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Long-term follow-up of HIV-positive men who have sex with men (MSM) with acute hepatitis C virus (HCV) infection: high rates of treatment and low rates of liver-related complications

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Introduction

Coinfection with the hepatitis C virus has been identified as a major factor of morbidity and mortality in individuals infected by the human immunodeficiency virus (HIV). In the last decade, HIV positive men who have sex with men (MSM) have drawn specific attention, as high incidences of acute HCV and HCV reinfections along with an unsually high interferon-based treatment uptake have been observed in many countries, especially in Europe. The most logical approach to reducing morbidity is treating patients in early phase HCV infection with the hope of inducing high response rates.

However, the benefits related to interferon-based treatment remain unknown in this population, bringing into question the ideal timing for treatment in the setting of acute HCV in the era of directly acting antivirals.

Methods

Retrospective analysis of HIV-positive MSM with acute HCV infection from a single center in Berlin from 2002 to 2013. Liver fibrosis was estimated by Fibroscan® and/or Fibrotest®.

The following endpoints were documented: significant fibrosis, cirrhosis, HCC, liver-related death, liver transplant, non-liver-related death, non-fatal cardiac event.

Results

In the 12-year observation period, 212 episodes of acute HCV infections occured in 178 HIV-positive MSM. The baseline characteristics are summarized in table 1 and 2. Of note, 65/173 (38%) patients claimed to have used intravenous drugs at least once in their lifetime.

Results cont.

The spontaneous clearance rate was 10.9% (23 out of 212 episodes). In 85% of patients, HCV treatment was initiated. The overall sustained virological response (SVR) rate was 59.7%. In patients who were treated in the acute phase, SVR rate was 65% (65/100 cases). In multivariable analysis, spontaneous clearance was significantly associated with HCV viral load (OR=0.53, 95%CI: 0.35-0.80, p=0.002) and ALT levels (OR=1.17, 95%CI: 1.09-1.25, p<0.001).

SVR was only associated with the number of reinfection episodes (OR=2.07, 95%CI: 0.18-3.34, p=0.003).

The median follow-up time was 47 months (IQR 28.1-77.6). Overall, 11 patients (6.2%, IR=1.6/100 p·y) died, 47 (26.4%, IR=6.6/100 p·y) developed significant fibrosis, and 14 (8.9%, IR=1.9/100 p·y) were diagnosed with liver cirrhosis (Table 3).

Results cont.

In multivariable analysis, the development of significant fibrosis was associated with ART duration, NNRTI use, and non-response to HCV treatment. Liver cirrhosis was only associated with non-response to HCV treatment (OR=3.60, 95%CI: 1.21-10.72, p=0.02).

Conclusions

During the last decade in an HIV-infected MSM population with acute HCV from Berlin, we found:

- **a large proportion of IV-drug use**
- **a spontaneous clearance rate of 11%**
- **a mortality rate higher than expected**
- **an extremely high treatment uptake with moderate SVR rates**

While interferon-based treatment has probably saved many lives, its use is now questionable due to less toxic HCV treatment options.

Demographic characteristics	*n*	
Age (years)	178	39 (32-45)
Male/female (% males)	178	178/0 (100)
BMI (kg/m²), median (IQR)	172	22.3 (20.7-33.1)
Diabetes, n (%)	171	3 (1.8)
Chronic drinker, n (%)	171	22 (12.9)
Intravenous-drug user, n (%)	173	65 (37.6)
HIV-related characteristics		
Detectable HIV-RNA viral load	174	81 (46.6)
HIV-RNA viral load (log_{10} copies/mL)[2]	81	4.44 (3.15-5.06)
CD4+ cell count (/mm³)	177	514 (386-676)
Nadir CD4+ cell count (/mm³)	138	347 (233-495)
Antiretroviral-naïve	176	41 (23.3)
Duration of previous ART (years)[3]	128	5.6 (2.5-9.4)
Previous exposure[3]		
Didanosine, n (%)	176	29 (16.5)
Stavudine, n (%)	176	37 (21.0)
Zidovudine, n (%)	177	80 (45.2)
NNRTI, n (%)	177	100 (56.5)
Protease inhibitor, n (%)	178	119 (66.9)
Evidence of lipodystrophy (clinical) , n (%)	172	44 (25.6)

[1]For patients with more than one acute episode, at the first HCV acute episode. [2]Among patients with detectable HIV-RNA viral load. [3]Among those undergoing antiretroviral therapy.

Table 1: Baseline characteristics of 178 HIV-positive MSM with 212 episodes of acute HCV infection

HCV-related characteristics	*n*	
Number of acute episodes	178	
1, n (%)		152 (85.4)
2, n (%)		19 (10.7)
3, n (%)		6 (3.4)
4, n (%)		1 (0.6)
HCV-RNA (log_{10} copies/mL), median (IQR)	169	6.09 (5.05-6.67)
HCV genotype	147	
1a, n (%)		116 (78.9)
1b, n (%)		4 (2.7)
Mixed 1a/1b, n (%)		2 (1.4)
2, n (%)		2 (1.4)
3, n (%)		2 (1.4)
4, n (%)		16 (10.9)
Mixed 1a/3, n (%)		5 (3.4)
IL28b genotype	145	
C/C, n (%)		65 (44.8)
C/T, n (%)		68 (46.9)
T/T, n (%)		12 (8.3)
Maximum ALT (IU/mL), median (IQR)	176	421 (157-881)
Treatment initiated	178	134 (75.3)
Pegylated-interferon[4] , n (%)	134	133 (99.3)
Directly-acting antiviral[4] , n (%)	134	10 (7.5)
HBsAg-positive, n (%)	161	12 (7.5)

[4]Only for those with initiation of anti-HCV therapy.

Table 2: HCV-related characteristics of 178 HIV-positive MSM with 212 episodes of acute HCV infection

Overall death	11 (6.2)
AIDS-related	2 (1.2)
Cardiovascular*	4 (2.3)
Overdose	1 (0.6)
Suicide	1 (0.6)
Other	3 (1.7)
Significant fibrosis or above**	47 (26.4)
Cirrhosis**	14 (8.9)

*Aortic aneurysm, cardiac failure, and 2 myocardial infarctions.

**Determined from non-invasive markers.

Table 3: Non-liver related and liver-related outcomes during a follow-up period of 47 months (IQR: 28.1-77.6)

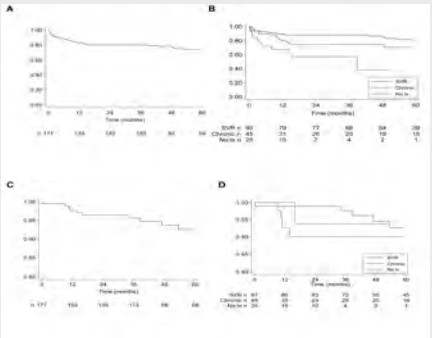

Figure 1: Kaplan-Meier curves time to significant fibrosis (A), by treatment outcome (B), and time to non-liver related endpoint (C), by treatment outcome (D)

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