

HIV associated comorbidities: matters of the heart

OC 54 Incidence of metabolic syndrome in people with HIV in Italy who started ART since 2008: data from the ICONA cohort

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ABSTRACT

Background: The prevalence of metabolic syndrome (MetS) in people with HIV (PWH) on ART is higher than in general population; age, BMI, and certain ART regimen have been identified as predictors. Nevertheless, the role of CD4 count at diagnosis has not been investigated yet.

Material and methods: We included PWH enrolled in ICONA who started ART from 2008 and excluded those with MetS, or MACE before ART. Primary endpoint is time to diagnosis of MetS, as defined by modified NCEP ATP III criteria, in PWH enrolled in ICONA cohort who started ART when recently HIV infected (RHI), or when chronically infected with CD4 count above (CHI) or below 200 cells/mm³ (advanced HIV disease). Abdominal fat accumulation was assessed by waist circumference or, if missing, by formula $31.2 + 2.4 \times \text{BMI}$ for men and $33.2 + 2.1 \times \text{BMI}$ for women. RHI was defined as reporting acute/primary infection and having started ART within 100 days since diagnosis or includes those with a negative HIV test within 1 year that have started ART within 6 months since estimated time of infection.

Incidence rates (IRs) of MetS were calculated as the number of events per 100-person-years-of-FU (PYFU) with 95% confidence intervals (95% CIs). Kaplan-Meier curves estimated cumulative probabilities of the first incident metabolic syndrome. Univariable and multivariable Cox proportional hazard models were applied to estimate factors associated with the event, adjusting for age, year of ART start, sex, risk factor for HIV acquisition, ethnicity, HCV and HBV coinfection, ART class of the first line, HIV-RNA and CD8 count at ART initiation.

Results: Among 13,034 PWH starting ART after 2008 enrolled in ICONA, 11,137 were included in the analysis after excluding those with a diagnosis of MetS (974, 7.47%) or MACE (63, 0.48%) and those lost-to-follow up: 685 (6.15%) were diagnosed with RHI, 7,253 (65.1%) with CHI and 3,199 (28.72%) were advanced HIV disease (Table 1).

Overall, IR of MetS was 3.96×100 PYFU (3.8 - 4.1) with an overall prevalence of 18.5% (17.8-19.2). In depth, MetS were 82 (12.0%) in RHI, 1,201 (16.6%) in CHI and 775 (24.2%) in advanced HIV disease ($p < 0.001$). The cumulative 5-year probability of MetS with advanced disease (25.6% [95% 23.8%, 27.4%]) was higher than that observed in the CHI (15.7% [14.8%, 16.7%]) and RHI (12.9% [10.2%, 16.3%], $p < 0.001$) (Figure 1).

At multivariable analysis, a higher adjusted hazard of MetS was found for advanced HIV disease vs CHI [aHR 1.39 (95%CI 1.23-1.57)] ($p < 0.001$) (Table 2), while no difference was observed between CHI and RHI and when comparing calendar period 2008-2015 to 2016-2023 ($p = 0.146$).

Conclusions: Our findings show that PWH who start ART with CD4 count < 200 cell/mm³ are at higher risk of developing MetS. This risk is independent of calendar period and other key confounders factors and unlikely to be mediated by first-line ART regimen. The role of chronic inflammation and activation should be further investigated.

Table 1. Demographic and immuno-virological characteristics of PWH enrolled in ICONA, who started ART from 2008.

	Advance HIV				P value
	CHI >200 CD4	disease	RHI	Total	
F	7,253 (65.1%)	3,199 (28.7%)	685 (6.2%)	11,137 (100.0%)	
M	1,311 (18.1%)	706 (22.1%)	36 (5.3%)	2,053 (18.4%)	<0.001
Age ^	38.0 [30.0-46.0]	43.0 [35.0-51.0]	34.0 [27.0-43.0]	39.0 [31.0-47.0]	<0.001
Year ^	2015 [2012-2018]	2016 [2012-2018]	2,017.0 [2015-2019]	2,015.0 [2012-2018]	<0.001
Months to ART start	7.8 [2.5-60.9]	1.9 [1.0-4.0]	1.6 [0.7-3.2]	4.0 [1.6-29.9]	<0.001
Ethnicity					<0.001
Asian	82 (1.1%)	60 (1.9%)	7 (1.0%)	149 (1.3%)	
Black	61.9 (8.5%)	398 (12.4%)	36 (5.3%)	1,053 (9.5%)	
Caucasian	6,087 (83.5%)	2,533 (79.2%)	609 (88.9%)	9,229 (82.9%)	
Hispanic/Latino	401 (5.5%)	183 (5.7%)	27 (3.9%)	611 (5.5%)	
Other/Unknwon	6.4 (0.9%)	25 (0.8%)	6 (0.9%)	95 (0.9%)	
Transmission mode					
Hetero	2,507 (34.6%)	1,629 (50.9%)	115 (16.8%)	4,251 (38.2%)	<0.001
IDU	472 (6.5%)	215 (6.7%)	31 (4.5%)	718 (6.4%)	
MSM	3,805 (52.5%)	1,049 (32.8%)	506 (73.9%)	5,360 (48.1%)	
Other/Unknown	469 (6.5%)	306 (9.6%)	33 (4.8%)	808 (7.3%)	
Diagnosis of AIDS	208 (2.9%)	1,032 (32.3%)	17 (2.5%)	1,257 (11.3%)	<0.001
Log HWRNA>5^	1,941 (26.9%)	2,113 (67.3%)	353 (52.3%)	4,407 (40.0%)	<0.001
CD4 count ^	413 [313-554]	73 [30-136]	484 [347-646]	335 [165-492]	<0.001
Percentage of PWH with CD4 between:					
200-350	2,466 (34.0%)	0 (0.0%)	130 (19.0%)	2,596 (23.3%)	<0.001
350-500	2,428 (33.5%)	0 (0.0%)	183 (26.7%)	2,611 (23.4%)	
<200	0 (0.0%)	3,199 (100.0%)	45 (6.6%)	3,244 (29.1%)	
>500	2,359 (32.5%)	0 (0.0%)	327 (47.7%)	2,686 (24.1%)	
Positive HCV status	687 (10.1%)	291 (9.8%)	43 (6.6%)	1,021 (9.8%)	0.019
Positive HBsAg status	325 (5.0%)	170 (5.9%)	18 (2.9%)	513 (5.1%)	0.007
Abacavir exposure	1,638 (22.6%)	815 (25.5%)	140 (20.4%)	2,593 (23.3%)	0.001
On same backbone drug					
NNRTI	1,431 (19.7%)	172 (5.4%)	54 (7.9%)	1,657 (14.9%)	<0.001
INSTI	2,545 (35.1%)	1,252 (39.1%)	309 (45.1%)	4,106 (36.9%)	<0.001
PI	625 (8.6%)	466 (14.6%)	29 (4.2%)	1,120 (10.1%)	<0.001
Years off follow up at ART start	5.4 [2.4-8.4]	4.8 [1.9-8.2]	4.2 [2.0-6.5]	5.1 [2.2-8.2]	<0.001

Abbreviations: RHI, recently HIV infected; CHI, chronically infected with CD4 count above 200 CD4 cells; IDU, injective drug users; MSM, men who have sex with men; ART, antiretroviral therapy; INSTI, integrase inhibitors; NNRTI, non-nucleoside reverse transcriptase inhibitors; HR, hazard rate; aHR, adjusted hazard rate.

Figure 1. Cumulative probability of developing metabolic syndrome among the 3 groups.

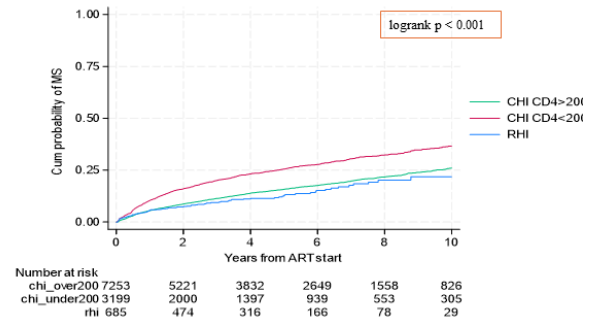


Table 2. Risk of developing metabolic syndrome among recently HIV infected (RHI), chronically infected with CD4 count above (CHI) or below 200 cells/mm3 (advanced HIV disease)

	Hazard Ratio	95%CI	P-value	aHR*	95%CI	P-value
Chronic HIV infection	1			1		
Advanced HIV infection	1.67	1.52-1.83	<.001	1.27	1.15-1.41	<.001
Recent HIV infection	0.83	0.67-1.04	0.111	1.02	0.81-1.29	0.855

*Adjusted for age at ART, year of ART start, sex, risk factor for HIV acquisition, ethnicity, HCV and HBV coinfection, first line ART regimen, HIV-RNA and CD8 count at ART initiation.