Alcohol and the Liver: A Clinical Update

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Objectives: Alcohol Associated Liver Disease

• Provide an update on the prevalence and epidemiology of ALD
• Impact of ALD on Healthcare costs and Resource utilization
• Update on liver transplant for patients with ALD
• Social and behavioral characteristics predictive of alcohol relapse
• Discuss predictors of outcomes for patients with ALD
• Impact of metabolic syndrome and obesity on ALD
Epidemiology of ALD

• We are moving in the wrong direction
• ALD remains the leading cause of liver disease in the US
• 2009 NHANES data
  • 31,000 deaths related to cirrhosis
  • 48% of these deaths due to (ALD)

Steatosis $\rightarrow$ Steatohepatitis $\rightarrow$ Cirrhosis $\rightarrow$ Death

Prevalence of ALD in the United States

- Using strictest definition of ALD
  - Men > 20g/day + ALT > 35U/L
  - Women > 10g/day + ALT > 25 U/L
- Review of the NHANES
  - Prevalence of ALD
  - ALD with advanced fibrosis (AF)
- Highest at risk
  - Older
  - Women
  - Hispanic

11 million ALD → 4 million AF

Abstract 157: Wong, Dang et al.
ALD: Lead Indication for Liver Transplant

• HCV indication has dramatically dropped
• Since 2015 ALD has overtaken NAFLD as leading indication
• Resulting effects on transplant programs and hospital resources
  More active substance abuse
  More likely to be unemployed
  Less likely to be listed
  More likely to be delisted
• Transplant programs are adapting to these needs
Financial and Resource Burden of ALD

• Alcoholic Hepatitis associated with morbidity and mortality
• Often seen in younger adults

• Looking at patients ≤ 35 years of age hospitalized 2006-14
  • Overall ALD admissions ↑
  • Alcoholic hepatitis ↑ 23.5% → 42.3%
  • Caucasian males
  • More likely to require ongoing medical care post discharge

Axley et al. #160
Increase in Hospital Resource Utilization

- Increase hospitalizations for AH in younger population
- Younger Population mortality increasing
- Longer Hospital stays
- Higher Hospital costs
- Less likely to be transplanted
- Increase use of Palliative services

Axley et al. #160
What about Readmissions

• Patients with ALD and cirrhosis have high readmission rates
• What is this rate of readmission and what factors predict it?
• Used NRD 2010-2014
• 61,750 admissions → 23.9% readmitted w/in 30 days
• Causes for readmission
  • AH (15.8%)
  • Alcoholic cirrhosis (15%)
  • HE (6.6%)
Predictors of Readmissions

**Increased Risk**
- Female sex (OR 1.14)
- Discharge AMA (1.89)
- Comorbidities (1.2)
- Ascites (1.8)
- Bariatric surgery (1.59)

**Decreased Risk**
- Ages 65-84 (0.78)
- Private insurance (0.77)
- Other insurance (0.7)
- Discharged to SNF (0.7)

Garg et al #1429
Referral for Early Alcohol Rehab is Critical

• Those with AH are not fee of risk once discharged
• Retrospective cohort (Validated prospective cohort 2013-2017)

• RESULTS
  • 30% 30 day readmission rate
  • 35% Relapse
  • 39% died

• Early Rehab (20%) → ↓Readmissions
  ↓Relapse
  ↓Death

Peeraphatdit et al #1414
Early Transplantation for Patients with AH

• Comparable post transplant survival
  • 94% one year
  • 84% three year

• The six month rule does not correlate with relapse risk
  • Overall relapse: 25% one year and 34% three year
  • Sustained relapse: 10% one year ad 17% three year

• Are we transplanting too early?

Giard, et al #161
Waitlist Removals for Patients with ALD
Review of the SRTR data 2002-2016

- Cumulative WL removal: death or too sick
  - ALD (HR 0.84, 95%CI 0.81-0.86, p<0.001)

- Cumulative WL removal: improvement
  - ALD (HR 1.58, 95%CI 1.39-1.79 p<0.001) women > men

- Standardized listing criteria for AH especially needed

Giard et al. #161
How to Predict who is going to improve

• Sequential MELD scores can be useful
• Prospective International cohort study (n=192; 640 MELD values)
  • MELD @ baseline 7/30/60/90 days, discharge
  • Association between serial MELD and mortality
Can Noninvasive scores Predict Outcome in ALD

• Fibroscan, ELF, Fibrotest Versus Histology
• Prospective study (=250)
  • Heavy ETOH for 5 years
  • Excluded decompensated cirrhosis
• Heavy ETOH for 5 years followed median of two years
• F0 (13%) F1(34%) F2(28%) F3(6%) F4(18)
• All baseline studies performed on same day
• Followed for decompensating events

Thiele et al #1357
Non-Invasive Testing versus Liver Biopsy outperformed predicting outcomes and deaths

11% died 20% had an decompensating event

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<td>13.10 (2.84-60.31)</td>
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Thiele et al #1357
### Scoring Systems To Predict Relapse

Evaluate various risk factors  
Assign Point system  
Can be used to guide decision

<table>
<thead>
<tr>
<th>Scoring System</th>
<th>Risk Factors</th>
<th>Author</th>
<th>Validated</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRAR</td>
<td>Duration</td>
<td>Yates et al. 1993</td>
<td>Yes Prospectively</td>
</tr>
<tr>
<td></td>
<td># of drinks</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td># prior rehab</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARRA</td>
<td>Absence of HCC</td>
<td>Rodrigue et al. 2013</td>
<td>Yes Retrospectively</td>
</tr>
<tr>
<td></td>
<td>Tobacco</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ETOH after diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Low motivation</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Poor stress manage</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lack of rehab</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social support</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lack of consequences</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social activity with ETOH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIPAT</td>
<td>Patients readiness</td>
<td>Maldonado et al. 2015</td>
<td>Yes Prospectively</td>
</tr>
<tr>
<td></td>
<td>Social Support</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psychopathology</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lifestyle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAPS</td>
<td>Acceptance of alcoholism, social stability</td>
<td>Beresford et al. 1992</td>
<td>No Retrospectively</td>
</tr>
</tbody>
</table>
Proposed Scoring System for Relapse Risk

• Used ACCELERATE-AH cohort:
  • 134 patients
  • Severe alcoholic hepatitis who underwent early OLT
  • Median sobriety pre LT of 54 days
  • Follow up median 1.6 years

• Overall outcomes
  • 74% were abstinent
  • 16% had slips
  • 10% sustained ETOH use

Lee et al #12
Variables which predict low Sustained Relapse

- **Sustained Alcohol use post-LT score**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10 drinks/day</td>
<td>4</td>
</tr>
<tr>
<td>Multiple prior rehab attempts</td>
<td>4</td>
</tr>
<tr>
<td>Prior alcohol related legal issues</td>
<td>2</td>
</tr>
<tr>
<td>Prior illicit substance abuse</td>
<td>1</td>
</tr>
</tbody>
</table>

- Score > 5 Can predicts low risk for sustained ETOH post OLT
  - 25% PPV
  - 95% NPV
- Performed better than the HRAR score

Lee et al #12
Mitigating relapse in the Transplant Patients

• Key is to minimize relapse especially high-dose relapse
• Retrospective analysis of 236 transplants
• Follow up 84.8 months (56.4 months)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Total Relapse %</th>
<th>High-dose Relapse %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire cohort</td>
<td>17.4</td>
<td>8.1</td>
</tr>
<tr>
<td>PTT alone</td>
<td>50.4</td>
<td>9.85</td>
</tr>
<tr>
<td>AA alone</td>
<td>62.8</td>
<td>10.1</td>
</tr>
<tr>
<td>AA + Sponsor</td>
<td>21.4</td>
<td>11.2</td>
</tr>
<tr>
<td>PTT + AA</td>
<td>11.6</td>
<td>6.6 (p = 0.04)</td>
</tr>
<tr>
<td>PTT + AA + Sponsor</td>
<td>10.1</td>
<td>5.9 (p = 0.03)</td>
</tr>
<tr>
<td>PTT + AA + Sponsor + Post TX AA</td>
<td>9.9 (p = 0.002)</td>
<td>5.8 (p = 0.002)</td>
</tr>
</tbody>
</table>

Pablo Arab et al. # 1426
What about Heavy ETOH in Obese Patients?

• Both follow similar fatty liver pathway of injury
• Mayo Clinic biobank non liver disease patients (n=18,506)
• Baseline breakdown
  • No drinking ➔ moderate ➔ heavy drinking
  • Normal weight ➔ overweight ➔ obese
• Outcomes
  • Development of FLD
  • Development of CV mortality and all cause mortality

Peeraphatdit et al #1362
Risk of FLD based on BMI and ETOH Use
Median of 5.8 years

• Majority were moderate drinkers (76.9%)
• FLD risk compared to non-drinkers

<table>
<thead>
<tr>
<th>BMI</th>
<th>MODERATE ETOH (AHR)</th>
<th>HEAVY ETOH (AHR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>0.48</td>
<td>3.12</td>
</tr>
<tr>
<td>25-30</td>
<td>0.86</td>
<td>2.06</td>
</tr>
<tr>
<td>&gt;30</td>
<td>1.31</td>
<td>1.94</td>
</tr>
</tbody>
</table>

Peeraphatdit et al #1362
Mortality Outcomes with Moderate ETOH

• Normal BMI
  • Moderate ETOH protective for CV and all cause mortality

• Overweight BMI
  • Moderate ETOH protective for all cause mortality
  • Moderate ETOH had similar CV mortality

• Obese BMI
  • Moderate ETOH no longer protective

Peeraphatdit et al #1362
Presence of Metabolic Syndrome: Impact on ACLF due to ETOH

- Large cohort from the AARC database (Asian Pacific ACLF Research Consortium)
- Prospective enrollment of ETOH-ACLF patients
- Compared outcomes between those with and without MetS
- Total of 2030 patients (60% due to alcohol)
- Overall 32% 30 day and 43% 90 day mortality

Duseja et al. #1415
Impact of MetS on Patients with ACLF

• Severity of disease Presentation related
  • Presence of obesity
  • Presence of HLD
Impact of MetS on Patients with ACLF

• Severity of disease Presentation related
  • Presence of obesity
  • Presence of HLD

• Impact on Mortality
  • Obesity or being overweight → 30 day mortality (HR 1.54, 95% C.I. 1.06-2.24)
  • No other metabolic risk factors impacted mortality

Duseja et al. # 1415
Impact of Bariatric Surgery on ALD

• Bariatric surgery seems to be risk for ↑ severity of ALD
  • Reduced gastric metabolism
  • Addiction transfer from food to alcohol

• Used NIS data

• Total AH discharges 610744 (.23%)

• Presence of AH
  • 0.23% without BS
  • 0.52% with BS

Garg et al. #1408
Bariatric Surgery Patients Vulnerable to AH

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (p&lt; 0.0001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bariatric Surgery</td>
<td>2.342</td>
</tr>
<tr>
<td>Age 45-64</td>
<td>2.631</td>
</tr>
<tr>
<td>Medicaid</td>
<td>1.558</td>
</tr>
<tr>
<td>Uninsured</td>
<td>3.411</td>
</tr>
<tr>
<td>Native American</td>
<td>1.782</td>
</tr>
<tr>
<td>Wealth</td>
<td>1.36</td>
</tr>
<tr>
<td>Morbid Obesity</td>
<td>0.342</td>
</tr>
</tbody>
</table>

• Risk Factors for relapse in BS Population
  • Young females
  • Psychiatric history
  • Drug abuse
  • DUI
  • History of abuse

Garg et al. #1408

Lagarde Mussa et al. #1427
In Summary

• The prevalence of ALD is increasing at a faster pace than NAFLD
• ALD contributes significantly to the rising healthcare burden
  • Transplant centers pre and post liver transplant
  • Hospital resources with recurrent admissions
• Palliative services and discharge planning is critical in these patients
• Predicting the appropriate time to list patients is not so simple
• Predicting relapse is not so straightforward but scoring systems help
• Metabolic syndrome and ALD are a unique subgroup of patients
• Bariatric surgery patients are particularly vulnerable to ALD
THANK YOU!!!!