Incidence of end-stage liver disease and causes of death in a cohort of HIV/HCV infected patients in France ‘HEPAVIH ANRS C013’

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Introduction

• HCV related mortality has recently overcome HIV mortality in the United States\textsuperscript{1}.

• Evidence suggests that in HCV mono-infected cirrhotic patients, sustained virological response (SVR) to interferon/ribavirin is associated with a decrease of the incidence of hepatocellular carcinoma (HCC)\textsuperscript{2}.

• This effect of antiviral therapy on prevention of HCC and decompensated cirrhosis in HIV/HCV co-infected patients is unclear.

Aims

• To assess:
  – the incidence of end-stage liver disease (HCC or decompensated cirrhosis)
  – the influence of anti-HCV therapy on this incidence,
  – the incidence and causes of death in a multicenter national cohort of cirrhotic patients co-infected with HIV and HCV.
Methods (1)

- The study was performed within HEPAVIH-ANRS CO13 cohort (1175 HIV/HCV co-infected patients included between 2006 and 2008).

- For incidence of ESLD, the study focused on the patients with cirrhosis at inclusion or during follow-up.
  - Cirrhosis was assessed using an algorithm combining liver biopsy and non-invasive fibrosis tests (Elastometry and/or Fibrotest)
  - Patients with decompensated cirrhosis or HCC at inclusion were excluded.
• **Causes of death** were evaluated for the entire cohort and validated by an expert committee.

• Time from enrolment to the **first** ESLD or liver-related death was reported as function of cirrhosis status.
Results (1)

Incidences of ESLD events

- Study population: 310 cirrhotic patients
  - 247 cirrhosis at cohort inclusion
  - 63 developed cirrhosis during follow-up
- Median follow-up: 38 months (IQR: 25-49)
- 37 ESLD events

<table>
<thead>
<tr>
<th>ESLD events</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCC</td>
<td>10</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>23</td>
</tr>
<tr>
<td>Decompensated cirrhosis + HCC</td>
<td>4</td>
</tr>
</tbody>
</table>
# Characteristics of patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>No ESLD events (n=273)</th>
<th>At least one ESLD event (n=36)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46 (27-70)</td>
<td>46 (40-70)</td>
<td>0.886</td>
</tr>
<tr>
<td>Male sex</td>
<td>78</td>
<td>83</td>
<td>0.494</td>
</tr>
<tr>
<td>ALT (upper limit of normal)</td>
<td>1.5 (0.2-30.8)</td>
<td>1.4 (0.2-6.6)</td>
<td>0.715</td>
</tr>
<tr>
<td>Alpha-foetoprotein (ng/ml)</td>
<td>6 (1-482)</td>
<td>12 (1-555)</td>
<td>0.001</td>
</tr>
<tr>
<td>HIV viral load (undetectable)</td>
<td>70</td>
<td>51</td>
<td>0.030</td>
</tr>
<tr>
<td>CD4</td>
<td>395 (3-1496)</td>
<td>270 (12-809)</td>
<td>0.006</td>
</tr>
<tr>
<td>CDC stage (AIDS)</td>
<td>30</td>
<td>42</td>
<td>0.063</td>
</tr>
<tr>
<td>HCV genotype 1</td>
<td>60</td>
<td>58</td>
<td>0.236</td>
</tr>
<tr>
<td>Previous exposure to HCV treatment (IFN, IFN + ribavirin, PEG or PEG + ribavirin)</td>
<td>59%</td>
<td>15%</td>
<td>0.049</td>
</tr>
<tr>
<td>SVR (viral eradication)</td>
<td>14%</td>
<td>6%</td>
<td>0.195</td>
</tr>
<tr>
<td>Owner or renter of their house</td>
<td>78</td>
<td>58</td>
<td>0.020</td>
</tr>
<tr>
<td>Good housing conditions</td>
<td>84</td>
<td>67</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Results are expressed as median (IQR) or %
Cumulative incidence of ESLD events

Actuarial Estimate

At 5 years: 16%
Cumulative incidence of ESLD events as function of SVR

Actuarial Estimate

- Absence of viral eradication
- SVR, viral eradication

- at 5 years: 17%
- at 5 years: 5%

p = 0.12
Results (2)
Causes of death in the entire cohort

78 validated deaths between 2006 and 2011

- **HCV (including HCC)**: 43.2%
- **Non AIDS cancer**: 13.5%
- **AIDS**: 9.5%
- **Cardiovascular**: 8.1%
- **Non AIDS infection**: 8.1%
- **Pulmonary**: 4%
- **Overdose**: 2.7%
- **Suicide**: 2.7%
- **Other**: 1.4%
- **Unknown**: 9.5%
## Causes of death as function of cirrhosis status

<table>
<thead>
<tr>
<th>Cirrhosis status</th>
<th>HCV</th>
<th>Cancer</th>
<th>AIDS</th>
<th>Other</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cirrhosis</td>
<td>1 (3)</td>
<td>9 (30)</td>
<td>2 (6)</td>
<td>18 (60)</td>
<td>30</td>
</tr>
<tr>
<td>Compensated cirrhosis</td>
<td>10 (50)</td>
<td>1 (9)</td>
<td>3 (15)</td>
<td>6 (22)</td>
<td>20</td>
</tr>
<tr>
<td>Decompensated cirrhosis</td>
<td>21 (66)</td>
<td>1 (9)</td>
<td>3 (11)</td>
<td>3 (11)</td>
<td>28</td>
</tr>
<tr>
<td>TOTAL</td>
<td>32</td>
<td>11</td>
<td>8</td>
<td>27</td>
<td>78</td>
</tr>
</tbody>
</table>

X² test, p-value <10^-4
Cumulative incidence of mortality according to cirrhosis stage

Actuarial Estimate

- No cirrhosis (at 5 years: 8%)
- Compensated cirrhosis (at 5 years: 8%)
- Decompensated cirrhosis (at 5 years: 66%)
Conclusion

• Incidence of liver-related deaths in cirrhotic patients coinfected with HIV and HCV
  – is 17% at 5 years, in patients who remain HCV chronically infected versus 5% in those who have cleared the virus (p=0.12)
  – however, the risk of HCC is still present, despite clearance of the virus
  – Limitations: non randomized study in which prevalence of factors limiting access to anti HCV therapy could possibly be higher in the non treated group compared to that in the RVS group
Conclusion

• Causes of death:
  – remain predominantly liver-related in patients with cirrhosis.
  – but in non cirrhotic patients, these causes are similar to those observed in HIV monoinfected patients.

• These results emphasize that progression towards cirrhosis should be stopped by an earlier access to anti HCV therapy.
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