COMPLICATIONS OF CIRRHOSIS: STRATEGIES TO IMPROVE LONG-TERM PATIENT OUTCOMES
Program Disclosure

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Annenberg Center for Health Sciences at Eisenhower and the Chronic Liver Disease Foundation (CLDF). The Annenberg Center for Health Sciences at Eisenhower is accredited by the ACCME to provide continuing medical education for physicians.

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This program is supported by an educational grant from AbbVie, Bristol-Myers Squibb and Salix.
Educational Objectives

• Recognize the signs of complications due to cirrhosis and the importance of early intervention.

• Describe evolving patient management strategies for hepatic encephalopathy in the hospital/outpatient setting.

• Apply the latest patient management strategies in order to decrease hospital readmissions due to hepatic encephalopathy.
Prevalence of Cirrhosis

- The prevalence of cirrhosis, both worldwide and in the US, is unknown
  - Compensated cirrhosis often goes undetected for prolonged periods of time
- Experts estimate that up to 1% of the population (~3 million) may have histological cirrhosis
Compensated Cirrhosis May Be Difficult to Recognize

- Asymptomatic
  - Subtle clues may be overlooked
    - Thrombocytopenia
    - Muscle wasting
    - AST>ALT without alcohol consumption
    - Liver enzymes may not be abnormal
  - Etiology may be remote
    - Prior alcohol use
    - Uncontrolled diabetes mellitus and obesity
Cumulative Proportion of Patients Transitioning from Compensated to Decompensated Stage Over Time

Once decompensation occurs median survival is 2 years.

Decompensated Cirrhosis

- Primary complications include:
  - Hepatic encephalopathy
  - Ascites
  - Variceal hemorrhage

- Other possible complications include:
  - Spontaneous bacterial peritonitis
  - Hepatic hydrothorax
  - Hepatorenal syndrome
  - Portopulmonary hypertension
  - Hepatocellular carcinoma
  - Portal vein thrombosis
Topics

• Hepatic Encephalopathy
• Economic and Social Burden
• Hospital Readmissions
• Cognitive Impairment
Treatment Goals for Overt HE

• Provision for supportive care
• Identification and removal of precipitating factors
  – Infection, GI bleed, dehydration
• Reduction of nitrogenous load from gut
• Correction of electrolyte abnormalities
• Long-term therapy assessment
  – Control of potential precipitating factors
  – Higher likelihood of recurrent encephalopathy
  – Assessment of need for liver transplantation

# Current Therapy Options for HE

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Drug Class</th>
<th>Indication</th>
</tr>
</thead>
</table>
| Lactulose | Poorly absorbed disaccharide | • Decrease blood ammonia concentration  
• Prevention and treatment of portal-systemic encephalopathy |
| Rifaximin | Non-aminoglycoside semi-synthetic, nonsystemic antibiotic | Reduction in risk of overt hepatic encephalopathy (HE) recurrence in patients ≥ 18 years of age. |
| Neomycin  | Aminoglycoside antibiotic | Not to be used, renal and ototoxic risk |
| Metronidazole | Synthetic antiprotozoal and antibacterial agent | Not approved for HE |
| Vancomycin | Aminoglycoside antibiotic | Not approved for HE |
Lactulose

- Currently the mainstay of therapy of HE; ~70% to 80% of patients with acute and chronic HE improve with lactulose treatment
- Mechanism of action:
  - A non-absorbable disaccharide that is fermented in the colon
  - Metabolism by the bacterial flora in the colon to lactic acid lowers the colonic pH
  - Cathartic effect can increase fecal nitrogen excretion with up to a 4-fold increase in stool volume

Lactulose (Cont.)

- Administered orally, by mouth or through a nasogastric tube or via retention enemas
- Dose: 45 to 90 g/day, titrated to achieve 2 to 3 soft stools per day with a pH below 6
- Principal side effects include abdominal distension, cramping, diarrhea, electrolyte changes, and flatulence
- Systematic review of clinical studies found insufficient evidence to support or refute the use of lactulose for HE

Rifaximin

- Minimally absorbed (<0.4%) oral antibiotic
- Broad-spectrum in vitro activity against aerobic and anaerobic enteric bacteria
- No clinical drug interactions reported
- No dosing adjustment required in patients with liver disease or renal insufficiency
- Approved for overt recurrent HE risk reduction in patients ≥18 years of age

Rifaximin Trial: Time to First Breakthrough HE Episode Primary Endpoint

- 91% of patients in both arms received concomitant lactulose

*Proportion of Patients Without Breakthrough HE (%)

Rifaximin* (77.9%)
Placebo* (54.1%)

*Rifaximin 550 mg or placebo twice daily
Hazard ratio with rifaximin, 0.42 (95% CI, 0.28–0.64)
P<0.001

Topics

• Hepatic Encephalopathy
• Economic and Social Burden
• Hospital Readmissions
• Cognitive Impairment
US Hospital Discharges Due to Cirrhosis Are Increasing

*ICD-9-CM diagnosis codes 571.2, 571.5, 571.6; all listed diagnoses.
### Resource Utilization for Patients Hospitalized with Hepatic Encephalopathy, 2005-2009

Increase health care utilization in patients discharged with the diagnosis of hepatic encephalopathy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of procedures</td>
<td>1.91 ± 0.06</td>
<td>1.92 ± 0.05</td>
<td>2.10 ± 0.07</td>
<td>2.20 ± 0.07</td>
<td>2.24 ± 0.06</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Length of stay, d</td>
<td>8.04 ± 0.17</td>
<td>7.95 ± 0.11</td>
<td>7.98 ± 0.11</td>
<td>8.40 ± 0.18</td>
<td>8.53 ± 0.17</td>
<td>.0191</td>
</tr>
<tr>
<td>Average charge (2009 $)</td>
<td>46,663 ± 2180</td>
<td>47,297 ± 1728</td>
<td>51,889 ± 2308</td>
<td>59,786 ± 3546</td>
<td>63,107 ± 3244</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Average cost (2009 $)</td>
<td>16,512 ± 709</td>
<td>15,851 ± 449</td>
<td>16,588 ± 615</td>
<td>17,832 ± 762</td>
<td>17,812 ± 764</td>
<td>.1697</td>
</tr>
<tr>
<td>Total national charge, (2009 $) millions</td>
<td>4676.7</td>
<td>5059.5</td>
<td>5603.5</td>
<td>6484.0</td>
<td>7244.7</td>
<td></td>
</tr>
<tr>
<td>Total national cost, (2009 $) millions</td>
<td>1651.1</td>
<td>1695.6</td>
<td>1791.3</td>
<td>1932.0</td>
<td>2044.5</td>
<td></td>
</tr>
</tbody>
</table>

Frequency and Duration of Hospitalization During the Lactulose and Rifaximin Period in Patients with Hepatic Encephalopathy

<table>
<thead>
<tr>
<th></th>
<th>Mean Number of Hospitalizations</th>
<th>Mean Days per Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During Lactulose</strong></td>
<td>1.6 (1.1)</td>
<td>7.3 (4.1)</td>
</tr>
<tr>
<td>n = 145</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>During Rifaximin</strong></td>
<td>0.5* (0.7)</td>
<td>2.5* (3.6)</td>
</tr>
<tr>
<td>n = 141</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P <0.001 rifaximin period versus lactulose period, paired t-test
Total Time Hospitalized and Charges During the Lactulose and Rifaximin Period in Patients with Hepatic Encephalopathy

*P <0.001 rifaximin period versus lactulose period, paired t-test

Charges were calculated in 2005 dollars based on average cost per hospital day as determined by the 2003 Healthcare Cost Utilization Project for ICD-9-CM principal diagnosis code 572.2. A healthcare cost index was used to predict 2004 and 2005 costs.

Demographic and Hospitalization Information for Both Groups

<table>
<thead>
<tr>
<th></th>
<th>Gender (male/female)</th>
<th>MELD (average)</th>
<th>Age (mean) (years)</th>
<th>Hospitalizations (total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group one (lactulose)</td>
<td>18/6</td>
<td>14 (range 10-19)</td>
<td>48</td>
<td>19</td>
</tr>
<tr>
<td>Group two (rifaximin)</td>
<td>10/5</td>
<td>15 (range 10-18)</td>
<td>47</td>
<td>3</td>
</tr>
</tbody>
</table>

Notes: Hospitalization number and treatment cost in patients with hepatic encephalopathy who received lactulose or rifaximin therapy. Treatment with rifaximin therapy reduced the number of hospitalizations compared with treatment with lactulose therapy concurrent with a reduction in total cost of therapy per patient (2005 US dollars).
Abbreviation: MELD, Model for End-Stage Liver Disease.
Therapy received affected hospital stays and costs in patients with OHE

<table>
<thead>
<tr>
<th>Group (outpatient therapy → added hospital therapy)</th>
<th>n</th>
<th>MELD score (mean)</th>
<th>Length of stay (days)</th>
<th>Time to start of full diet (days)</th>
<th>HCUP (7,500/d)</th>
<th>Insured/MC/MD costs (8,382/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Lac→Lac</td>
<td>18</td>
<td>11.5</td>
<td>5.75</td>
<td>4.1</td>
<td>43,125</td>
<td>48,197</td>
</tr>
<tr>
<td>(2) RFX→Lac</td>
<td>19</td>
<td>12.5</td>
<td>3.4</td>
<td>2.25</td>
<td>25,500</td>
<td>28,329</td>
</tr>
<tr>
<td>(3) Lac→RFX</td>
<td>20</td>
<td>10.5</td>
<td>4.25</td>
<td>3.5</td>
<td>31,875</td>
<td>35,624</td>
</tr>
<tr>
<td>(4) NT→Lac/RFX</td>
<td>14</td>
<td>11.5</td>
<td>5.25</td>
<td>3.8</td>
<td>39,375</td>
<td>44,006</td>
</tr>
<tr>
<td>(5) NT→Lac</td>
<td>28</td>
<td>13</td>
<td>6.5</td>
<td>4.5</td>
<td>48,750</td>
<td>54,483</td>
</tr>
</tbody>
</table>

Notes: There were five groups of patients with three admission treatments: no treatment, lactulose, or rifaximin. Patients were then treated with lactulose, rifaximin, or both. The most expensive group in terms of length of stay and overall costs were the no-treatment groups. The least expensive in terms of length of stay and overall costs was the group presenting on rifaximin therapy.

Abbreviation: d, day; HCUP, Healthcare Cost and Utilization Project; Lac, lactulose; Lac/RFX, lactulose and rifaximin combination therapy; MC, Medicare; MD, Medicaid; MELD, Model for End-Stage Liver Disease; NT, no treatment; OHE, overt hepatic encephalopathy; RFX, rifaximin monotherapy.

Impact of Affordable Care Act (ACA) on Patients with Hepatic Encephalopathy

• Under the ACA, the Centers for Medicare & Medicaid Services (CMS) assign penalties to hospitals for underperformance in certain conditions

• In an effort to decrease costs and improve quality of care, CMS has selected certain core conditions to measure and evaluate

• Measures
  – 30-day readmission rates
  – Average length of stay
  – Mortality

<table>
<thead>
<tr>
<th>Care Measure Conditions</th>
<th>Hospital-Acquired Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Acute myocardial infarction (AMI)</td>
<td>• Central-line associated blood stream infection (CLA-BSI)</td>
</tr>
<tr>
<td></td>
<td>• Methicillin-resistant <em>staphylococcus aureas</em> (MRSA)</td>
</tr>
<tr>
<td>• Heart failure (HF)</td>
<td>• Catheter-associated urinary tract infection (CA-UAT)</td>
</tr>
<tr>
<td></td>
<td>• <em>Clostridium difficile</em> (C. diff)</td>
</tr>
<tr>
<td>• Chronic obstructive pulmonary disorder (COPD)</td>
<td>• Sepsis</td>
</tr>
<tr>
<td></td>
<td>• Falls</td>
</tr>
<tr>
<td>• Pneumonia</td>
<td>• Pressure ulcers</td>
</tr>
</tbody>
</table>

• While the ACA does not currently include regulations for HE, in a retrospective review of 21 million inpatient admissions in 2014, 42% of patients admitted with HE presented with a core measure comorbidity.
HE Disrupts Caregiver’s Lives

- Overt episodes of HE are debilitating, can render the patient incapable of self-care\(^1\)
- HE caregivers report greater disruptions compared to cirrhosis caregivers\(^2\)

**Complications of Cirrhosis\(^3\):**
- Encephalopathy
- Ascites
- Varices, Bleeds
- Coagulopathy
- Malnutrition
- HCC
- HPS/HRS

**Complications of Aging:**
- COPD
- CVA
- DM
- Arthritis
- Cancer
- Dementia
- CHF
- CAD
- MI

**Informal Caregiver Burden**
- Cost
- Strain
- Time

ADL, activities of daily living; IADL, instrumental activities of daily living; CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM, diabetes mellitus; GI, gastrointestinal; HCC, hepatocellular carcinoma; HPS, hepatopulmonary syndrome; HRS, hepatorenal syndrome; MI, myocardial infarction

Impact of Hepatic Encephalopathy on Affected Family Within the Last Three Years

Hepatic encephalopathy impacts family daily functioning compared to previous three years of patient diagnosis

Hepatic Encephalopathy Impact on Caregivers

Increase caregiver burden with increasing severity of hepatic encephalopathy
Mean (±SE) caregivers’ scores in the ‘objective burden’ domain of the
Caregiver Burden Inventory (CBI)

Incremental Cost-Effectiveness Ratios


Bozkaya D, Barrett AC, Migliaccio-Walle K. AASLD Annual Liver Meeting Poster. 2014.
Topics

• Hepatic Encephalopathy
• Economic and Social Burden
• Hospital Readmissions
• Cognitive Impairment
Hospital Readmissions Among Patients with Decompensated Cirrhosis are Common

- Retrospective study of 402 patients from an academic transplant center
- Follow-up time censored at death, elective admissions such as transplant or post-procedure observation, or the date of last clinic note; median follow-up was 203 days
- Included cirrhotic patients hospitalized for ascites, SBP, renal failure, hepatic encephalopathy, or variceal hemorrhage
- Median time to readmission was 67 days
- Median number of readmissions was 2 (range 0-40); overall rate was 3 hospitalizations/person-year

All-Cause and HE-Related Re-Hospitalization for Patients with Hepatic Encephalopathy

N=8,125 alive at discharge

## Unadjusted and Adjusted Odds Ratios for 30-Day Readmissions by Condition for Complications of Liver Disease

<table>
<thead>
<tr>
<th></th>
<th>30-Day Hepatology Readmission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted OR (95% CI)</td>
</tr>
<tr>
<td><strong>Number of complications</strong></td>
<td></td>
</tr>
<tr>
<td>1 vs 0</td>
<td>1.58 (1.47-1.71)</td>
</tr>
<tr>
<td>2 vs 0</td>
<td>4.20 (3.81-4.62)</td>
</tr>
<tr>
<td>3+ vs 0</td>
<td>5.42 (4.61-6.37)</td>
</tr>
<tr>
<td><strong>Type of complication</strong></td>
<td></td>
</tr>
<tr>
<td>Ascites</td>
<td>1.28 (1.20-1.37)</td>
</tr>
<tr>
<td>Variceal hemorrhage</td>
<td>1.85 (1.71-2.00)</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>2.62 (2.41-2.83)</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>2.33 (1.90-2.85)</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>1.79 (1.61-2.00)</td>
</tr>
<tr>
<td><strong>Other specified conditions</strong></td>
<td></td>
</tr>
<tr>
<td>Alcoholic liver disease</td>
<td>1.27 (1.19-1.35)</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1.85 (1.72-1.98)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1.46 (1.25-1.70)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>1.28 (1.18-1.38)</td>
</tr>
<tr>
<td>Infection</td>
<td>0.96 (0.90-1.02)</td>
</tr>
</tbody>
</table>
## Unadjusted and Adjusted Odds Ratios for 90-Day Readmissions by Condition for Complications of Liver Disease

<table>
<thead>
<tr>
<th>Number of complications</th>
<th>Unadjusted OR (95% CI)</th>
<th>Model 1 OR (95% CI)</th>
<th>Model 2 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 vs 0</td>
<td>1.44 (1.35-1.53)</td>
<td>1.62 (1.52-1.73)</td>
<td></td>
</tr>
<tr>
<td>2 vs 0</td>
<td>3.83 (3.54-4.14)</td>
<td>4.03 (3.71-4.37)</td>
<td></td>
</tr>
<tr>
<td>3+ vs 0</td>
<td>4.70 (4.11-5.37)</td>
<td>5.22 (4.55-6.00)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of complication</th>
<th>Unadjusted OR (95% CI)</th>
<th>Model 1 OR (95% CI)</th>
<th>Model 2 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascites</td>
<td>1.11 (1.05-1.18)</td>
<td>1.31 (1.23-1.39)</td>
<td>1.60 (1.52-1.69)</td>
</tr>
<tr>
<td>Variceal hemorrhage</td>
<td>2.03 (1.90-2.16)</td>
<td>1.83 (1.71-1.95)</td>
<td>1.70 (1.60-1.82)</td>
</tr>
<tr>
<td>Hepatic encephalopathy</td>
<td>2.44 (2.28-2.60)</td>
<td>2.53 (2.37-2.70)</td>
<td>3.07 (2.86-3.30)</td>
</tr>
<tr>
<td>Hepatorenal syndrome</td>
<td>2.06 (1.75-2.43)</td>
<td>2.31 (1.96-2.73)</td>
<td>1.43 (1.20-1.71)</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>1.98 (1.82-2.15)</td>
<td>1.79 (1.63-1.96)</td>
<td>1.83 (1.67-2.01)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other specified conditions</th>
<th>Unadjusted OR (95% CI)</th>
<th>Model 1 OR (95% CI)</th>
<th>Model 2 OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcoholic liver disease</td>
<td>1.27 (1.21-1.33)</td>
<td>1.17 (1.11-1.24)</td>
<td>1.10 (1.04-1.16)</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>1.97 (1.87-2.09)</td>
<td>1.78 (1.69-1.88)</td>
<td>2.09 (1.97-2.22)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1.48 (1.30-1.68)</td>
<td>1.32 (1.16-1.51)</td>
<td>1.41 (1.23-1.61)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>1.12 (1.05-1.20)</td>
<td>1.37 (1.28-1.47)</td>
<td>1.23 (1.15-1.32)</td>
</tr>
<tr>
<td>Infection</td>
<td>0.89 (0.85-0.94)</td>
<td>1.03 (0.98-1.09)</td>
<td>1.02 (0.96-1.08)</td>
</tr>
</tbody>
</table>

Reducing 30 Day Readmission by Intervention Phase

- Electronic phase ~ Checklist items incorporated into electronic provider order system
- Check list phase ~ QI checklist prompted medication review and dosing

## Univariate Analysis of Admission Number and Hospital Length of Stay (HLOS) Before and During Rifaximin

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Admissions</th>
<th>HLOS</th>
<th>Before Rifaximin</th>
<th>During Rifaximin</th>
<th>Δ</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months n=227 (69.9%)</td>
<td>Admissions</td>
<td>1.17 (1.15)</td>
<td>0.64 (0.96)</td>
<td>45.3%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HLOS</td>
<td>15.84 (22.46)</td>
<td>7.40 (14.66)</td>
<td>53.3%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>6 months n=189 (60.0%)</td>
<td>Admissions</td>
<td>1.62 (1.48)</td>
<td>1.02 (1.47)</td>
<td>37.0%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HLOS</td>
<td>20.66 (25.46)</td>
<td>9.66 (16.59)</td>
<td>53.2%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>12 months n=158 (48.5%)</td>
<td>Admissions</td>
<td>2.11 (1.96)</td>
<td>1.56 (2.39)</td>
<td>26.1%</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HLOS</td>
<td>24.40 (29.69)</td>
<td>11.53 (18.60)</td>
<td>52.7%</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>All data annualised n=315 (96.6%)</td>
<td>Admissions</td>
<td>3.12 (9.77)</td>
<td>1.98 (4.52)</td>
<td>36.5%</td>
<td>0.042</td>
<td></td>
</tr>
<tr>
<td></td>
<td>HLOS</td>
<td>30.50 (21.03)</td>
<td>21.03 (54.18)</td>
<td>31.0%</td>
<td>0.006</td>
<td></td>
</tr>
</tbody>
</table>

Pattern of **Mean Number of Admissions**

Mean Length of Emergency Hospital Admissions

The Majority of Overt HE Patients Do Not Receive Proper Management Therapy After Discharge

- It was determined that >60% of patients did not receive ongoing prophylactic therapy to reduce the risk of HE recurrence after discharge
- Within an analysis of medical and hospital claims among outpatients who had 1 or more overt HE episodes from 2009 to 2011 during a 3-year period

Saab S. *Int J Gen Med.* 2015; Neff GW, Frederick RT. *Hepatology.* 2012;56(suppl 1):945A.
Rehospitalization Rates Due to Recurrent HE Can Potentially Be Prevented

- In one study, HE was one of the most common causes for possibly preventable rehospitalizations within 1 month after discharge for decompensated cirrhosis†

- Some of these rehospitalizations could have been potentially prevented with:
  - Improved Patient Education
  - Telephone Management
  - Other Disease Management Interventions

† In a retrospective study of adult patients originally hospitalized with cirrhosis (N=402) and any of the following complications: HE (34%), variceal hemorrhage (20%), spontaneous bacterial peritonitis (13%), renal failure with ascites (24%), or ascites requiring paracentesis (54%) during a 3-year period.1,2

Topics

- Hepatic Encephalopathy
- Economic and Social Burden
- Hospital Readmissions
- Cognitive Impairment
Changes in Resting-State Functional MR Imaging

Reduction in Functional Connectivity

A. Healthy control subjects

B. The cirrhotic patients without MHE and without previous OHE

C. The cirrhotic patients with current MHE and without previous OHE

D. The cirrhotic patients with previous OHE

Learning Impairment in Patients with Cirrhosis with a Previous Episode of Overt Hepatic Encephalopathy (HE)

Patients with cirrhosis without prior overt HE episode

Patients with cirrhosis with a prior overt HE episode

Overt HE Impairs Learning in Patients with Cirrhosis

- Inhibitory control test (ICT)
- Learning impairment in overt HE but not in minimal HE or normals

Greater Decline in Brain Volume in Patients with History of HE After Liver Transplantation

Decreased Cognitive Functions Before and After Liver Transplant According to History of Overt HE

Cognitive Function May Be Compromised, Even Post Liver Transplant

- Study objective: evaluate cognitive function and quality of life in OLT recipients who had suffered from overt HE prior to their procedure
- Patients with cirrhosis with and without overt HE scheduled for liver transplantation (n=39) underwent 2 psychometric batteries* an average of 18 months after liver transplant

*Includes the psychometric hepatic encephalopathy score and Repeatable Battery for the Assessment of Neuropsychological Status. Error bars indicate standard deviation.
†Based on results of Repeatable Battery for the Assessment of Neuropsychological Status. 
‡P<0.001 vs normative values. §P<0.05 vs normative values.
## Employment in Liver Transplant Recipients, in the United States

<table>
<thead>
<tr>
<th>Authors (Year)</th>
<th>Number</th>
<th>Follow-up (Months)</th>
<th>Mean Age (Years)</th>
<th>Return to Work</th>
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<tbody>
<tr>
<td>Cowling et al (2004)</td>
<td>152</td>
<td>53</td>
<td>53</td>
<td>36%</td>
</tr>
<tr>
<td>Rongey et al (2005)</td>
<td>186</td>
<td>41</td>
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<tr>
<td>Sahota et al (2006)</td>
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<td>54</td>
<td>49%</td>
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<td>Saab et al (2007)</td>
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<tr>
<td>Huda et al (2012)</td>
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<td>Duffy et al (2010)</td>
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<td>&gt;240</td>
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<td>Gorevski et al (2011)</td>
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<td>-</td>
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<td><strong>Weighted</strong></td>
<td>22,861</td>
<td></td>
<td></td>
<td><strong>45%</strong></td>
</tr>
</tbody>
</table>

Conclusions

- Hepatic encephalopathy is an economic and social burden. Increased burden is realized not only by patients but also experienced by caregivers.
- Hepatic encephalopathy is an important cause of hospital readmission.
- Hepatic encephalopathy is not a completely benign complication of cirrhosis. It may affect future learning that may persist even after liver transplantation.