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Correlation among bone, endothelial and hepatic damage in PLWH

Masiello1, V. Iodice1, F. Laguardia2, A. Boccia2, I. Capriglione2, A. Iodice1, F. Simeone1, and P. Maggi1
1. Infectious Diseases Unit, AORN Sant'Anna e San Sebastiano, Caserta, Italy; 2 Infectious Disease Unit, University Hospital Luigi Vanvitelli, Naples, Italy

Introduction/Summary

Patients with HIV infection (PLWH) are at increased risk of non-AIDS-related comorbidities such as osteoporosis and atherosclerosis. These two comorbidities are generally associated with aging, but there are currently few studies on their correlation. Recent analyses of the general population have shown that patients with osteoporosis have a higher risk of developing cardiovascular disease than those with normal bone mass density. Few studies have evaluated the association between liver damage, in terms of liver fibrosis, HF, and steatosis, HS) and atherosclerosis in PLWH. The aim of our study is to evaluate the possible correlation between bone, endothelial and hepatic damage in PLWHs on antiretroviral therapy (ART).

Patients and Methods

We enrolled 200 patients, 56 females and 144 males. We divided the patients in 2 groups based on cIMT: A) (#121) with normal cIMT (<1.3 mm) and B) (#79) with pathologic cIMT (>1.3 mm). Patients were submitted to measurement of carotid intima-media thickness (cIMT) with high resolution B mode Doppler USG and evaluation of HF using a process based on vibration-controlled transient elastography (Fibroscan) and HS by an ultrasonic controlled attenuation parameter (CAP) and assessment of mineral bone density with bioelectrical impedence analysis The cut-off value for defining the presence of c-IMT is 1,3 mm, for significant HS is CAP > 260 dBm and for HF is > 7 kPa. For both groups we evaluated T and Z score values. For patients >50 years and for menopausal women we have considered the T score (normal >-1, osteopenia between -1 and -2,5, osteoporosis <-2,5) , for patients<50 years we have considered the Z score(<-2 pathologic, >-2 normal) For each group we also considered CD4, CD4 nadir, CD4/CD8 ratio, years of HAART, type of ART, total, HDL and LDL cholesterol and triglycerides levels. For statistical analysis we used t-student and X-square tests.

Results

Data are shown in Table 1. No statistically significant differences emerged between the two groups for age, CD4, CD4/CD8 ratio, years of ART, and vitamin D. A statistical significance was highlighted for the type of ART, showing that in group A there is a prevalence of dual therapies (2DR) compared to group B (p 0.03), for CD4 nadir, triglyceridemia, total cholesterolemia and LDL values. In addition, statistical significance was found in T/Z scores values and in HS with pathological bone density and higher steatosis values in group B (p<0.006 and p0,00000, respectively). We did not observe statistically significant differences between the two groups in fibrosis values (p 0.69).

TABLE 1

BASELINE DATA	TOTAL	IMT< 1,3	IMT≥ 1,3	p
Numbers of patients	200	121	79	///
Age, median (range)	52 (23-83)	47 (23-62)	58 (29-83)	///
Male patients n(%)	144 (72)	89 (73,5)	55 (69,6)	0,64
Years on HAART, median (range)	10 (1-33)	7,5 (1-29)	10 (1-33)	///
ARV Regimens n (%)	DUAL 43 (23,2) 2NRTI+PI 8 (4,3) 2NRTI+INSTI 105 (56,7) 2NRTI+1NNRTI 29 (15,6)	DUAL 32 (26,4) 2NRTI+PI 8 (6,6) 2NRTI+INSTI 72 (59,5) 2NRTI+ 1NNRTI 9 (7,4)	DUAL 17 (21,5) 2NRTI+PI 5 (6,3) 2NRTI+INSTI 54 (68,3) 2NRTI+1NNRTI 3 (3,7)	**0,03** 0,28 0,10 0,89
CD4, cell/uL M +SD	574,84±266,67	589,47±254,21	565,49±276,83	0,47
CD4+ NADIR , cell/µL (M ± SD)	296,7±212,6	336,4±230,2	271±197,8	**0,03**
CD4/CD8 ratio>1 n (%)	71 (38,3)	29 (36,2)	42 (40)	0,85
Triglycerides (mg/dl) M± SD	125,76±68,88	114,58±73,35	144,18±64,51	**0,003**
Total cholesterol (mg/dl) M ± SD	188,23±57,26	181,42±47,07	200,16±63,57	**0,02**
HDL cholesterol (mg/dl) M ± SD	54,43±19,73	54,81±13,37	56,81±23,62	0,49
LDL cholesterol (mg/dl) M± SD	119,12±46,64	107,15±43,36	128,1±47,39	**0,002**
Vitamin D (ng/ml) M± SD	24±11,5	26,45±12,23	24,18±11,89	0,19
% of Elevated Triglycerides >150 mg/dl	45 (22,5)	20 (16,5)	25 (31,6)	**0,01**
% of Elevated Cholesterol > 200 mg/dl	40 (20)	15 (20,6)	25 (31,6)	**0,001**
% of patients with T/Z score alterations n (%)	84 (44,4)	39 (32,2)	48 (60,7)	**0,0001**
Liver stiffness >F2, n (%)	30 (16,2)	16 (20)	14 (13,3)	0,69
Steatosis grade (CAP score>260 dB/m) n (%)	58 (31,3)	23 (19)	35 (44,3)	0,00000

Conclusion

These data confirm a strong correlation between bone and endothelial damage in ART-treated PLWHs: patients with increased cIMT (>1.3 mm) more often show bone density alterations with osteopenia or osteoporosis. Furthermore, PLWH show higher values of liver steatosis than patients with normal c-IMT suggesting that in PLWH liver, bone and heart are closely connected and the type of ART may play a decisive role in the development or in the protection from of comorbidities based on the alteration of lipid metabolism. However, these data suggest the importance and need for broader diagnostic evaluation in PLWH.

References

Higher Levels of Osteoprotegerin and Immune Activation/Immunosenescence Markers Are Correlated with Concomitant Bone and Endovascular Damage in HIV-Suppressed Patients.D'Abramo A, Zingaropoli MA, Oliva A, et al.PLoS One. 2016 Feb 25;11(2):e0149601. doi: 10.1371/journal.pone.0149601. eCollection 2016.PMID: 26913505