Changes in cardiometabolic parameters after ART initiated within 1 year of HIV acquisition

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BACKGROUND

- Whilst some studies have reported that the use of integrase strand transfer inhibitors (INSTIs) is associated with minimal impact on lipid profiles compared to other drug classes, others have shown that the risk of dyslipidaemia and hypertension is increased when an INSTI is combined with TAF
- Findings from these studies are, however, often limited as participants may have been living with untreated HIV for prolonged periods of time which may have had an impact on lipid levels.
- Analyses of cohorts of individuals initiating antiretroviral therapy (ART) shortly following HIV acquisition may minimize this potential confounding impact of long-term

METHODS

We analysed data from CASCADE, a multinational study of cohorts from France, the Netherlands, Spain, Sweden, Greece, Canada and the UK, in which all participants have well estimated dates of HIV-1 seroconversion (SC) with a HIV-1 test window ≤12 months or other laboratory evidence of seroconversion

Inclusion criteria

- Seroconverted 2007-2022 whilst aged ≥16 years
- Started ART within 12 months of SC
- Information available at baseline (ART initiation) on BMI, CD4 cell count and HIV-RNA viral load. In addition:

  Lipid analyses: information on total cholesterol or triglyceride measurements available at baseline and post-ART

  Hypertension analyses: Without hypertension at baseline and with information on arterial blood pressure (BP) available at baseline and post-ART

Definitions

- *Hyperlipidaemia*: total cholesterol>240 mg/dL or triglycerides >200 mg/dL or initiation of lipid-lowering therapy
- *Hypertension*: systolic BP≥140, or diastolic BP≥90mmHg or initiation of antihypertensives

Statistical analysis

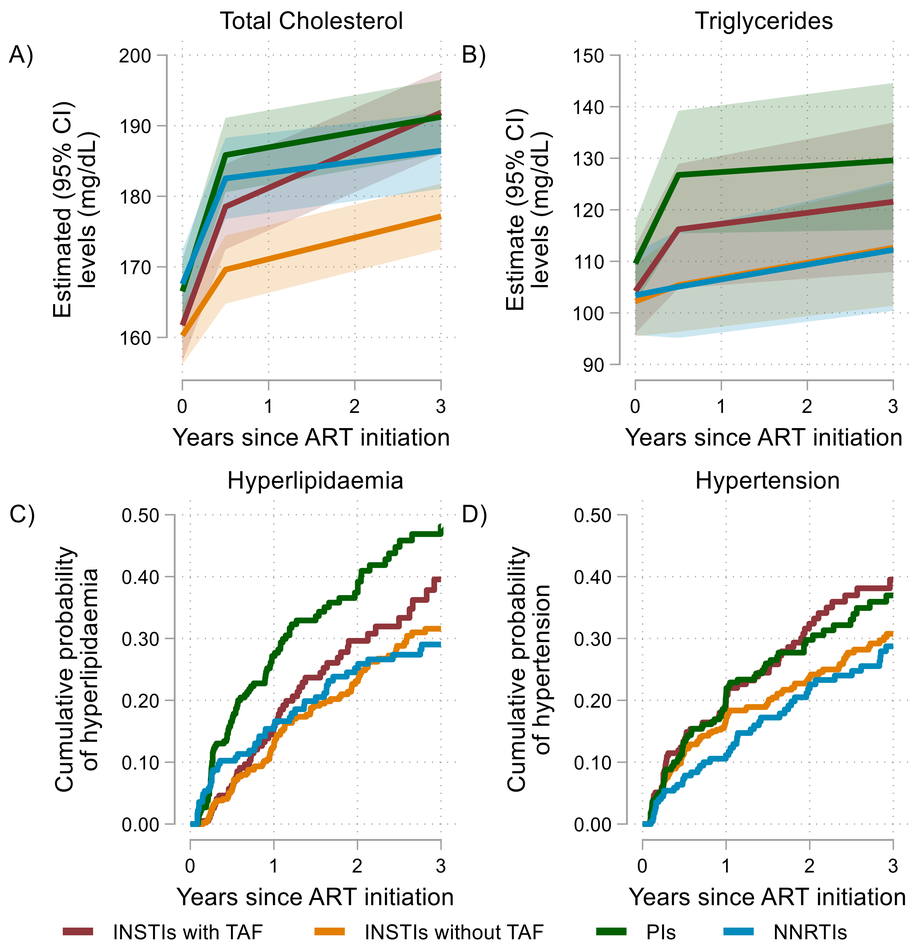
- Lipid levels were modelled through piecewise linear mixed models with a knot at 6 months; the risk of hypertension or hyperlipidaemia was modelled using time-to-event methods. Multivariable models were adjusted for age, sex at birth, probable exposure route, region of origin, and baseline CD4 cell count, HIV-RNA viral load and BMI
- Follow-up started at ART initiation and was censored if there was a change in the type of the ART regimen or (for the mixed models lipids analyses) initiation of lipid-lowering therapy.

RESULTS

- 6587 of 28545 fulfilled the general inclusion criteria; 1555 and 1417 were eligible for the lipid and hypertension analyses, respectively
- Most common regimens were based on INSTI without TAF, followed by PI, NNRTI, and INSTI with TAF (**Table**)

- Lipid levels and blood pressure appear to rapidly increase after ART initiation even in individuals starting ART very soon after HIV-1 seroconversion
- INSTIs+TAF and PIs are associated with faster increases in cholesterol and triglyceride levels compared to other ART types
- INSTI+TAF is associated with an increased risk of hypertension, and PIs with an increased risk of hyperlipidaemia
- INSTIs without TAF seem to have milder effects on cardiometabolic parameters similar to those of NNRTIs

Figure. Evolution of total cholesterol (A) and triglyceride (B) levels and cumulative risk of hyperlipidaemia (C) and hypertension (D) by time since ART initiation and type of ART



(A) and (C) based on multivariable models and estimates shown for men having sex with men, aged 30-39 at SC, originating from Europe/N America, with normal BMI and average baseline CD4 and VL. *Hyperlipidaemia*: TCHOL>240 mg/dL or TG>200 mg/dL or antilipidemic treatment. *Hypertension*: systolic ≥140, or diastolic ≥90mmHg or initiation of antihypertensives

Table. Baseline characteristics of study population by type of ART regimen. All figures are Median (IQR) or N (%) and refer to the lipids analyses sample (N=1555); characteristics were similar for the hypertension analyses sample (N=1417)

Variable	INSTI+TAF	INSTI, no TAF	PI	NNRTI
	n=285 (18.3%)	n=590 (37.9%)	n=382 (24.6%)	n=298 (19.2%)
Age at seroconversion (years)	34 (28, 44)	34 (27, 43)	37 (29, 45)	37 (30, 45)
Sex/probable exposure				
Men having sex with men	239 (83.9%)	516 (87.5%)	309 (80.9%)	269 (90.3%)
Injecting drug use	1 (0.4%)	1 (0.2%)	8 (2.1%)	0 (0.0%)
Men having sex with women	24 (8.4%)	21 (3.6%)	29 (7.6%)	16 (5.4%)
Women having sex with men	8 (2.8%)	33 (5.6%)	25 (6.5%)	8 (2.7%)
Unknown	13 (4.6%)	19 (3.2%)	11 (2.9%)	5 (1.7%)
Year of seroconversion	2019 (17, 20)	2015 (14, 17)	2013 (11, 14)	2012 (09, 13)
CD4 count (cells/μL)	496 (370, 631)	496 (364, 640)	448 (313, 605)	460 (320, 605)
HIV-RNA (log_{10} copies/mL)	4.9 (4.3, 5.8)	5.0 (4.4, 5.7)	5.3 (4.7, 5.9)	4.8 (4.3, 5.2)
BMI (Kg/m^2)	23 (21, 25)	23 (21, 25)	23 (21, 25)	23 (22, 25)
Triglycerides (mg/dL)	113 (85, 152)	107 (77, 160)	114 (82, 159)	106 (77, 141)
Total cholesterol (mg/dL)	159 (133, 184)	159 (137, 186)	162 (140, 189)	164 (143, 193)
Diastolic BP (mmHg)	75 (70, 80)	73 (70, 80)	70 (68, 80)	72 (69, 80)
Systolic BP (mmHg)	121 (112, 128)	120 (111, 127)	120 (110, 126)	120 (110, 130)

- INSTI with TAF: associated with fastest total cholesterol increase after month 6 (p<0.001), and faster triglyceride increase only during first 6 months (p=0.038) compared to NNRTIs.
- INSTI without TAF: only associated with relatively slow increase in total cholesterol after month 6 (p=0.027) compared to NNRTIs. PIs had similar effects to those of INSTI with TAF **(Figure: A, B)**
- In 1189 individuals with no baseline hyperlipidaemia, only PIs were significantly associated with increased hazard of hyperlipidaemia (aHR=1.75 vs. NNRTIs; 95% CI:1.26-2.43; p=0.001) (**Figure: C**)
- Hypertension risk elevated for INSTI+TAF but not INSTI without TAF (aHR=1.51; 95% CI:1.07-2.13; p=0.019 and aHR=1.14; 95% CI:0.85-1.53; p=0.392 vs. NNRTIs, respectively). (**Figure: D**)

CONCLUSIONS

- Lipid levels and blood pressure appear to rapidly increase after ART initiation even at this early stage of infection
- Our findings stress the importance of informed ART regimen decisions, acknowledging the potential for different effects on cardiometabolic parameters.

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