Managing Ascites in 2013

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Fabulous Lake Louise June 14, 2013

Disclosures

Nothing To Disclose

Off Label Uses: Midodrine, Baclofen

Outline

• Case of Ascites & “Rhabdomyolysis” AKI
• Evaluation of the Patient with Ascites
• Tap & Ascitic Fluid Analysis
• Complications of Ascites
• Treatment of Patients with Ascites

Sleisenger and Fordtran 9th Edition
Gastrointestinal and Liver Diseases
2010: pp 1517-41
Hepatology 2013;57:1651-3
J Hepatol 2010;53:397-417
Internat J Hepatol 2011: ID 801983
UpToDate
64 y/o White Male

- New Clinic Visit June 4, 2013
- CC: Ascites
- Admitted May 16-20, 2013
  When Clinic Labs: Na 115, K 3.6, BUN 45, Cr 6.2, WBC 6.7, Hb 9.5, Plt 131
- TP 5.5, Alb 3.3, Bili 1.7, AST 105, ALT 28, INR 1.3, MELD 25

64 y/o White Male

- HPI: Cirrhosis on CT 2-3 y Prior
- 4-5 Drinks/d PTA
- 1st Decompensation of ALD
- UGIB on NSAIDs 10 y Prior
- No Hep Encephalopathy
- No IVDA or Street Drugs

64 y/o White Male

- PMH: DU on NSAID, HTN, Dyslip, CAD c Stent, Alc Cirr
- PSH: Arthroscopic Knee, Stent
- Meds On Adm: ASA, PPI, Ezetimibe, Metoprolol 100 mg bid, Crestor, Valsartan 320 mg/d, Talsulosin
64 y/o White Male

- Hosp Adm PE: BP 90/60, P 68
- Obese, Alert, Ascites, Firm Liver
- No Edema
- Vascular Spiders
- No Asterixis

64 y/o White Male

- Adm Dx: “?Rhabdo From Playing Golf in the Sun”
- ARB D/C, Azotemia Resolved
- Sent Home with BP 90s/60s Off ARB, but on BB & Alpha B

64 y/o White Male: DDx

- Not Rhabdo
- Not HRS
- Not ATN
- Hypotension/Hypoperfusion Induced by ARB, Alpha B & BB
- ASA Reduces Renal PG
- “Cirrhosis Cures Hypertension”
**64 y/o White Male: DDx**

- In My Clinic: BP 99/65, P 65
- 3+ Ascites, 1 cm Edema
- Na 131, K 4.9, BUN 16, Cr 1.3
- Plan: 100 mg Aldac, Furo 40 mg, D/C BB, D/C Tamsulosin, Start Dutasteride
- Avoid Anti-HTN Rx

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**64 y/o White Male: DDx**

- 1 Week Later: 10# Wt Loss
- BP 119/67
- Na 126, 4.2, BUN 7, Cr 1.1
- UNa 108/UK 48
- One of My Goals in Cirrhosis c Ascites is MAP >82=Sys BP >100

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**Differential Diagnosis of Ascites**

- Causes of Ascites
  - Mostly Cirrhosis & Alcoholic Hepatitis
  - Special Attention to Curable Diseases: TB, Chlamydia, Pericarditis
- Evaluation
  - History & Physical Examination
  - Ascitic fluid Analysis
  - Ultrasound of Liver & Spleen c Doppler
  - Special Testing
Paracentesis

• Routine for New Onset, Admission, or Deterioration
• Diagnostic Tap = 22 ga 1.5 inch
• Therapeutic Tap = 15-18 ga
• 1% Complication Rate
• ~1/1000 Serious Complication

[References]
Arch Intern Med 1986;146:2259-61
Transfusion 1991;31:164-71
Hepatology 2004;40:484-8
Video NEJM 2006;355:e21
UpToDate—17 Pages

Special Testing

• Cardiac Echo
  • Suspected Cardiac Ascites
  • Serum Pro-BNP 6100 vs 166 for Cirrhosis
• Upper GI Endoscopy
  • Screening for Large Varices
  • May Detect H. pylori or Gastric Ca
• Laparoscopy to Rule in TB

[References]
Hepatology 2006;44:449A
J Clin Gastro 2010;44:e23-6

Rx of Cirrhosis & Ascites

• Abstinence from Alcohol
• "News Flash" Baclofen to Reduce Alcohol Craving: “Miracle”
  • 5 mg tid x 3d, Then 10 mg tid, Maybe 5-10 5/d
• Dietary Sodium Restriction: 2g (88 mmol/d)
• Diet Education of Patient & Cook
• Oral Spironolactone & Furosemide
  • Usual Starting Doses 100 mg & 40 mg q AM
• Follow Weight & Urine Na/K

[References]
Hepatology 2012;57:1651-3
Lancet 2007;370:1915-22
Science 2011;332:653
Hepatology 2010;52:1104A
Hepatology 2012;56:1091A
Random UNa/K

- Pts on 88 mmol/d Diet Must Have Ur Na>K to Lose Weight
- If UNa>K & They Are Not Losing Weight, More Diet Education
- If UNa<K, Increase Dose of Diuretics

Diuretics

- Starting Doses
  - 100 mg/d Spironolactone & 40 mg/d Furosemide
  - Follow Wt & Na/K
  - If No Wt Loss & Ur Na/K <1, Double to 200 & 80
  - Max Doses=400 & 160—Seldom Used
  - Amiloride Can Be Substituted (10-40 mg/d)

Diuretics: Special Populations

- Alcoholic Hepatitis
  - Days/Wks of Low K Requiring Supplementation
  - Start with Spironolactone Alone
  - Only Add Furosemide When K Normal
  - D/C Diuretics for Azotemia
- Parenchymal Renal Disease, inc Elderly
  - Prone to Hyperkalemia
  - Use More Furosemide & Less Spironolactone
BP & Survival in Cirrhosis

- Patients Admitted with Tense Ascites & Cirrhosis
- Multivariate Analysis: MAP p=0.00001
  - MAP >82 mmHg 70% 24 Mo Survival
  - MAP ≤82 mmHg 20% 24 Mo Survival

Gastroenterology 1988;94:482-7

"Window Hypothesis" of Beta Blockers in Cirrhosis

Gut 2012;61:967-9
Sir William Osler
Paraphrased by TB Reynolds

“Patients Do the Teaching, If We Just Pay Close Enough Attention”

Midodrine for Ascites
• BP Drops as Ascites Becomes Refractory
  • Nurses & Diuretics
• Midodrine: Oral Alpha Agonist
• Midodrine Can Increase BP & Improve Response to Diuretics
• 40 Patient RCT for Refrac or Recurrent
  • Inc Uvol, UNa, MAP, SVR, Control, Survival
  • Decrease PRA, CO

J Hepatol 2007;46:213-21
Liver Int 2009;29:109-74
J Hepatol 2012;56:348-54
Propranolol & Ascites

- Lebrec: “Propranolol Does Not Decrease BP in Cirrhosis”
- Conflicts with My Experience
- Accumulating Data Suggesting Harm in Refractory Ascites
  - Prospective Study: 5 mo vs 20 mo Survival
  - 80% vs 10% PICD p LVP in Refractory
- My Advice: Individualize & Monitor BP & Creatinine

Vaptans & Ascites

- Older Studies for Hyponatremia: CHF
- $15,000/mo to Increase Thirst
- FDA May 20, 2013 Announced that Tolvaptan May Cause Liver Injury Leading to Organ Transplant or Death in Cirrhosis
- Largest RCT: Cirrhosis-Specific
  - 1200 Patients: Uncomplicated Ascites & DTT
  - “Satavaptan is Not Clinically Beneficial in the Long-Term Management of Ascites in Cirrhosis”. Mortality Was Increased.

Rx of Patients with Ascites

- Medical Rx: 90% Effective
- D/C Propranolol, ACEi, ARB, NSAID, Alpha B
- Options for Diuretic-Resistant Patients
  - Midodrine to Increase BP, Uvol & Una, & Surv
  - LVP –q 2 Weeks (8 liters)
  - TIPS
  - Liver Transplantation
  - Peritoneovenous Shunt: Denver (Leveen Gone)
Pseudorefractory Ascites

- High Sodium Intake
- Non-Compliance
- No Diet Education
- Favorite Food
- IV Saline or Na Medication
- NSAIDs
- Propranolol, ACE, ARB, Alpha B

Tap Equipment

- Tri-Med Caldwell 15-ga 3.25 inch
- End Hole & Side Holes
- GI Supply RP System
  - Peristaltic Pump 1 L/2 Minutes
  - Longest Needle
  - Remanufacture May Occur
- Requires #11 Scalpel Nick
**Large-Volume Paracentesis (LVP)**

- LVP Does Not Cause “Vacuum”
- Fluid Forms Slowly, Weeping Across Liver Capsule
- LVP Improves Breathing & Appetite
- Increases Vital Capacity
- Prevents Leaks from Tap Sites
- Edema Refills Abdomen Rapidly

*Am J Gastro 1993;88:905-7*

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**Albumin After LVP**

- Study Design is a Problem
- In the 1st Study 31% of Patients Had Not received Diuretics
- Most Pts in these Studies are Diuretic-Sensitive, But Have Tense Ascites
- Albumin Not Needed for Taps <5L
- Albumin May Improve Survival for >5L, (6-8g/L)

*Am J Gastro 1997;92:371-3
Liver Internat 2009;29:636-41
Hepatology 2012;55:1172-81*

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**TIPS**

- Transjugular Intrahepatic Portasystemic Stent-Shunt
- Initial Wild Enthusiasm
- ~$20,000 Insertion Fee
- Now Much Better Selection
TIPS for Refractory Ascites

- Side-to-Side Radiologic Shunt
- Usually Converts Diuretic-Resistant to Diuretic-Sensitive
- ~25% Encephalopathy but Treatable
- Much Better Control of Ascites Than Taps
- Possible Survival Advantage

Gastroenterology 2002;123:1839-47
Gastroenterology 2003;124:634-41
Hepatology 2010;51:1-16

TIPS

- Indications
  - Diuretic-Resistant Ascites
  - Multiple Rapid Readmissions for Ascites
  - Refractory Hepatic Hydrothorax
  - Avoid Chest Tubes
  - Thin Umbilical Hernia

Gastroenterology 2003;124:1700-10
Hepatology 2005;41:386-400
Am J Gastro 1986;81:566-7
Hepatol Int 2009;3:582-6

Large-Scale RCTs: Uncoated TIPS for Ascites

<table>
<thead>
<tr>
<th>Ref</th>
<th>No.</th>
<th>Control</th>
<th>Survival</th>
<th>Enceph</th>
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<tbody>
<tr>
<td>NEJM 2000 342:1701</td>
<td>60</td>
<td>61 vs 18% p=0.006</td>
<td>69% vs 52% p=0.02 mul</td>
<td>58% vs 48% NS</td>
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<tr>
<td>Gastro 2002 123:1839</td>
<td>70</td>
<td>51% vs 17% p=0.003</td>
<td>43% vs 35% NS</td>
<td>All 77 vs 66 NS Sev 60 vs 54 p=0.18</td>
</tr>
<tr>
<td>Gastro 2003 124:634</td>
<td>109</td>
<td>58% vs 16% p&lt;0.001</td>
<td>40% vs 37% NS</td>
<td>Mod-Sev 38 vs 12, p= .06</td>
</tr>
<tr>
<td>Hep 2004 40:629-35</td>
<td>66</td>
<td>79% vs 42% p=0.0012</td>
<td>77% vs 52% p=0.021</td>
<td>61% vs 39% NS</td>
</tr>
</tbody>
</table>
Coated TIPS

- Coated: Less Stenosis, No Day 1 U/S
- Vienna Multi-Center Retrospective Study
  - 419 Bare vs 89 Goretx (45 for Ascites)
  - Goretx Had Better Survival: 3 mo, 1 yr & 2 yr
- International RCT
  - 80 Patients (32 Ascites)
  - PPG at 6, 12, 24 Months
  - 13% vs 44% Shunt Dysfunction, p<0.001
  - 8% vs 29% Clinical Relapse, p<0.05
  - No Change in PSE or Survival

My Personal Tips on TIPS

- It Is Difficult to Show Survival Advantage
- TIPS is Getting Better and Better
- TIPS Improves Hepatologist’s QOL & Maybe Pt’s
- Choose Patients Wisely
  - <65 y/o, Caregiver in House, Child-Pugh ≤12
  - Check MELD for Predicting 3-mo Survival, <18
  - No Alcoholic Hepatitis (80% mort)
  - Ejection Fraction ≥60% (nl EF=76% Hep 2002;35:1441-8)
  - Target PPG <8 mm Hg
  - No Severe Spontaneous HE or 2nd CNS Hit
- Use Diuretics post TIPS
- Coated TIPS Appears Is a Major Step Forward

Automated Low Flow Ascites (ALFA) Pump
Automated Low Flow Ascites (ALFA) Pump

- Start in 2004: Pumps fluid from peritoneal cavity to urinary bladder
- Chargeable 20 min/day with wand
- Prevents the waste of energy heating the fluid
- Could improve nutrition if patients can eat more
- Eases breathing

J Hepatol 20013;58:922-7

ALFA Pump: More Applicable Than TIPS

- Can be performed in elderly
  - Increasing population, even 90 y/o
- Hepatic encephalopathy
- Poor cardiac function
- High MELD
- Surgeon or IR insertion

ALFA Pump: Other Applications

- Cardiac ascites
- Malignancy-related ascites
  - Peritoneal carcinomatosis
  - Chylous ascites
- Hepatic hydrothorax
- "Pump Paracentesis"
Splenic Art Embo for PHT

- 1973 Autologous Clot Was Embolized
- 1982 Rx of Hypersplenism
- May Rx Refractory Variceal Hemorrhage
  - PVT & Failed TIPS Attempt
- May Improve Refractory Hep Encephalopathy
- 1 Successful Case of SAE To Rx Refractory Ascites in PVT After Liver Transplantation

PEG in Patients with Ascites

- Ascites is a Contraindication to PEG
- Omentum Cannot Seal a Leak with Fluid Bathing the Surfaces
- I Have Seen No Survivors
- 90% 30-Day Mortality in Recent Review
- I Disagree with AGA PG: “...if reaccumulation [of ascites] can be prevented for a period of 7-10 days”...

Survival after decompensation in 1150 patients with cirrhosis

JVIR 2007;18:463-81
Liv Transpl 2007;113:1532-7

Hepatology 2009;49:2087-107
Am J Gastro 2010;72:1072-5
Gastroenterology 2011;141:742-65
Treatment Options

• First Line
  • Abstinence from Alcohol
  • Na-Restricted Diet & Diuretics
  • Consideration of Transplant

Treatment Options

• Second Line
  • Discontinue BBs, ACEi, ARB, Alpha B
  • Midodrine
  • Q 2 Week Outpatient Taps
  • TIPS
  • Consideration of Transplant

Treatment Options

• Third Line
  • Denver Shunt
  • Splenic Artery Embolization
  • Experimental
    • ALFA Pump