>522±163</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other hemodynamic endpoints</th>
<th>Baseline</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macitentan N=43</td>
<td>Placebo N=42</td>
<td>Macitentan N=43</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>7.3±3.7†</td>
<td>6.7±3.6</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>46.4±7.9</td>
<td>43.8±8.5</td>
</tr>
<tr>
<td>Cardiac Index, L/min/m²</td>
<td>3.1±0.8</td>
<td>2.9±0.8</td>
</tr>
<tr>
<td>HVPG, mmHg</td>
<td>10.5±3.5‡</td>
<td>10.5±3.8**</td>
</tr>
</tbody>
</table>

Krowka M et al. AASLD 2018, San Francisco #111
Liver Transplantation

• Transplant at least halts progression of PoPH
• MELD exception of 22 may be obtained
• Traditional criteria for liver transplantation
  – mPAP > 35 mmHg
  – mPAP > 50 mmHg associated with high mortality
• PoPH can develop in as little as 3 months
  – Routine screening advised
Hepatic Encephalopathy

• Spectrum of reversible neuropsychiatric disorders attributed to elevated toxins in patients with liver disease

• Advanced HE is equivalent to 6-7 MELD pts

<table>
<thead>
<tr>
<th>Normal</th>
<th>Covert HE, Grade 0-1</th>
<th>West Haven II</th>
<th>West Haven III</th>
<th>West Haven IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>No signs</td>
<td>No signs</td>
<td>Confused Asterixis</td>
<td>Obtunded Responds to noxius stimuli</td>
<td>Comatose</td>
</tr>
<tr>
<td>No sx</td>
<td>No Sxs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal tests</td>
<td>Abnormal special tests</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Hepatic Encephalopathy

- Develops 2% - 3% per year
- Median survival post onset is 1-2 years
- Manifestations
  - Subtle personality changes → coma
- Treatment
  - Correct the cause
    - Infection, Dehydration, Bleeding, Electrolyte changes, Constipation
    - Lactulose
    - Rifaximin

Conn HO et al. Lippincott Williams & Wilkins.1979
LOLA Improved Encephalopathy

- L-ornithine L-aspartate
  - AA salt of Ornithine and Aspartate
  - Enhances the metabolism of ammonia to glutamine
- Minimal high quality clinical data
- Double-blind, RCT in patients with OHE (n=193)
  - Control – Lactulose and Ceftriaxone
  - Treatment – Control + IV LOLA (30g)
- Mean time for recovery 1.92 vs 2.5 days (p=0.002)
- Venous ammonia on day 5 and LOS also lower in treatment group
- No difference in adverse events

Sidhu SS et al. Hepatol. 2018;67:700-710
CRRT Reduces Ammonia in ALF

- CRRT may reduce ammonia on chronic liver disease
- No data in ALF and therapeutic limited
- Multicenter cohort study 1998-2016, n = 340
- Studied effect CRRT on ammonia x 3 days for CRRT, Intermittent RRT, and no RRT
  - Ammonia decrease CRRT – 38%, IRRT – 23%, no RRT – 19% (p=0.007)
- CRRT may be effective adjunct to improve ammonia levels

Slack AJ et al. Liver Int. 2014;34:42-48
Cardsoso FS et al. Hepatol. 2018;67:711-720
Role of Benzos and PPIs in HE

- Meds that interact with neurotransmitters and gut flora impact HE
- Reviewed 20% random sample of US medicare database
- 184,481 medicare enrollees with cirrhosis
  - Excluded patients with HE within 3 months of diagnosis
- Pharmacological data showed 27% used PPIs, 27% used opiates, and 14% used benzodiazepines
- Incident HE diagnosed 26%, and Incidence Rate Ratio for portal htn was 3.66 (3.59-3.72)
- PPIs and Opiates demonstrated potentially modifiable risk factors

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Person-years at risk (thousand, % of total)</th>
<th>HE Events (% of HE events)</th>
<th>Unadjusted Hazard Ratio</th>
<th>Adjusted Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine use</td>
<td>65 (14%)</td>
<td>9377 (19%)</td>
<td>1.23 (1.20, 1.26)</td>
<td>1.13 (1.10, 1.16)</td>
</tr>
<tr>
<td>GABAergic use</td>
<td>60 (13%)</td>
<td>8579 (18%)</td>
<td>1.24 (1.21, 1.27)</td>
<td>1.14 (1.11, 1.17)</td>
</tr>
<tr>
<td>Opiate use</td>
<td>125 (27%)</td>
<td>18212 (37%)</td>
<td>1.37 (1.34, 1.39)</td>
<td>1.23 (1.21, 1.26)</td>
</tr>
<tr>
<td>Antipsychotic use</td>
<td>18 (4%)</td>
<td>2421 (5%)</td>
<td>1.14 (1.10, 1.19)</td>
<td>1.01 (0.96, 1.05)</td>
</tr>
<tr>
<td>Proton Pump Inhibitor use</td>
<td>127 (27%)</td>
<td>19685 (40%)</td>
<td>1.58 (1.55, 1.61)</td>
<td>1.47 (1.44, 1.50)</td>
</tr>
</tbody>
</table>

Co-variates used for adjustment included: age, sex, race, etiology of cirrhosis, Medicaid co-enrollment, hemodialysis, portal hypertension (varices, ascites, TIPS placement), and management by a gastroenterologist.

Tapper EB et al. AASLD 2018, San Francisco #220
Frailty and Opiate Use Correlate with QOL in Cirrhotics

- Cirrhosis associated with decreased QOL
- Severity of illness most important factor
- 300 patients with cirrhosis
  - portal htn (varices, ascites or plt < 80)
  - No HE
- Katz Activity of Daily Living score, self reported falls, hand grip, chair stands , and cognitive function (inhibitory control test)

Baki J et al. AASLD 2018, San Francisco #177
Frailty and Opiate Use Correlate with QOL in Cirrhotics

- 70% CPT A, median MELDNa 9
- 76% varices
- 41% h/o ascites
- 91% performed all ADLs
- 22% chronic opiates

Beta coefficient represents adjusted, incremental effect of each factor on QOL

Conclusion: Opiate deprescribing and PT may be modifiable factors for QOL improvement

Table 1: Multivariable Linear Regression of Factors Associated with Quality of Life (QOL)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta Coefficient (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.18 (0.01 – 0.36)</td>
<td>0.04</td>
</tr>
<tr>
<td>Education</td>
<td>1.32 (0.33 – 2.32)</td>
<td>0.01</td>
</tr>
<tr>
<td>MELD-Na</td>
<td>-0.54 (-0.19 - -0.86)</td>
<td>0.009</td>
</tr>
<tr>
<td>Incomplete ADL</td>
<td>-5.56 (-11.1 - -2.06)</td>
<td>0.005</td>
</tr>
<tr>
<td>Falls</td>
<td>-3.61 (-6.57 - -0.64)</td>
<td>0.02</td>
</tr>
<tr>
<td>Chair stands (per 10)</td>
<td>8.97 (4.60 – 13.33)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>-3.36 (-6.36 - -0.36)</td>
<td>0.03</td>
</tr>
<tr>
<td>Opiates</td>
<td>-7.43 (-10.3 - -4.57)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Liver Frailty Index (LFI) Predicts Waitlist Mortality

- Frailty predicts mortality, independent of MELDNa
  - Unclear if Frailty also predicts mortality independent of ascites and HE (not captured in MELDNa)
- Studied OLT waitlist at 9 US centers
- Liver Frailty Index – grip, chair stands, balance
  - Frail = LFI > 4.5
- HE defined as Numbers Connection Test score > 45 seconds

Lai J et al. AASLD 2018, San Francisco #217
Liver Frailty Index (LFI) Predicts Waitlist Mortality

• Frailty is common
• Frailty higher with ascites or HE
• Frail patients were more likely to die or be delisted if ascites or HE
• In competing risk regression, HE and Frailty associated with wait list mortality (not ascites)

Lai J et al. AASLD 2018, San Francisco #217
Liver Frailty Index (LFI) Predicts Waitlist Mortality

• In Multivariate models adjusted for MELDNa, age, race, albumin, ascites and HE, only frailty was associated with wait list mortality (HR 1.8, 95% CI 1.3-2.5 p < 0.01)
  – Neither ascites or HE were predictive

• Conclusion: LFI should be recognized as independent complication of cirrhosis
  – May help predict those who need intensive PT (“pre-habilitation”) or accelerated path to transplant to prevent falling off list or mortality
Alcohol Liver Disease Rising

• Mortality due to cirrhosis increasing since 2009
  – Driven by alcohol mediated cirrhosis in people aged 25-34
  – Highlights new challenge for care of patients with liver disease in post HCV era

Tapper EB and Parikh ND. BMJ. 2018;362:k2817
Rising Burden of ACLF from ETOH in the Young

- Reviewed National Inpatient Sample 2006-14
- Of 112,174 admissions with ACLF from 2006-2014, 5772 (5.15%) patients were young (<35 yo)
  - 2.7% in 2006 and increasing to 4.9% in 2014

Axley P et al. AASLD 2018, San Francisco #282
Rising Burden of ACLF from ETOH in the Young

- Younger patients (mean age 31 vs. 56 years) were more likely to be... (p<0.0001 for all)
  - female (35.3 vs. 28.5%),
  - obese (11.1 vs. 7.6%),
  - Hispanic (28.7 vs. 17.9%),
  - hospitalized in the southern US (46.2 vs. 32.6%)
  - admitted with alcoholic hepatitis (40.6 vs. 16.5%)

- ACLF severity was greater in young adults
- Young adults were more likely to have... (p<0.001 for all)
  - variceal bleeding (11 vs. 8%),
  - hepatic encephalopathy (72.7 vs. 68.3%)
  - hepatorenal syndrome (28.5 vs. 19i%)
  - increased use of mechanical ventilation (79 vs. 76%)
  - renal replacement therapy (31.9 vs. 27.9%)

Axley P et al. AASLD 2018, San Francisco #282
Costs of Liver Disease Rising

- Data from National Inpt Sample – 2005-2011
- 3,644,332 cirrhosis admissions – 44% liver-related
- Between 2005 and 2011, the total number of cirrhotic admissions increased 52%
- Total cost of liver admissions per year increased 59%, from $6.08 billion to $9.66 billion
- National cost $55.8 billion overall and $15.2 billion for liver-related admissions

Zou B et al. AASLD 2018, San Francisco #175
Early Discharge Visits Improves Survival But Not Readmission Rate

• Early outpatient visits after hospitalization promoted as a method to reduce readmissions
• Reviewed cirrhotics discharged 2015-16
• 256 patients
  – 77% had visit scheduled before d/c
  – 60% were within 30 days
    • 83 kept visit and 70 non-adherent

Rao BB et al. AASLD 2018, San Francisco #176
Early Discharge Visits Improves Survival But Not Readmission Rate

- Readmission rates at 1, 3, 6 months statistically similar
- Survival at 3 and 6 months higher in adherent group (p = 0.029)
- HE patients were less likely to adhere
- Commercial insurance more adherent
- Dissociation between readmission and survival should be considered when measuring quality

Rao BB et al. AASLD 2018, San Francisco #176
Einstein Telehealth Monitoring

- All patients discharged from Liver unit
- First launched 4/27/18
- Program readmission rate
  - 27% vs 48.1% prior
  - Diverse readmissions
    - Bronchitis, ERCP complications, Hyponatremia
- Patient satisfaction 97%
Take Home Points

• Midodrine + Albumin may decrease PICD
• Tolvaptan may reduce dose of diuretics used for ascites and improve renal function (?survival)
• Low dose Terlipressin is a safe adjunct in variceal bleeding (if you live outside the US or Canada)
• Using LS cutoff may reduce unnecessary variceal screening (supported by guidelines and evidence)
• Macitentan is safe in PoPH
• Reducing PPI and Opiate use in HE is helpful
• Frailty is essential to recognize in liver patients and may be considered a unique complication
• Liver related hospitalizations and cost are rising
  – And post discharge visits don’t help readmission rates but may improve survival
THANK YOU
Complications of Portal Hypertension – A Practical Management Approach

Advances in Liver Disease 2018: A Year in Review
12/8/18
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