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Long-term liver stiffness dynamics after sustained virological response in patients with HIV/HCV co-infection and advanced fibrosis

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Objective: This study analyses liver stiffness (LS) dynamics in people with HIV (PWH) and advanced liver fibrosis who achieved sustained virological response (SVR) and assess factors associated with LS normalization or progression, after long-term follow-up.

Design: Prospective multicenter cohort study.

Methods: This study included individuals with HIV/HCV co-infection from the Spanish GEHEP-011 cohort, fulfilling: pretreatment LS $\geq$9.5 kPa; sustained virological response (SVR) with direct-acting antiviral regimen; available measurement of LS at SVR. Factors

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associated with LS normalization (achieving ≤7.2 kPa in two consecutive measurement) and progression (increase of >20% LS at the last measurement available) were analyzed.

Results: A total of 678 patients were included. The median follow-up was 40 (17–71) months. The repeated measures ANOVA revealed a significant main effect of time on LS. Overall, 221 (32.6%) achieved normalization. Lower probability of normalization was associated with advanced liver disease [baseline LS: sHR = 0.26 (95% CI, 0.19–0.37), $P < 0.001$; liver decompensation before SVR: sHR = 0.22 (0.05–0.97), $P < 0.001$; baseline MELD score: sHR = 0.81 (0.69–0.94), $P = 0.006$]. LS progression occurred in 50 (7.4%). Progression was associated with higher baseline LS [sHR = 1.04 (1.01–1.07), $P = 0.007$], controlled attenuation parameter (CAP) [CAP ≥ 280 dB/m: sHR = 2.94 (1.16–7.44)] and older age [sHR 1.06 (1.00–1.13), per year, $P = 0.04$].

Conclusions: In PWH, LS significantly decreases after HCV cure in the long-term, achieving values of ≤7.2 kPa. In a substantial proportion of patients, LS remain stable or even increases. Older age and concomitant steatotic liver disease are associated with LS progression.

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Introduction

In individuals with chronic active hepatitis C virus (HCV) infection, liver stiffness (LS) is a valuable noninvasive test to assess the extent of liver disease due to its correlation with the histological stage of fibrosis [1]. Furthermore, LS provides important prognostic information regarding patient outcomes before [2] and after sustained virological response (SVR) [3,4]. The achievement of SVR halts the progression of liver damage. In most cases, LS undergoes a significant reduction [5], which is associated with a lower risk of liver-related events [6]. However, in a substantial proportion of patients, LS increases after HCV cure and may be linked to a higher risk of developing liver complications [7]. In this context, LS serves as a useful parameter to guide clinical decision-making [8]. More specifically, while consistent posttreatment improvements in LS may justify discontinuing surveillance for complications [6], patients who experience worsening LS remain at risk of developing liver-related events [9] and should be closely monitored.

People with HIV (PWH) experience a slower regression of LS after SVR [10]. Although some factors, such as immunosuppression, may compromise hepatic injury reversal [11], those individuals who will show LS normalization are not well identified. In some cases, LS gets worse [12]. In the same way, it is not well known which patients will develop LS progression. Certain factors may be associated, such as concomitant causes of liver injury or metabolic factors [13]. Identifying individuals at risk of LS progression is crucial for improving monitoring efforts. Understanding the dynamics of LS after SVR could be therefore a pivotal element in the long-term care of patients with HCV/HIV co-infection. However, long-term evidence on the LS changes in patients with HCV/HIV co-infection and advanced fibrosis after HCV cure is still lacking.

Therefore, this study aims to analyze LS dynamics in patients with HCV/HIV co-infection and advanced fibrosis who achieved SVR with direct-acting antiviral (DAA) therapy and to assess the factors associated with LS normalization or progression, after a long-term follow-up.

Methods

Study design and patients

This was a prospective multicenter cohort study, in which infectious diseases units of 17 hospitals were involved across Spain. For this study, only PWH from the GEHEP-011 cohort (clinicaltrials.gov; ID: NCT04460157) were analyzed. In this cohort, which recruits individuals, either with HCV mono-infection or HIV/HCV co-infection, inclusion criteria were: SVR with a DAA-based regimen; LS value ≥ 9.5 kPa before treatment; and LS determination by vibration-controlled transient elastography (VCTE) available at the SVR time-point. People with positive serum hepatitis B surface antigen at any point of the follow-up were excluded.

Follow-up and vibration-controlled transient elastography examinations

The time of DAA initiation was considered the baseline time point. Follow-up clinical and laboratory assessments

were conducted at each site every six months following a standardized common protocol. Participants were monitored until the earliest occurrence of death, liver transplantation, HCV reinfection, loss to follow-up, or the censoring date (November 30, 2023). LS and controlled attenuation parameter (CAP) were assessed by VCTE (FibroScan, Echosens, Paris, France), within the 30 days prior to initiating DAA therapy and on the day of SVR assessment, according to a standardized procedure. Then, LS was measured annually at each center if VCTE was available. Examinations were performed by a trained operator, using the M probe. To be considered valid, each examination it had to include at least 10 measures with a success rate of >60% and the median of the interquartile range should be <30%.

Outcomes and definitions

The primary endpoint was the time elapsed from the baseline time-point to the achievement of LS normalization. LS normalization was defined as achieving a LS value ≤7.2 kPa in two consecutive measurements [14]. This cut was chosen because this value is thought to correlate with the absence of significant fibrosis [15]. Additionally, a decrease in liver stiffness to values below 7 kPa is indicative of absence of compensated liver disease, suggesting significant improvement in liver health [16]. The date of the LS normalization attainment was established as the first date where this endpoint was met. The co-primary endpoint was the time elapsed from the baseline time-point to the achievement of significant LS progression. Significant LS progression was defined as an increase of 20% or more considering the first and the last LS measurement available [17]. The categorization according to LS levels was carried out according to the "rule of five", as the proposed cutoff values correlate with progressively higher risk of liver-related death and decompensation [6]. The diagnosis of cirrhosis was established for an LS value ≥14 kPa before treatment initiation [18]. To detect severe steatotic liver disease (34–66% of the hepatocytes affected), a CAP above 280 dB/m was chosen [19].

Data analysis

Descriptive analyses were performed. Continuous variables are presented as medians [quartile 1–quartile 3 (Q1–Q3)] and categorical variables as counts (%). To assess the effect of time on LS, a repeated measures analysis of variance (ANOVA) was performed. The time-to-event was calculated as the months elapsed from the baseline LS determination to primary and co-primary endpoints. Survival curves were constructed using the Kaplan–Meier method. Comparisons were performed by the log-rank test. A fine-gray regression model for competing risk was conducted, where competing event was death from any cause. Variables associated with the main endpoint in the univariate analysis with a *P*-value ≤0.10 were included in the multivariable model, along with sex at birth and age. For the co-primary endpoint, the *P*-value threshold was set at 0.20 for inclusion in the multivariable model. SPSS statistical software package release 25 (IBM, Chicago, IL, USA) and Stata 16.0 Statistics/Data Analysis (StataCorp College Station, TX, USA) package were used to perform statistical analyses.

Ethical statement

All participants provided informed written consent before being enrolled in the cohort. This study has been designed according to the Helsinki Declaration and was approved by the local ethics committee.

Results

Characteristics of the study population

A total of 678 individuals were included in the study. All of them were receiving ART and 563 (83.0%) had a plasma HIV-RNA load below 50 copies/ml. The median (Q1–Q3) $CD4^+$ cell counts was 573 (351–786) cells/mm^3. Four hundred twenty-one (62.1%) had LS ≥14 kPa before treatment. At the SVR time-point, 288 (42.5%) patients showed LS ≥14 kPa. Additional relevant baseline characteristics are displayed in Table 1.

Eighty-four (12.4%) patients died, 28 (4.1%) were lost-to-follow-up, 7 (1.0%) underwent a liver transplant, and in 4 (0.6%) individuals HCV reinfection was documented. In 378 (55.8%) patients, LS were measured in all visits. There was a 26.5% loss of LS determinations out of the total visits.

Liver stiffness dynamics during follow-up

The median (Q1–Q3) time between the first and the last LS measurements was 40 (17–71) months. The repeated measures ANOVA revealed a significant main effect of time on LS, indicating that LS differed across time-points (Fig. 1). Compared to baseline, LS mean value decreased by 29.9% at the SVR time-point. Twelve and twenty-four months after SVR, the mean of LS declined by 34.9% and 41.9% compared to baseline, respectively. When considering LS categories, 448 (66%) individuals improved, in 192 (28%) there was no change, and 38 patients (6%) worsened (Figure 1, Supplementary Material, http://links.lww.com/QAD/D676, Table 1, Supplementary Material, http://links.lww.com/QAD/D675).

Liver stiffness normalization and factors associated therewith

Two hundred and twenty-one (32.6%) individuals reached a level of LS ≤7.2 kPa during the follow-up. Relevant characteristics of patients with LS normalization are displayed in Table 2. The probability (95% CI) of attaining a LS value <7.2 kPa at 1, 3, and 5 years was: 11.2% (9.0–13.1%), 26.7% (23.2–30.7%), and 38.7% (34.4–43.4%), respectively (Fig. 2). In the multivariable analysis, having a more advanced liver disease was

Table 1. Baseline characteristics of the study population (*N* = 678).

Characteristic	Value
Previous to treatment	
Sex at birth, male, *n* (%)	584 (86.1)
Age (years)[a]	50 (47–53)
IDU, *n* (%)	571 (84.2)
GT3, *n* (%)	114 (16.8)
LS (kPa)[a]	17.3 (11.8–27.0)
Baseline cirrhosis, *n* (%)	421 (62.1)
Liver decompensation, *n* (%)	53 (7.8)
MELD score[a]	6 (6–7)
CPT class A, *n* (%)	533 (78.6)
After SVR	
Interferon-free treatment, *n* (%)	642 (94.7%)
LS ≥14 kPa, *n* (%)	288 (42.5)
CAP[b] (dB/m)[a]	236.5 (204.0–271.5)
Diabetes, *n* (%)	37 (5.5)
Alcohol[c] ≥50 g/day, *n* (%)	27 (4.0)
CPT class A, *n* (%)	644 (95.0)
MELD score[a]	6 (6–7)
Platelets count (10^9/l)[a]	141 (100–192)
AST (U/l)[a]	21 (16–75)
ALT (U/l)[a]	24 (20–32)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; CPT, Child–Pugh–Turcotte; GT3, hepatitis C virus genotype 3; IDU, injected drugs use; LS, liver stiffness; MELD, model for end-stage liver disease; SVR, sustained virological response.
[a]Median (Q1–Q3).
Data are number (%) of patients.
[b]Available at 213 patients.
[c]Available at 581 patients.

significantly associated with a lower probability of reaching LS ≤7.2 kPa (Table 3). Additionally, the coexistence of diabetes mellitus showed an association with a reduced likelihood of LS ≤7.2 kPa which was close to the statistical signification level (Table 3).

Characteristics of patients with liver stiffness progression and associated factors

In total, 50 (7.4%) patients showed LS progression during the follow-up. Among patients who presented LS progression, 3 (6%) had diabetes mellitus and 2 (4%) drunk over 50 g/day of alcohol at the time of progression. Other characteristics of this subpopulation are depicted at Table 2. In the bivariable analysis, IFN-free therapy was significantly associated with the outcome (Table 4). However, this variable was not included in the multivariable model due to the absence of events in one of its categories, which led to model instability and unreliable subhazard ratio estimation. In the multivariable analysis, having a higher LS value at SVR, a CAP value at SVR above 280 dB/m and being older, were significantly associated with a higher probability of LS progression (Table 4).

Discussion

In patients with HCV/HIV co-infection and advanced liver fibrosis, LS significantly decreases after achieving SVR with DAA-based regimens in the long-term. For an important proportion of patients, this improvement leads to values of LS ≤7.2 kPa. However, almost one-third of patients experience no change or even an increase in LS. Showing a more advanced liver disease prior to HCV infection cure was associated with a lower probability of achieving LS normalization. On the other hand, the presence of severe steatotic liver disease, a higher LS value, both measured at SVR, and an older age are predictors of LS progression after SVR.

The dynamics of LS improvement following HCV cure remain poorly defined in patients with HIV in the long term. LS reflects different aspects of HCV-associated liver injury (inflammation, fibrosis, and portal hypertension). Several works have shown an important decrease in LS after SVR [12,20–22]. The magnitude of LS reduction is greatest in the first year post-SVR because reflect resolution of necroinflammation [23]. However, the vast majority of them were conducted in patients with HCV mono-infection, with short follow-up after SVR. It can

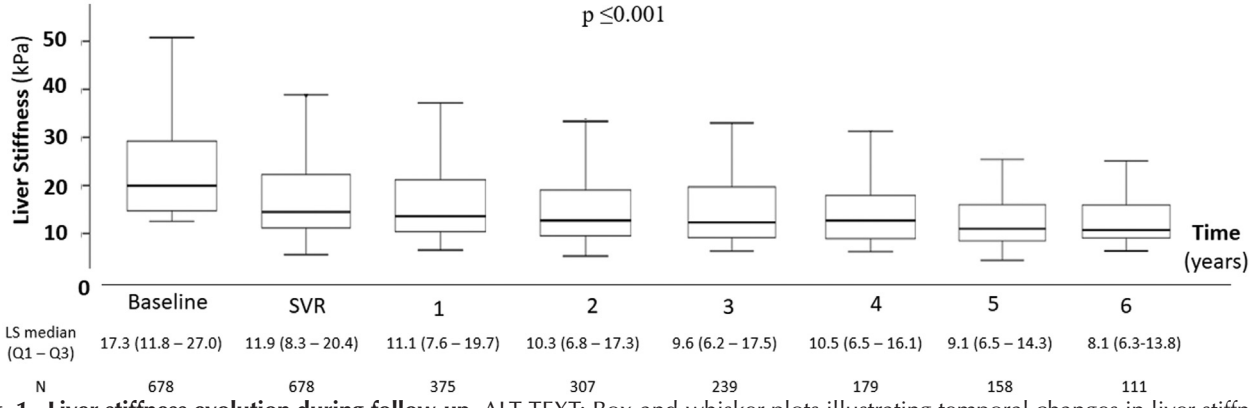

Fig. 1. Liver stiffness evolution during follow-up. ALT TEXT: Box-and-whisker plots illustrating temporal changes in liver stiffness measurements.

Table 2. Baseline characteristics of patients with clinically relevant changes.

Characteristic	LS normalization ($n=221$)	LS progression ($n=50$)
Sex at birth, male, *n* (%)	188 (85.1)	46 (92.0)
Age (years)*	51 (48–54)	52 (52–55)
IDU, *n* (%)	179 (81.0)	44 (88.0)
Weight (kg)[a]*	72.0 (62.0–83.0)	71.8 (64.4–81.1)
Diabetes mellitus[b], *n* (%)	5 (2.3)	3 (6.0)
Alcohol[c] ≥50 g/day, *n* (%)	9 (4.1)	2 (4.0)
GT3, *n* (%)	42 (19.0)	12 (24.0)
Cirrhosis, n (%)	76 (34.4)	36.0 (72.0)
MELD score*	6 (6–6)	7 (6–9)
CPT class A[d], *n* (%)	218 (98.6)	46 (92.0)
Liver decompensation, *n* (%)	2 (0.9)	8 (16.0)
$CD4^+$ cell count nadir*	169.5 (67.3–311.0)	130.0 (57.5–263.5)
$CD4^+$ cell count at SVR*	647 (423.3–826.3)	617.5 (340.0–699.3)
HIV-RNA <50 copies/ml at SVR[e], *n* (%)	179 (81.0)	41 (82.0)
LS value at SVR ≥ 14 kPa, *n* (%)	16 (7.2)	43 (86.0)
CAP[f] (dB/m)*	231.5 (207.0–276.8)	241.0 (192.0–329)

CAP, controlled attenuation parameter; CPT, Child–Pugh–Turcotte; GT3, hepatitis C virus genotype 3; HIV, human immunodeficiency virus; IDU, injected drugs use; LS, liver stiffness; MELD, model for end-stage liver disease; RNA, ribonucleic acid; SVR, sustained virological response.
*Median (Q1–Q3).
[a]Available at 145/221 and 28/50 patients.
[b]Available at 210/221 and 48/50 patients.
[c]Available at 199/221 and 43/50 patients.
[d]Available at 219/221 and 39/50 patients.
[e]Available at 202/221 and 44/50 patients.
[f]Available at 68/221 and 19/50 patients.

be hypothesized that LS may experience a greater improvement after a more prolonged follow-up. The overall reduction in LS aligns with the hypothesis that SVR reduces hepatic inflammation, halts fibrosis progression, and may lead to fibrosis regression [24,25]. Achieving 7.2 kPa presumably correlates with the absence of significant fibrosis or with minimal fibrosis in patients with active HCV infection [15]. This decrease might reflect structural and functional changes of cirrhosis after removing the etiology of liver injury [26]. It is not surprising that individuals with a more severe liver disease had a lower probability of attaining LS normalization. Knop *et al.* demonstrated that, while LS significantly decreased in patients with HCV-associated cirrhosis post-SVR, the degree of improvement was more substantial in those with compensated cirrhosis compared to those with decompensated cirrhosis. In the present study, diabetes mellitus showed a trend towards association with the primary endpoint, acting as a factor avoiding LS normalization. Certainly, diabetes mellitus has been described as a risk factor for liver fibrosis progression and hepatocellular carcinoma, even after HCV eradication [26]. Pontual *et al.* found that while LS significantly decreased in nondiabetic patients with SVR, diabetic patients with SVR exhibited a positive rate of LS progression [27]. This can be explained by the link

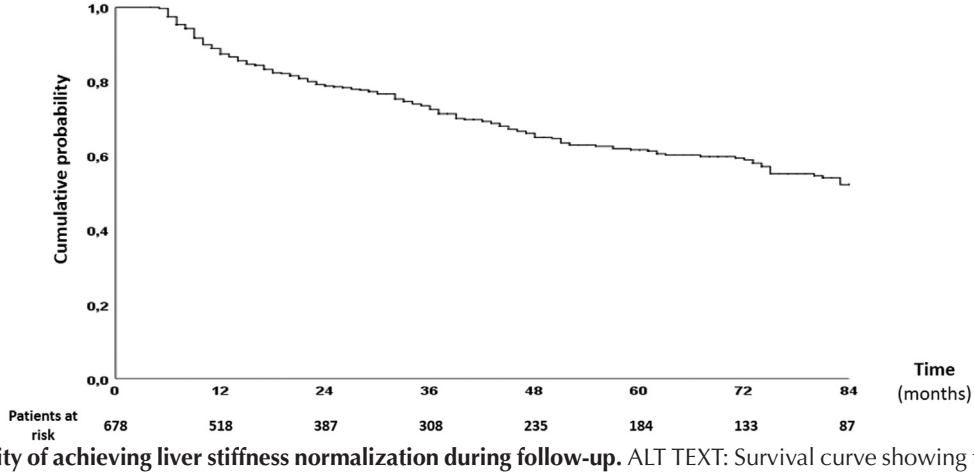

Fig. 2. Probability of achieving liver stiffness normalization during follow-up. ALT TEXT: Survival curve showing the probability of achieving target liver stiffness over the follow-up period.

Table 3. Predictors of LS normalization (*N* = 221).

Characteristic	Categories	*n*/*N* (%)	Bivariable *P*-value	sHR (95% CI)	Multivariable *P*-value
Sex at birth	Female	33/94 (35.1)	0.438	Ref.	0.214
	Male	188/584		0.77 (0.50–1.16)	
Age (years)	< 50	127/377 (33.7)	0.238	0.99 (0.95–1.02)[a]	0.430
	≥ 50	94/301 (31.2)			
IDU	No	42/107 (39.3)	0.075	Ref.	0.123
	Yes	179/571 (31.3)		0.77 (0.54–1.08)	
Nadir $CD4^+$ cell counts (cells/$mm^{3)}$	< 350	158/457 (34.6)	0.038	–[b]	–
	≥ 350	36/93 (38.7)			
GT	Others	179/564 (31.7)	0.134	–	–
	3	42/114 (36.8)			
Diabetes mellitus	No	205/608 (33.7)	0.027	Ref.	0.054
	Yes	5/37 (13.5)		0.42 (0.17–1.01)	
Alcohol	< 50g/day	190/554 (34.3)	0.988	–	–
	≥ 50g/day	9/27 (33.3)			
Baseline MELD score	< 10	206/608 (33.7)	<0.001	Ref.	0.006
	≥ 10	5/77 (6.5)		0.81 (0.69–0.94)	
Baseline CPT class	A	191/533 (35.8)	<0.001	–	–
	B or C	0/31 (0)			
LS value before treatment	< 14	145/257 (56.4)	<0.001	Ref.	< 0.001
	≥ 14	76/421 (18.1)		0.26 (0.19–0.37)[a]	
Liver decompensation before SVR	No	219/625 (35.0)	<0.001	Ref.	0.045
	Yes	2/53 (3.8)		0.22 (0.05–0.97)	
$CD4^+$ cell counts at SVR (cells/mm^3)	< 350	33/144 (22.9)	0.007	Ref.	0.967
	≥ 350	167/447 (37.4)		0.99 (0.67–1.46)	
LS value at SVR (kPa)	< 14	205/390 (52.6)	<0.001	–[c]	–
	≥ 14	16/288 (5.6)			
CAP value at SVR (dB/m)	< 280	52/167 (31.1%)	0.679	–	–
	≥ 280	16/46 (34.8%)			
HCV therapy	IFN-based	12 (33.3)			
	IFN-free	209 (32.6)	0.135	–	–

CPT, Child–Pugh–Turcotte; GT, hepatitis C virus genotype; IDU, injected drugs use; LS, liver stiffness; MELD, model for end-stage liver disease; SVR, sustained virological response.
[a]Entered as a continuous variable. Per one unit increase.
[b]Excluded from the model because of collinearity with $CD4^+$ cell counts at SVR.
[c]Excluded from the model due to collinearity with baseline LS.

Table 4. Predictors of LS progression (N = 50).

Characteristic	Categories	*n*/*N* (%)	Bivariable p-value	sHR (95% CI)	Multivariable *P*-value
Sex at birth	Female	4/94 (4.3)	0.234	–	–
	Male	46/584 (7.9)			
Age (years)	<50	22/377 (5.8)	0.167	1.06 (1.00–1.13)*	0.04
	≥ 50	28/301 (9.3)			
IDU	No	6/107 (5.6)	0.438	–	–
	Yes	44/571 (7.7)			
Alcohol	< 50g/day	41/554 (7.4)	0.977	–	–
	≥ 50g/day	2/27 (7.4)			
Nadir $CD4^+$ cell count (cells/$mm^{3)}$	< 200	25/333 (7.5)	0.498	–	–
	≥ 200	12/217 (7.5)			
$CD4^+$ cell count at SVR (cells/mm^3)	< 350	31/447 (6.9)	0.712	–	–
	≥ 350	11/114 (7.6)			
HIV-RNA (copies/mL)	< 50 cp/mL	41/563 (7.3)	0.599	–	–
	≥ 50 cp/mL	3/53 (5.7)			
HCV GT	Others	38/564 (6.7)	0.112	–	–
	3	12/114 (10.5)			
LS value at SVR (kPa)	No	14/257 (5.4)	0.200	1.04 (1.01–1.07)*	0.007
	Yes	36/421 (8.6)			
Liver decompensation before SVR	No	42/625 (6.72)	0.013	–	–
	Yes	8/53 (15.1)			
CAP value at SVR (dB/m)[a]	< 280	12/167 (7.2)	0.064	Ref.	0.023
	≥ 280	7/46 (15.2)		2.94 (1.16–7.44)	
HCV therapy	IFN-based	0	0.031	–	–
	IFN-free	43 (6.7)			

CAP, controlled attenuation parameter; GT, hepatitis C virus genotype; HIV, human immunodeficiency virus; IDU, injected drugs use; LS, liver stiffness; Ref, reference; RNA, ribonucleic acid; SVR, sustained virological response.
*Entered as a continuous variable. Per one unit increase.
[a]Available at 221 patients.

between diabetes mellitus and steatotic liver disease through interconnected mechanisms. These include insulin resistance, hyperinsulinemia, oxidative and endoplasmic reticulum stress, chronic inflammation, macrophage activation, and upregulation of RAGE/TLR4 signaling pathways [28–30].

Despite the encouraging overall trend, a significant proportion of patients did not show LS improvement or even experienced LS progression after HCV cure. Also, the fact that LS remains stable overall 2–3 years after HCV cure in these patients raises the question of whether there is a point of no return [31]. Factors such as ongoing liver injury from non-HCV causes or metabolic syndrome are likely involved in LS progression. In the present work, steatotic liver disease was associated with LS progression after SVR. Research on this topic has primarily focused on patients with HCV mono-infection [13,32]. However, studies involving PWH remain scarce. Severe steatotic liver disease promotes liver inflammation and a fibrogenic response through hepatic stellate cell activation and oxidative stress, which contribute to fat accumulation within hepatocytes [33]. Besides, severe steatotic liver disease is often accompanied by insulin resistance [34], which exacerbates hepatic fat accumulation and inflammation, further promoting fibrosis and potentially contributing to the progression of LS [35]. Age is another factor significantly associated with the LS progression. Aging-related processes contribute to dysregulations driving the progression of liver fibrosis. Mechanisms such as cellular senescence, chronic inflammation, and impaired immune function play a central role in promoting fibrosis [36,37], which could ultimately lead to an increase in LS. Recent evidence suggests that increased cellular aging, as indicated by telomere length, may contribute to reduced liver regeneration following SVR [38]. Further studies focusing on these factors are needed to properly understand the dynamics of LS. Identifying factors associated with LS progression after SVR could help to select patients in whom screening measures for liver events after HCV cure should be intensified. The impact of interferon-based regimens on residual liver inflammation after SVR remains unclear. While interferon has immunomodulatory properties, current evidence from large cohort studies indicates that persistent hepatic inflammation after SVR is common regardless of the antiviral regimen used [39]. In this study, the association between IFN-free therapy and the outcome was significant in bivariable analysis. However, due to the absence of events in the untreated group, this variable could not be reliably assessed in the multivariable model. While this may reflect a clinically meaningful difference, the small size and event-free nature of that subgroup limit the interpretability of this finding.

This study may have some limitations. The most important is the lack of several LS measurements, primarily due to the unavailability of VTCE in certain centers during the clinical evaluation period. However, when normalization or progression could not be assessed due to missing data, the outcome was neither imputed nor assumed. As a result, it is possible that the incidences of both normalization and progression were underestimated. However, we believe this conservative approach enhances the accuracy of outcome classification. Second, data for key variables that may influence LS dynamics, such as body mass index, alcohol consumption and CAP values were missing in a considerable proportion of individuals. All these factors may have a negative impact on the LS dynamics. On the one hand, the prevalence of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH) in people with HIV is higher than in the general population [40], linked to overweight and metabolic disorders. On the other hand, alcohol use can produce synergism in liver injury, enhancing necroinflammatory responses. Alcohol use independently promotes hepatic inflammation, oxidative stress, and fibrosis, influencing epigenetic regulation [41]. Third, it is possible that certain ART regimens, as nonnucleoside reverse transcriptase inhibitors, may have a beneficial impact of LS normalization [42]. However, some ART toxicity is linked with liver disease progression. Tenofovir Alafenamide is associated with weight gain and hepatic steatosis [43,44]. Older ART (e.g. didanosine, statvudine) are associated with an important mitochondrial injury and hepatic steatosis [45]. Unfortunately, ART information was not available and no analysis could be conducted in this sense. Finally, the study had a limited follow-up period, so it did not capture the long-term changes in LS beyond this time frame. However, this study has some strengths. In this sense, this work, provides data on a large population of HIV/HCV co-infected patients after SVR, with the longest follow-up of the studies reported so far, in a real-life setting. We have identified factors associated with LS progression after SVR in people with HIV/HCV co-infection. Finally, this is the first study to explore the impact of steatotic liver disease on the dynamics of progression and normalization of LS in PWH.

In conclusion, in most PWH and HCV co-infection and advanced fibrosis who achieve SVR after DAA-based therapy, there is a significant decrease in LS. Over a long-term follow-up, a vast majority of patients experience an improvement, with many achieving LS $\leq$7.2 kPa, indicating an important reduction in risk of liver events. Despite this, one-third of the cohort exhibit stable or even increasing LS values. Premature immunosenescense and concomitant steatotic liver disease may underlie LS progression after SVR in this setting. There is a need for continuous monitoring and identifying factors influencing LS dynamics postcure. The identification of predictors for LS evolution could be pivotal to improve postcure management and to implement preventive measures for liver-related complications in PWH with HCV co-infection, after SVR.

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Data availability: Anaïs Corma Gómez (A.C.G.) and Juan Macías had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The data that support the findings of this study are available from the corresponding author (A. C.G.), upon reasonable request.

Conflicts of interest

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