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Cardiovascular events in delayed presentation of HIV: the prospective PISCIS cohort study.

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PISCIS POPULATIONAL HIV COHORT FROM CATALONIA AND BALEARIC ISLANDS

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Introduction

People living with HIV (PLWH) have an increased cardiovascular (CV) risk compared to the background population. Late HIV presenters (LP; CD4 ≤350 cells/μL) have increased risks of AIDS and non-AIDS comorbidities, but their impact on cardiovascular events (CVE) remains unclear.

Objectives

We aimed to assess if the risk of CV disease (CVD) is increased in individuals diagnosed at a late stage of HIV infection compared to those diagnosed early

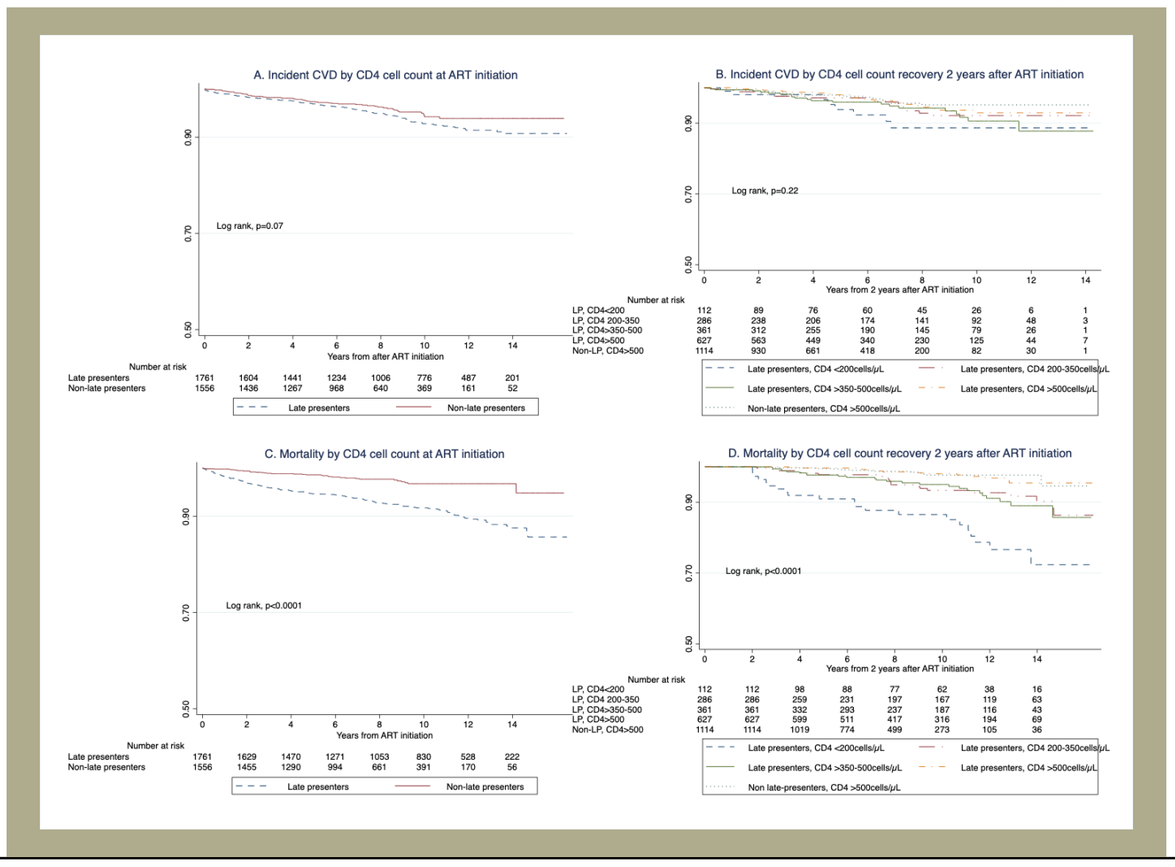
Methodology

From the prospective, multicentre PISCIS cohort, we included all adult PLWH initiating antiretroviral therapy (ART) between 2005-2019 without prior CVE. Additional comorbidity data were extracted from PADRIS, which is a central research-oriented database that gathers and crossmatches real-world health data generated by the different public health systems information (SISCAT), provided by the Catalan Agency for Health Quality and Evaluation (AQuAS).

The primary outcome was incidence of first CVE (ischemic heart disease, congestive heart failure, cerebrovascular or peripheral vascular disease).

The secondary outcome was all-cause mortality after first CVE. We used Poisson regression.

Figure 1. Kaplan-Meier curves of time to CV events or all-cause mortality. A. Incident cardiovascular events by CD4 cell count at ART initiation; B. Incident CV events by CD4 cell count 2 years after ART initiation; C. Mortality by CD4 cell count at ART initiation and D. Mortality by CD4 cell count 2 years after ART initiation.



Results

We included 3,317 PLWH (26,589.1 person/years [PY]): 1,761 LP and 1,556 non-LP. Overall, 163 (4.9%) experienced a CVE (IR 6.1/1000PY [95%CI: 5.3-7.1]): 105 (6.0%) LP versus 58 (3.7%) non-LP. No differences were observed in the multivariate analysis adjusting for age, transmission mode, comorbidities, and calendar-time, regardless of CD4 at ART initiation (aIRR 0.92 [0.62-1.36] and 0.84 [0.56-1.26] in LP with CD4 count <200 and 200-≤350 cells/μL, respectively, compared to non-LP) (Figure 1A and Table 1).

Overall mortality was 8.5% in LP versus 2.3% in non-LP (p<0.001) (Figure 1C). Mortality after the CVE was 31/163 (19.0%), with no differences between groups (aMRR 1.24 [0.45-3.44]. Women versus MSM, and individuals with chronic lung and liver disease experienced a particularly high mortality after the CVE (aMRR 5.89 [1.35-25.60], 5.06 [1.61-15.91] and 3.49 [1.08-11.26], respectively).

Sensitivity analyses including only PLWH surviving the first two years, yielded similar results, also among immunological non-responders with two-year CD4 <200 cells/μL (Figure 1B, 1D).

Table 1: Incidence rate of a first CV event in the overall cohort, including all LP and non-LPs

	CVD Events (n)	IR per 1000 PY (95% CI)	IRR (95% CI)	aIRR (95%CI)[1]
Total	163	6.1 (5.3-7.1)		
Age (time-updated) (years)				
<40	29	2.4 (1.7-3.4)	Ref (1)	Ref (1)
40-49	55	6.1 (4.7-8.0)	2.58 (1.64-4.04)	2.11 (1.33-3.33)
50-59	54	13.1 (10.0-17.1)	5.49 (3.50-8.62)	3.87 (2.42-6.20)
≥60	25	19.1 (12.9-28.3)	8.04 (4.71-13.72)	4.56 (2.53-8.20)
Transmission mode				
MSM	57	3.6 (2.8-4.7)	Ref (1)	Ref (1)
Heterosexual men	47	12.5 (9.4-16.6)	3.48 (2.37-5.12)	2.43 (1.62-3.67)
Women	16	4.7 (2.9-7.7)	1.32 (0.76-2.30)	1.14 (0.65-1.99)
IDU	28	13.7 (9.5-19.9)	3.82 (2.43-6.01)	2.23 (1.35-3.71)
Unknown/other	15	9.9 (5.9-16.4)	2.75 (1.56-4.85)	1.98 (1.11-3.55)
CD4 cell count at ART initiation				
Late presenters, CD4 200-≤350 cells/μL	105	6.9 (5.7-8.3)	1.35 (0.98-1.86)	
Non-late presenters, Cd4 >350 cells/μL	58	5.1 (3.9-6.6)	Ref (1)	
CD4 cell count at ART initiation				
Late presenters, CD4 <200 cells/μL	63	8.7 (6.8-11.2)	1.71 (1.19-2.44)	0.92 (0.62-1.36)
Late presenters, CD4 200-≤350 cells/μL	42	5.3 (3.9-7.1)	1.03 (0.69-1.53)	0.84 (0.56-1.26)
Non-late presenters, Cd4 >350 cells/μL	58	5.1 (3.9-6.6)	Ref (1)	Ref (1)
Calendar time (time-updated)				
2005-2009	8	4.5 (2.2-9.0)	0.72 (0.35-1.48)	0.81 (0.39-1.69)
2010-2014	47	6.3 (4.8-8.4)	1.02 (0.72-1.44)	1.16 (0.82-1.64)
2015-2021	108	6.2 (5.1-7.5)	Ref (1)	Ref (1)
AIDS defining event at ART initiation				
Yes	29	13.8 (9.6-19.9)	2.52 (1.69-3.77)	1.49 (0.95-2.34)
No	134	5.5 (4.6-6.5)	Ref (1)	Ref (1)
Comorbidities at ART initiation				
Diabetes	6	32.0 (14.4-71.3)	5.38 (2.38-12.17)	1.32 (0.51-3.39)
Arterial hypertension	16	14.3 (8.8-23.3)	2.48 (1.48-4.15)	1.83 (1.07-3.11)
Dyslipidaemia	13	16.5 (9.6-28.5)	2.84 (1.61-5.01)	1.34 (0.71-2.55)
Chronic kidney disease	3	31.0 (10.0-96.1)	5.13 (1.64-16.08)	1.98 (0.58-6.76)
Chronic lung disease	6	26.5 (11.9-59.0)	4.45 (1.97-10.06)	1.67 (0.71-3.90)
Chronic liver disease	25	20.3 (13.7-30.1)	3.74 (2.44-5.72)	2.38 (1.48-3.82)
Malignancy	11	22.4 (12.4-40.5)	3.85 (2.09-7.10)	2.27 (1.20-4.30)
Depression	14	9.9 (5.9-16.8)	1.68 (0.97-2.90)	1.08 (0.61-1.91)

Conclusion

PLWH presenting late to care without prior CV events did not have an increased long-term CV risk compared with non-late presenters.
Mortality after a first cardiovascular event was high, but no differences were observed between late and non-late presenters.

With today's treatment options, late HIV presentation does not increase the risk of CV events. Risk stratification and identification of PLWH at risk of future CVD should be individualized based on risk factors or comorbidities associated with increased CV risk.

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