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FRAGILITY FRACTURES AND RISK ASSESSMENT IN A COHORT OF ADULT WOMEN LIVING WITH HIV IN ARGENTINA.

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BACKGROUND

- A rising number of women living with HIV (WLHIV) are now reaching menopausal age.
- Low bone mineral density (BMD) is a common finding with elevated fracture risk (FR) in this population.
- Modified-FRAX® is widely used for fracture prediction but a few concerns about its accuracy have arisen recently, mainly related to its cut-offs for therapeutic intervention.
- The aim of this study was to evaluate the prevalence of fragility fractures (FF) and associated factors in a cohort of adult WLHIV receiving care at our institution.

MATERIALS AND METHODS

- Retrospective and observational study including WLHIV over 50 years old assisted at an HIV reference center in Buenos Aires, Argentina from 1997 to 2017.
- Clinical, laboratory and demographic data were reviewed to stablish the prevalence of common co-morbidities, including low BMD assessed by DXA scan, and FF defined as events evidenced by imaging techniques that occurred spontaneously or by low-level trauma.
- FR-assessment was performed using modified-FRAX® scores for hip fracture and major osteoporotic fracture.
- These scores were calculated for all women at the time of enrollment and for women with FF was also calculated for the last visit before the date on which the FF occurred.
- Information was collected in an Ad Hoc database and T-test, Chi^2 , Fisher exact or Mid P tests, and maximum likelihood odds ratio were used as appropriate.
- Variables with p-values < 0.15 in the univariate analysis were used to built two multiple regression models -Model 1 and 2-, excluding and including the modified-FRAX® scores calculated before the occurrence of FF, respectively.

RESULTS

- Two hundred and fifty patients were included. Demographic and clinic characteristics are shown in Table 1.
- Prevalence of low BMD was 67% (88/132 women) and FF 6.4% (16/250 patients). Factors associated with FF according to univariate analysis are shown in Table 2.
- No significative difference was obseved between modified-FRAX® scores in patients without FF and modified-FRAX® scores calculated before the ocurrence of FF. Factors associated with FF in Model 1 were: increased age (p = 0.007), HCV co-infection (p = 0.001), increased modified-FRAX® score for hip fracture (p = 0.002) and major osteoporotic fracture (p < 0.001).
- Factors associated with FF in Model 2 were: ARV regimens not based on Efavirenz (p = 0.011), low BMD assessed by DXA (p = 0.005), and HCV co-infection (p < 0.001). Those patients without FF showed a 75th percentile for both modified-FRAX® scores of 1.2 and 4.7, respectively (Figures 1 and 2). Taking into account this percentiles as cut-off values, scores for hip fracture ≥ 1.2 or major osteoporotic fracture ≥ 4.7 were associated with a significantly higher likelihood of FF with an OR: 8.42 (95%CI: 2.71-31.26, p < 0.001) and OR: 11.9 (95%CI: 3.1-67.2, p < 0.001), respectively.

Table 1. **Demographic and clinical characteristics.**

Variable	Result
Mean age, y (SD)	58,1 (6,1)
Mean time since HIV diagnosis, y (SD)	13,8 (6,9)
Mean BMI, kg/m^2 (SD)	26,9 (5,1)
Current or Former Smoker, n (%)	116 (46,4)
History of Alcohol/substance abuse, n (%)	22 (8,8)
AIDS at diagnosis, n (%)	116 (46,4)
On ARV Therapy, n (%)	246 (98,4)
Mean total cART duration, y (SD)	11,7 (5,9)
Plasma HIV-1 RNA < 20 copies/ml, n (%)	217 (88,2)
Mean current CD4 count, cells/μl (SD)	673 (312)

Table 2. **Univariate analysis.**

Variable	FF (16)	No FF (234)	P-value	OR(95%CI)
Mean age, y, (SD)	60.8 (6)	57.9 (6.1)	0.079	--
Mean time since HIV diagnosis, y, (SD)	13.6 (6.1)	13.8 (7)	0.901	--
AIDS at HIV diagnosis	6	110	0.478	--
On ARV therapy	16	230	0.922	--
Viral Load < 20 copies/ml	15	202/230	0.828	--
Current mean CD4 count, cells/μl (SD)	604 (193)	678 (318)	0.174	--
Tenofovir DF exposure	9	117/230	0.689	--
Abacavir exposure	13	168/230	0.697	--
TNA/1st gen PI* exposure	13	200/230	0.731	--
Atazanvir or Darunavir exposure	7	88/230	0.665	--
Efavirenz exposure	2	80/230	0.107	--
Integrase inhibitor exposure	3	25/230	0.538	--
ARV-related adverse events (any)	13	34/230	***< 0.001***	***24.5 (6.3-140.8)***
Mean BMI (SD)	27.7 (5.2)	26.8 (5.1)	0.511	--
Current of former smoker (Tobacco)	6	110	0.478	--
LDL-cholesterol > 130 mg%	11	148	0.879	--
Diabetes/Glucose intolerance	2	48	0.476	--
Chronic Kidney Disease	0	7	--	--
Low BMD by DXA scan	14/14	74/118	***0.013***	***12.45 (1.41-709)***
Mean Frax at enrollment -Hip- (SD)	2.6 (2.2)	1.0 (1.5)	*0.011*	--
Mean Frax before FF -Hip- (SD)	1.0 (1.6)	--	0.981	
Mean Frax at enrollment -MO- (SD)	8.7 (4.4)	3.8 (3.1)	***< 0.001***	--
Mean Frax before FF -MO- (SD)	3.7 (3.3)	--	0.939	
Vitamin D deficiency	8/10	53/71	0.999	--
Psychiatric disorders	9	144	0.676	--
HCV Coinfection	5	16	***0.012***	***6.11 (1.48-22.2)***
Malignancies	2	18	0.908	--
Menopause	14/14	158/178	0.994	--
Exposición a Esteroides	1	9	0.981	--
Mean of Co-medications (SD)	3.7 (1.6)	1.9 (1.7)	***< 0.001***	--

* Thymidin nucleoside analogues / First generation Protease Inhibitors

Figure 1. **Box-Plot for Modified-FRAX® for hip fracture. (A) Patients without fragility fractures. (B) Patients with fragility fracturs previous to bone fracture episode. (C) Patients with fragility fractures at study enrollment.**

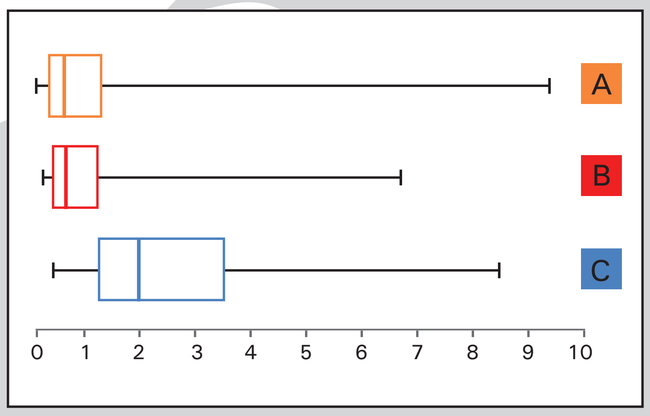
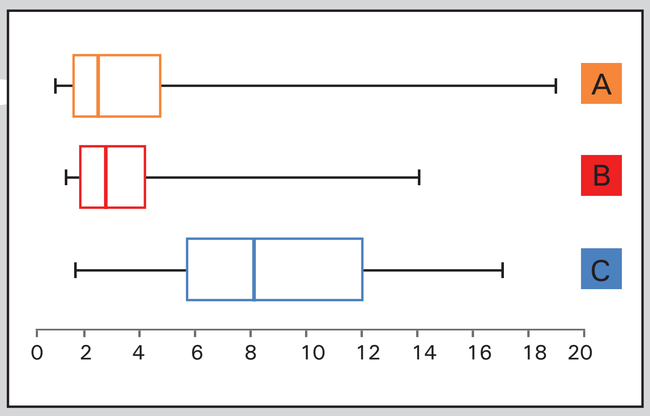


Figure 2. **Box-Plot for Modified-FRAX® for major osteoporotic fracture. (A) Patients without fragility fractures. (B) Patients with fragility fracturs previous to bone fracture episode. (C) Patients with fragility fractures at study enrollment.**



CONCLUSIONS

- Risk factors for FF found in this study were similar to those previously described in the literature, highlighting the impact of HCV co-infection.
- Despite of known modified-FRAX® limitations, our findings suggest that a new cut-off could be more accurate for risk prediction in order to perform a therapeutic intervention and deserve further investigation in a prospective study.