Trends in incidences and risk factors for hepatocellular carcinoma & other liver events in HIV/HCV co-infected individuals from 2001 to 2014: a multi-cohort study

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On behalf of EuroSIDA in EuroCoord and the HCC Study Group
Background

• Individuals with HIV are often co-infected with HCV
  Alter, J Hepatol, 2006

• Co-infection accelerates the progression of liver disease
  Lo Re et al., Ann Int Med, 2014

• In HIV/HCV co-infected individuals
  - Liver disease is a major cause of death, but seems to be declining
    Grint et al., AIDS, 2015
  - Hepatocellular carcinoma (HCC) seems to be increasing
    Ioannou et al., Hepatology, 2013
Aim

In HIV/HCV co-infected individuals:

- Describe incidences of HCC and other liver events from 2001 to 2014
- Compare risk factors for HCC versus other liver events
Study population

- 7,229 adults with HIV and positive HCV antibody-test
- EuroSIDA Study (n = 4,132)
- Swiss HIV Cohort Study (n = 2,044)
- Canadian Co-infection Cohort (n = 840)
- Southern Alberta Clinic Cohort (n = 213)
Outcomes

1) Hepatocellular carcinoma (HCC)

2) Other liver events
   • Liver decompensations
   • Liver-related deaths (excluding HCC)
Statistical analyses

• Poisson regressions to estimate incidence rate ratios separately for
  1) HCC
  2) Other liver events

• Univariate predictors with $p < 0.10$ were included in the multivariate models
Predictor variables

- Age*
- Gender
- Race
- HIV risk group
- Region
- BMI*
- Calendar year of diagnosis
- Smoking*
- Alcohol*
- Cirrhosis*
- HBV status*
- Prior HBV drugs*
- Prior HCV drugs*
- Prior cART*
- Prior AIDS*
- HIV RNA*
- CD4 cell count nadir*
- CD4 cell count current*

* Time-updated variable
Definition of cirrhosis as predictor variable

- Subjects had cirrhosis if they had at least one of the following:

  1) Liver biopsy with METAVIR score F4
  2) FibroScan elasticity > 12.5 kPa
  3) Aspartate aminotransferase-to-platelet ratio index (APRI) > 2
  4) Plasma hyaluronic acid level > 200 ng/ml
Baseline characteristics (subset)  
- in HIV/HCV co-infected individuals

<table>
<thead>
<tr>
<th>Study subjects</th>
<th>n = 7,229</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>38 (33–43)(^a) years</td>
</tr>
<tr>
<td>Male gender</td>
<td>68 %</td>
</tr>
<tr>
<td>White race</td>
<td>90 %</td>
</tr>
<tr>
<td>IDU HIV risk group</td>
<td>59 %</td>
</tr>
<tr>
<td>HBV positive</td>
<td>5 %</td>
</tr>
<tr>
<td>Prior cART</td>
<td>71 %</td>
</tr>
<tr>
<td>Prior HCV drugs</td>
<td>5 %</td>
</tr>
</tbody>
</table>

\(^a\) Median (IQR)
### Overall crude incidence rates
- in HIV/HCV co-infected individuals

<table>
<thead>
<tr>
<th></th>
<th>Number of events</th>
<th>Person-years of follow-up</th>
<th>Crude incidence rate(^a)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCC</td>
<td>72</td>
<td>45,192</td>
<td>1.6</td>
<td>1.3–2.0</td>
</tr>
<tr>
<td>Other liver events</td>
<td>375</td>
<td>43,718</td>
<td>8.6</td>
<td>7.8–9.5</td>
</tr>
</tbody>
</table>

\(^a\) per 1,000 person-years of follow-up
Trends in crude incidence rates
- in HIV/HCV co-infected individuals

-4 % per year (95% CI: -2%, -7%)
+11 % per year (95% CI: +4%, +19%)
Characteristics at event (subset)  
- in HIV/HCV co-infected individuals

<table>
<thead>
<tr>
<th>Event</th>
<th>HCC (n = 72)</th>
<th>Other liver event (n = 375)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50 (46–56)\textsuperscript{a} years</td>
<td>44 (39–50)\textsuperscript{a} years</td>
</tr>
<tr>
<td>White race</td>
<td>94 %</td>
<td>92 %</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>74 %</td>
<td>70 %</td>
</tr>
<tr>
<td>HBV positive</td>
<td>8 %</td>
<td>6 %</td>
</tr>
<tr>
<td>Ever HCV drugs</td>
<td>32 %</td>
<td>18 %</td>
</tr>
<tr>
<td>Current cART</td>
<td>89 %</td>
<td>60 %</td>
</tr>
<tr>
<td>CD4 cell count current</td>
<td>286 (201–438)\textsuperscript{a} cells/mm\textsuperscript{3}</td>
<td>242 (110–397)\textsuperscript{a} cells/mm\textsuperscript{3}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Median (IQR)
Risk factors
- in HIV/HCV co-infected individuals

- also adjusted for gender, region (Europe East/Argentina vs. Europe West vs. Canada), prior AIDS, prior HCV drugs, prior HBV drugs, prior cART, and CD4 cell count nadir
- also adjusted for: gender, region (Europe East/Argentina vs. Europe West vs. Canada), prior AIDS, prior HBV drugs, prior cART, CD4 cell count nadir, HIV risk group, BMI*, smoking*, alcohol abuse, diabetes, and HIV RNA *p<0.05
Conclusion

- in HIV/HCV co-infected individuals

• Opposing trends in crude incidence rates
  - Increasing for HCC (driven by cirrhosis?)
  - Decreasing for other liver events

• Common risk factors for HCC and other liver events
  - Cirrhosis
  - High age
  - Low CD4 cell count
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www.cocostudy.ca
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Thank you for your attention!