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Impact of HIV Infection on the Dynamics of Liver Stiffness After HCV Cure

753

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BACKGROUND

After sustained virological response (SVR), liver stiffness (LS) usually decreases. However, information related to the impact of HIV co-infection in patients with advanced fibrosis is scarce. The aim was to analyse the impact of HIV co-infection on the LS dynamics after HCV cure.

METHODS

- **Design:** prospective study conducted in the GEHEP-011 multicenter cohort (ID NCT04460157)
- **Patients:** chronic HCV infection, with or without HIV co-infection, fulfilling: 1) SVR with direct-acting antivirals; 2) pre-treatment LS ≥9.5kPa; 3) available measurement of LS at SVR. Pre-treatment, SVR and annual post-treatment LS were assessed.
- **Primary outcome:** time to LS normalization achievement (≤7.2kPa) in two consecutive examinations.
- **Analysis:** Missing LS values were handled using multiple imputation methods, up to the last available measurement, and the imputed data were then used for further analysis. To address potential confounding biases due to baseline differences between people with and without HIV co-infection, a propensity score (PS) was calculated. For the primary analysis, two different approaches were conducted: 1) Fine-Gray regression model for competing risks was performed using the PS as a covariate as well as variables associated with the main endpoint in the bivariate analysis with a p-value <0.05. 2) Fine-Gray regression analysis after HIV/HCV co-infected and HCV mono-infected matching of the sample by PS was performed.

RESULTS

Table 1. Baseline characteristics (N=1,138)

Characteristics	HCV (N=460)	HCV/HIV (N=678)	p-value
Sex assigned at birth, Male, n (%)	332 (72.2)	584 (86.1)	<0.001
Age (years)*	54 (48-60)	51 (48-54)	<0.001
GT3, n (%)	74 (16.1)	114 (16.8)	0.811
Past use of injected drugs, n (%)[a]	166 (36.1)	571 (84.2)	<0.001
Cirrhosis, (LS ≥ 14kPa), n (%)	266 (57.8)	421 (62.1)	0.149
LS ≥ 21kPa, n (%)	161 (35.0)	256 (38.2)	0.272
MELD score[b, *]	6 (6-7)	6 (6-8)	0.125
CPT class A, n (%)[c]	442 (91.7)	533 (78.6)	0.021
Liver decompensation, n (%)	14 (3.0)	53 (7.8)	0.001
Diabetes, n (%)[d]	26 (5.7)	37 (5.5)	0.888
Alcohol ≥ 50g/day, n (%)[e]	41 (8.9)	70 (10.3)	0.242

Data are number (%) of patients. *Median (Q1-Q3)
[a]Available for 1,133 patients. [b]Available for 1,069 patients. [c]Available for 997 patients. [d]Available for 886 patients. [e]Available for 909 patients. [f]Available for 1,110. [g]Available for 1,053. [h]Available for 1,103.

After SVR, the probability of reaching LS normalization is significantly lower in PLWH. This could have implications on the development of long-term clinical events

Figure 1. Dynamics of liver stiffness according to HIV co-infection status.

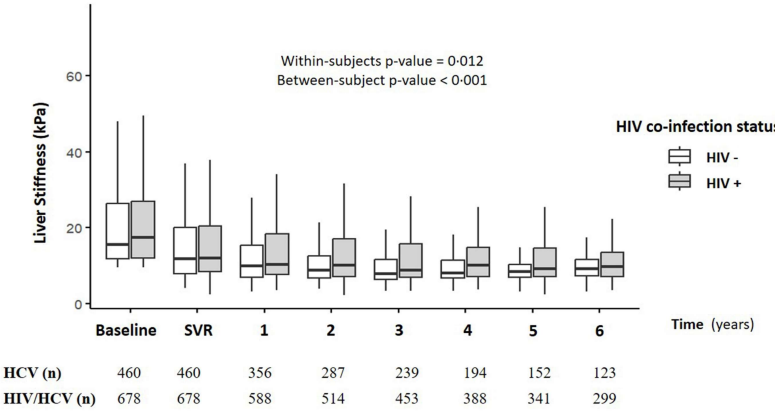


Table 2. Predictors of LS normalization after SVR (N= 1,138)

	Categories	LS normalization n/N (%)	p-bivariate	Adjusted sHR (95% CI)	p-multivariate
HIV co-infection	No	167/460 (36)	0.003	Ref.	0.045
	Yes	217/678 (32)		0.82 (0.67-1.00)	
Diabetes	No	351/987 (36)	<0.001	Ref.	0.006
	Yes	9/64 (14)		0.40 (0.21-0·76)	
PS[a]	----	----	----	0.95 (0.61-1.48)*	0.890

[a] Available for 1,104 patients. *Entered as a continuous variable.
To calculate PS, variables included in the logistic regression were: age, sex, way of HCV infection, prior hepatic decompensation, pre-treatment CPT score, and baseline LS value

Fig. 2. Probability of attaining LS normalization according to HIV co-infection

Probability (95% CI) at 1, 3 and 5 years:
- HIV/HCV: 14% (11%-17%), 49% (41%-57%) and 80% (74%-87%)
- HCV: 19% (15%-23%), 60% (52%-68%) and 83% (76%-99%)

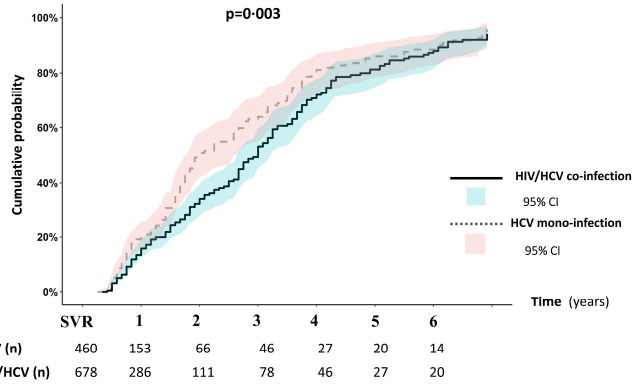


Table 3. PS matching analysis for the prediction of LS normalization after SVR (n=546)

	Categories	Adjusted sHR (95% CI)	p-multivariate
HIV co-infection	No	Ref.	p<0.001
	Yes	0.76 (0.56-0.97)	

CONCLUSIONS

- A substantial proportion of people with chronic HCV infection and advanced fibrosis, both with and without HIV co-infection, are able to achieve LS normalization during a long-term follow-up after HCV eradication.
- The probability of achieving LS normalization is significantly lower and later among PLWH compared to those with HCV mono-infection. These findings were observed even after adjusting for multiple potential confounders through the competing risks model and PS matching, reinforcing the robustness of the results.
- This suggests that HIV co-infection has a negative impact on the long-term evolution of LS following successful HCV treatment.

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