Management of cirrhosis in HIV infected patients

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Figure 1 Causes of death in patients with HIV infection

Deepak Joshi, John O'Grady, Doug Dieterich, Brian Gazzard, Kosh Agarwal

**Increasing burden of liver disease in patients with HIV infection**

The Lancet, Volume 377, Issue 9772, 2011, 1198 - 1209

http://dx.doi.org/10.1016/S0140-6736(10)62001-6
Cirrhosis in the HIV-infected
Cirrhosis in the HIV-infected

**Viruses**
- **Chronic**
  - HBV ± HDV
  - VHC, VHE
- **Acute**
  - HAV, HCV, HEV
  - HBV ± HDV
  - CMV, Toxoplasmosis, HSV, VZV, EBV

**Other**
- Autoimmune hepatitis
- Non-cirrhotic portal hypertension

**HAART**
- Metabolic syndrome
- Lipodystrophy
- Alcohol
- HCV
- Mitochondrial toxicity

**ASH NASH**
- NRTI > NNRTI > PI > Entry inhibitors
Natural History of chronic liver disease in HIV-infected patients

- Normal liver
- ASH/NASH
  - Viruses
  - Other
- Chronic liver disease
- No further progression
- Cirrhosis
- Not all patients have progressive disease
- HCC
- ESLD
The relation between alcohol and outcome from chronic HCV infection

Kim WR Hepatology 2001
## Alcohol and HIV/HCV: Interlaced Stories

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>HCV alone (n=72)</th>
<th>HBV alone (n=14)</th>
<th>HCV and HBV (n=16)</th>
<th>Neither HCV nor HBV (n=8)</th>
<th>$P^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatocarcinoma</td>
<td>7</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>0.002</td>
</tr>
<tr>
<td>Excessive alcohol consumption</td>
<td>44</td>
<td>3</td>
<td>9</td>
<td>8</td>
<td>0.003</td>
</tr>
<tr>
<td>Antiretroviral toxicity as a possible contributing factor</td>
<td>6</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0.59</td>
</tr>
</tbody>
</table>

$^a$ According to the Bonferroni correction, the significance level for the $P$-value is 0.02.
Alcohol is a major contributor to liver related (and unrelated) mortality in HIV-infected patients
Effect of abstinence from alcohol on survival of patients with alcoholic cirrhosis: A systematic review and meta-analysis
Provider Awareness of Alcohol

• HCV Negative
  – 23 (12%) of 186 drinkers were recognized by provider
    • Kappa 0.07
    • Sensitivity 12% (8% - 18%)
    • Specificity 94% (90% - 97%)

• HCV Positive
  – 29 (33%) of 88 drinkers were recognized by provider
    • Kappa 0.28
    • Sensitivity 33% (23% - 44%)
    • Specificity 91% (87% - 95%)

Conigliaro J JAIDS 2003
Liver mortality by HIV1/HBsAg status

- HIV1 NEG HBsAg NEG: REF 0.8
- HIV1 NEG HBsAg POS: 0.8
- HIV1 POS HBsAg NEG: 1.7
- HIV1 POS HBsAg POS: 14.2

P values:
- P=0.04
- P<0.0001
- P<0.0001

Successful Hepatitis B Treatment Reduces Clinical Endpoints

- HBV suppression with nucleos(t)ide analogue therapy reduces risk of hepatic decompensation and HCC in pts with advanced fibrosis or cirrhosis

Kaplan-Meier Estimate of Time to Disease Progression in Asians With CHB (Mos)

This is a key message

Treat HBV regardless of fibrosis
The near future...
(expected for HCV POS/HIV NEG patients)

1990
The Empiric Phase

2003
The Refinement Phase
- Optimal dosing
- Viral kinetics
- Challenging populations
- Nonresponders

2011
The Phase of Directly Acting Antivirals

2015-2017
The Final Phase
Small Molecule Combinations

You are Still here

Survival Outcomes in Pts With CHC and F3/F4 disease With/Without SVR


**All-Cause Mortality**

- **Without SVR**
  - Pts at Risk, n: 405 393 382 363 344 317 295 250 207 164 135
  - Yrs: 0 1 2 3 4 5 6 7 8 9 10
- **With SVR**
  - Pts at Risk, n: 192 181 168 162 155 144 125 88 56 40 28

**Liver-Related Mortality or Liver Transplantation**

- **Without SVR**
  - Pts at Risk, n: 405 392 380 358 334 305 277 229 187 146 119
  - Yrs: 0 1 2 3 4 5 6 7 8 9 10
- **With SVR**
  - Pts at Risk, n: 192 181 168 162 155 144 125 88 56 40 28

**Hepatocellular Carcinoma**

- **Without SVR**
  - Pts at Risk, n: 405 390 375 349 326 294 269 229 191 151 122
  - Yrs: 0 1 2 3 4 5 6 7 8 9 10
- **With SVR**
  - Pts at Risk, n: 192 181 167 161 152 142 124 86 54 39 27

**Liver Failure**

- **Without SVR**
  - Pts at Risk, n: 405 384 361 337 314 288 259 216 184 143 113
  - Yrs: 0 1 2 3 4 5 6 7 8 9 10
- **With SVR**
  - Pts at Risk, n: 192 180 166 160 152 141 123 88 56 40 28

10-year incidence of liver-related outcomes
HCV POS/HIV NEG Patients with F3-F4 disease


96 HCV patients
METAVIR score F3-F4
Median FUP 118 months; IQR=86-138 months
51-year-old white female; HIV before 1987; No OI; HAART 1997; ATZ/TDF/FTC/RTV since 2008; 300-350 CD4 (23%); HIV RNA NEG; No metabolic syndrome; Alcohol 30 g/d

- HCV G1, SVR to PR in 2005 (Metavir F4)
- March 2011: ALT N, PLT Nl, PT 90%, Bilirubin 86µmol/L, Alb N, US N, FT A3F4 (ATV), Fscan 8.6 kPa
- October 2012: unique HCC (5 cm), partial portal vein thrombosis, AFP 4859 UI
- November 2012: uncontrolled metastatic disease, AFP > 25.000 UI. Palliative care.
This is a key message

Patients with cirrhosis should undergo regular surveillance for HCC, irrespective of SVR... and of noninvasive tests
Is this a simple case?

- 42-year-old HIV-/HCV coinfected patient
- 12 units of alcohol per day
- 6-8 joints of marijuana per day
- Deep venous thrombosis 3 years earlier
- Refered for evaluation anti-HCV Rx
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<th>Result</th>
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<td>FIB-4 index</td>
<td>0.97</td>
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<tr>
<td>FibroTest</td>
<td>A2F3 (Total bilirubin 37 µmol / l)</td>
</tr>
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<td>Fibroscan</td>
<td>4.9 Kpa (IQR 0.6)</td>
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- **What is your interpretation?**
  - a) Nil to mild fibrosis (Metavir F0-F2)
  - b) Extensive fibrosis or cirrhosis (Metavir F3-F4)
  - c) Other?
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**Discordance = liver biopsy**
Nodular regenerative hyperplasia

- Nodulation without fibrosis
- Atrophic hepatic plates
- Thickened hepatic plates
- Sinusoidal dilatation
NRH = vascular disease of the liver

Reshamwala, 2004
This is a key message

Interlaced stories of chronic liver disease in HIV-infected patients
Take home messages

• The neglected role of alcoholism
• Viral suppression is an objective
• Do not alleviate HCC surveillance, regardless of SVR
• Screen for esophageal varices
• Search for other causes of chronic liver disease
• First decompensation, including HCC = referral to transplant center