Overview of Liver Disease Associated With HCV

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Los Angeles, CA: April 28, 2015 (ADVANCED)

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Learning Objectives

After attending this presentation, participants will be able to:

- Describe HCV in 2015
- Describe how to diagnose advanced liver disease and cirrhosis
- Identify the clinical presentation and risks associated with decompensated cirrhosis
- Describe HCV treatment 4-2015

Worldwide prevalence of each HCV genotype by GBD Region. Size of pie charts proportional to the number of seroprevalent cases estimated by Hanafiah et al 2014: Messina 2015

HCV genotype 1 (63.4 million cases: 46.2%) - one third of which are in East Asia.
Genotype 3 (54.3 million: 39.1%); genotypes 2, 4, and 6 (22.8%); genotype 5 <1%.
While genotypes 1 and 3 dominate in most countries irrespective of economic status, largest proportions of genotypes 4 and 5 are in lower-income countries.
Future Burden of Hepatitis C Related Morbidity and Mortality in the US

- Markov model of health outcomes
  - Of 2.7 M HCV infected persons in primary care
  - 1.47 M will develop cirrhosis
  - 350,000 will develop liver cancer
  - 897,000 will die from HCV-related complications


Effects of SVR on the risk of liver transplant, hepatocellular carcinoma, death and re-infection: meta analysis, 129 studies, 34,563 patients

5-year risk of death (all-cause) by SVR

5-year risk of hepatocellular carcinoma by SVR

Benefits may be offset by re-infection over 5 years

- 0.9% in ‘low-risk’ persons
- 8.2% in persons who inject drugs
- 23.6% in persons coinfected with HIV

HCV SVR and All Cause Mortality

**Steps in Assessing Fibrosis**

1. **Clinical evidence of cirrhosis**
   - Labs (elevated INR, low albumin, bilirubin)
   - Radiology evidence of portal HTN
   - Exam (ascites, varices, encephalopathy)

2. **Transient elastography**

3. **Noninvasive markers**
   - E.g. APRI Fib 4- uses AST, platelets, ALT

4. **If further delineation is needed → Liver biopsy**
   - Not needed in many/ most situations with HCV

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**Transient Elastography**

- Measures elasticity using sound waves
- Stiffness determined by multiple factors
  - Degree of Fibrosis
  - Degree of Inflammation- not good for AVH, high ALT
- Degree of Steatosis
  - Not effective in morbidly obese patients >3.5cm
- Approved in U.S. 4-2013
  - now have XL probes

*J Gastrointestin Liver Dis. 2008 Jun;17(2):155-163*
Elastography: HCV Fibroscan

- 2.5 kPa
- 5
- 70
- 95
- 125
- 150

Affected by weight, access of probe (2 cm), steatosis

Diagnosing Cirrhosis – Labs

**EXAM:**
- Spider nevi, splenomegaly

**Most labs not helpful**
- 50% Child’s A normal
- AST: ALT often >1

**Synthetic dysfunction**
- Hypoaalbuminemia
- Prolonged PT/ INR
- Hyperbilirubinemia

**Portal Hypertension**
- Thrombocytopenia
- Leukopenia
- Anemia

**Renal dysfunction**
- Elevated creatinine;
  remember depends on muscle mass

**Hyponatremia** with ascites

Survival Time from First Liver Decompensation to Death in HCV

- Death during study
  - 366/1037 HCV
  - 100/180 HIV/HCV
- Risk factors for death:
  - HIV
  - Baseline CTP
  - MELD >13
  - Age

Decompensation with Ascites
- Encephalopathy
- Variceal bleed
- Synthetic dysfunction (INR, Bili, Alb)

Pineda, Hepatology 2005
Prognosticating Decompensated Cirrhosis

### Child-Turcotte-Pugh Classification for Severity of Cirrhosis

<table>
<thead>
<tr>
<th>Clinical and Lab Criteria</th>
<th>Points*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
</tr>
<tr>
<td>Acites</td>
<td>None</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
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<tr>
<td>Prothrombin time</td>
<td>&lt;4</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>&lt;1.7</td>
</tr>
</tbody>
</table>

*Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)

- Class A: 5 to 6 points
- Class B: 7 to 9 points
- Class C: 10 to 15 points

3-Month Mortality Based on CTP

![Graph showing 3-month mortality based on CTP scores](http://hepatitisc.uw.edu/go/management-cirrhosis-related-complications/liver-transplantation-referral/core-concept/all)


MELD and Liver Transplantation

- **MELD**
  - Prioritization on liver transplant list
  - Most IMPORTANT single value in prognosis
  - Easy to calculate prior to referral
- **MELD = 15 or greater**
  - Benefit from OLT
- Important predictor of liver-related outcomes
MELD

**MELD Formula**
The MELD score is calculated using the following formula:

\[
\text{MELD Score} = 0.957 \times \text{log}(\text{creatinine mg/dL}) \\
+ 0.378 \times \text{log}(\text{bilirubin mg/dL}) \\
+ 1.120 \times \text{log}(\text{INR}) \\
+ 6.432
\]

Multiply the score by 10 and round to the nearest whole number.

Laboratory values less than 1.0 are set to 1.0 for the purposes of the MELD score calculation.

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3-Month Survival Based on MELD

http://hepatitisc.uw.edu/go/management/cirrhosis-related-complications/liver-transplantation-referral/core-concept/all

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Risk of Bleeding from Esophageal Varices

Cirrhosis

- **Prevalence**: 35%-80%
- **Risk of Bleeding**: 25%-40%
- **Survive**: 50%-70%
- **Die**: 30%-50%
- **Rebleed**: 70%
Variceal Surveillance

All cirrhotics require Esophagogastroduodenoscopy

- No varices
- Small varices (< 5 mm), Child B/C
- Medium or large varices

- Repeat endoscopy in 3 years (well compensated); in 1 year if decompensated
- No beta-blocker prophylaxis
- Nonselective Beta-blocker prophylaxis
- Child Class A, no red wales: beta blockers
- Child class B/C, red wales: beta blockers or band ligation

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Hepatic Venous Pressure to Predict Portal Hypertension

Robic J Hep 2011: 100 pts followed for 2y: ETOH 38; v hep 28: 75 F3-4

Liver Stiffness to predict Portal Hypertension

Robic J Hep 2011
Hepatocellular Carcinoma (HCC)

- Late complication of end-stage liver disease
  - Exceptions: HBV seen in non cirrhotics
- Diagnosis by US, CT scan, MRI
  - Histology is not essential
- Alpha-fetoprotein level may be elevated
  - 20-40% with HCC have normal AFP
  - 20-30% without HCC have abnormal AFP
  - The higher the AFP, the more likely the diagnosis of HCC

Hepatocellular Carcinoma (HCC)

- Surveillance
  - Screen all patients with cirrhosis for HCC
    - Up to 8% risk of HCC/year
    - Also male HBV carriers >40 and female HBV >50 (even if they don’t have cirrhosis)
    - Up to 0.6% risk of HCC/year
  - If recertifying... “screen with ultrasound q 6 months”
    - No benefit to shortening interval
    - No benefit to screening with AFP
    - In practice many still use cross-sectional imaging and AFP to screen as well

Quad phase CT Appearance of HCC

Arterial Phase
Portal venous Phase washout
Hypervascular lesion that washes out on portal venous phase
Treatment of HCC

- Resection
- Local-regional therapy
  - TACE
  - RFA
  - Ethanol ablation
- Liver transplantation
- Systemic
  - Sorafenib

LOCAL REGIONAL THERAPIES FOR HCC

CHEMOEMBOLIZATION
  - Conventional and Drug-eluting beads

ABLATION

- CHEMICAL
  - Percutaneous ethanol injection (PEI)
- THERMAL
  - Radiofrequency ablation (RFA)
    (Laparoscopic, percutaneous or open)
  - Microwave/ Cryo- ablation

RADIOEMBOLIZATION (YITTRIUM - 90)

Take Home: HCC

- Screen ALL patients with u/s q6 months if they have cirrhosis
- Usually radiographic diagnosis
  - Biopsy rarely needed if classic imaging
  - Cross-sectional imaging look for "arterial enhancement" and "washout"
- Treatment:
  - Possibly "curative": ablation, resection, transplant
  - Palliative: TACE, sorafenib
HCV treatment in cirrhotics

- 5% to 7% of Child’s A cirrhotics decompensate per year
- Diagnosis of Child’s A, even B cirrhosis may be subtle
- Screen for HCC
- Perform EGD
- Monitor closely on therapy
- Child’s B can be treated - OLT back up plan

### Treatment of HCV: 4-2015 USA

<table>
<thead>
<tr>
<th>Genotype</th>
<th>No cirrhosis</th>
<th>Cirrhosis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Regimen</td>
<td>wk</td>
</tr>
<tr>
<td>1a</td>
<td>SOF+LDV (&lt;6M)</td>
<td>12 (8)</td>
</tr>
<tr>
<td></td>
<td>3D +RBV</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>SMV +SOF±RBV</td>
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<td></td>
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<td>wk</td>
</tr>
<tr>
<td>2</td>
<td>SOF+RBV</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td><strong>SOF + RBV TE</strong></td>
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<tr>
<td>3</td>
<td>SOF+RBV</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>SOF+PEG/R</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>(DAC + SOF)</td>
<td>12</td>
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