



Magnetic resonance imaging of cerebral small vessel disease in HIV positive and HIV negative men aged 50 and above

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Background

- Cerebral small vessel disease (CSVD) is associated with circulating inflammatory mediators
- The association between HIV and stroke raises the question of whether HIV is also associated with CSVD

Aim

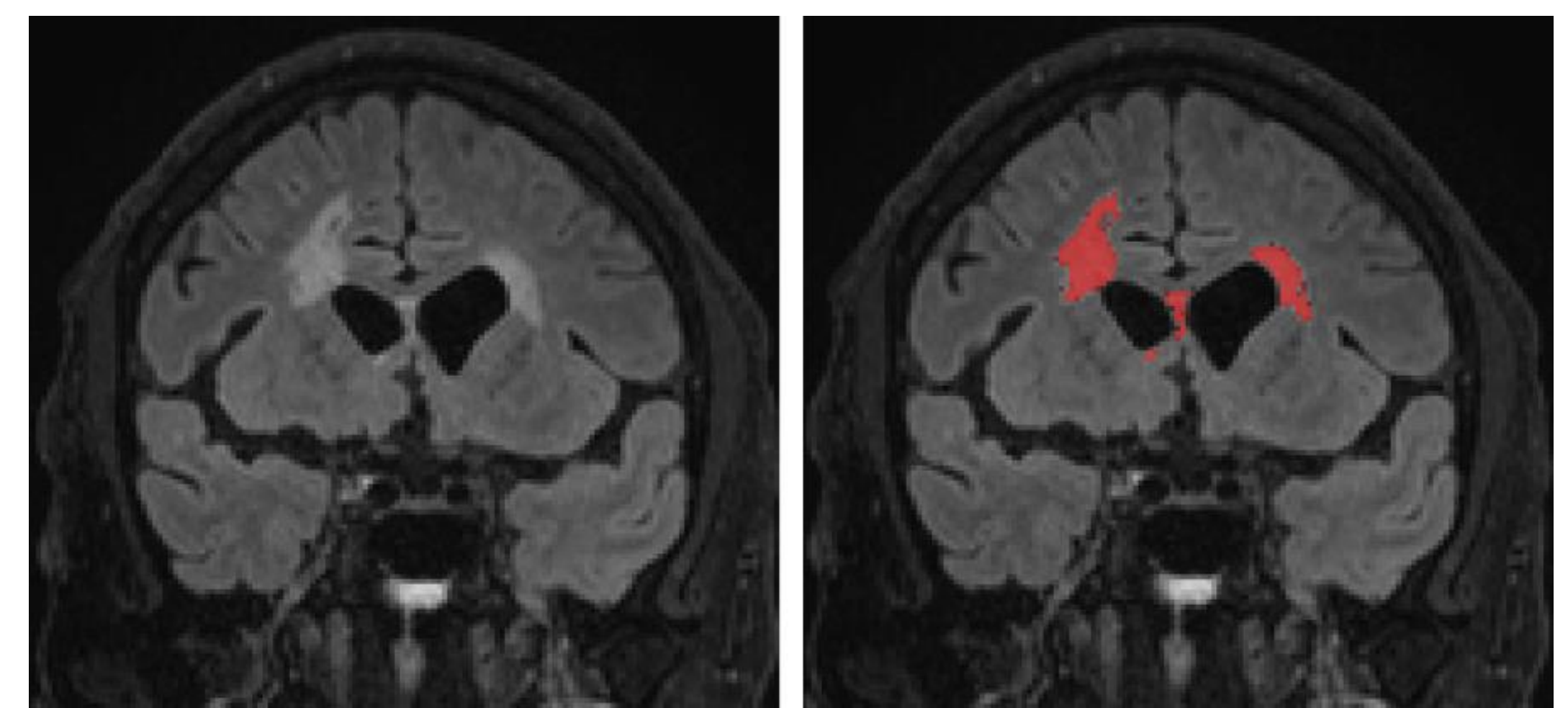
- To assess whether HIV serostatus was associated with white matter hyperintensities (WMH), a neuroimaging correlate of cerebral small vessel disease, in UK-based men aged ≥ 50 years

Methods

- POPPY is a cohort study of 3 demographically matched groups (PLWH aged ≥ 50 years; PLWH aged < 50 years; HIV-negative people aged ≥ 50 years)
- The present sub-study included white, male participants in POPPY aged ≥ 50 years; all HIV-positive participants were on ART with VL < 50 copies/ml
- Participants underwent magnetic resonance imaging (MRI) at 3 Tesla. WMH volume (WMHV) was extracted from volumetric 3D T1 and FLAIR images using automated image processing algorithms [1] (Figure 1) and compared between groups (Mann-Whitney test)
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- Participants underwent magnetic resonance imaging (MRI) at 3 Tesla. WMH volume (WMHV) was extracted from volumetric 3D T1 and FLAIR images using automated image processing algorithms [1] (Figure 1) and compared between groups (Mann-Whitney test)
- The association between HIV serostatus and WMHV (assessed as a proportion of intracranial volume [ICV] and log transformed) was described using linear regression models, with adjustment for all factors associated with WMHV in bivariate models ($p < 0.2$): age, waist circumference, and high density lipoprotein concentration

Figure 1. Example of a coronal FLAIR slice (left) and corresponding WMH segmentation overlaid in red (right)



Results

- 38 HIV positive and 37 HIV negative men were included. Traditional atherosclerosis risk factors were similar between groups, but there were some differences in past medical history (Table 1)
- HIV positive participants had median CD4 count 570 cells/ μ L (interquartile range [IQR] 470–700 cells/ μ L), time since diagnosis was median 20 y (IQR 14–24 y), and duration of ART was median 15 y (IQR 11–20 y)
- There were no differences in WMH between groups (Table 2)

Table 1. Participant characteristics

	HIV positive (n=38)	HIV negative (n=37)	p value
Age, median years (IQR)	60 (55–64)	59 (54–63)	0.61
Blood pressure, median (IQR)			
Systolic	125 (117–131)	126 (116–138)	0.45
Diastolic	79 (73–84)	76 (72–82)	0.37
Current smoker, n (%)	9 (23.7)	7 (18.9)	0.62
Ever smoked, n (%)	24 (63.2)	21 (56.8)	0.57
Drug use in past 6 months, n (%)	12 (31.6)	11 (29.7)	0.86
Lipids, median mmol/L (IQR)			
Total cholesterol	4.8 (3.9–5.4)	5.1 (4.2–5.8)	0.14
HDL	1.3 (1.0–1.5)	1.3 (1.1–1.6)	0.55
LDL	2.4 (1.8–3.3)	3.1 (2.6–3.5)	0.06
Framingham 10y risk, median % (IQR)	6.5 (5.0–9.4)	7.4 (6.0–10.4)	0.41
Medical history, n (%)			
Coronary heart disease	5 (13.2)	0	0.05
Stroke or TIA	2 (5.3)	0	0.49
Syphilis	18 (47.4)	8 (21.6)	0.02
Hepatitis C	2 (5.3)	0	0.49

Abbreviations: HDL, high density lipoprotein; IQR, interquartile range; LDL, low density lipoprotein; TIA, transient ischaemic attack

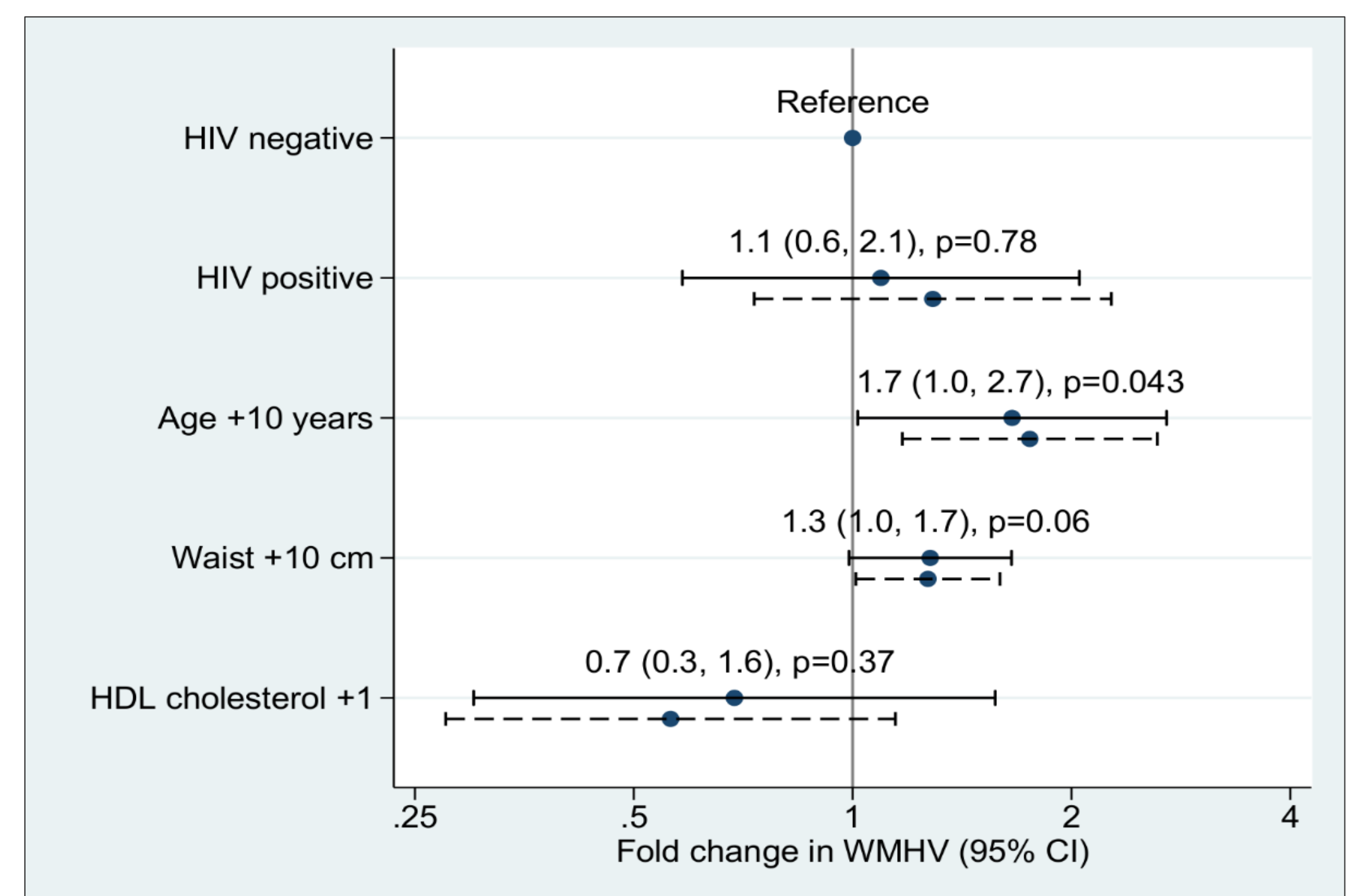
Table 2. Comparison of white matter hyperintensity volume between groups

	HIV positive (n=38)	HIV negative (n=37)	p value
Median (IQR) white matter hyperintensity volume (WMHV), μ L	962 (428–2628)	825 (347–1969)	0.31
Median (IQR) WMHV, as % of intracranial volume	0.06 (0.03–0.17)	0.05 (0.02–0.13)	0.29

Abbreviations: IQR, interquartile range.

- In a multivariable linear regression model (Figure 2), WMHV/ICV was not associated with HIV status ($p=0.78$). There were associations between a larger volume of WMHV/ICV and older age (1.7-fold increase in WMHV/ICV per +10 years, 95% confidence interval [CI] 1.1–2.7, $p=0.043$) and larger waist circumference (1.3-fold increase in WMHV/ICV per +10 cm, 95% CI 1.0–1.7, $p=0.06$).

Figure 2. Multivariable analysis of factors associated with WMHV



Abbreviations: CI, confidence interval; HDL, high density lipoprotein; WMHV, white matter hyperintensity volume

Conclusion

- We found no difference in WMHV between middle aged HIV positive men and demographically matched HIV negative controls. This suggests there is no association between HIV status and CSVD

Discussion

- Our null findings agree with two MRI studies measuring WMHV [2,3]
- An autopsy study measuring arteriolar wall thickness in cerebral white matter also found no difference in CSVD between PLWH and HIV-negative controls [4]

- In contrast, two other MRI studies (one measuring WMHV, the other using radiological visual rating scales) did find more CSVD in HIV positive participants than in HIV-negative controls [5,6]
- Studies of retinal vascular measurements (biomarkers of CSVD) have also found no difference between HIV positive participants and HIV negative controls [7,8]
- In order to synthesize these contrasting studies, one needs to consider the selection of controls and the measurement techniques used in each study
- Signs, symptoms and risk factors associated with CSVD should be addressed in PLWH in the same manner as in HIV-negative individuals

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