Major Vascular Events in Adults on ART in a South African HIV Management Programme

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BACKGROUND

- People living with HIV (PLWH) have an increased risk of major vascular events (MVEs), based on studies in high-income settings.[1,2]
- Data on MVE incidence in PLWH in Africa are limited.[3,4]
- We aimed to describe incidence of, and associations with, MVEs in PLWH on antiretroviral therapy (ART) in the Aid for AIDS (AfA) cohort.

METHODS

- AfA is an HIV management programme for employed / insured people in Southern Africa. Patients are managed according to established AfA protocols, which are in line with World Health Organization ART guidelines for low- and middle-income countries.
- This cohort analysis includes adults (≥18 years) who had a first ART claim through AfA from 1 January 2011 to 30 September 2018. Cohort entry was on date of first ART claim. Persons were censored on their date of death, last contact, first MVE, or 30 September 2018.
- We defined MVE as hospitalisation claims for stroke, acute coronary syndrome, or coronary revascularization procedure. We excluded hospitalisations with evidence for concomitant infectious or neoplastic diseases that may mimic stroke presentations.
- We calculated MVE incidence and explored associations with MVE using Cox regression.
- We identified hypertension, diabetes, and dyslipidaemia from hospitalisation claims, drug claims, and laboratory results, and included these as time-updated covariates in the regression model.

RESULTS

- We included 125,978 patients with 320,176 person-years of follow up. Baseline characteristics are summarized in Table 1; ART exposure in Table 2.
- We found 788 first MVEs (Figure 1). Incidence was 2.5 per 1,000 PYFU.
- Figure 2 shows the cumulative incidence of MVE, stratified by sex, from a Kaplan-Meier analysis.
- In the Cox regression model (Table 3), after adjustment for other variables, MVE was associated with older age, male sex, longstanding HIV infection, lower CD4 count and unsuppressed viral load at first claim, hypertension, diabetes, and dyslipidaemia. ART regimens consisting of two NRTIs with a protease inhibitor, or two NRTIs with rilpivirine/etravirine were associated with increased risk of MVE, versus a regimen of two NRTIs with efavirenz/nevirapine.

Incidence of major vascular events was 2.5 per 1,000 person-years. Strokes predominated (58% of events)

Table 1. Baseline characteristics of the cohort

	Number		
Age*, median (IQR) years	125,978	38	(33 to 45)
Female, n (%)	125,978	75,485	(60%)
CD4 count*, median (IQR) cells / µL	125,520	276	(140 to 446)
HIV viral load *, median (IQR) $\log_{10}$ copies / mL	124,614	4.4	(2.6 to 5.1)
Has **hypertension**, n (%)	125,978	22,930	(18%)
Has **diabetes**, n (%)	125,978	10,131	(8.0%)
Has **dyslipidaemia**, n (%)	125,978	11,528	(9.2%)
Died, n (%)	125,978	5,344	(4.2%)

Table 2. ART regimen exposure-time in the cohort

	Patient-years	
2 NRTIs + **efavirenz / nevirapine**	284,166	(89%)
2 NRTIs + **PI**	24,753	(7.8%)
2 NRTIs + **rilpivirine / etravirine**	3,854	(1.2%)
2 NRTIs + **INSTI**	350	(0.11%)
Other regimens	5,426	(1.7%)

Figure 1. Major vascular events (MVE) and their subtypes

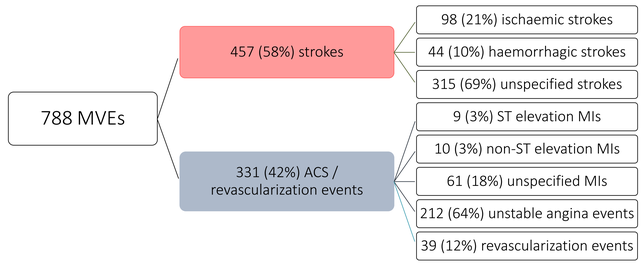

Figure 2. Kaplan-Meier estimates of MVE prevalence, stratified by sex

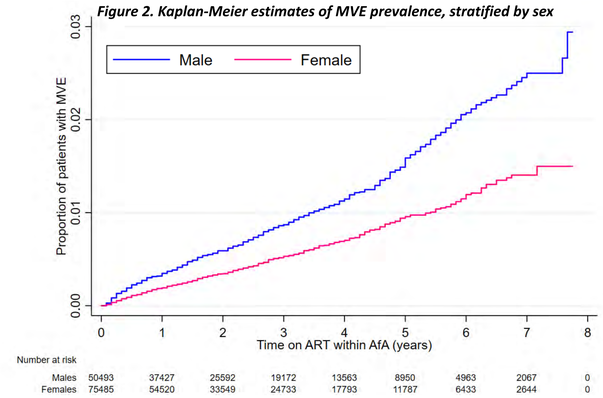

Table 3. Major vascular event hazard ratio estimates from Cox regression analysis

	Unadjusted analysis		Adjusted analysis	
Variable	**Hazard ratio (95% CI)**	**p**	**Adjusted HR (95% CI)**	**p**
Age				
Per 10-year increase	1.8 (1.7 to 2.0)	<0.001	1.2 (1.1 to 1.4)	<0.001
Gender				
Male (versus female)	1.7 (1.5 to 2.0)	<0.001	1.3 (1.1 to 1.5)	0.001
Year of HIV diagnosis				
Up to 2001 (versus 2002 and later)	1.7 (1.1 to 2.6)	0.017	1.8 (1.1 to 2.7)	0.013
Not known (versus 2002 and later)	0.89 (0.77 to 1.0)	0.12	1.0 (0.90 to 1.2)	0.60
CD4 cell count at first AfA ART claim				
<50 (versus ≥350) cells / mm^3	1.5 (1.2 to 1.9)	0.001	1.3 (1.0 to 1.7)	0.031
50 to 199 (versus ≥350) cells / mm^3	1.2 (0.99 to 1.4)	0.070	1.1 (0.92 to 1.3)	0.27
200 to 349 (versus ≥350) cells / mm^3	1.0 (0.83 to 1.2)	0.99	1.0 (0.83 to 1.2)	0.93
HIV viral load at first AfA ART claim				
Unsuppressed (≥ 400 versus suppressed < 400 copies/mL)	1.5 (1.2 to 1.8)	<0.001	1.4 (1.1 to 1.6)	0.01
Hypertension				
Present (versus not present)	6.5 (5.6 to 7.5)	<0.001	4.4 (3.7 to 5.1)	<0.001
Diabetes mellitus				
Present (versus not present)	4.9 (4.2 to 5.8)	<0.001	1.9 (1.6 to 2.3)	<0.001
Dyslipidaemia				
Present (versus not present)	3.9 (3.3 to 4.6)	<0.001	1.6 (1.3 to 1.9)	<0.001
Current ART regimen (all versus 2NRTIs with efavirenz or nevirapine)				
2 NRTIs with rilpivirine or etravirine	1.9 (1.2 to 3.0)	0.011	1.6 (1.0 to 2.6)	0.050
2 NRTIs with a protease inhibitor	1.4 (1.1 to 1.7)	0.009	1.4 (1.1 to 1.7)	0.009
2 NRTIs with an integrase inhibitor	2.3 (0.58 to 9.3)	0.23	1.7 (0.43 to 7.0)	0.44
Other regimen	0.79 (0.42 to 1.5)	0.46	0.73 (0.39 to 1.4)	0.33

CONCLUSIONS

- In this young, mostly female, African cohort, MVE incidence was 2.5 per 1,000 person-years. Background incidence data from this setting is lacking.
- Stroke predominated, in contrast to high-income settings, where coronary disease is more common.
- The MVE associations with specific ART regimens we identified deserve further study.

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ADDITIONAL KEY INFORMATION

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