Aging & HIV in the ANRS CO3 Aquitaine Cohort

Cross-sectional results of the Skin, Muscle & Bone Aging Determinants: The SIMBAD study

Mercié P[1,8], Richert L[6,8], Le Marec F[8], Duffau P[1], Lawson-Ayayi S[8,9], Milpied B[7], N Barthe[10], Lazaro E[1], Bonnet F[1,8], Pellegrin I[3], Amiéva H[8], Dehail P[4], Reigadas S[4], Cazanave C[2], Dupon M[2], Neau D[2], Dabis F[8,9] and the SIMBAD study group of the ANRS CO3 Aquitaine Cohort. *[1]Service de médecine interne et immunologie clinique, [2]Service de maladies infectieuses et maladies tropicales, [3]Laboratoire d'immunologie, [4]Laboratoire de virologie, [5]Service de médecine physique et réadaptation, [6]Pôle de santé publique, [7]Service de dermatologie. CHU de Bordeaux. [8]INSERM U897, Université de Bordeaux, France. [9] COREVIH Aquitaine, [10]Service de médecine nucléaire. Bordeaux, France.* *Supported by ANRS, Paris, France.*

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Background. With increasing life expectancy, comorbidities have become a concern for ART-treated people living with HIV (PLHIV). These comorbidities are more frequent at a given age than in the general population without clear explanations, except for ART- or hepatitis co-infection related complications. We prospectively investigated age-related comorbidities and functional limitations and their clinical and biological determinants in PLHIV in care.

Methods. The SIMBAD study enrolled consenting adult PLHIV from the ANRS CO3 Aquitaine Cohort with a previous bone DXA measurement. Participants underwent standardized neurocognitive and functional locomotor tests, a repeat DXA, measurement of plasma 25-OH vitamin D, T-cell immune activation (CD4+/CD8+DR+) and immunosenescence (CD4+/CD8+CD57+CD28-) markers. Functional test results were compared to age-specific norms of the general population when available. Correlations between different tests were described in a principal component analysis (PCA), and determinants for pre-defined tests assessed by multivariable linear regression.

Results. 109 patients were assessed. Detailed results are indicated in Table 1. Main results are expressed as median (IQR) : median vitamin D level was 29.0 (18.8;35.5) ; vitamin D subgroups were < 20ng/ml (n=29); 20-30 (n=30) and ≥ 30 (n=48). T-cell immune activation markers were CD4+DR+: 9.5 (6.8;12.6) and CD8+DR+: 23.7 (17.2;40.2. T-cell immunosenescence marker CD8+CD57+CD28- was 29.7 (18.8;35.7).

Table 1. Characteristics of SIMBAD study participants compared to the rest of the Aquitaine cohort participants under follow-up in the study sites in 2012-2013

Characteristics	SIMBAD participants N=109		Rest of the Aquitaine cohort participants N=2966		p
Age (years)	51.6	(46.6;61.0)	48.8	(42.3;54.8)	**<10⁻³**
Gender, n (%)					0.193
Male	87	(79.8)	2143	(72.3)	
Female	22	(20.2)	820	(27.6)	
Transgender	0	(0.0)	3	(0.1)	
Transmission risk group, n (%)					**<10⁻³**
MSM	70	(64.2)	1248	(42.1)	
Heterosexual	31	(28.4)	1043	(35.2)	
Drug users	4	(3.7)	413	(13.9)	
Others	4	(3.7)	262	(8.8)	
CDC classification, n (%)					0.500
A	66	(60.6)	1632	(55.0)	
B	24	(22.0)	712	(24.0)	
C	19	(17.4)	622	(21.0)	
Duration since first reported seropositivity (years)	17.1	(12.5;21.3)	15.8	(8.2;21.9)	**0.027**
ART treatment, n (%)					**0.034**
2 NRTIs + PI/r	35	(32.4)	1286	(44.8)	
2 NRTIs + NNRTI	32	(29.6)	813	(28.3)	
Other cART	13	(12.0)	226	(7.9)	
ART no-cART	25	(23.1)	438	(15.2)	
No treatment	3	(2.8)	110	(3.8)	
Missing data	1	(.)	93	(.)	
Undetectable viral load, n (%)					**0.011**
No	7	(6.9)	487	(16.4)	
Yes	94	(93.1)	2479	(83.6)	
Missing data	8	(.)	0	(.)	
Last CD4+ count (cells/mm3)	538	(441;729)	581	(419;760)	0.335
CD4+ nadir (cells/mm3)	253	(168;389)	270	(175;371)	0.700

Results (continued). Test results differed significantly from population norms for spine and femoral neck bone mineral density (BMD), the timed-up-and-go locomotor test and neurocognitive tests; mean differences were modest and seemed to attenuate with increasing age (Figures 1,2; Table 2). Marked alterations (locomotor Z-score >|2|, 2 neurocognitive Z-scores >|1|, osteoporosis) were found in <25% per domain.

Figure 1. Distribution of bone mineral density results in SIMBAD study participants compared to the theoretical mean according to age-specific norms of the general population

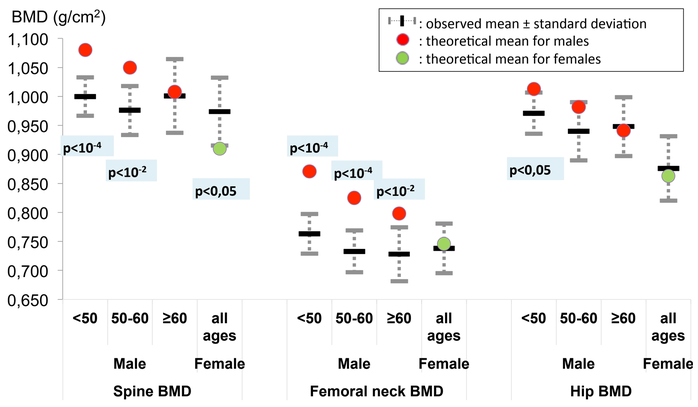


Figure 2. Distribution of locomotor test results in SIMBAD study participants compared to the theoretical mean according to age-specific norms of the general population

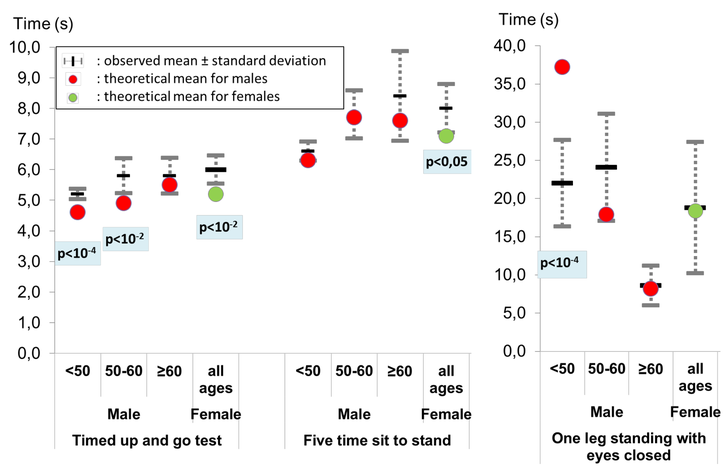
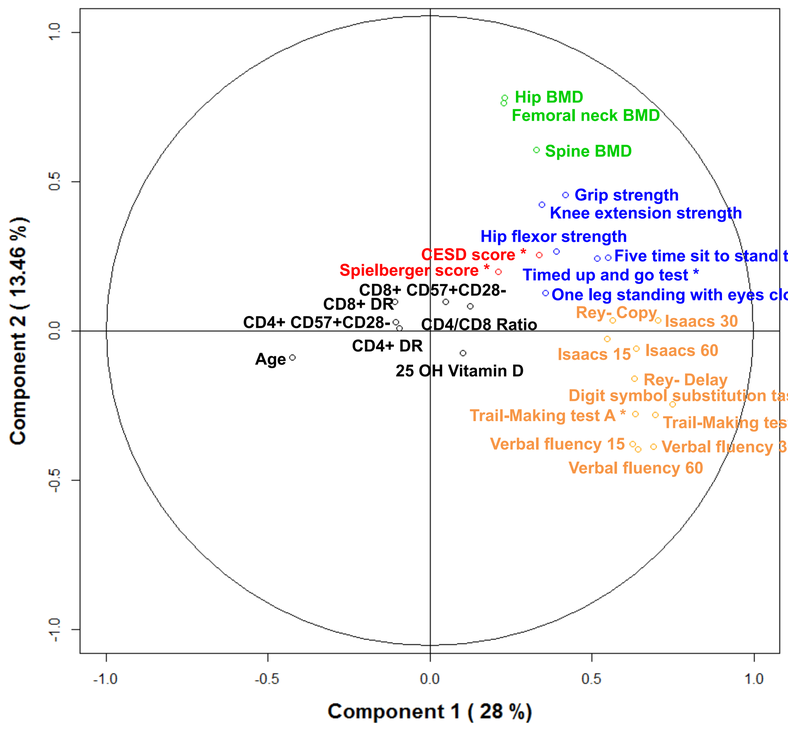


Table 2. Distribution of neurocognitive test results in SIMBAD study participants compared to the theoretical mean according to age-specific norms of the general population

Tests	Age	Education level	N	Observed proportion (%)	Theoretical proportion (%)	p
Rey figure (copy) > 16th centile	<55		63	19 (30.1)	(16.0)	**0.002**
	≥55		39	16 (41.0)	(16.0)	**<10⁻³**
Rey figure (delayed recall) > 16th centile	<55		64	17 (26.6)	(16.0)	**0.021**
	≥55		39	10 (25.6)	(16.0)	0.101
Trail-Making Test A > 16th centile	<55	-	65	10 (15.4)	(16.0)	0.892
	≥55	No college diploma	27	9 (33.3)	(16.0)	-
		College diploma	10	5 (50.0)	(16.0)	-
Trail-Making Test B > 16th centile	<55	-	65	17 (26.2)	(16.0)	**0.026**
	≥55	No college diploma	25	5 (20.0)	(16.0)	-
		College diploma	10	3 (30.0)	(16.0)	-

Figure 3. PCA – Correlations between tests of different domains (and projection of illustrative variables)



Legend : * These tests were transformed (-1 x test result) to standardize interpretation across all tests: the higher the value, the better the test performance

Tests of different domains correlated weakly (r<|0.4|).

Multivariable linear regression models of a pre-defined subset of tests (femoral neck BMD, lower limb muscle performance, verbal fluency and psychomotor speed) showed that increasing age was the only consistently significant determinant of poorer test results (Table 3). Other determinants (lean mass index, lipoatrophy, CD4 nadir, type of ART) varied between tests. No associations were found with vitamin D levels or T-cell immune activation/senescence markers in any of the regression models.

Table 3. Summary of results from multivariable linear regression models

Explanatory variables	Dependent variable: Femoral neck BMD Beta	p-value	Five times sit-to-stand test Beta	p-value	Psychomotor speed (Wechsler codes) Beta	p-value	Verbal Fluency Test Beta	p-value
Age (years)	-0.012	0.2570	-0.037	0.0010	-0.038	0.0003	-0.024	0.0284
Lean mass index (kg/m⁻²)	0.345	0.0254	0.354	0.0281	-	-	-	-
Lipo-atrophy								
No	0	0.0089	-	-	-	-	0	0.0409
Yes	-0.546		-		-		0.443	
Type of ART								
cART	0		-		-		-	
ARV, no-cART	-0.473	0.0249	-	-	-	-	-	-
Naive	0.971		-		-		-	
CDC stage								
Stage A	-		0		-		-	
Stage B	-	-	-0.445	0.0541	-	-	-	-
Stage C	-		-0.518		-		-	
Nadir (/mm³)	-		-	-	0.002	0.0267	-	-
Viral load indetectability								
No	-	-	-	-	-	-	0	
Yes	-		-		-		0.766	0.0444

Conclusions. In this cross-sectional analysis of the SIMBAD study, bone, muscular and neurocognitive alterations appeared to be of low severity and not related to biologic markers in PLHIV care. Ongoing longitudinal analyses will allow for further assessment of the relationships with aging.

References

Appay V, Almeida JR, Sauce D et al. Accelerated immune senescence and HIV-1 infection. Exp Gerontology 2007;42:432-437.
Cazanave C, Dupon M, Lavignolle-Aurillac V et al. Reduced Bone Mineral Density in HIV-Infected Patients: Prevalence and Associated Factors. AIDS 22, no 3 (Jan 30, 2008) : 395-402.
De Biasi Sara, Pinti M, Nasi M et al. HIV-1 infection and the aging of the immune system: facts, similarities and perspectives. J Exp Clin Med 2011;3(4):143-150.
Duffau P*, Wittkop L*, Lazaro E et al. Association of Immune-activation and -senescence Markers With non AIDS defining Comorbidities in HIV suppressed Patients. Accepted for Publication in AIDS the 19.06.2015. * equally contributors.
Richert L, Brault M, Mercié P, et al. Decline in Locomotor Functions over Time in HIV-Infected Patients ». AIDS 28, no 10 (19 juin 2014): 1441-49.

Acknowledgements ANRS CO3 Aquitaine Cohort - 2015
Coordination: F. Bonnet, F. Dabis
Scientific committee: F. Bonnet, S. Bouchet, D. Breilh, G. Chêne, F. Dabis, M. Dupon, H. Fleury, V. Gaborieau, D. Lacoste, D. Malvy, P. Mercié, P. Morlat, D. Neau, I. Pellegrin, JL. Pellegrin, S. Reigadas, S. Tchamgoué
Epidemiology and Methodology: M. Bruyand, G. Chêne, F. Dabis, C. Fagard, S. Lawson-Ayayi, L. Richert, R. Thiébaut, L. Wittkop.
Infectious Diseases and Internal Medicine: K. André, F. Bonnet, N. Bernard, O. Caubet, L. Caunègre, C. Cazanave, J. Ceccaldi, I. Chossat, C. Courtault, FA. Dauchy, S. De Witte, D. Dondia, M. Dupon, A. Dupont, P. Duffau, H. Dutronc, S. Farbos, I. Faure, V. Gaborieau, Y. Gerard, C. Greib, M. Hessamfar-Joseph, Y. Imbert, D. Lacoste, P. Lataste, E. Lazaro, D. Malvy, J. Marie, M. Mechain, JP. Meraud, P. Mercié, E. Monlun, P. Morlat, D. Neau, A. Ochoa, JL. Pellegrin, M. Pillot-Debelleix, T. Pistone, I. Raymond, MC. Receveur, P. Rispal, L. Sorin, S. Tchamgoué, C. Valette, MA. Vandenhende, MO. Vareil, JF. Viallard, H. Wille, G. Wirth.
Immunology: JF. Moreau, I. Pellegrin.
Virology: H. Fleury, ME. Lafon, S. Reigadas, P. Trimoulet.
Pharmacology: S. Bouchet, D. Breilh, F. Haramburu, G. Miremont-Salamé
Data collection, Project Management and Statistical Analyses: MJ. Blaizeau, I. Crespel, M. Decoin, S. Delveaux, F. Diarra, C. D'Ivernois, C. Hanappier, D. Lacoste, S. Lawson-Ayayi, O. Leleux, F. Le Marec, E. Lenaud, J. Mourali, E. Pernot, A. Pougetoux, B. Uwamaliya-Nziyumvira, A. Tsaranazy, A. Valdes.
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