EFFECTS OF ADVANCED HIV DISEASE ON INFLAMMATION FOLLOWING ART INITIATION

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BACKGROUND

- Early antiretroviral treatment (ART) initiation has been shown to reduce immune activation in HIV patients.
- We explored the differences associated with later versus earlier presentation on changes on biomarkers of inflammation, coagulation, monocyte activation and gut barrier damage after ART initiation in the Cohort of the Spanish HIV/AIDS Research Network (CoRIS).

MATERIALS AND METHODS

- We performed our study in the Cohort of the Spanish HIV Research Network (CoRIS) —a national ongoing prospective multicenter cohort of people living with HIV (PLWHIV), adults and treatment-naïve recruited from 46 Spanish centres from 2004-onward.

- **Inclusion criteria:**
    - We selected 100 CoRIS participants aged ≥ 18 years recruited from 1 January 2004 to 30 November 2018 with earlier (CD4 >350/mm^3) or later (CD4<100/mm^3) presentation at enrollment (50 early presenters (EP) and 50 late presenters (LP) respectively).
    - To be eligible, each of these patients must have a baseline (pre-ART), 48 weeks and 96 weeks after ART initiation blood sample avalaible in HIV BioBank.
    - In addition, an attempt was made to guarantee equitable representation in both groups of the three main families of ART, for which it was planned to select 20 patients treated with integrase inhibitors (II), 15 with protease inhibitors (IP) and 15 with Non-nucleosides analogues (NN) in each group as long as samples were available.

- **Outcomes** were changes in 4 plasma biomarkers (hs-CRP, D-dimer, sCD14 and IFABP as indicators of inflammation, coagulation, monocyte activation and bacterial translocation respectively) at baseline (pre-ART), week 48 and week 96 after ART initiation.

- **Laboratory procedures:**
    - We measured levels of hs-CRP, D-dimer, sCD14 and IFABP in plasma and each sample was assayed in triplicate.

- **Stadistical Analysis:** We modelled the biomarker changes using linear mixed models, which included the interaction term time-versus-treatment group as a fixed-effect and a random effect for each patient. We adjusted for sex, age, ART regimen, period of enrolment, risk factor for HIV acquisition and region of origin. Continuous outcome variables were log-transformed to satisfy model assumptions

- All CoRIS participants provided their written informed consent prior to enrolling in the cohort. The study was approved by the Research Ethic Committee of 12 de Octubre Hospital.

RESULTS

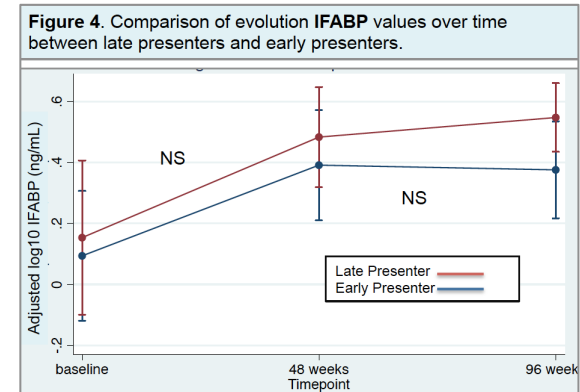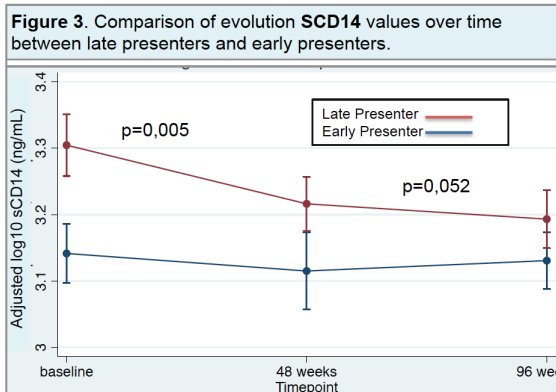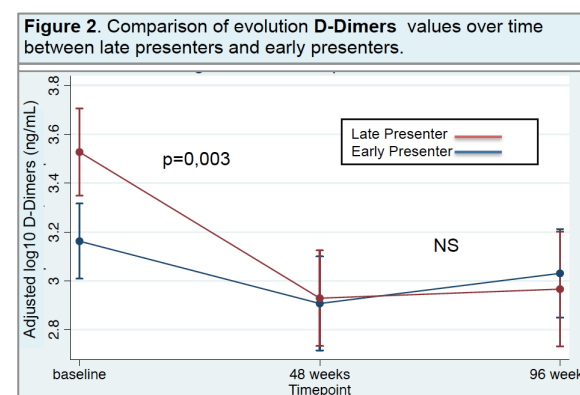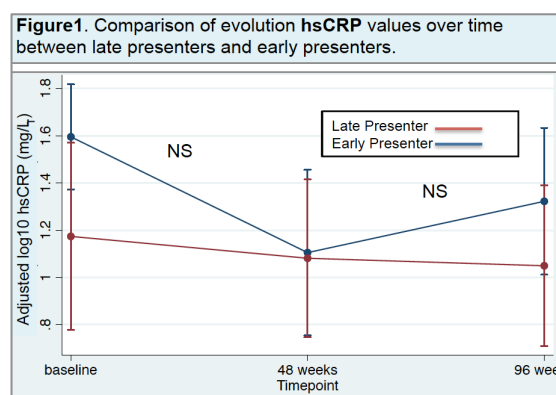**Table 1: Sociodemographic and clinical characteristics at cohort entry**

	Early presenters (EP) N= 50	Late presenters (LP) N=48	P value
Sex [n (%)]			
Females	6(12%)	10 (21%)	
Males	44 (88%)	38 (79%)	0,24
Age (mean/SD)	38 (11%)	39 (10%)	0,61
Transmission group [n (%)]			
MSM	37 (74%)	28 (58%)	
IDU	1 (2%)	3 (6%)	
Heterosexual	11 (22%)	13 (27%)	
Other/unknown	0 (0%)	4 (8%)	0,12
Educational level [n (%)]			
Primary education or less	2 (4%)	6 (12%)	
Secondary education	8 (16%)	5 (10%)	
University	18 (36%)	12 (25%)	
Other/unknown	6 (12%)	10 (21%)	0,21
Country of origin [n (%)]			
Spain	29 (58%)	30 (62%)	
Eastern Europe	1 (2%)	2 (4%)	
Western Europe	8 (16%)	1 (2%)	
Sub-Saharan Africa	1 (2%)	2 (4%)	
Latin America	11 (22%)	12 (25%)	0,21
Initial ART regimen			
2NRTI + I1NI	20 (40%)	18 (38%)	
2NRTI+1IP	15(30%)	15 (31%)	
2NRTI+1NNRTI	15 (30%)	15 (31%)	0,97
CD4+cell count , cells/µL (mean/SD)	484 (177)	44 (34)	<0,001
AIDS-defining event *			
No	50 (100%)	23 (48%)	
Yes	0 (0%)	25 (52%)	<0,001
Viral load copies/ml (mean/SD)	124229 (391451)	818141 (1284 164)	<0,001

MSM: male-male sexual contact; IDU: injection drug use; ART: antiretroviral therapy, NRTI: nucleoside reverse transcriptase inhibitor; INI: integrase inhibitor, NNRTI: non-nucleoside reverse transcriptase inhibitor; PI: protease inhibitor

Table 2: Differences of inflammatory biomarkers values at cohort entry

	Early presenters (EP) N= 50	Late presenters (LP) N=48	P value
hs CRP (ng/ml) (mean/SD)	83717,26 (74348,77)	100740,56 (102473,2)	0,35
D-Dimers (ng/ml) (mean/SD)	2309,77 (1874,49)	6339,39 (7273,67)	<0,001
sCD14 (ng/ml) (mean/SD)	1470, 29 (560, 75)	2156,99 (737,84)	<0,001
IFABP (ng/ml) (mean/SD)	3,43 (6,26)	3,94 (4,70)	0,67

Evolution of inflammatory biomarkers in HIV early presenters (CD4 >350/mm^3) versus HIV late presenters (CD4<100mm^3)

Figure 1. Comparison of evolution **hsCRP** values over time between late presenters and early presenters.

Figure 2. Comparison of evolution **D-Dimers** values over time between late presenters and early presenters.

Figure 3. Comparison of evolution **SCD14** values over time between late presenters and early presenters.

Figure 4. Comparison of evolution **IFABP** values over time between late presenters and early presenters.

CONCLUSIONS

- Despite the fact that late presenters exhibit higher baseline sCD14 and D-dimer levels than early presenters, these levels tended to converge after 96 weeks of ART.
- No differences were found in hsCRP and IFABP. Our study suggests that advanced HIV disease impacts on monocyte activation and pro-thrombotic pathways, although this effect is attenuated following ART.