TELOMERE LENGTH OF CIRRHOTIC HIV/HCV PATIENTS INCREASES AFTER HCV CLEARANCE WITH DAAs

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BACKGROUND

One-third of HIV patients coinfected with HCV develop cirrhosis throughout their lives. Cirrhosis is associated with a senescent phenotype that affects telomeric length, among other mechanisms. It is unknown if the telomere is restored after HCV eradication in these patients. We evaluated the impact of HCV elimination with new direct-acting antivirals (DAAs) on telomeric length dynamics in HIV/HCV coinfected patients with advanced cirrhosis.

METHODS

A longitudinal study was conducted in 60 HIV/HCV coinfected and 30 HCV monoinfected cirrhotic patients at baseline and 48 weeks after anti-HCV treatment with DAAs (final) (Figure 1). The relative telomere length (RTL) was quantified with a real-time multiplex PCR (MMqPCR) on peripheral blood mononuclear cells (PBMCs) DNA. Generalized linear models adjusted for the most relevant clinical and epidemiological variables and generalized mixed linear models were also used.

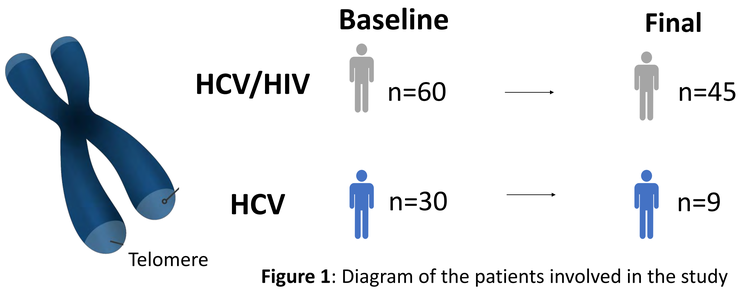


Figure 1: Diagram of the patients involved in the study

Table 2. Clinical characteristics of the patients related to HIV markers.

HIV markers	All patients		HIV/HCV patients		
	HIV/HCV	HCV	p Compensated	Decompensated	p
No.	60	30	35	25	
Nadir CD4+ T cells	130 (66-245)	-	- 86.5 (40.0-242.0)	150 (99-273)	0.082
Nadir CD4+ T cells<200 cells/mm3	37 (67.3%)	-	- 21 (70.0%)	16 (64.0%)	0.637
Baseline CD4+ T cells	439 (234-717)	-	- 427 (234-721)	444 (227-685)	0.857
Baseline CD4+ T cells<500 cells/mm3	35 (58.3%)	-	- 20 (57.1%)	15 (60.0%)	0.825
Prior AIDS	22 (36.7%)	-	- 12 (34.3%)	10 (40.0%)	0.651
Antiretroviral therapy					
NRTI+NNRTI	7 (11.9%)	-	- 6 (17.1%)	1 (4.2%)	0.104
NRTI+II	31 (52.5%)	-	- 17 (48.6%)	14 (58.3%)	
NRTI+PI	8 (13.6%)	-	- 7 (20.0%)	1 (4.2%)	
PI+II+NNRTI/MVC	4 (6.8%)	-	- 1 (2.9%)	3 (12.5%)	
Others	9 (15.3%)	-	- 4 (11.4%)	5 (20.8%)	

RESULTS

In comparison with HCV-monoinfected patients, HIV/HCV-coinfected patients were younger, had lower BMI, and had been exposed less frequently to interferon. Besides, they were more frequently men, smokers, prior IDUs and alcohol abusers (**Table 1**). There were no differences in HIV markers between compensated and decompensated patients (**Table 2**).

Table 1. Clinical and epidemiological characteristics of the patients related to HIV markers.

	All patients			HIV/HCV patients		
	HIV/HCV	HCV	p	Compensated	Decompensated	p
No.	60	30		35	25	
Age (years)	51.7 (48.7-53.8)	58.5 (52.3-69.6)	**<0.001**	51.6 (48.7-53.6)	52.1 (48.7-53.8)	0.887
Gender (male)	49 (81.7%)	17 (56.7%)	0.011	29 (82.9%)	20 (80.0%)	0.778
BMI (kg/m^2)	23.8 (21.7-26.4)	27.7 (23.1-32.5)	**0.002**	23.8 (21.2-26.5)	23.5 (21.8-25.0)	0.705
Current smoker	38 (64.4%)	10 (33.3%)	**0.005**	22 (62.9%)	16 (66.7%)	0.764
Alcohol drinker (>50 g/day)	37 (61.7%)	9 (30%)	**0.005**	21 (60%)	16 (64.0%)	0.753
Previous IFNα therapy	23 (38.3%)	20 (67%)	**0.011**	12 (34.3%)	11 (44.0%)	0.445
IVDU	48 (80.0%)	4 (13.3%)	**<0.001**	27 (77.1%)	21 (84.0%)	0.513
Liver markers						
Child-Pugh-Turcotte	5 (5-5)	5 (5-7)	0.056	5 (5-5)	5 (5-6)	0.039
MELD	9 (8-11)	10 (7-11)	0.608	9 (7-10)	9 (8-12)	0.408
LSM	33.1 (23.6-39.3)	30.7 (27.3-48.0)	0.171	33.3 (26.0-39.3)	31 (18-39.7)	0.382
HVPG	15.3 (12.5-17.3)	16.5 (13-18)	0.467	15.5 (11.5-17.0)	15.3 (13.5-18.0)	0.883
Decompensation	25 (41.7%)	14 (46.7%)	0.652	0 (0%)	25 (100%)	-
HCV markers						
HCV genotype						
1	38 (65.5)	24 (80%)	0.173	21 (60.0%)	17 (73.9%)	0.531
2	0 (0%)	1 (3.3%)		0 (0%)	0 (0%)	
3	9 (15.5%)	3 (10%)		6 (17.1%)	3 (13.0%)	
4	11 (19.0%)	2 (6.7%)		8 (22.9%)	3 (13.0%)	
Log_{10} HCV-RNA (IU/mL)	6.2 (5.7-6.7)	6.11 (5.50-6.41)	0.405	6.4 (5.8-6.7)	6.0 (5.3-6.3)	**0.015**

HCV eradication with DAAs was associated with a significant increase in telomere length in HIV/HCV-coinfected patients with advanced cirrhosis, particularly in compensated patients.

EVOLUTION OF THE RELATIVE TELOMERE LENGTH (RTL)

RTL was significantly lower in HIV/HCV-coinfected patients than in HCV-monoinfected patients both at baseline (p<0.001), and at the end of follow-up (p=0.032).

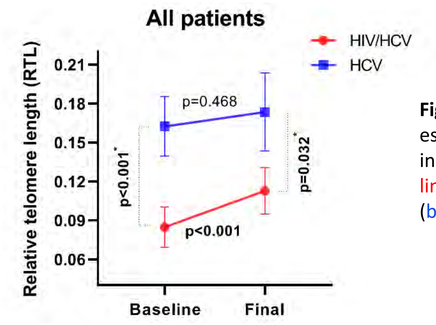


Figure 2: Comparison of the estimated mean of RTL values in HIV/HCV-coinfected (red line) and HCV-monoinfected (blue line) patients

A significant RTL increase over time was found only for HIV/HCV-coinfected patients (p<0.001), especially in those patients with compensated cirrhosis (p<0.001).

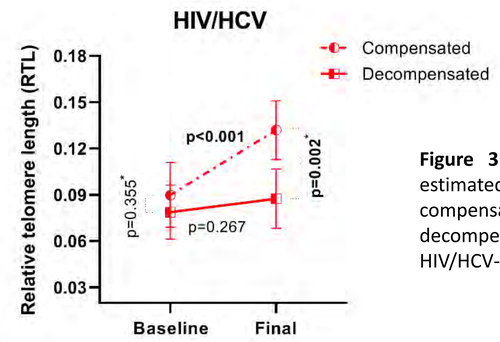


Figure 3: Comparison of the estimated mean of RTL values in compensated (dashed line) and decompensated (solid line) HIV/HCV-coinfected patients

CONCLUSIONS

HCV eradication with all-oral DAAs was associated with an increase in telomere length in HIV/HCV-coinfected patients with advanced cirrhosis, particularly in compensated patients. This finding suggests that HCV clearance may have implications in age-related conditions in this population group.

ADDITIONAL KEY INFORMATION
Additional Resources
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