Cirrosis Descompensada y Alcohol

Hugo Cheinquer

Professor Titular de Gastroenterología e Hepatología da UFRGS
Hospital de Clínicas de Porto Alegre
Porto Alegre, RS, Brasil
I have no conflict of interests related to this presentation
Natural history of alcoholic liver disease

- Healthy liver
- Alcohol → Steatosis/fibrosis, alcoholic steatohepatitis
- Alcohol → Liver cirrhosis
- Alcohol → Liver cancer

90%-100% steatosis
10%-35% alcoholic hepatitis
8%-20% cirrhosis
1%-2% of cirrhotics/year develop HCC
20%-40%

Adapted from:
Issues in alcoholic decompensated cirrhosis

- Nutrition
- Overlap of alcoholic hepatitis
- Different prognostic models
- Impact of alcohol abstinence
- Infection
- Alcohol withdrawal syndrome
Prognostic models

MADDREY  MELD  GLASGOW  LILLE
# Lille Model for Alcoholic Hepatitis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>57</td>
<td>years</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.9 g/dL</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (initial)</td>
<td>5.3 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (day 7)</td>
<td>3.4 mg/dL</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.1 mg/dL</td>
<td></td>
</tr>
<tr>
<td>PT</td>
<td>17 sec</td>
<td></td>
</tr>
</tbody>
</table>

**0.185 points**  
Low score = low mortality  
Good prognosis. Scores < 0.45 predict a 6-month survival of 85%.

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**The Lille Model: A New Tool for Therapeutic Strategy in Patients with Severe Alcoholic Hepatitis Treated with Steroids**

- Survival
  - <0.45
  - \( p < 0.0001 \)
  - \( \geq 0.45 \)


Decompensated cirrhosis
Impact of removing the etiology of the liver disease
Treating HBV increases SV in decompensated B cirrhosis

Treating HCV increases SV in decompensated C cirrhosis

HCV

Observed versus expected mortality

- Expected (historical)
- Observed (SVR with DAAs)

Standardized mortality ratio at 1 year = 0.39 (95% CI: 0.24-0.65); p < 0.001

Kim WR, AASLD 2017, Abs. LB-27
Persistence of alcohol use was the main determinant of long-term mortality

### Significant Prognostic Variables for Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistence of alcohol use</td>
<td>2.68</td>
<td>1.74–4.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Development of HE</td>
<td>1.73</td>
<td>1.14–2.64</td>
<td>0.11</td>
</tr>
<tr>
<td>Age (per year)</td>
<td>1.07</td>
<td>1.05–1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin [per g(dL)]</td>
<td>0.93</td>
<td>0.89–0.97</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline MELD (per point)</td>
<td>1.05</td>
<td>1.01–1.09</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Abstinence was identified as an independent predictor of prognosis in the subgroup of patients with histological ASH.

Lackner C, et al. J Hepatol 2017
How can we promote abstinence and help the patients to avoid alcohol relapse? Baclofen 10mg

Ideal dosage: 30-80mg/day

Administer between 2-4x/day

Start with 5-10mg and increase every 3 days
Impact of baclofen in alcohol-dependant patients: the French “OBADE-ANGH” series

N=103

Improvement of hepatic function at Month 12

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Month 12</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT, %</td>
<td>70.4</td>
<td>76.5</td>
<td>0.0034</td>
</tr>
<tr>
<td>Bilirubin, µmol/l</td>
<td>29.6</td>
<td>20.6</td>
<td>0.0279</td>
</tr>
<tr>
<td>Albumin, g/l</td>
<td>34.5</td>
<td>36.6</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Conclusions: Baclofen is well tolerated and combined with medical and psychosocial monitoring, can help patients reduce or stop alcohol consumption.

Barrault C, et al. ILC 2018, PS-072
Nutrition in decompensated ALD

• Malnutrition and sarcopenia occur in 60-70% of the patients with decompensated ALD

• Poor nutritional status has adverse effect on prognosis

• Parenteral thiamine can reduce alcohol related brain damage and Wernicke-Korsakoff’s

Intensive Enteral Nutrition Is Ineffective for Patients With Severe Alcoholic Hepatitis Treated With Corticosteroids

Moreno et al. Gastroenterology 2016
Lower mortality with higher caloric intake

Recommended daily intake:

**Protein:**
1.2 to 1.5 g/kg

**Calories:**
35 kcal/kg

Moreno et al. Gastroenterology 2016

Singal AK, et al. Am J Gastroenterol 2018
Management of Alcohol Withdrawal Syndrome

3-5% have severe AWS: short acting benzodiazepines (lorazepan/oxazepan) are the treatment of choice

Singal AK, et al. Am J Gastroenterol 2018
Investigate and manage infection

Most common infections:
- Spontaneous bacterial peritonitis
- Urinary tract infections
- Pneumonia
- *Clostridium difficile* enterocolitis
- Cellulitis

Antibiotics (EASL Guidelines)
- β lactams
- Cephalosporins
- Quinolones
  (with modifications guided by culture)

EASL Guidelines, 2018
Treat superimposed alcoholic hepatitis

- Glucocorticoids → ↓ 28-day mortality (several meta-analysis)
- Glucocorticoids + N-Acetylcysteine → ↓ 28-day mortality (Nguyen-Khac, NEJM 2011)
- Granulocyte Colony-Stimulating Factor → ↓ 90-day mortality (Singh et al, AJG 2014)
Liver Transplant

Not possible in Brazil unless 6 month abstinence from alcohol

Increased difficulty to get admitted to intensive care unit because of this
Conclusions

• Decompensated cirrhosis is a complex multisystem disorder with a high mortality rate

• When the condition is alcohol-related, management should focus on some special issues, such as:
  - Complete alcohol abstinence
  - Adequate nutritional management
  - Investigation and treatment of infections
  - Treat superimposed alcoholic hepatitis (glucocorticoids, etc)