

# Exploring cardiovascular risk in people with HIV: the critical role of intima-media thickness

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## Introduction/Summary

People living with HIV (PLWH) are ageing because of reduced mortality due to ART effectiveness (1). This has led to a global increase in their life expectancy by more than 50 years. As result, chronic diseases such as cardiovascular disease (CVD) are increasing in PLWH population (2). The association between HIV infection and cardiovascular diseases, particularly atherosclerosis, is a significant area of concern (3). Our study aimed to evaluate the correlation and risk factors between HIV infection and increased intima-media thickness (IMT) and assess differences between unilateral or bilateral localization.

## Methods

We performed a cross-sectional study from April 2023 to January 2024. People with HIV (PWH) from ARNAS Garibaldi and San Marco hospitals in Catania (Italy) were screened using doppler ultrasound of the supra-aortic trunks. IMT  $\geq 1$  mm was considered pathological. Therefore, patients were distinguished in 2 different groups: A (IMT < 1 mm), and B (IMT  $\geq 1$  mm). Demographic, laboratory and clinical data were collected. (table 1). We assessed differences using the chi-squared test, Fisher exact test and Mann-Whitney U, as appropriate. A logistic regression model assessed the association between demographical, viro-immunological, clinical characteristics, and IMT  $\geq 1$  mm. The study was conducted in accordance with the declaration of Helsinki and approved by the Provincial Ethics

committee of Messina (SHICohorth-protocol code 34/17 of the 22/03/2017, date of approval 22/05/2017).

## Results

197 PLWH 155 males (78.7%), median age 53.8 (IQR 44.1-60.6) were screened. A IMT  $\geq 1$  mm was found in 67 (34%) participants [group B: 55 males (82.1%); median age 58.2 years (IQR 52.4-63)]. Age, obesity, hypertension, smoking, and total and LDL cholesterol were higher in group B.

and LDL cholesterol were higher in group B. Median duration of infection was 9 (IQR 15-19) years in group A and 15 (6-24) in group B, while the median of ART years was 9 years (5-17) and 12.5 (6-22), respectively (Table 1). In both univariate and multivariate logistic regression models, age ( $p < 0.0001$ ), smoking ( $p 0.017$ ), total cholesterol ( $p 0.03$ ), serum LDL ( $p 0.045$ ), were associated with IMT  $\geq 1$  mm (Table 2). In multivariate analyses, years of infection, hypertension, diabetes and obesity were not significantly associated with IMT  $\geq 1$  mm. In group B, years of infection is significantly associated with an IMT  $\geq 1$  mm bilaterally in both univariate (OR: 1.07, 95%CI: 1.02-1.14) and multivariate logistic regression adjusted for age (aOR = 1.01, 95% CI: 1.01-1.14), maintaining a  $p$ -value  $< 0.05$  ( $p 0.016$ ) (Table 3).

## Conclusion

Our study highlights the significance of traditional cardiovascular risk factors such as age, smoking, and lipid profile in PLWH, showing their association with IMT  $\geq 1$  mm. Notably, while certain factors like years of infection and comorbidities did not directly correlate with IMT, a sub-analysis revealed a potential link between longer infection duration and bilateral IMT  $\geq 1$  mm. These findings underscore the importance of early screening and targeted intervention for cardiovascular health in PLWH. Further research is needed to explore the underlying mechanisms and tailor preventive strategies for this population.

Table 1. Characteristics of 197 people with HIV screened for doppler ultrasound of the supra-aortic trunks divided by IMT < 1mm and  $\geq 1$  mm.

	Overall (197)	Group A [IMT < 1 (130)]	Group B [IMT $\geq 1$ (67)]	p-value
Age (years), median (IQR)	53.8 (44.1-60.6)	51.0 (40.1-58.1)	58.2 (52.4-63.0)	<0.0001
Gender, n (%)				
Cis Male	155 (78.7%)	100 (76.9%)	55 (82.1%)	0.2
Cis Female	39 (19.8%)	29 (22.3%)	10 (14.9%)	
Female transgender	3 (1.5%)	1 (0.8%)	2 (3%)	
Risk factor for HIV acquisition, n (%)				0.23
Heterosexual	73 (37.1%)	45 (34.6%)	28 (41.8%)	
MSM	97 (49.2%)	70 (53.8%)	27 (40.3%)	
IDU	14 (7.1%)	7 (5.4%)	7 (10.4%)	
Bisexual	11 (5.6%)	6 (4.6%)	5 (7.4%)	
Other	2 (1%)	2 (1.5%)	0 (0%)	
HBsAg positive, n (%)	1 (0.51%)	1 (0.51%)	0 (0%)	0.05
HBcAb positive, n (%)	41 (21%)	21 (16.2%)	20 (30%)	
HCV coinfection:				0.5
Treated	14 (7.1%)	8 (6.1%)	6 (9%)	
Untreated	2 (1%)	2 (1.5%)	0 (0%)	
History of AIDS, n (%)				0.5
Yes	43 (21.8%)	26 (20%)	17 (25.4%)	
No	145 (73.6%)	99 (76.2%)	46 (68.7%)	
In progress	9 (4.6%)	5 (3.8%)	4 (6%)	
Smoking, n (%)				0.018
Yes	107 (54.3%)	62 (47.7%)	45 (67.2%)	
No	55 (28%)	44 (33.8%)	11 (16.4%)	
Former	35 (17.7%)	24 (18.5%)	11 (16.4%)	
Diabetes, n (%)	9 (4.57%)	3 (2.31%)	6 (8.9%)	0.064
Hypertension, n (%)	60 (30.5%)	31 (23.8%)	29 (43.3%)	0.005
BMI, n (%)				0.006
$\leq 24.9$	96 (48.7%)	73 (56.2%)	23 (34.3%)	
$\geq 25 < 29.9$	69 (35%)	42 (32.3%)	27 (40.3%)	
$\geq 30 < 34.9$	22 (11.2%)	12 (9.2%)	10 (15%)	
$\geq 35$	10 (5.1%)	3 (2.3%)	7 (10.4%)	
Treatment with statins, n (%)	36 (18.3%)	16 (12.3%)	20 (30%)	0.003
Years of infection (IQR)	12 (5 - 22)	9 (5 - 19)	15 (6 - 24)	0.0849
Years of therapy (IQR)	9 (5 - 18)	9 (5 - 17)	12.5 (6 - 22)	0.0811
Nadir CD4 (cell/mm <sup>3</sup> ), median (IQR)	219 (50.5 - 353.5)	275 (89 - 372)	118 (35 - 300)	0.0085
Zenith HIV-RNA (log <sub>10</sub> copies/ml), median (IQR)	5.04 (4.65-5.62)	4.96 (4.61-5.46)	5.30 (4.79-5.88)	0.0181
Total cholesterol (mg/dL), median (IQR)	185 (161 - 213)	181 (156 - 203)	190 (172 - 223)	0.0048
LDL (mg/dL), median (IQR)	120.5 (99 - 142)	118 (98 - 139)	128 (102 - 149)	0.1072
HDL (mg/dL), median (IQR)	46 (38 - 55)	46 (38 - 55)	47 (39 - 59)	0.5615
Triglycerides (mg/dL), median (IQR)	97 (47 - 167)	165 (88 - 125)	126 (84 - 196)	0.0005

MSM: men who have sex with men; IDU: injecting drug use; BMI: body mass index; IQR: interquartile range

Table 2: Logistic regression analysis

	Univariate logistic regression			Adjusted logistic regression			Adjusted for
	OR	95%CI	p-value	aOR	95% CI	p-value	
Age	1.09	1.06-1.13	<0.0001				
Nadir CD4	0.99	0.99-1.00	0.062				
Zenith HIV-RNA	1	0.99-1.00	0.063				
Years of infection	1.03	0.99-1.06	0.06	0.99	0.95-1.02	0.47	age
LDL	1.01	0.99-1.02	0.047	1.01	1.00-1.02	0.045	Statin, diabetes, age, sex
Total cholesterol	1.01	1.01-1.02	0.024	1.01	1.01-1.02	0.03	Statin, diabetes, age, sex
Smoke	2.90	1.35-6.23	0.006	2.73	1.20-6.26	0.017	age, sex
Hypertension	2.43	1.30-4.60	0.006	0.75	0.33-1.67	0.47	Smoke, age, sex, obesity
Diabetes	4.16	1.01-17.2	0.049	1.7	0.40-7.80	0.45	Age, sex
BMI:							Age, sex
$\geq 25 < 29.9$	2.04	1.04-4.00	0.38	1.84	0.90-3.85	0.105	
$\geq 30 < 34.9$	2.64	1.01-6.91	0.47	2.48	0.85-7.22	0.094	
$\geq 35$	7.40	1.77-30.99	0.006	4.45	0.96-20.4	0.05	

OR: odds ratio; CI: confidence interval; aOR: adjusted odd ratio; BMI: body mass index

Table 3: Logistic regression analysis on bilateral IMT  $\geq 1$  mm

	Univariate logistic regression			Adjusted logistic regression			Adjusted for
	OR	95% CI	p-value	aOR	95% CI	p-value	
Years of infection	1.07	1.02-1.14	0.01	1.08	1.01-1.14	0.016	Age.

OR: odds ratio; CI: confidence interval; aOR: adjusted odd ratio

## References

- Rodés B, Cadiñanos J, Esteban-Cantos A, Rodríguez-Centeno J, Arribas JR. Ageing with HIV: Challenges and biomarkers. Vol. 77, eBioMedicine. 2022.
- Feinstein MJ, Hsue PY, Benjamin LA, Bloomfield GS, Currier JS, Freiberg MS, et al. Characteristics, Prevention, and Management of Cardiovascular Disease in People Living with HIV: A Scientific Statement from the American Heart Association. Circulation. 2019;140(2).
- Avagimyan A, Pogosova N, Kakturskiy L, Sheibani M, Urazova O, Trofimenko A, et al. HIV-Related Atherosclerosis: State-of-the-Art-Review. Vol. 48, Current Problems in Cardiology. 2023