Retinal vascular calibres in older HIV-positive men compared to HIV-negative and younger HIV-positive controls

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POPPY
Pharmacokinetic and clinical observations in people over 50

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Abstract # 1493

Background

- With effective antiretroviral therapy (ART), HIV is now a treatable, chronic condition, though chronic immune activation and elevated levels of circulating inflammatory markers may persist
- The associations between HIV and stroke [1], and HIV and cognitive impairment [2], raise the question of whether HIV is associated with CSVD, which is also associated with systemic inflammatory markers
- Retinal vascular measurements are biomarkers of the risk of CSVD, stroke, cognitive impairment and coronary heart disease

Aim

- To determine the association between HIV status, age and retinal vascular measures in a UK-based sample of men living with HIV and a comparable group of HIV-negative controls

Methods

- POPPY is a cohort study of 3 demographically matched groups (people living with HIV [PLWH] aged ≥50 years; PLWH aged <50 years; HIV-negative people aged ≥50 years)
- Inclusions: white, male participants in POPPY
- Exclusions: PLWH with viral load (VL) >50 copies/mL or not on antiretroviral therapy (ART); diabetes mellitus
- Optic disc-centred 45° colour fundus photography was carried out (**Figure 2**)
- Outcomes were: central retinal arterial estimate (CRAE); central retinal venous estimate (CRVE); arterial-venous ratio (AVR), compared between groups with 3-way ANOVA
- The association of participant group, and other factors, with AVR was estimated in linear regression models. The multivariable model included all variables found to be associated with p<0.2 in bivariate models

Results

- Groups were generally well-matched on cardiovascular risk variables, except for differing rates of hepatitis C (p=0.03 by 3-way Chi-square), syphilis (p=0.004) and previous stroke/TIA (p=0.07) (**Table 1**).

Table 1. Participant characteristics

	PLWH aged ≥50 (n=120)	PLWH aged <50 (n=39)	HIV-negative aged ≥50 (n=52)	p value *
Age, median y (IQR)	59 (54, 65)	44 (41, 48)	60 (55, 65)	0.48
BP, median (IQR)				
Systolic	127 (118, 139)	124 (114, 132)	129 (116, 140)	0.20
Diastolic	79 (72, 85)	78 (71, 84)	80 (72, 85)	0.62
Current smoker, n (%)	22 (18.3)	13 (33.3)	8 (15.4)	0.08
Ever smoked, n (%)	64 (53.3)	27 (69.2)	33 (63.5)	0.16
Drug use in past 6 months, n (%)	37 (30.8)	15 (38.5)	15 (28.8)	0.59
Lipids, median mmol/L (IQR)				
Total cholesterol	5.0 (4.4, 5.6)	5.1 (4.6, 5.7)	5.0 (4.3, 5.8)	0.73
HDL	1.3 (1.0, 1.6)	1.3 (1.1, 1.6)	1.3 (1.0, 1.6)	0.92
LDL	2.8 (2.3, 3.5)	2.9 (2.4, 3.3)	3.0 (2.3, 3.5)	0.78
Framingham 10y risk, median % (IQR)	7.3 (5.3, 9.6)	2.8 (2.1, 4.2)	7.6 (5.9, 13.7)	0.22
Medical history, n (%)				
CHD	17 (14.2)	1 (2.6)	5 (9.6)	0.11
Stroke or TIA	7 (5.8)	0	0	0.07
Syphilis	53 (44.2)	11 (28.2)	10 (19.2)	0.004
HCV	13 (10.8)	3 (7.7)	0	0.03
CD4+ count, median cells/mm^3 (IQR)	600 (470, 750)	740 (490, 930)	n/a	0.11
Time since starting ART, median y (IQR)	13.1 (6.8, 17.6)	6.8 (5.1, 11.5)	n/a	0.0009

* 3-way comparison except for age and Framingham risk (only the two over-50 groups were compared), and CD4 and ART duration (only the HIV positive groups were compared)

Abbreviations: ART, antiretroviral therapy; AVR, arterial-venous ratio; BP, blood pressure; CHD, coronary heart disease; HCV, hepatitis C virus; HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; PLWH, people living with HIV; TIA, transient ischaemic attack.

- There were no differences between the three groups on any of the retinal vascular outcome measures (**Table 2**).

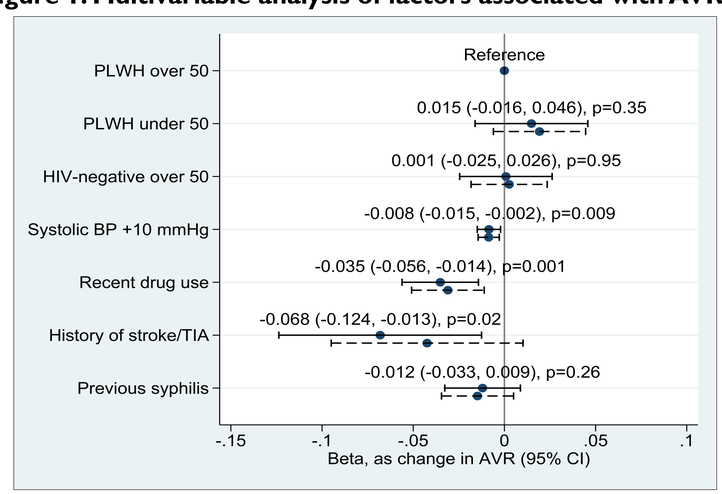
Table 2. Retinal vascular measurements

	PLWH aged ≥50 (n=120)	PLWH aged <50 (n=39)	HIV-negative aged ≥50 (n=52)	p (3-way comparison)
Central retinal arterial estimate	142.0 (20.2)	142.9 (20.3)	138.6 (20.4)	0.51
Central retinal venous estimate	199.1 (29.1)	195.6 (27.7)	193.4 (26.1)	0.46
Arterial-venous ratio (AVR)	0.72 (0.06)	0.74 (0.09)	0.72 (0.07)	0.32

Results are expressed as mean (SD). Abbreviations: PLWH, people living with HIV.

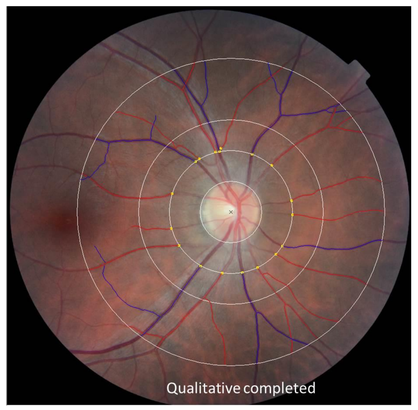
- In a linear regression model including study group and all factors with p<0.2 on bivariate analyses, there were associations between lower AVR (an indicator of worse cerebrovascular health) and higher blood pressure, reported history of stroke or TIA, and recent recreational drug use (**Figure 1**). Participant group was not associated any other outcome measure (not shown).

Figure 1. Multivariable analysis of factors associated with AVR



Abbreviations: AVR, arterial-venous ratio; BP, blood pressure; CI, confidence interval; PLWH, people living with HIV; TIA, transient ischaemic attack.

Figure 2. Sample image of retinal vascular measurement technique



In computer-assisted retinal vessel measurement, retinal arterioles (red) and venules (blue) are automatically identified and markers (yellow) are placed at 0.5 disc diameters distal to the disc margin. Trained readers confirm placement on the largest vessels passing between 0.5 and 1.0 disc diameters. The software then generates a "big 6" average calibre, giving a measure of central retinal vessel diameter.

Summary

- We found no association between participant group (PLWH aged ≥50 years; PLWH aged <50 years; HIV-negative aged ≥50 years) and retinal vascular measurements in white, UK-based men

Discussion

- Our findings agree with those of another study of retinal vascular measurements in a younger, predominantly female population in South Africa [3]
- Two MRI studies measuring the total volume of white matter hyperintensities (WMH), and one autopsy study measuring arteriolar wall thickness in cerebral white matter, found no difference in cerebral CSVD between PLWH and HIV-negative controls [4-6]
- In contrast, two MRI studies (one measuring volume of WMH, the other using radiological visual rating scales) found more CSVD in HIV positive participants than in HIV-negative controls [7,8]

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