Spontaneous HCV clearance in HCV/HIV coinfected patients from AIDS Center Prague

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Spontaneous HCV clearance (SHCVC) : background

- Approximately 30% of HIV infected persons have also HCV coinfection.\(^1\)
- Spontaneous HCV clearance (SHCVC) is generally observed in 15-45% of HCV infected persons; it is less frequent in HCV/HIV co-infected persons.
- **Male sex**\(^2\),\(^3\),\(^4\), higher **age**\(^4\), high HCV **viral load** (VL), asymptomatic course of acute VHC, low ALT levels or HIV coinfection\(^4\), HBsAg-, non-genotype 1 infection and IL28B **non-CC genotypes**\(^5\) are **negative predictors** for SHCVC.
- Approximately 59% of all HIV-infected persons in the Czech Republic are monitored by AIDS Center Prague (ACP).
- The aim of the study was to assess the proportion of SHCVC in HIV/HCV coinfected patients from ACP and to establish which elected factors contribute to SHCVC.

### Distribution of care for HIV+ patients in the Czech Republic (Feb 2018)\(^1\)

- **AIDS Center Bulovka:** 1639; 59%
- Other AIDS Centers: 1153; 41%

**Maly M, Nemecek V: National institute of Health, 2018**

\(^1\) Rockstroh JK, et al.: Does hepatitis C viremia or genotype predict the risk of mortality in individuals co-infected with HIV? *J Hepatol*. 2013 Aug;59(2):213-20...EuroSIDA (105 European Centers)


Sex as a cofactor contributing to SHCVC

Compared with males, females were more likely to have cleared the virus (44.6% vs 33.7%, respectively).\(^1\)

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**HCV clearance rate by sex**

(Zawyat Razin, Egypt, 2002) \(^1\)

- **Men**: 33.70%
- **Women**: 44.60%

**HCV clearance rate by sex**


- **Men**: 3%
- **Women**: 34%

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Sex as a cofactor contributing to SHCVC

Greater proportion of Female in HCV untreated group
Participants with acute HCV infection who did (estimated duration of infection > 26 W) and did not receive HCV treatment. N=632
The InC³ Study: nine cohorts (Australia, Canada, Netherlands and United States).

Age as a cofactor contributing to SHCVC

HCV clearance rate by age in heroin users
(Garten RJ, China, 2008)\(^1\)

<table>
<thead>
<tr>
<th>Age ≤25</th>
<th>Age &gt;25</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=125</td>
<td>n=222</td>
</tr>
<tr>
<td>13.6%</td>
<td>5.9%</td>
</tr>
</tbody>
</table>

Metaanalysis of studies 1994-2015
"The likelihood of spontaneous clearance was lower in males and individuals with HIV co-infection, the absence of HBV co-infection, asymptomatic infection, black or nonindigenous race, non-genotype 1 infection, older age and alcohol or drug problems."


Material & Methods:

- Data were collected retrospectively from medical records.
- Out of all 1,639 persons monitored by ACP 171 (10.4%) were anti-HCV positive.
- 147 (86%) of those were men and 24 (14%) women. The mean age was 37.4 y. (median=36.5).
- Factors as sex, age, ALT, bilirubin levels, CD4+ count, HCV VL and antiretroviral therapy (ART), which could possibly contribute to SHCVC were collected only in relation to patients with known time of acute HCV infection (data relating to 68 - 75 persons in different categories were validated).
- T-test, Fisher and Mann-Whitney tests were used for statistical analysis.
In 43 (25.1%) out of all 171 HCV/HIV co-infected patients SHCVC was observed.
The percentage of women with spontaneous HCV clearance was higher (33%), than in men (24%), but the difference was not statistically significant (Fisher’s test, \( p=0.319 \)).
## Impact of age on SHCVC

<table>
<thead>
<tr>
<th>SHCVC</th>
<th>N</th>
<th>mean</th>
<th>sd</th>
<th>p50</th>
<th>iqr</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>49</td>
<td>36.5</td>
<td>8.411605</td>
<td>35</td>
<td>6</td>
<td>17</td>
<td>63</td>
</tr>
<tr>
<td>YES</td>
<td>23</td>
<td>39.2</td>
<td>7.743925</td>
<td>39</td>
<td>13</td>
<td>24</td>
<td>54</td>
</tr>
<tr>
<td>Total</td>
<td>72</td>
<td>37.4</td>
<td>8.246484</td>
<td>36.5</td>
<td>10</td>
<td>17</td>
<td>63</td>
</tr>
</tbody>
</table>

No statistically significant differences in mean age between 23 patients with and 49 patients without spontaneous HCV clearance were documented. (t-test, p=0.200).
Impact of bilirubin levels on SHCVC

<table>
<thead>
<tr>
<th>Number of pts divided in three groups according to the bilirubin levels</th>
<th>Bilirubin (in umol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;20</td>
</tr>
<tr>
<td>Spontaneous HCV clearance</td>
<td></td>
</tr>
<tr>
<td>NO</td>
<td>26</td>
</tr>
<tr>
<td>YES</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
</tr>
</tbody>
</table>

No statistically significant differences between percentage of patients with and without SHCVC in particular categories divided according the bilirubin levels were confirmed. Fisher´s exact, \( p=0.324 \).
### Impact of ALT levels on SHCVC

<table>
<thead>
<tr>
<th>Spontaneous HCV clearance</th>
<th>ALT (ukat/L)</th>
<th>&lt;0.8</th>
<th>0.8-2.39</th>
<th>2.4-7.9</th>
<th>8+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td></td>
<td>4</td>
<td>12</td>
<td>15</td>
<td>17</td>
<td>48</td>
</tr>
<tr>
<td>YES</td>
<td></td>
<td>4</td>
<td>10</td>
<td>5</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>8</td>
<td>22</td>
<td>20</td>
<td>23</td>
<td>73</td>
</tr>
</tbody>
</table>

No statistically significant differences between percentage of patients with and without SHCVC in particular categories divided according to the ALT levels were confirmed. Fisher’s exact, \( p=0.312 \).
## Impact of $\text{CD4}^+$ cells counts on SHCVC

<table>
<thead>
<tr>
<th>SHCVC</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>p50</th>
<th>iqr</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>51</td>
<td>656</td>
<td>285.9</td>
<td>608</td>
<td>350</td>
<td>196</td>
<td>1500</td>
</tr>
<tr>
<td>YES</td>
<td>24</td>
<td>726</td>
<td>292.5</td>
<td>802.5</td>
<td>381</td>
<td>164</td>
<td>1379</td>
</tr>
<tr>
<td>TOTAL</td>
<td>75</td>
<td>678</td>
<td>287.2</td>
<td>619</td>
<td>344</td>
<td>164</td>
<td>1500</td>
</tr>
</tbody>
</table>

In patients with SHCVC slightly higher mean of $\text{CD4}^+$ cells counts (726) was observed in comparison to those without SHCVC (656), but no statistical difference was confirmed (t-test, $p = 0.330$).
## Impact of ART on SHCVC

<table>
<thead>
<tr>
<th>Spontaneous HCV clearance</th>
<th>Patients without ART</th>
<th>On ART patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>NO</td>
<td>20</td>
<td>83</td>
<td>31</td>
</tr>
<tr>
<td>YES</td>
<td>4</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>24</td>
<td>31</td>
<td>53</td>
</tr>
</tbody>
</table>

In the group of patients **without ART** spontaneous HCV clearance in **17%** was documented in contrary to **41% in on ART** group of patients. The difference is **statistically significant** (Fisher test, p=0.039).

Our results differs from results of Portugal study:
In 15 HIV/HCV coinfected patients with CHC followed spontaneous HCV clearance after temporary suspension of the ART. 

### Impact of HCV viral load on SHCVC

<table>
<thead>
<tr>
<th>SHCVC</th>
<th>N</th>
<th>mean</th>
<th>sd</th>
<th>p50</th>
<th>iqr</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>47</td>
<td>2378888</td>
<td>8285303</td>
<td>84100</td>
<td>1221330</td>
<td>9</td>
<td>54500000</td>
</tr>
<tr>
<td>YES</td>
<td>21</td>
<td>145375.6</td>
<td>5132773.7</td>
<td>537</td>
<td>5067</td>
<td>14</td>
<td>2340000</td>
</tr>
<tr>
<td>Total</td>
<td>68</td>
<td>1689127</td>
<td>6949083</td>
<td>13400</td>
<td>333067.5</td>
<td>9</td>
<td>54500000</td>
</tr>
</tbody>
</table>

Medians of HCV VL were lower (537) in 21 patients with SHCVC compared to 84,100 in 47 patients without SHCVC. The difference is statistically significant (p<0.001).
Case study

- Jan 43 y MSM
- unprotected sexual contacts, non smoker, non alcoholic, non IVDU, marihuana user. Condyloma ac. In 2001. Depression.
- End of y.2004: admitted to ID clinic for acute icteric VHB, became HBsAg negative
- Jan 2005: dg. HIV infection, introduced (including TDF, susp. HBV and HIV coinfection).
- Jan 2006: syphilis secundaria...1-st episode
- Apr 2007: ART stopped: Stage A1
- Sep 2008: syphilis reinfection (roseola)...1-st reinfection
- Mar 2009: HCV PCR positive, GT 3a
- Jan 2010: HCV therapy introduced by Peg-IFN+RBV, but the same day HCV PCR negative
- Feb 2010: HCV PCR negative, therapy stopped W6: spontaneous HCV clearance?
- Jun 2010: HCV PCR detectable, (weakly positive, unmeasurable)
Case study

- **Sep 2010:** HCV VL < 100 IU/ml, GT 3a
- **Nov 2011:** Caposi sarcoma (left sole, surgery) CD4+: 501
- **Dec 2011:** cART switch ATV+RTV+FTC/TDF (Caposi s.)
- **Feb 2012:** HCV VL 138 000 IU/ml
- **Oct 2012:** HCV VL 423 000 IU/ml GT 4c/4d
- **Feb 2013:** HCV therapy introduced by (Peg-IFN+RBV intolerance)
- **Mar 2013:** HCV PCR negative W4
- **Oct 2013** therapy stopped W34 (intolerance), SVR 24 and SVR 48 was achieved
- **Sep 2014** HCV PCR negative
- **July 2015** syphilis (by serology, syphilis latens)....2-nd reinfection
- **July 2016** switch from ATV/c+FTC/TDF
- **Aug 2016** switch from ATV/c+FTC/TDF to ATV/c 3TC+TDF (insurance rules)
- **Sep 2017** syphilis (ulcer)....3-rd reinfection
- **Sep 2017** Caposi sarcoma – (left sole, surgery) CD4: 960, CD4+/CD8+: 0,70 supressed
- **Sep 2018** HCV PCR negative CD4: 894, CD4+/CD8+: 0,73, supressed
Spontaneous elimination of HCV infection was confirmed in every 4th HCV/HIV coinfected person monitored by AIDS-Center Prague.

Low HCV VL and ART as statistically significant independent factors contributing to spontaneous HCV clearance were observed.

No relation in sex, age, bilirubin and ALT levels or CD4+ cell counts to spontaneous HCV clearance was observed.

Because of high effectiveness of DAA therapy, possibility of late HCV spontaneous clearance in HIV/HCV coinfected patients, “waiting“ and close monitoring seems to be reasonable strategy in patients with acute VHC.
Thank you for your attention

....and special thanks to my grandson for his help with the lecture.