



Supported by the European Commission
6th Framework Programme grant number
LSHP-CT-2006-037570

Liver fibrosis progression after acute HCV infection (AHC) in HIV-positive individuals

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Background:

Recent data suggested high fibrosis progression rates after sexually acquired AHC. This may be due to the fact that in contrast to traditional risk populations, where HCV is usually acquired prior HIV-infection (e.g. intravenous drug abusers), in most cases of sexually transmitted HCV infections occur in already HIV-infected individuals. Here we investigate into the impact of AHC on liver fibrosis progression in previously HIV-infected individuals.

Methods:

HIV-positive patients with AHC were asked to participate in a prospective study on the evaluation of liver fibrosis progression after AHC by means of transient elastometry (FibroScan®). A standardized questionnaire captured standard demographic factors, risk factors for liver fibrosis such as NASH, alcohol abuse and HAART exposure, and details of acute HCV infection. Stiffness values ≤ 6 kPa were assigned METAVIR fibrosis score F1, 6.1 – 9.0 kPa F2, 9.1 – 12 kPa F3 and > 12 kPa F4. Prior AHC no fibrosis (F0) was assumed unless biopsy / FibroScan were available. Fibrosis progression rate (FPR) was calculated dividing the difference in fibrosis units by the time of follow-up. Only patients with a chronic course of AHC or if FibroScan prior to anti-HCV therapy was available were included for analysis.

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Results:

30 male patients were enrolled, demographic details are shown in table 1. Median follow-up was 0.4 years (IQR 0.2 – 0.6) and the overall calculated fibrosis progression rate (FPR) was 3.8 METAVIR fibrosis units per year (IQR 1.9 – 6.2).

Plotting FPR over follow-up time revealed a logarithmic association between observation time and calculated fibrosis progression rate. Short observation times strongly correlated with calculated high fibrosis progression rates (figure 1).

No interaction of risk factors for cirrhosis or HAART exposure with follow-up time was observed (table 2a). ALT elevation $> 2.5 \times$ ULN at the time of FibroScan was associated with higher readouts but not with follow-up times (table 2b). Limiting analysis to patients with ALT < 2.5 ULN or liver biopsy only, however, resulted in similar findings (figure 2).

Conclusions:

Calculated high fibrosis progression rates after acute HCV infection in HIV-positive individuals are probably influenced by short observation periods. Higher liver stiffness in the acute phase of hcv infection may be at least partially explained by higher inflammatory activity which has been shown to increase stiffness leading to overestimation of fibrosis. A linear model for fibrosis progression, as is currently applied in the setting of chronic HCV infection, should be used with caution in the setting of acute HCV infection.

Tables and Figures:

Table 1: Demographic Data

all data as median (IQR) or numbers (%)

	All Patients N = 30
Male sex	30 (100%)
Age [Years]	39 (35 – 42)
HIV-Status at the time of AHC	
CD4-cellcount [μ l]	444 (374 – 587)
HIV-RNA [off HAART, log ₁₀]	4.2 (3.5 – 4.4)
HAART	21 (70%)
Transmission risk AHC	
MSM	27 (90%)
IVDA	1 (3%)
Nasal drugs	11 (37%)
Clinical presentation AHC	
any symptom / sign	8 (27%)
jaundice	3 (10%)
ALT > 350 IU/l	20 (67%)
HCV-RNA (log ₁₀)	5.9 (5.3 – 6.7)
HCV-Genotype 1	24 (80%)
Risk factor liver fibrosis	15 (50%)
Alcohol abuse	1 (3%)
Illicit drug use	10 (33%)
diabetes	1 (3%)
lipodystrophy	3 (10%)
Previous HAART exposure	
overall [duration in months]	43 (2 – 90)
to didanosine	5 (17%)
to stavudine	7 (23%)
to zidovudine	13 (43%)
to nevirapine	5 (17%)

Figures 1 and 2: Calculated fibrosis progression rates according to follow-up times

calculation of fibrosis progression rate: difference fibrosis units divided by follow-up

Figure 1: analysis including all patients (n=30)

Figure 2: analysis restricted to 12 patients with ALT < 2.5 ULN at FibroScan or liver biopsy

Figure 1

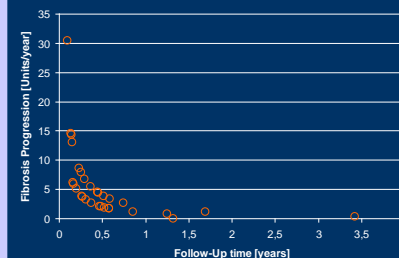
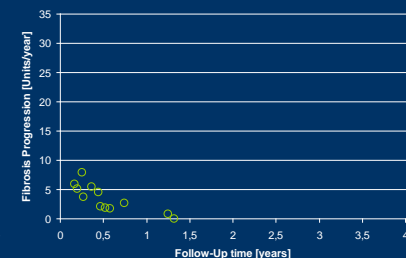


Figure 2



Tables 2a and b: Interaction analysis*

a) Interaction between risk factors for liver cirrhosis and HAART exposure with follow-up times (FU)

b) Interaction between ALT > 2.5 upper limit of normal (ULN) with FibroScan (FibroS) readouts and follow-up times (FU)

a)	Risk liver fibrosis	No risk liver fibrosis	P-value
FU [years]	0.3 (0.2 – 0.5)	0.5 (0.2 – 1.3)	0.233
	HAART	HAART	
	> 1 year	< 1 year	
FU [years]	0.4 (0.3 – 0.6)	0.3 (0.2 – 0.6)	0.642

b)	ALT < 2.5 ULN or biopsy	ALT > 2.5 ULN at FibroScan	P-value
FibroS [kPa]	5.4 (4.4 – 6.1)	6.9 (5.9 – 8.3)	0.030
FU [years]	0.5 (0.3 – 0.7)	0.3 (0.2 – 0.5)	0.164

*all data as median (IQR)