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The Influence of Antiretroviral Therapy on Hepatitis C Virus Viral Load and Liver Fibrosis in Human Immunodeficiency Virus-Coinfected Patients: An Observational Study

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Keywords
Antiretroviral therapy · Hepatitis C · HIV · Liver fibrosis · Viral load

Abstract
Background: The role of antiretroviral therapy (ART) for Hepatitis C viral load (HCV-VL) and liver fibrosis is poorly understood. This study aimed at evaluating the influence of ART on HCV-VL and liver fibrosis in human immunodeficiency virus (HIV)/HCV-coinfected patients. ***Methods:*** We conducted a retrospective cohort study of HIV/HCV-coinfected patients followed at a tertiary university hospital. ***Results:*** In total, 143 patients were included. In 61 patients, ART initiation was accompanied by an increase in HCV-VL and a decrease in HIV viral load (HIV-VL), whereas ART suspension led to a decrease in HCV-VL and an increase in HIV-VL. Among the 55 HIV-suppressed patients who switched to a raltegravir (RAL)-containing regimen, median HCV-VL levels decreased significantly, while switching to a rilpivirine-containing regimen did not yield a significant reduction. ***Discussion:*** If the treatment of chronic hepatitis starts before ART, ART initiation should be delayed as much as possible. If ART has been started, it is advisable to wait 1 year before initiating chronic hepatitis treatment. RAL as the third agent in an ART regimen could be beneficial in HIV/HCV-coinfected patients, in comparison to other antiretroviral drugs. ***Conclusion:*** The start and the suspension of ART significantly interferes with HCV-VL in HIV/HCV-coinfected patients.

Introduction

Hepatitis C virus (HCV) is a major public health problem and a leading cause of chronic liver disease [1, 2]. It is estimated that 70–170 million people are infected worldwide [3, 4]. Among the 33 million people living with human immunodeficiency virus (HIV) infection, around five million are also chronically infected with HCV [5].

HCV-related liver disease persists as the main cause of morbidity and mortality in HIV-coinfected patients [6]. Among these patients, HCV viral load (HCV-VL) is higher [7], and progression to advanced liver fibrosis is faster [8–10]. In general, basal HCV-VL and liver fibrosis are two of the most important indicators of HCV treatment

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efficacy, particularly of the newly available direct-acting antiviral agents (DAAs).

Little is known about the influence of beginning and discontinuing antiretroviral therapy (ART) and of different ART regimens on HCV-VL and liver fibrosis. Furthermore, few clinical reports have shown a spontaneous cure of chronic hepatitis C in HIV/HCV-coinfected patients [11–13]. Data from our group identified a group of 16 HIV/HCV-coinfected patients under ART on whom a spontaneous cure of chronic hepatitis C occurred without HCV treatment [14].

We conducted a study that aims to assess the influence of beginning and discontinuing ART as well as of different ART regimens on HCV-VL and hepatic elastography in a HIV/HCV-coinfected cohort. A better knowledge of these dynamics could lead to better outcomes in the treatment of chronic HCV in HIV-coinfected patients.

Methods

We conducted a retrospective cohort study in a HIV clinic of a tertiary university hospital in Porto, Portugal. The clinical data was collected between January 2007 and April 2015. Eligible patients were HIV infected with HCV chronic hepatitis. In accordance to EASL guidelines, HCV chronic hepatitis was defined by two positive reverse transcription polymerase chain reaction test results for HCV-RNA, separated by at least 1 year [15]. For elastography assessment (Fibroscan® score), patients were excluded if they had taken anti-HCV medication.

HCV and HIV-1 viral loads were determined using Cobas®AmpliPrep/Cobas® Taqman® HCV quantitative test v2.0 and Cobas AmpliPrep/Cobas Taqman HIV-1 quantitative test v2.0, respectively. For HIV-2 viral loads, an in-house protocol (with primers and probes by TIB Molbilol in LightCycler®2.0; Roche) were applied. HIV suppression under ART was defined as a plasma HIV-1 RNA <20 copies/mL and HIV-2 <180 copies/mL. HCV suppression was defined as a plasma HCV RNA <12 UI/mL.

For HCV genotype determination, an Abbott RealTime HCV Genotype II assay with Abbott m2000rt was used. To identify the interleukin (IL)28B promoter polymorphism at position 3,176 C/T (rs12979860), primers and probes by LightMix® Kit IL28B with the LightCycler 2.0 were used. Liver stiffness was defined using transient elastography (Fibroscan) and classified according to the METAVIR score: F0–F1 ≤7.2 KPa; F2–F3 = 7.3–11.8 KPa; F3–F4 = 11.9–14.8 KPa; F4 ≥14.9 KPa.

For the purposes of this study, we defined three groups:

- Group A: patients who began ART (not excluding that some of them later stopped ART).
- Group B: HIV-suppressed patients whose previous ART regimen was switched to a regimen containing raltegravir (RAL) as the third agent.
- Group C: HIV-suppressed patients whose previous ART regimen was switched to a regimen containing rilpivirine (RPV) as the third agent.

The patients had blood samples collected 1 month after the intervention (beginning of or switch to ART) for HCV-VL and HIV viral load (HIV-VL) assessment.

Demographic variables were analyzed descriptively. Descriptive data are presented as the most suitable measure of central tendency and dispersion. Shapiro-Wilk and Kolmorov-Smirnov tests were applied to test normality, according to sample size. To test differences between the groups in terms of HCV-VL and liver stiffness progression, a nonparametric Wilcoxon signed-rank test was applied. A p value of 0.05 was considered significant. Data analysis was conducted using the Statistical Package for the Social Sciences® (SPSS) 23.0.

Results

Group A: Patients Who Began ART

In total, we included 143 patients. Sixty-seven patients were included in Group A. All were Caucasian, 57 were male, and the risk factor for HIV/HCV co-infection was intravenous drug abuse in all but 3 patients. Out of these 3 patients, 2 had heterosexual risk, and 1 was a male who had sex with men (MSM). The median age of HIV/HCV diagnosis was 41 years. All were infected with HIV-1. The median CD4+ T lymphocyte count before treatment start was 200 cells/mm^3 (Table 1).

Forty-four patients were infected with HCV genotype 1, 17 patients were infected with HCV genotype 3, 5 patients were infected with HCV genotype 4, and in 1 patient, the HCV genotype was not determined. METAVIR liver fibrosis stage, assessed by transient elastography (Fibroscan), was F0–F1 in 27 patients, F2–F3 in 20 patients, F3–F4 in 3 patients, F4 in 12 patients, and not determined in 5 patients. IL28B was CC in 21 patients, CT in 25 patients, TT in 7 patients, and not determined in 14 patients. Basal liver enzyme values were elevated in 46 patients. Eight patients had an increase in the value of liver enzymes related to drug toxicity (including ART).

After the beginning of ART, a significant drop in HIV-VL and a significant rise in HCV-VL were found in 61 of these patients. When 27 out of these 61 patients self-suspended ART, the reverse occurred; I.E., HIV-VL increased and HCV-VL decreased. For some of these patients, these variations in VL occurred repeatedly with each ART initiation and suspension and especially in the first month after the beginning or the suspension of ART. VL values stabilized after this 1-month period, reaching nearly baseline values.

In 76 occasions of ART initiation, HCV-VL suffered a statistically significant increase ($p < 0.001$) relative to the preceding HCV-VL value, with a median of 5,471,732 IU/

Table 1. Baseline characteristics

	Group A (n = 67)	Group B (n = 55)	Group C (n = 21)
Male, *n* (%)	57 (85.07)	47 (85.45)	19 (90.48)
Median age, years	41	44	43
Transmission, *n* (%)			
Coinfection by injection	64 (95.52)	50 (90.91)	17 (80.95)
Heterosexual risk	2 (2.99)	2 (3.64)	3 (14.29)
MSM	1 (1.49)	0 (0.00)	1 (4.76)
Blood transfusion risk	0 (0.00)	3 (5.45)	0 (0.00)
HIV type, *n* (%)			
HIV 1	67 (100.00)	52 (94.55)	21 (100.00)
HIV 2	0 (0.00)	2 (3.64)	0 (0.00)
HIV 1 and 2	0 (0.00)	1 (1.82)	0 (0.00)
Median basal CD4+ T lymphocyte count, cells/mm^3	200	395	404
HCV genotype, *n* (%)			
1	44 (65.67)	43 (78.18)	14 (66.67)
3	17 (25.37)	6 (10.91)	5 (23.81)
4	5 (7.46)	6 (10.91)	2 (9.52)
ND	1 (1.49)	0 (0.00)	0 (0.00)
Fibroscan, *n* (%)			
F0–F1	27 (40.30)	24 (43.64)	13 (61.90)
F2–F3	20 (29.85)	20 (36.36)	5 (23.81)
F3–F4	3 (4.48)	3 (5.45)	1 (4.76)
F4	12 (17.91)	8 (14.55)	2 (9.52)
ND	5 (7.46)	0 (0.00)	0 (0.00)
IL28B, *n* (%)			
CC	21 (31.34)	20 (36.36)	8 (38.10)
CT	25 (37.31)	24 (43.64)	11 (52.38)
TT	7 (10.45)	8 (14.55)	1 (4.76)
ND	14 (20.90)	3 (5.45)	1 (4.76)
Basal liver enzymes, *n* (%)			
Elevated	46 (68.66)	–	–
Normal	21 (31.34)	–	–
Rise	8 (11.94)[a]	–	–

ND, not determined; HIV, human immunodeficiency virus; HCV, hepatitis C virus; IL, interleukins. [a] Related to antiretroviral therapy start or to the use of hepatotoxic drugs.

mL. On the other hand, in 29 instances of patient self-suspension of ART, HCV-VL suffered a statistically significant ($p < 0.001$) decline, with a median decrease of 2,592,000 IU/mL. Thus, the decrease in HCV-VL values related to the discontinuation of ART was higher than the increase related to the beginning of ART. These variations in HCV-VL do not seem to have been influenced by age, gender, HCV genotype, liver stiffness, or IL28 polymorphism.

RAL-containing regimens were taken by 4 out of the 61 patients in whom ART initiation was accompanied by HCV-VL increase and by 4 out of the 6 patients whose HCV-VL did not increase with ART initiation. Of the 6 patients in whom HCV-VL did not increase with the beginning of ART, 4 had begun ART with RAL and emtricitabine/tenofovir disoproxil fumarate (FTC/TDF), 1 with efavirenz (EFV) and FTC/TDF, and 1 with EFV and abacavir/lamivudine (ABC/3TC). In these 8 patients who began ART with RAL as the third agent, the median increase in HCV-VL was 1,550,204 IU/mL. The difference in HCV-VL values between the 8 patients who started ART with RAL as the third agent and the 59 other patients was statistically significant ($p < 0.001$). The only patient who did not have a decrease in HCV-VL with the suspension of ART was found to be taking a RAL-containing regimen and to be under the influence of toxics (alcohol and drugs).

Table 2. HIV-supressed patients who switched to a RAL-containing (Group B) or RPV-containing (Group C) ART regimen

	Group B RAL-containing ART regimen	Group C RPV-containing ART regimen
Before switching therapy, n (%)	*n* = 55	*n* = 21
Under ART + PI/r	44 (80.00)	13 (61.90)
Under ART + first-generation NNRTI	0 (0.00)	8 (38.10)
Taking a first-generation NNRTI	7 (12.73)	0 (0.00)
Taking PI/r + first-generation NNRTI	2 (3.64)	0 (0.00)
Second-generation NNRTI	2 (3.64)	0 (0.00)
Therapy after switching, n (%)	*n* = 55	*n* = 21
RAL or RPV + FTC/TDF	48 (87.27)	15 (71.43)
RAL or RPV + ABC/3TC	6 (10.91)	6 (28.57)
RAL + AZT+3TC	1 (1.82)	0 (0.00)
HCV-VL change (before and after the beginning of RAL or RPV)	*n* = 48	*n* = 13
Mean (median) difference	−3,438,965.7 (−2,346,940.8)	−516,881.9 (−390,293.8)
Mean (median) log	0.43 (0.4)	0.09 (0.09)
p value	<0.001	0.149

ART, antiretroviral therapy; PI/r, boosted protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; RAL, raltegravir; RPV, rilpivirine; FTC/TDF, emtricitabine/tenofovir disoproxil fumarate; ABC/3TC, abacavir/lamivudine; AZT, zidovudine.

Group B: HIV-Suppressed Patients Whose Previous ART Regimen Was Switched to a Regimen Containing Raltegravir as the Third Agent

Fifty-five HIV-suppressed patients who switched to a RAL-containing regimen were included in this group. RAL was associated with FTC/TDF in 48 patients, with ABC/3TC in 6 patients, and with lamivudine/zidovudine (AZT/3TC) in 1 patient. Before switching therapies, 44 patients were under ART with a boosted protease inhibitor (PI/r; PI/r monotherapy in 3 cases), 7 patients were taking a first- generation non-nucleoside reverse transcriptase inhibitor (NNRTI), 2 were taking a PI/r+ first-generation NNRTI, and 2 were taking a second-generation NNRTI (Table 2).

All were Caucasian, 47 were male, and the risk factor for HIV/HCV co-infection was intravenous drug abuse in all but 5 patients (2 had heterosexual risk and 3 blood transfusion risk). Median age at HIV/HCV diagnosis was 29 years, and the median age at the time of the switch to RAL was 44 years. Fifty-two patients were infected with HIV-1, 2 were infected with HIV-2, and 1 was infected with both HIV-1 and HIV-2. We excluded the HIV-2 monoinfected patients from the analysis. Patients had been HIV suppressed for a median of 46 months when the change to RAL took place. Median CD4+ T lymphocyte count, before the switch to RAL therapy, was 395 cells/mm^3 (Table 1).

A total of 43 patients were infected with HCV genotype 1, 6 with HCV genotype 3, and 6 with HCV genotype 4. METAVIR liver fibrosis stage was F0-F1 in 24 patients, F2-F3 in 20 patients, F3-F4 in 3 patients, and F4 in 8 patients. The IL28B polymorphism was CC in 20 patients, CT in 24 patients, TT in 8 patients, and not determined in 3 patients (Table 1).

With the switch to RAL, all but 1 patient maintained the HIV suppression. A decrease in HCV-VL was observed in all but 7 patients (a median of four determinations before RAL introduction and a median of four determinations after RAL introduction). The decrease in the median HCV-VL values after the RAL switch was statistically significant ($p < 0.001$), with a median reduction of 2,346,940.8 IU/mL (Table 2). In 40 cases, the first measurement of HCV-VL after switching to RAL showed a statistically significant decrease ($p < 0.001$) relative to the measurement made prior to the introduction of RAL. Out of the 7 patients who did not have a decrease in HCV-VL, 4 patients were under the effect of toxics (alcohol or drugs), and 3 had only one determination of HCV-VL after switching to a RAL-containing regimen.

Fibroscan assessments were made with a median interval of 25 months (of which 20 months were on treatment with RAL-containing regimens). The patients had already been HIV-suppressed for a median of 57 months

Table 3. Fibroscan assessments for Group B and Group C

	Group B (n = 55)	Group C (n = 21)
Fibroscan assessments, n (%)		
Fibrosis regression	23 (41.82)	11 (52.38)
Maintain F0–F1 stage	5 (21.74)	5 (45.45)
Maintain F2–F3 stage	4 (17.39)	1 (9.09)
F2–F3 to F0–F1 stage	6 (26.09)	3 (27.27)
F3–F4 to F2–F3 stage	2 (8.70)	1 (9.09)
Maintain F4 stage	3 (13.04)	0 (0.00)
F4 to F2–F3 stage	1 (4.35)	0 (0.00)
F4 to F3–F4 stage	1 (4.35)	0 (0.00)
F4 to F0–F1 stage	1 (4.35)	1 (9.09)
Fibrosis progression	16 (29.09)	4 (19.05)
Median progression (Kpa)	1.70	0.90
Maintain F0–F1 stage, *n* (%)	9 (56.25)	3 (75.00)
Maintain F2–F3 stage, *n* (%)	1 (6.25)	1 (25.00)
Maintain F4 stage, *n* (%)	2 (12.5)	0 (0.00)
Increase stage, *n* (%)	4 (25.00)[a]	0 (0.00)
Did not experience any change	2 (3.64)	0 (0.00)
Excluded	14 (25.45)	6 (28.57)
Mean fibrosis variation, KPa (p value)	–0.65 (0.139)	–0.90 (0.041)

[a] Two patients from F0–F1 to F2–F3, 1 from F0–F1 to F3–F4, and 1 from F3–F4 to F4 to F2–F3, 1 patient from F4 to F3–F4, and 1 patient from F4 to F0–F1.

when the first determination of Fibroscan was performed. After switching to RAL-containing regimens, 23 patients had stiffness regression, 16 patients had slight progression, and 2 patients did not experience any change. Fourteen patients were excluded from this group: 12 who had undergone treatment for HCV infection, and 2 for whom data on liver stiffness was not available. This variation in Fibroscan assessments was not statistically significant (p = 0.139) (Table 3).

In the 16 patients who had stiffness progression, the median progression was 1.70 KPa, with 9 patients maintaining the METAVIR fibrosis stage of F0–F1. Four patients suffered an increase in the METAVIR fibrosis stage (two from F0–F1 to F2–F3, one from F0–F1 to F3–F4, and one from F3–F4 to F4). Among the 23 patients who had stiffness regression, 11 had METAVIR fibrosis stage improvement (6 patients from F2–F3 to F0–F1, 1 patient from F4 to F2–F3, 2 patients from F3–F4 to F2–F3, 1 patient from F4 to F3–F4, and 1 patient from F4 to F0–F1), indicating that the METAVIR fibrosis stage either regressed or stabilized in 90.2% of the patients (Table 3).

There were no differences between patients making use of FTC/TDF or ABC/3TC, neither in terms of HCV-VL nor in terms of METAVIR liver fibrosis score.

Group C: HIV-Suppressed Patients Whose Previous ART Regimen Was Switched to a Regimen Containing Rilpivirine as the Third Agent

Twenty-one HIV-suppressed patients who switched to an RPV-containing ART regimen were included in this group. RPV was taken in association with FTC/TDF by 15 patients and in association with ABC/3TC by 6 patients. Before switching therapies, 13 patients were under ART with PI/r, and 8 patients were under ART with a first-generation NNRTI (Table 2).

All of these patients were Caucasian, 19 were male, and the risk factor for HCV-HIV co-infection was intravenous drug abuse in all but 4 patients (3 heterosexual risk and 1 MSM). The median age at HIV/HCV diagnosis was 30 years, and the median age at the time of switching to RPV was 43 years. All patients were infected with HIV-1. Patients had been HIV suppressed for a median of 59 months when the change to RPV took place. The median CD4+ T lymphocyte count before switching to RPV was 404 cells/mm^3 (Table 1).

A total of 14 patients were infected with HCV genotype 1, 5 with HCV genotype 3, and 2 with HCV genotype 4. The METAVIR liver fibrosis stage was F0-F1 in 13 patients, F2–F3 in 5 patients, F3–F4 in 1 patient, and F4 in 2 patients. The IL28B polymorphism was CC in 8 pa-

tients, CT in 11 patients, TT in 1 patient, and not determined in 1 patient (Table 1).

With the switch to RPV, all but 1 patient maintained HIV suppression. A decrease in HCV-VL was observed in 13 patients (a median of four determinations before RPV introduction and a median of four determinations after RPV introduction). The decrease in the median HCV-VL after switching to the RPV-containing regimen was not statistically significant ($p = 0.149$), with a median reduction of 390,293.7 IU/mL (Table 2). In 15 patients, the first measurement of HCV-VL after switching to RPV did not show a statistically significant decrease ($p = 0.092$) relative to the measurement made prior to the introduction of RPV.

Fibroscan assessments were made with a median interval of 20 months (of which 15 were on treatment with RPV-containing regimens). Patients had already been HIV-suppressed for a median of 50.5 months when the first determination of METAVIR liver fibrosis score was done. After switching to RPV-containing regimens, 11 patients had liver stiffness regression, and 4 patients had progression (Table 3). This variation was statistically significant ($p = 0.041$).

In the 4 patients with stiffness progression, the median progression was 0.90 kPA. Three patients maintained the METAVIR fibroses stage F0–F1, and 1 patient remained at stage F2–F3. Two of these 4 patients were on RPV for less than 6 months. Among the 11 patients with stiffness regression, 5 had a change in the METAVIR fibrosis stage (3 patients from F2–F3 to F0–F1, 1 patient from F3–F4 to F2–F3, and 1 patient from F4 to F0–F1); i.e., the METAVIR fibrosis stage either regressed or stabilized in 100% of the patients (Table 3).

Three HCV-treated patients without sustained virologic response (SVR) and 3 patients without elastography data were excluded from this stiffness evaluation. There were no differences between patients making use of FTC/TDF or ABC/3TC, neither in terms of HCV-VL nor in terms of METAVIR liver fibrosis score.

Discussion

The variation in HCV-VL observed with the beginning or suspension of ART could be related to the endogenous levels of interferon alfa, restrained by HIV replication levels, and/or influenced by the higher hepatotoxicity related with the beginning of ART versus less hepatotoxicity related with ART suspension. The endogenous alfa interferon may play an important role in the replication of HCV, given that high levels of HIV have been associated with high levels of endogenous alfa interferon. With the onset of ART, there is a decrease in HIV levels and, therefore, a decrease in endogenous alfa interferon levels [16]. This decrease in endogenous alfa interferon levels leads to an increase of HCV viremia [17] as well as to a possible increase in liver enzyme values [18]. Thus, when ART is suspended, HIV and endogenous interferon alfa levels increase, which may cause HCV-VL to decrease. Nevertheless, HCV-VL variations can also occur irrespective of ART initiation or suspension. A better knowledge of the dynamic between HCV-VL and ART could lead to better outcomes in the treatment of HCV-related chronic hepatitis on HIV/HCV-coinfected patients.

A transitory ART interruption is regarded as counterproductive. However, such an interruption could make HCV-VL values fall significantly and be under 800,000 IU/mL at the time HCV treatment is started [19–22].

We hypothesize that RAL as the third agent in an ART regimen could be beneficial in HIV/HCV-coinfected patients, in comparison to other antiretroviral drugs. In our study, we observed that in patients taking RAL as the third agent in an ART regimen, HCV-VL values decreased, and liver stiffness decreased. This HCV-VL decrease was statistically significant ($p < 0.001$) and presumably would have been higher if, in 12 patients, the HCV-VL decrease had not been impaired by ART toxicity. This toxicity was noticeable through a significant increase on HCV-VL and liver enzyme values.

Despite the fact that the progression to advanced METAVIR fibrosis scores is faster in coinfected HIV/HCV patients [8–10], we found that, after the switch to RAL and according to the transient elastography assessment, liver stiffness decreasing was found in 23 patients. This variation in the METAVIR fibrosis stage was not statistically significant ($p = 0.139$). Nevertheless, it is worth noting that stiffness increasing was expected to be found in all patients. The average METAVIR fibrosis scores would have presumably been lower if, once more, some patients had not been impaired by toxicity [23]. For this evaluation of liver stiffness, we excluded HCV-treated patients, with or without SVR, and patients who were not HIV-suppressed when starting a RAL-containing regimen, given that in both of these situations, stiffness regression could occur regardless of the antiretroviral drug [24, 25].

RAL is not only safe but can also be appropriate for HCV/HIV-coinfected patients [26, 27]. It is a less hepa-

totoxic agent, with a favorable behavior of liver enzyme values observed during its use [28–31]. RAL is well tolerated and does not have interactions with the new DAAs, or with ribavirin [32, 33]. It can even be used in patients with a Child-Pugh score C [34], and it is the preferential drug for hepatic transplant candidates [35, 36]. Furthermore, the HCV virus is in itself a negative predictor for cardiovascular risk [37, 38], and HIV/HCV-coinfected patients should be treated with antiretroviral drugs with an improved impact on the lipid profile, as is RAL [39].

RPV is also a well-tolerated agent [40, 41] and, as RAL, does not have significant pharmacokinetic interactions with most of the new DAAs for HCV [26, 29, 42–44]. In patients doing RPV, the progression to advanced METAVIR fibrosis scores could be lower, but its positive impact on HCV-VL values appears to be less than that seen with RAL. Overall, the HCV-VL reduction found in Group C was lower than that seen in Group B, and it was not statistically significant ($p = 0.149$).

Despite the fact that progression to advanced METAVIR fibrosis scores is faster in HIV/HCV-coinfected patients, we found that 11 patients experienced liver stiffness regression after the switch to RPV. This variation was statistically significant ($p = 0.041$). In this liver stiffness evaluation, we excluded 3 HCV-treated patients without SVR because regression could have occurred in this situation regardless of the antiretroviral drug used [12]. To confirm the positive impact of RAL and RPV on HCV treatment response, it would be important to have a review comparing the rapid viral response (RVR) and SVR between RAL- and RPV-containing regimens versus regimens containing other antiretroviral drugs.

With the proposed treatment strategies for HCV/HIV-coinfected patients, we hypothesize that obtaining better treatment outcomes in this patient population are possible, even in countries where the new DAAs are not yet available. In countries with new DAAs already available, obtaining better results or at least the same level of good results but with shorter treatments or/and less drugs regimens are possible.

The main limitation of our study was the fact that it included a small number of patients, which compromises the power of the statistical analyses. Additionally, the investigation was conducted at a single center where the studied patients were all Caucasian and to a large percentage male. Conclusions are also limited by the fact that in the groups taking RAL or RPV, the median time between one transient elastography and the other was just 25 and 20 months, and the median time of evolution was just 20 and 15 months, respectively. Finally, the lack of a control group did not allow for a comparison of these groups' results with those of patients making use of other possible ART regimens. It is important to note that patient follow-up did not extend beyond April 2015, since from this date onwards, the most recent DAAs became available for chronic hepatitis C treatment in Portuguese hospitals.

Conclusion

Our study suggests that the start and the suspension of ART significantly interferes with HCV-VL in HIV/HCV-coinfected patients. RAL seems to exert a good impact on HCV-VL and on liver fibrosis, while RPV appears to influence only liver fibrosis. Further investigations are needed to establish the role of ART in HCV-VL and liver fibrosis variation.

Statement of Ethics

This study was approved by the Hospital's Commission for Medical Ethics, and the research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written informed consent could not be obtained as this is a retrospective cohort study.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Jorge Soares conducted the research and wrote the manuscript; António Ferreira and Francisco Almeida contributed to the data collection and data analysis; André Silva-Pinto reviewed the data analysis and wrote the manuscript; Carmela Piñeiro and Rosário Serrão collected data; and António Sarmento reviewed the manuscript.

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