Differences in Predictors for Ischaemic and Haemorrhagic Strokes in HIV+ Individuals

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BACKGROUND

• HIV+ individuals are known to have a higher risk of stroke compared to HIV- individuals.1,2 They also have a higher burden of traditional cardiovascular disease (CVD) risk factors and exposure to antiretroviral therapy (ART) may pose additional risk.3-5

• In the general population, several shared risk factors for ischaemic and haemorrhagic strokes have been identified (hypertension, renal impairment, age, diabetes, prior stroke1), and hypertension and low estimated glomerular rate (eGFR) may be more strongly linked to ischaemic strokes than haemorrhagic strokes.6

As it is unknown whether there are differences in risk factors for ischaemic and haemorrhagic strokes in HIV+ individuals, the aim of our study was to investigate this in the large, heterogeneous D:A:D cohort.

METHODS

• D:A:D Study participants were followed from the time of the first blood pressure (BP) measurement at/after 1/1/1999 or individual study entry and until the first of a validated stroke, 6 months after last follow up or 1/2/2014.

• Elevated BP during follow-up was defined as one time-updated measurement of systolic BP ≥140 mm Hg and/or diastolic BP≥90 mm Hg, and incidence rates (IRs) for strokes were calculated for both stroke subtypes and stratified by presence/absence of elevated BP.

• Separate univariable and multivariable Poisson regression models were used to identify associations between possible risk factors and each subtype of stroke. Risk factors considered were:

  - Demographic/CVD-related: Gender, atrophy (time-fixed), age (5 years older), calendar year, dyslipidaemia (total cholesterol≥6.2, HDL<0.9, TC:HDL ratio≥6.5), previous CVD event (myocardial infarction/stroke), family history of CVD, body mass index (BMI), diabetes, smoking status (all time-updated)

  - HIV-related: Mode of HIV-acquisition (time-fixed), previous AIDS diagnosis, HIV-RNA viral load, CD4 count, cumulative exposure (5 years) to ART (protease inhibitors (PIs), non-nucleoside transcriptase inhibitors (NNRTIs), nucleoside reverse transcriptase inhibitors (NRTIs)), HIV and HCV infection (all time-updated)

  - In sensitivity analyses, we additionally included Cockcroft Gault estimated eGFR as one time-updated covariate after restricting follow-up to the start of systematic collection of eGFR on 1/2/2004.

Risk factors differing in multivariable Poisson models were selected and formally tested for whether their predictive ability differed on each stroke subtype, using the method described by Wei et al.10 These analyses used Cox proportional hazards models, restricted to fixed baseline covariates only.

RESULTS

• General characteristics of study participants at time of inclusion (baseline) and at time of stroke are displayed in Table 1.


CONCLUSIONS

• Of the 43,564 included persons, there were 590 strokes over 339,979 person years (PYRS) (IR of 1.74 (95%CI [1.60, 1.88]), 83 (14%) were haemorrhagic, 296 (50%) were ischaemic and the remaining 211 (35.8%) strokes were of unknown etiology. Crude IRs for stroke were higher in White individuals, 22,418 51.5 310 52.5 262 23.7, compared to Black individuals, 10,331 48.3 162 54.7 5 0.5.

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• Age, elevated BP and low CD4 count were the strongest predictors for both stroke subtypes.

• As has been reported in the general population, haemorrhagic strokes seemed to be more strongly associated with elevated BP than ischaemic strokes, and with low eGFR in sensitivity analyses.

• In sensitivity analyses, eGFR <60 ml/min seemed to show a stronger association with the risk of haemorrhagic than ischaemic strokes (adjusted relative rate 3.01 [1.28, 7.04] vs. 1.08 [0.68, 1.72]).

• In the formal comparative analysis, the direction of effects for selected risk factors were mostly similar to findings from separate Poisson models. None of the factors differed significantly in their predictive ability for either stroke subtype, except for male gender; stronger predictive ability for ischaemic stroke (p=0.001), and IDU; stronger predictive ability for haemorrhagic stroke (p=0.04) (Figure 3).

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