



# Influence of CD4+/CD8+ ratio on early age of stroke in persons living with HIV: a single university center study in Portugal

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**Background.** Ischemic stroke (iSk) is one of the important causes of morbidity in people living with HIV (PLWH)<sup>1</sup>, either due to the virus itself and immunosuppression at all ages, or due to the traditional risk factors (RF) which, generally, increase with age<sup>2,3</sup>. CD4+/CD8+ ratio is proposed as a potential marker for PLWH at increased risk for non-AIDS comorbidities<sup>4</sup>. The current study aims to relate low CD4+/CD8+ ratios with the early ages of a diagnosis of iSk, compared to the ages of its occurrence in uninfected individuals.

**Patients and Methods.** A population of 6.446 hospitalized patients with iSk, during a 6-year period, was analysed, divided into 2 groups (Gr.): Gr. 1 - population uninfected with HIV (n = 6.395), Gr. 2 - PLWH (n = 51). Gr. 2 was further divided into 3 subgroups according to the CD4+/CD8+ ratio (< 0,4; 0,4 to 1; ≥ 1).

Statistical analysis was carried out with tests for equality of means for all variables and n-way analysis of variance for the entire population (PLWH and HIV-) including both the effect of HIV infection and the CD4+/CD8+ ratio, while maintaining control of the remaining potential RF.

**Results.** The average age of an iSk in Gr. 2 was 12,2 years earlier (p < 0,001) than the one observed in Gr. 1. PLWH had less RF than Gr.1 patients (High blood pressure 53 v/s 73% p=0,002; Dyslipidemia 25 v/s 44% p=0,007; Diabetes 14 v/s 25% p= 0,004).

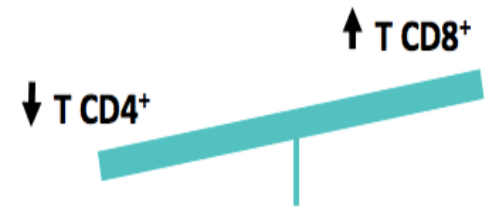
Multivariate analyses confirmed the association of a low CD4+/CD8+ ratio with the anticipation of the ischemic stroke in Group 2, about 9,3 years earlier in the subgroup with a ratio < 0,4 when compared to the subgroup with a normalized (≥ 1) ratio (p = 0,0366). The reduction in the number of years in the diagnosis of an iSk among PLWH with a CD4+/ CD8+ ratio <0,4 and the uninfected population was 18 years.

**Conclusions.** PLWH who have a CD4/CD8 ratio <0,4 have an increased risk of stroke at an earlier age.

“Normalization” of this ratio value may lead to a delay in the occurrence of iSk by around 9 years. The CD4+/CD8+ ratio can distinguish PLWH requiring more aggressive control of modifiable RF in the prevention of early iSk, particularly when it remains <0,4.

**References.** 1. Bogorodskaya M, Chow FC, Triant VA. Stroke in HIV. Can J Cardiol. 2019;35:280-7; 2. Shah ASV, Stelzle D, Lee KK, Beck EJ, Alam S, Clifford S, et al. Global burden of atherosclerotic cardiovascular disease in people living with HIV. Circulation. 2018;138:1100-12; 3. Benjamin LA, Allain TJ, Mzinganjira H, Connor MD, Smith C, Lucas S, et al. The role of human immunodeficiency virus-associated vasculopathy in the etiology of stroke. J Infect Dis. 2017;216:545-53; 4. Saracino A, Bruno G, Scudeller L, Volpe A, Caricato P, Ladisa N, et al. Chronic inflammation in a long-term cohort of HIV-infected patients according to the normalization of the CD4:CD8 ratio. AIDS Res Hum Retroviruses. 2014;30:1178-84

**Inflammation and immune activation typically associated with HIV infection**



CD4/CD8 (Normal: 1,5 - 2,5)  
Ratio inversion: < 1

**Population:**  
6.446 pts. with ischemic stroke (6 year period)



**Control group (Gr1) 6395 pts.**



**PLWH group (Gr2) 51 pts.**

ICD 9: iSk - 433, 434; PLWH - 042, V08

**Subgroups by CD4/CD8 ratios**  
< 0,4      0,4-1      ≥ 1

## Results



**Gr1(contr.)**

43,39%

56,61%

Median age:

70,34 years

**Age difference: 12,2 years (p<0.001)**



**Gr2(PLWH)**

35,29%

64,71%

Median age:

58,16 years

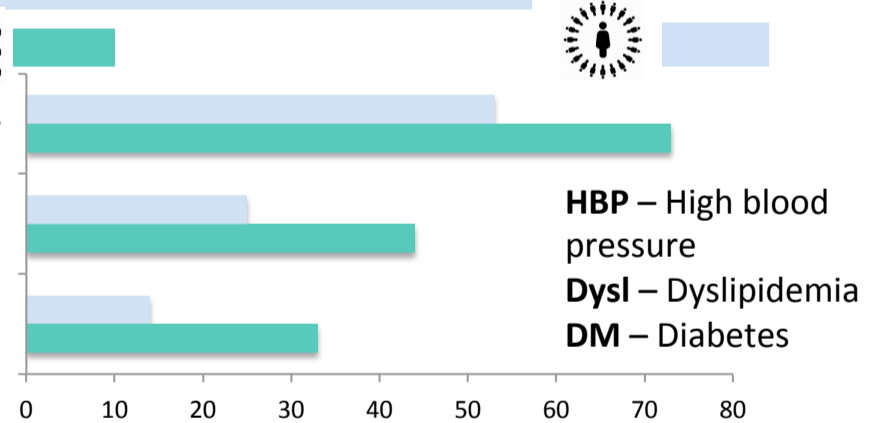
## Comorbidities (%)



HBP

Dysl

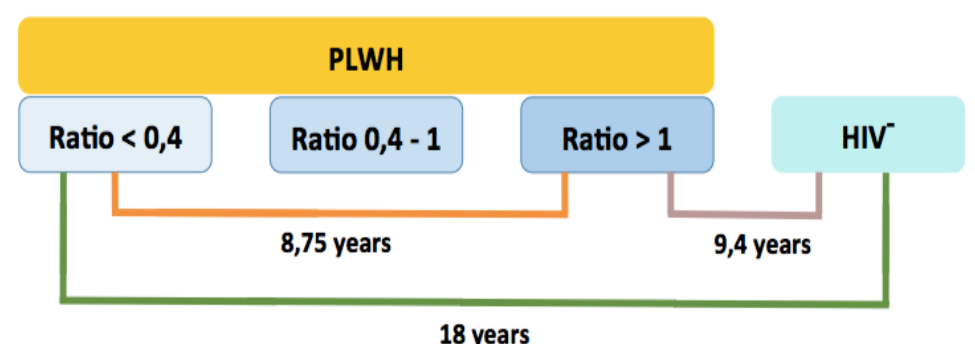
DM



**HBP** – High blood pressure  
**Dysl** – Dyslipidemia  
**DM** – Diabetes

**PLWH had less risk factors than Gr.1 patients**

**Multivariate analyses adjusted for CD4/CD8 ratio, age, sex, HBP, Dysl and DM**



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