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Trabecular bone score assessed by dual-energy X ray absorption predicts vertebral fractures in HIV infected young adults

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ABSTRACT

Introduction: Bone mineral density (BMD) is reduced in patients with human immunodeficiency virus (HIV) infection. Trabecular bone score (TBS) is an additional feature calculated by dual-energy X ray absorption (DXA) that measures texture inhomogeneity at lumbar spine level, providing an index of bone microarchitecture. However, its clinical value still needs to be fully addressed. Aims of the study were to assess BMD and TBS in a cohort of patients with HIV compared to a population of healthy subjects and to investigate the prognostic value of TBS in HIV infected patients.

Method: Bone health was assessed by DXA in 165 patients with HIV infection (120 men, mean age 40 ± 7 years) and in 164 healthy subjects (53 male, mean age 37 ± 10 years). BMD was measured at level of lumbar spine (L1-L4), femoral neck and total hip. TBS was computed from the images of lumbar spine using machine proprietary software.

Results: BMD at femoral neck level was similar in HIV infected patients and healthy subjects ($p = 0.57$), whereas BMD measured in total femur was lower in HIV infected patients compared to healthy subjects ($p < 0.05$). Although mean BMD in lumbar spine was similar between HIV infected patients and healthy subjects ($p = 0.90$), mean lumbar TBS was lower in patients with HIV infection compared to healthy subjects ($p < 0.05$). Age, sex and HIV infection resulted independent predictors of reduced TBS. In HIV infected patients age, sex and protease inhibitor duration resulted independent predictors of reduced TBS. TBS was a significant predictor of vertebral fractures during follow-up ($p < 0.05$).

Conclusion: Patients with HIV infection have a significant reduction of TBS, a texture parameter related to bone microarchitecture that may provide skeletal information that is not captured from the standard BMD measurement.

1. Introduction

Management of patients with human immunodeficiency virus (HIV) infection has significantly evolved during the last decades (Brazier et al., 2024; Vandekerckhove et al., 2011; Moali et al., 2023). HIV infected patients have increased risk of osteoporosis (Mallon, 2010). This represents a multifactorial challenge related to the fact that some risk factors for osteoporosis such as smoking habit, low body weight and alcohol abuse are more prevalent in HIV infected patients as compared to healthy subjects (Pollock et al., 2009). Moreover, the introduction of antiretroviral therapy (ART) has substantially extended the overall survival and the quality of life of HIV infected patients, leading to similar life expectancy of the general population (Teeraananchai et al., 2017). However, ART, especially protease inhibitor treatments, seems to increase the risk of osteoporosis and fragility fractures in long-life treated patients (Brown and Qaqish, 2006; Bedimo et al., 2012; Caglar et al., 2024). Dual energy X-ray absorption (DXA) is the gold standard for the clinical evaluation of bone health, and it allows a non-invasive

Abbreviations: HIV, human immunodeficiency virus; DXA, dual energy X-ray absorption; BMD, bone mineral density; TBS, trabecular bone score; ART, antiretroviral therapy.

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quantitative assessment of the bone structure, including the estimation of bone mineral density (BMD) (Camacho et al., 2020). Trabecular bone score (TBS) is an additional feature provided by DXA examination. TBS measures texture inhomogeneity at lumbar spine level, providing an indirect index of bone microarchitecture within one single examination (Harvey et al., 2015). It has been demonstrated that DXA-derived TBS correlates with other microstructural parameters such as trabecular thickness, trabecular bone volume and structural model index, and it can be considered a predictor of vertebral mechanic behavior (Muschitz et al., 2015; Roux et al., 2013). Although the evaluation of TBS and its potential clinical value has been demonstrated to be a useful tool in the general population to predict the risk of fragility fractures in addition to FRAX® algorithm (McCloskey et al., 2016), its clinical utility in specific categories of patients still needs to be fully addressed. Some studies evaluated the added value of TBS in predicting fractures in post-menopausal women (Briot et al., 2013). TBS has also been investigated in Asian population with HIV (Kim et al., 2020; Guan et al., 2021a). However, there is no normal reference range for TBS and specific analysis especially in young Caucasian population which may help clinicians in interpreting such a potential tool is still lacking. The aim of the present retrospective cross-sectional study was to assess BMD and TBS in an Italian young cohort of patients with HIV, compared to a population of healthy subjects. Secondary endpoint was to evaluate the impact of ART on the bone health and to investigate the prognostic value of TBS in HIV infected patients.

2. Material and methods

2.1. Study population

Between January 2021 and December 2023, bone health was assessed in 714 patients referred to DXA examination in a single-center University hospital in Italy. For the purpose of the present study and in order to minimize the impact of age and hormonal factors on bone assessment, subjects <18 years old, postmenopausal women and male subjects >50 years old were excluded. Final population comprised 165 HIV infected patients and 164 healthy subjects. Demographic information, as well as clinical history, prevalence of smoking habits, alcohol and/or drug abuse, were collected. Duration of HIV infection, type of transmission, HIV category, CD4 cells count, ART type and duration were evaluated in the HIV infected patients' cohort. All the data were verified and complemented with demographic and clinical information collected from medical records. Consent was obtained according to Institutional Review Board-approved protocol, abiding by the principles of the Declaration of Helsinki.

2.2. Bone assessment using DXA

All patients underwent DXA examination using a commercially available densitometer (GE Lunar Prodigy, GE Healthcare, Madison, WI). DXA machine underwent daily calibration measures using anthropometric phantom to assure accurate BMD measurements. Scan acquisition and analysis were performed using the proprietary software (enCORE ver. 18). Lumbar spine (L1-L4), femoral neck and total hip images were acquired in all patients. Since population was made by adult men and pre-menopausal women, T-score was not used for the analysis. TBS was computed from the images of lumbar spine using machine proprietary software. TBS was categorized as normal (>1.31), intermediate (1.31–1.23), or degraded (<1.23) (Kim et al., 2020).

2.3. Follow-up

Follow-up in HIV subjects was obtained by a questionnaire assessed during phone call to the patients or by review of hospital or physicians' records when phone calls were not successful, by individuals blinded to the patient's DXA results. Clinically overt vertebral fractures were considered as endpoint. The date of the last examination or consultation was used to determine the length of follow-up.

2.4. Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorical data as percentage. Student two-sample *t*-test and chi-square test were used to compare the differences, as appropriate. A p value <0.05 (two-sided) was considered statistically significant. Pearson correlation coefficient was used to analyze relationship between BMD and TBS. Univariable and multivariable logistic regression analyses were performed to determine the variables associated with reduced TBS. Odds ratios with 95 % confidence interval (CI) were calculated by univariable and multivariable Cox regression analysis to identify the variables associated with vertebral fractures during follow-up. Variables showing a p value <0.05 at univariable analysis were considered for multivariable analysis. Receiver operating characteristics (ROC) area under curve (AUC) was applied to evaluate the diagnostic ability of TBS in identifying vertebral fractures and to establish the best trade-off between sensitivity and specificity in such identification. The optimal cut-off point was determined by ROC curve based on the Youden index. Statistical analysis was performed using IBM SPSS statistics software (ver. 29.0.1, IBM Corp., Armonk, NY, USA).

3. Results

Clinical characteristics of the study population according to HIV infection are summarized in Table 1. Patient with HIV were older, more likely male and with a significant higher prevalence of alcohol usage, smoking habit and drug abuse history as compared to healthy subjects.

Mean BMD values measured in HIV infected patients and healthy subjects are depicted in Fig. 1. BMD at femoral neck level showed no significant differences between HIV infected patients and healthy subjects ($p = 0.29$), whereas BMD measured in total hip was significantly lower in HIV infected patients compared to healthy subjects ($p < 0.05$). Although mean BMD in lumbar spine was similar between HIV infected patients and healthy subjects ($p = 0.53$), mean lumbar TBS was significantly lower in patients with HIV infection compared to healthy subjects (1.33 ± 0.15 vs. 1.38 ± 0.12, $p < 0.005$) (Fig. 2). Moreover, patients with HIV showed higher prevalence of intermediate or degraded TBS ($\chi^2 = 6.62$, $p < 0.01$). Nevertheless, lumbar BMD and TBS showed a significant albeit modest correlation ($r = 0.30$, $p < 0.001$). *Z*-score resulted not different at lumbar spine level between HIV infected and non-infected subjects ($p = 0.10$), whereas it was significantly lower in patients with HIV in femoral neck and total hip (both $p < 0.01$).

The results of logistic regression univariable and multivariable

Table 1
Clinical characteristics of the study population according to HIV infection.

	All patients (n = 329)	HIV+ (n = 165)	HIV- (n = 164)	p value
Age (years)	38 ± 9	40 ± 7	37 ± 10	<0.001
Male gender, n (%)	174 (53)	120 (72)	54 (33)	<0.001
Body mass index, kg/m^2	25 ± 5	25 ± 4	25 ± 6	0.15
Alcohol usage, n (%)	24 (7)	18 (11)	6 (4)	<0.05
Never alcohol usage, n (%)	305 (93)	147 (89)	158 (96)	<0.05
Smoking habit, n (%)	142 (43)	116 (70)	26 (16)	<0.001
Never smoking, n (%)	187 (57)	49 (30)	138 (84)	<0.001
Drug abuse, n (%)	27 (8)	27 (16)	0 (0)	<0.001
Previous fractures, n (%)	28 (8)	6 (4)	22 (13)	<0.005

Values are expressed as mean value ± standard deviation or as number (percentage) of subjects.

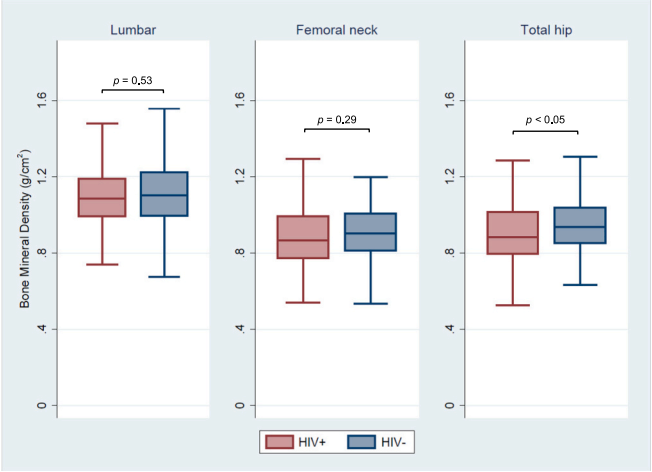

Fig. 1. Bone mineral density in HIV infected patients (HIV+) and healthy subjects (HIV-) in lumbar spine, femoral neck and total hip.

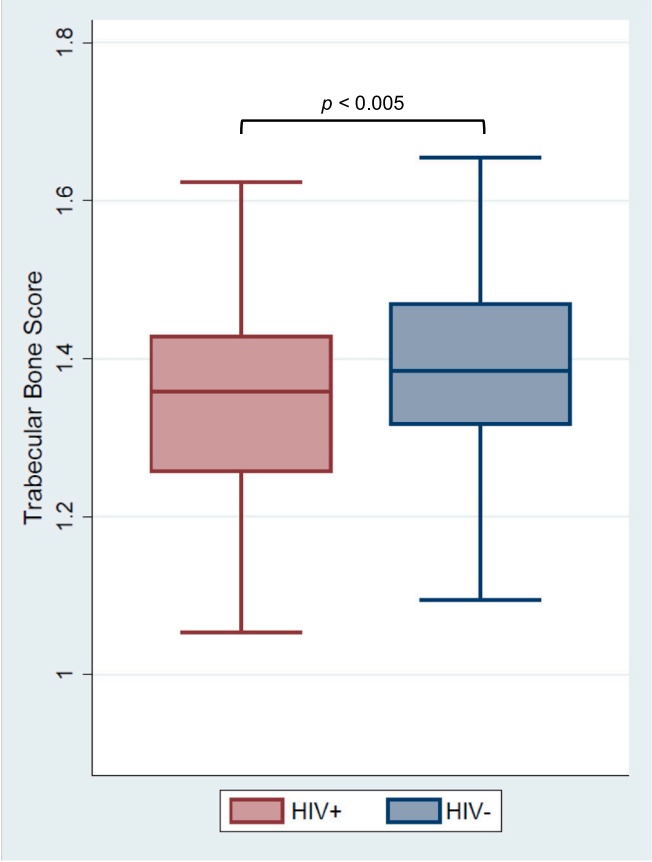

Fig. 2. Trabecular bone score in HIV infected patients (HIV+) and healthy subjects (HIV-).

analyses are depicted in Table 2. As shown, age, sex and HIV infection were significant predictors of reduced TBS. In multivariable analysis, age, sex and HIV infection resulted as independent predictors of reduced TBS ($p < 0.005$).

3.1. Sex-based analysis

Table 3 shows clinical characteristics of our study population according to sex and HIV infection. In men, BMD at lumbar spine ($p = 0.92$) and femoral neck level ($p = 0.31$) was not different between HIV infected patients and healthy subjects, whereas BMD measured in total hip was significantly lower in HIV infected patients compared to healthy subjects ($p < 0.05$). TBS was significantly lower in men with HIV infection compared to healthy subjects (1.35 ± 0.11 vs. 1.39 ± 0.13, $p < 0.05$). In women, BMD at lumbar spine was not different between HIV infected patients and healthy subjects ($p = 0.10$). However, BMD at femoral neck ($p < 0.05$), BMD in total hip ($p < 0.001$) and TBS (1.26 ± 0.12 vs. 1.37 ± 0.11, $p < 0.001$) were significantly lower in HIV infected women as compared to healthy women.

Table 2
Univariable and multivariable predictors of reduced TBS.

	Univariable analysis		Multivariable analysis	
	Odds ratio (95 % CI)	*p* value	Odds ratio (95 % CI)	*p* value
Age	1.057 (1.026–1.088)	<0.001	1.056 (1.024–1.089)	<0.001
Male gender	0.611 (0.377–0.990)	<0.05	0.381 (0.217–0.669)	<0.001
Body mass index	0.993 (0.946–1.042)	0.76		
Alcohol usage	0.649 (0.235–1.792)	0.40		
Smoking habit	1.611 (0.994–2.612)	0.06		
Drug abuse	1.845 (0.822–4.140)	0.14		
HIV infection	1.877 (1.150–3.062)	<0.005	2.438 (1.383–4.298)	<0.005

Table 3
Clinical characteristics of the study population according to sex and HIV infection.

	All patients (n = 329)	HIV+ (n = 165)	HIV- (n = 164)	*p* value
Men (n)	174	120	54	
Age (years)	40 ± 8	41 ± 7	38 ± 10	<0.05
Body mass index, kg/m^2	25 ± 4	25 ± 3	25 ± 4	0.95
Alcohol usage, n (%)	20 (11)	16 (13)	4 (7)	0.31
Never alcohol usage, n (%)	154 (89)	104 (87)	50 (92)	0.31
Smoking habit, n (%)	95 (55)	86 (72)	9 (17)	<0.001
Never smoking, n (%)	79 (45)	34 (28)	45 (83)	<0.001
Drug abuse, n (%)	19 (11)	19 (16)	0 (0)	<0.001
Previous fractures, n (%)	12 (7)	4 (3)	8 (15)	<0.05
Women (n)	155	45	110	
Age (years)	37 ± 9	40 ± 6	35 ± 10	<0.001
Body mass index, kg/m^2	24 ± 6	25 ± 5	24 ± 6	0.57
Alcohol usage, n (%)	4 (3)	2 (4)	2 (2)	0.58
Never alcohol usage, n (%)	151 (97)	43 (95)	108 (98)	0.58
Smoking habit, n (%)	47 (30)	30 (66)	17 (15)	<0.001
Never smoking, n (%)	108 (70)	15 (33)	93 (84)	<0.001
Drug abuse, n (%)	8 (5)	8 (18)	0 (0)	<0.001
Previous fractures, n (%)	16 (10)	2 (4)	14 (13)	0.15

Values are expressed as mean value ± standard deviation or as number (percentage) of subjects.

3.2. HIV infected subgroup analysis

Table 4 reports the clinical characteristics of the HIV infected patients. As shown, almost the whole cohort (99 %) was receiving ART and

Table 4
Characteristics of HIV infected subjects (n = 165).

Characteristics	Value
HIV duration (years)	18 ± 11
Type of transmission	
Drug addiction, n (%)	30 (18)
Heterosexual, n (%)	58 (35)
Homosexual, n (%)	63 (38)
Transfusion, n (%)	6 (4)
Vertical, n (%)	7 (4)
CD4 cells count (cells/μl)	796 ± 955
HIV-RNA viral load <40 copies/ml, n (%)	160 (97)
Anti-retroviral therapy, n (%)	165 (99)
Tenofovir disoproxil fumarate, n (%)	123 (75)
Tenofovir alafenamide, n (%)	125 (76)
Protease inhibitor, n (%)	88 (54)
Anti-retroviral therapy duration (years)	15 ± 10
HIV category	
A1, n (%)	12 (7)
A2, n (%)	45 (27)
A3, n (%)	15 (9)
B1, n (%)	2 (1)
B2, n (%)	24 (15)
B3, n (%)	33 (20)
C2, n (%)	3 (2)
C3, n (%)	31 (19)

Values are expressed as mean value ± standard deviation or as number (percentage) of subjects.

showed a good control of the infection. Of note, HIV viral load was <40 copies/ml in 97 % of the patients. In HIV infected patients, age, sex, HIV infection duration, ART duration, protease inhibitor therapy usage and duration were significant predictors of reduced TBS. Only age, sex and protease inhibitor therapy duration resulted as independent predictors of reduced TBS (Table 5).

3.3. Follow-up in HIV infected patients

Follow-up was 75 % completed in HIV infected patients, leaving 123 subjects for the analysis. Five vertebral fractures occurred during a median follow-up of 16 months (range 3–31 months). Cox regression analysis showed that reduced TBS was a significant predictor of vertebral fractures ($p < 0.05$) whereas lumbar BMD was not. Similarly, age, sex, alcohol usage, smoking habit, tenofovir disoproxil fumarate, tenofovir alafenamide and protease inhibitor usage were not significant predictors of vertebral fractures in our cohort. By ROC curve analysis, TBS showed an AUC of 0.802 in predicting vertebral fractures (Fig. 3). Based on the Youden index, TBS value of 1.21 provided the best trade-off in predicting vertebral fractures in HIV infected patients.

Table 5
Univariable and multivariable predictors of reduced TBS in HIV infected subjects.

	Univariable analysis		Multivariable analysis	
	Odds ratio (95 % CI)	*p* value	Odds ratio (95 % CI)	*p* value
Age	1.115 (1.057–1.177)	<0.001	1.123 (1.039–1.215)	<0.005
Male gender	0.291 (0.142–0.594)	<0.001	0.275 (0.078–0.965)	<0.05
Body mass index	1.002 (0.923–1.089)	0.95		
Alcohol	0.703 (0.237–2.080)	0.52		
Smoking habit	1.127 (0.555–2.289)	0.74		
HIV-RNA load	1.000 (1.000–1.000)	0.68		
CD4 cell count	1.000 (1.000–1.001)	0.37		
HIV infection duration	1.057 (1.025–1.089)	<0.001	0.980 (0.878–1.093)	0.72
Anti-retroviral therapy duration	1.067 (1.030–1.105)	<0.001	1.041 (0.908–1.193)	0.57
Tenofovir disoproxil fumarate usage	1.158 (0.544–2.463)	0.70		
Tenofovir alafenamide usage	0.637 (0.307–1.322)	0.23		
Protease inhibitor usage	2.499 (1.245–4.817)	<0.01		
Protease inhibitor duration	1.011 (1.005–1.018)	<0.001	1.010 (1.002–1.018)	<0.05

4. Discussion

The results of this study demonstrate that HIV infected patients have lower values of TBS as compared to healthy subjects. To our knowledge this is the first study that attempts to identify a possible TBS cut-off to predict vertebral fractures in patients with HIV. As previously demonstrated, subjects with HIV infection have increased risk of osteoporosis and fragility fractures, due to infection but mostly related to the long-term ART (Pollock et al., 2009; Teeraananchai et al., 2017; Brown and Qaqish, 2006). A recent metanalysis by Chang et al. (Chang et al., 2021) demonstrated that people with HIV have lower BMD than controls and a higher prevalence of fractures. Thus, we expected to observe lower BMD values in HIV infected subjects as compared to healthy controls. Surprisingly, in our cohort we did not find significant differences in lumbar and femoral neck BMD values of HIV patients as compared to healthy subjects, whereas the total hip appeared as the most affected area by reduced BMD in HIV patients as compared to controls. TBS in lumbar spine, on the other hand, resulted significantly lower in HIV infected patients as compared to healthy subjects. Considering that trabecular bone is more prone to turnover and to remodeling, being a more active site in the bone, it can be hypothesized the HIV status played a role in this finding. Accordingly, the results by Chang et al. (Chang et al., 2021) suggest that screening for osteoporosis should be started earlier in HIV subjects, regardless of age. Despite in our study age resulted as independent predictor of impaired bone microarchitecture together with HIV infection, it has to be considered that our study population was quite young (median age 38 years-old), confirming that early screening may provide important diagnostic information in these patients. Moreover, it is already known the strong association between ART and bone health impairment (Guan et al., 2021a; Chang et al., 2021; Guan et al., 2021b). In particular, Guan et al. (Guan et al., 2021b) investigated that long-term exposure to ART has impact on both BMD and TBS in an Asian population. These results were consistent with a previous study (Güerri-Fernández et al., 2017) which demonstrated that BMD and TBS were lower in HIV patients, particularly when treated with tenofovir disoproxil fumarate. In our study ART duration resulted significantly associated with reduced TBS but tenofovir disoproxil fumarate usage did not. On the other hand, in our population protease inhibitor treatment resulted as significant predictor and treatment duration was an independent predictor of reduced TBS. This result confirmed the known association between protease inhibitor usage and bone loss (Moran et al., 2016). The explanation of this association remains to be fully addressed. Some in-vitro studies demonstrated that protease inhibitor treatment may either induce an alteration of the osteoblast gene expression (Malizia et al., 2007) or reduce osteoblast differentiation (Hernandez-Vallejo et al., 2013), but it may also contribute to increase osteoclast differentiation from peripheral blood cells (Yin et al., 2011), suggesting a direct role of this therapy in bone deterioration. Several studies analyzed BMD and TBS changes, focusing on women with HIV infection (Lo Re 3rd et al., 2015; Milic et al., 2023; Sharma et al., 2018). Of course, bone health in female subjects is strongly dependent by hormonal status and thus we excluded post-menopausal women from our study population, in order to minimize the impact of the estrogen level on bone assessment, and still our results are consistent with the previous studies in literature. Some authors have also proposed the

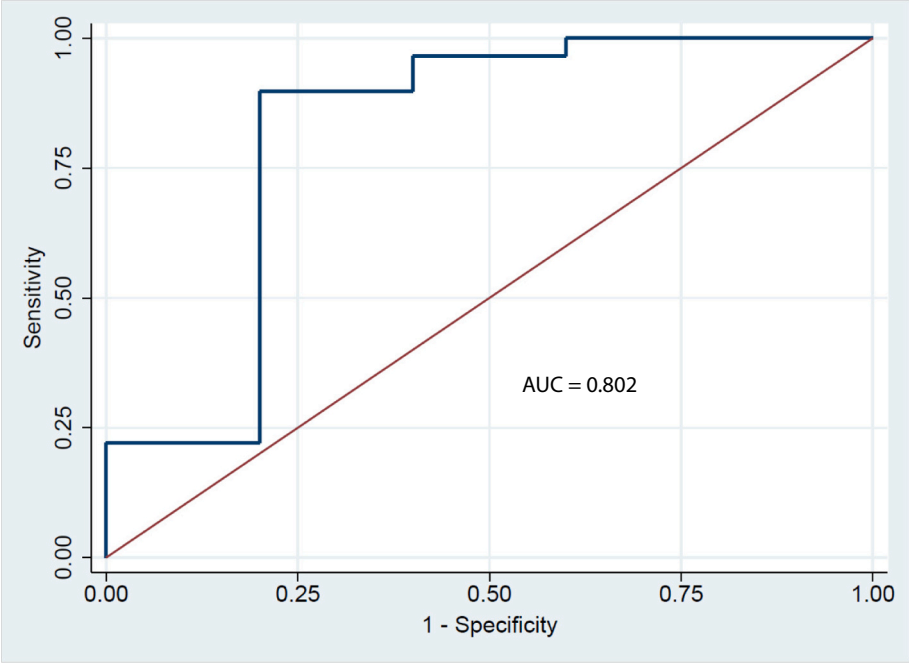

Fig. 3. Receiving operating characteristic curve for identification of vertebral fractures using trabecular bone score in HIV infected patients.

evaluation of TBS using computed tomography of radius and tibia (Yin et al., 2013; Macdonald et al., 2020; Foreman et al., 2020; Calmy et al., 2013), demonstrating impaired TBS in HIV patients. The reduction of TBS highlighted in our study has the great advantage of being assessed by DXA which is the common methodology to screen patients for osteoporosis and it can be derived by one single examination. BMD, T-score and Z score by DXA are in fact the most reliable parameters to evaluate bone health and they are milestones in the diagnosis of osteoporosis (Camacho et al., 2020).

Finally, concerning the risk of fracture, our results showed that reduced TBS was a significant predictor of vertebral fractures whereas lumbar BMD was not. This confirms previous findings (Kim et al., 2020; McGinty et al., 2019) demonstrating that HIV patients receiving ART are not only at higher risk of developing osteoporosis and vertebral fractures, but mostly important, that evaluation of BMD and *Z*-score may still not be enough for prognostic purposes in selected categories of patients. Indeed, the introduction of TBS evaluation in FRAX® algorithm has been proposed (Leslie et al., 2014), but this has not been still fully implemented in the clinical practice. Our findings substantially confirmed the results by Ciullini et al. (Ciullini et al., 2018), demonstrating the correlation between low TBS evaluated by DXA and vertebral fractures in HIV patients. Whilst the authors (Ciullini et al., 2018) considered as endpoint sub-clinical fractures diagnosed by lateral thoracic and lumbar spine X-ray examination, our study evaluated during follow-up only clinically overt fractures. This can be considered a limitation, taking into account that not all fragility vertebral fractures are clinically diagnosed and this may be the explanation for the limited number of events in our observations. A further limitation of our study is that scans and TBS data were not collected at the time of follow-up. However, in our albeit limited findings, TBS showed an AUC of 0.802 in predicting vertebral fractures. In particular, TBS value of 1.21 was identified as the best cut-off to predict the event. More studies, including prospective randomized trials, are needed to confirm and explore this possible cut-off value, considering that there is no normal reference range for TBS.

5. Conclusions

Patients with HIV infection have a significant reduction of TBS, a texture parameter related to bone microarchitecture that may provide skeletal information that is not captured from the standard BMD measurement. In HIV patients, ART and protease inhibitor usage are related to reduced TBS. Moreover, TBS is a strong predictor of vertebral fractures in HIV patients. These findings suggest that integrating DXA with TBS evaluation may help in refining risk stratification, identifying HIV patients at higher risk of fragility fractures in which a change of patient management can be hypothesized. Further studies are requested to determine whether TBS could integrate the clinical value of DXA in bone health assessment in HIV patients.

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CRediT authorship contribution statement

Teresa Mannarino: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Adriana D'Antonio:** Writing – review & editing, Formal analysis, Data curation. **Simona Mercinelli:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Maria Falzarano:** Writing – review & editing, Data curation. **Federica Volpicelli:** Writing – review & editing, Data curation. **Ciro Gabriele Mainolfi:** Writing – review & editing, Investigation, Data curation. **Emanuela Zappulo:** Writing – review & editing, Investigation, Data curation. **Giovanni Di Filippo:** Writing – review & editing, Investigation, Data curation. **Maria Rosaria Cotugno:** Writing – review & editing, Investigation, Data curation. **Ivan Gentile:** Writing – review & editing, Supervision, Conceptualization. **Alberto Cuocolo:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization.

Declaration of competing interest

The authors have no conflicts of interest associated with the material presented in this paper.

Data availability

Data will be made available on request.

References

Bedimo, R., Maalouf, N.M., Zhang, S., Drechsler, H., Tebas, P., 2012. Osteoporotic fracture risk associated with cumulative exposure to tenofovir and other antiretroviral agents. AIDS 26, 825–831.

Brazier, E., Tymejczyk, O., Wools-Kaloustian, K., Jiamsakul, A., Torres, M.T.L., Lee, J.S., et al., 2024. International epidemiology databases to evaluate AIDS (IeDEA). Long-term HIV care outcomes under universal HIV treatment guidelines: a retrospective cohort study in 25 countries. PLoS Med. 21, e1004367.

Briot, K., Paternotte, S., Kolta, S., Eastell, R., Reid, D.M., Felsenberg, D., et al., 2013. Added value of trabecular bone score to bone mineral density for prediction of osteoporotic fractures in postmenopausal women: the OPUS study. Bone 57, 232–236.

Brown, T.T., Qaqish, R.B., 2006. Antiretroviral therapy and the prevalence of osteopenia and osteoporosis: a meta-analytic review. AIDS 20, 2165–2174.

Caglar, B., Durcan, E., Karaali, R., Balkan, I.I., Kaya, S.Y., Yavuzer, H., et al., 2024. Bone metabolism in men who live with HIV aged 50 years and over: impact of infection duration. Curr. HIV Res. 22 (1), 65–71.

Calmy, A., Chevalley, T., Delhumeau, C., Toutous-Trellu, L., Spycher-Elbes, R., Ratib, O., et al., 2013. Long-term HIV infection and antiretroviral therapy are associated with bone microstructure alterations in premenopausal women. Osteoporos. Int. 24, 1843–1852.

Camacho, P.M., Petak, S.M., Binkley, N., Diab, D.L., Eldeiry, L.S., Farooki, A., et al., 2020. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal Osteoporosis-2020 update. Endocr. Pract. 26 (Suppl. 1), 1–46.

Chang, C.J., Chan, Y.L., Pramukti, I., Ko, N.Y., Tai, T.W., 2021. People with HIV infection had lower bone mineral density and increased fracture risk: a meta-analysis. Arch Osteoporos. 16, 47.

Ciullini, L., Pennica, A., Argento, G., Novarini, D., Teti, E., Pugliese, G., et al., 2018. Trabecular bone score (TBS) is associated with sub-clinical vertebral fractures in HIV-infected patients. J. Bone Miner. Metab. 36, 111–118.

Foreman, S.C., Wu, P.H., Kuang, R., John, M.D., Tien, P.C., Link, T.M., et al., 2020. Factors associated with bone microstructural alterations assessed by HR-pQCT in long-term HIV-infected individuals. Bone 133, 115210.

Guan, W., Pan, W., Yu, W., Cao, W., Lin, Q., Zhang, Z., et al., 2021b. Long-term trabecular bone score and bone mineral density changes in Chinese antiretroviral-treated HIV-infected individuals. Arch. Osteoporos. 16, 41.

Guan, W.M., Pan, W., Yu, W., Cao, W., Lin, Q., Zhang, Z.Z., et al., 2021a. Changes in trabecular bone score and bone mineral density in Chinese HIV-infected individuals after one year of antiretroviral therapy. J Orthop Translat. 29, 72–77.

Güerri-Fernández, R., Molina-Morant, D., Villar-García, J., Herrera, S., González-Mena, A., Guelar, A., et al., 2017. Bone density, microarchitecture, and tissue quality after long-term treatment with Tenofovir/Emtricitabine or Abacavir/lamivudine. J. Acquir. Immune Defic. Syndr. 75, 322–327.

Harvey, N.C., Glüer, C.C., Binkley, N., McCloskey, E.V., Brandi, M.L., Cooper, C., et al., 2015. Trabecular bone score (TBS) as a new complementary approach for osteoporosis evaluation in clinical practice. Bone 78, 216–224.

Hernandez-Vallejo, S.J., Beaupere, C., Larghero, J., Capeau, J., Lagathu, C., 2013. HIV protease inhibitors induce senescence and alter osteoblastic potential of human bone marrow mesenchymal stem cells: beneficial effect of pravastatin. Aging Cell 12, 955–965.

Kim, Y.J., Kang, K.Y., Shin, J., Jun, Y., Kim, S.I., Kim, Y.R., 2020. Trabecular bone scores in young HIV-infected men: a matched case-control study. BMC Musculoskelet. Disord. 21, 94.

Leslie, W.D., Johansson, H., Kanis, J.A., Lamy, O., Oden, A., McCloskey, E.V., et al., 2014. Lumbar spine texture enhances 10-year fracture probability assessment. Osteoporos. Int. 25, 2271–2277.

Lo Re 3rd, V., Lynn, K., Stumm, E.R., Long, J., Nezamzadeh, M.S., Baker, J.F., et al., 2015. Structural bone deficits in HIV/HCV-coinfected, HCV-monoinfected, and HIV-monoinfected women. J Infect Dis 212, 924–933.

Macdonald, H.M., Maan, E.J., Berger, C., Dunn, R.A., Côté, H.C.F., Murray, M.C.M., et al., 2020. Deficits in bone strength, density and microarchitecture in women living with HIV: a cross-sectional HR-pQCT study. Bone 138, 115509.

Malizia, A.P., Cotter, E., Chew, N., Powderly, W.G., Doran, P.P., 2007. HIV protease inhibitors selectively induce gene expression alterations associated with reduced calcium deposition in primary human osteoblasts. AIDS Res. Hum. Retroviruses 23, 243–250.

Mallon, P.W., 2010. HIV and bone mineral density. Curr. Opin. Infect. Dis. 23, 1–8.

McCloskey, E.V., Odén, A., Harvey, N.C., Leslie, W.D., Hans, D., Johansson, H., et al., 2016. A Meta-analysis of trabecular bone score in fracture risk prediction and its relationship to FRAX. J. Bone Miner. Res. 31, 940–948.

McGinty, T., Cotter, A.G., Sabin, C.A., Macken, A., Kavanagh, E., Compston, J., et al., 2019. HIV UPBEAT (Understanding the Pathology of Bone Diseases in HIV-infected Subjects) Study Group. In: Assessment of trabecular bone score, an index of bone microarchitecture, in HIV positive and HIV negative persons within the HIV UPBEAT cohort, 14. PLoS One. e0213440.

Milic, J., Renzetti, S., Morini, D., Motta, F., Carli, F., Menozzi, M., et al., 2023. Bone mineral density and trabecular bone score changes throughout menopause in women with HIV. Viruses 15, 2375.

Moali, B., Tlale, L.B., Nkomo, B., Otieno, M., Sirili, N., Nsoh, M., et al., 2023. Comparison on treatment outcomes of patients enrolled on anti-retroviral therapy at different levels of the health-care system in a high HIV/AIDS setting. AIDS Rev. 25, 173–178.

Moran, C.A., Weitzmann, M.N., Ofotokun, I., 2016. The protease inhibitors and HIV-associated bone loss. Curr. Opin. HIV AIDS 11, 333–342.

Muschitz, C., Kocijan, R., Haschka, J., Pahr, D., Kaider, A., Pietschmann, P., et al., 2015. TBS reflects trabecular microarchitecture in premenopausal women and men with idiopathic osteoporosis and low-traumatic fractures. Bone 79, 259–266.

Pollock, E., Klotsas, A.E., Compston, J., Gkrania-Klotsas, E., 2009. Bone health in HIV infection. Br. Med. Bull. 92, 123–133.

Roux, J.P., Wegrzyn, J., Boutroy, S., Bouxsein, M.L., Hans, D., Chapurlat, R., 2013. The predictive value of trabecular bone score (TBS) on whole lumbar vertebrae mechanics: an ex vivo study. Osteoporos. Int. 24, 2455–2460.

Sharma, A., Ma, Y., Tien, P.C., Scherzer, R., Anastos, K., Cohen, M.H., et al., 2018. HIV infection is associated with abnormal bone microarchitecture: measurement of trabecular bone score in the Women's interagency HIV study. J. Acquir. Immune Defic. Syndr. 78, 441–449.

Teeraananchai, S., Kerr, S.J., Amin, J., Ruxrungtham, K., Law, M.G., 2017. Life expectancy of HIV-positive people after starting combination antiretroviral therapy: a meta-analysis. HIV Med. 18, 256–266.

Vandekerckhove, L.P., Wensing, A.M., Kaiser, R., Brun-Vézinet, F., Clotet, B., De Luca, A., et al., 2011. European consensus group on clinical management of tropism testing. European guidelines on the clinical management of HIV-1 tropism testing. Lancet Infect. Dis. 11, 394–407.

Yin, M.T., Modarresi, R., Shane, E., Santiago, F., Ferris, D.C., McMahon, D.J., et al., 2011. Effects of HIV infection and antiretroviral therapy with ritonavir on induction of osteoclast-like cells in postmenopausal women. Osteoporos. Int. 22, 1459–1468.

Yin, M.T., Shu, A., Zhang, C.A., Boutroy, S., McMahon, D.J., Ferris, D.C., et al., 2013. Trabecular and cortical microarchitecture in postmenopausal HIV-infected women. Calcif. Tissue Int. 92, 557–565.