

Estimating the 10-year fracture risk among persons with HIV and persons without HIV: A comparative study

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Abstract

Background: The risk of osteoporotic fracture among persons with HIV was higher than the persons without HIV. Traditional factors are also found as the risk factor affecting fracture risk among persons with HIV and general population. Predicting the fracture risk among the high-risk group is important to develop a comprehensive fracture prevention program.

Purpose: This study aimed to compare the estimation of the 10-year fracture risk between persons with HIV and persons without HIV using the FRAX™ algorithm.

Methods: This study recruited 245 participants from August to November 2023, while 221 participants agreed to participate. The participants consist of 107 persons with HIV and 114 persons without HIV. The estimation of the ten-year probability of major osteoporotic and hip fractures was calculated using the FRAX™ algorithm. The participant's characteristics related to osteoporotic fracture risk was analyzed using a Chi-Square analysis.

Results: The overall mean score of 10-year probability of major osteoporotic fracture (MOF) was 3.1% (SD 1.9) for the HIV group and 2.7% (SD 2.3) for non-HIV. For the 10-year probability, hip fracture (HF) risk was 0.5% (SD 0.5) for the HIV group and 0.6% (SD 0.9) for non-HIV. For MOF, HIV persons with fracture history showed a lower score (3.5%) compared to persons without HIV (5.3%). Smoker HIV persons showed the same MOF score (4.6% vs. 4.6%) but lower HF score (0.8% vs. 1.6%) when comparing to persons without HIV, respectively. HIV persons with glucocorticoid use showed a higher MOF probability score than persons without HIV (2.8% vs 2.7%).

Conclusion: The 10-year fracture risk was higher among persons with HIV compared to persons without HIV. Fracture history, smoking behavior, and glucocorticoid use were identified as the potential factors associated with the risk. Further analysis using multivariate regression analysis may require to confirm the factors associated with high fracture risk.

Keywords: FRAX™, hip fractures, HIV, osteoporotic fractures, 10-year risk of fracture

Introduction

Persons with HIV were having higher bone fracture risk as high as three times compared to the persons without HIV (Prieto-Alhambra et al., 2014). As a consequence, it may lead to an increase of up to 12% in non-AIDS-related mortality (Hasse et al., 2011). An earlier study found that bone fractures prevalence among persons with HIV was 11.1% (Ilha et al., 2018). According

to the guidelines of bone fracture management from the United States, all persons with HIV should be evaluated for their fracture risk using an estimation tool such as FRAX™ (Brown et al., 2015). The FRAX™ tool is an algorithm that integrates clinical risk factors, with or without the inclusion of bone mineral density measurements, to evaluate an individual's fracture risk (McCloskey, 2009).

Fracture is a disease related to the associated factors. Among persons with HIV, there were several types of factors may affect the fracture risk, including traditional, ART, and HIV-related factors (Bedimo et al., 2016; Bedimo et al., 2012; Gedmintas et al., 2017; Gonciulea et al., 2017; Pramukti, Liu, et al., 2020). Identifying fracture risk among the population with HIV is crucial to investigating the leading cause of fracture (McGee & Cotter, 2024). Therefore, further comprehensive prevention programs may link the baseline need (Brown et al., 2015).

Over five million individuals living with HIV reside in the Asia and Pacific region (UNAIDS, 2023). Nevertheless, limited research has examined fracture risk among persons with HIV within this population. Previous research demonstrated that individuals with HIV infection exhibit a higher fracture risk when comparing to the individual without HIV (Pramukti et al., 2020). Moreover, age was identified as a significant factor affecting fracture risk (Pramukti et al., 2020). However, it is still unclear whether HIV condition or older age that affecting the fracture risk more. The present study aimed to estimate the 10-year risk of major osteoporotic fractures (MOF) and hip fractures (HF) among persons with HIV and middle-age persons without HIV using the FRAX™ tool, as well as to identify HIV-specific and general risk factors associated with fracture risk.

Materials and Methods

Design

A multi-center cross-sectional study was conducted at outpatients in the center of Bandung Referral Hospital and Sumedang Referral Hospital.

Sample and setting

All persons with HIV attending the HIV outpatient clinic, as well as patients without HIV who visited the general medical outpatient clinic between August and November 2023, were invited to participate in the study. Patients with active opportunistic infections, those who declined participation, and pregnant individuals were excluded. Among the 245 eligible participants, 24 (9.7%) declined participation for unspecified reasons, resulting in a final sample of 221 participants (107 persons with HIV and 114 persons without HIV) who were consecutively enrolled. In addition to demographic information, participants provided data necessary for FRAX™ assessment.

Variable

The primary variable measured in this study was the

10-year fracture risk, calculated using the FRAX™ tool, which incorporates clinical risk factors such as age, sex, weight, history of previous fractures, parental history of hip fracture, current smoking status, glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, and alcohol consumption (>3 units per day). Data on all clinical risk factors, except for bone mineral density (BMD), were collected through a structured questionnaire. The 10-year probability of major osteoporotic fractures (MOF) generated by the FRAX™ algorithm was expressed as an absolute percentage score (Brown et al., 2015).

Instruments

The FRAX™ algorithm served as the primary instrument in this study and has previously been validated in HIV-infected populations. A 2014 study conducted in the United States involving 17,387 HIV-positive male veterans and 7,064 HIV-negative male veterans demonstrated comparable predictive accuracy for osteoporotic fracture risk, with scores of 1.62 and 1.69, respectively ($p = 0.03$) (Yin & Falutz, 2016). Similarly, a study in Italy reported that the FRAX™ tool exhibited a sensitivity of 77.3% and a specificity of 69% ($p = 0.02$) in assessing fracture risk among 57 Caucasian HIV-positive and 50 HIV-negative men (Pepe et al., 2012).

Data collection

Following approval from the facility's Research Ethics Committee, data collection was conducted from mid-August to December 2023. Eligible patients were identified through the HIV/AIDS information system by the HIV case manager and subsequently referred to the research team during clinic visits. Written informed consent was obtained from all participants, who were then asked to complete the demographic and FRAX™ questionnaires. HIV-related clinical data were extracted from medical records provided by the HIV case manager.

Data analysis

The 10-year probabilities of major osteoporotic fractures (MOFs) and hip fractures were calculated by inputting the relevant data into the FRAX™ computerized algorithm. Descriptive analysis was performed to summarize the study variables. A Chi-Square was used to identify the participant's characteristics related to osteoporotic fracture risk. All statistical analyses were performed using SPSS software version 27 for Windows.

Ethical consideration

The IRB approval has been obtained from the Research Ethics Committee Universitas Padjadjaran with the registration number 1002/UN6.KEP/EC/2023. Prior to the data collection, the subjects were explained about the study procedures including the assurance of confidentiality and anonymity principles. Afterward, the subjects asked for their consent to join the study. Those

Table 1. Participant characteristic (n=221)

Variable	n (%)
Sex, male (%)	102 (46.2)
Age (years) (mean) (SD)	41.6 (13.8)
Body weight (kg) (mean + SD)	56.9 (11.8)
Body height (cm) (mean + SD)	157.6 (16.9)
Marital status	
Not married	71 (32.1)
Married	128 (57.9)
Divorced	22 (10.0)
HIV status	
HIV positive	107 (48.4)
HIV negative	114 (51.6)
Traditional risk factor	
Fracture history (%)	12 (5.4)
Parental hip fracture history (%)	63 (28.5)
Smoking (%)	19 (8.6)
Glucocorticoid use (%)	63 (28.5)
Rheumatoid Arthritis (%)	41 (27.0)
Alcohol abuse (%)	12 (5.4)
HIV-related risk factor	
Viral load (copies) (n=76)	
- > 40/ml	14 (18.5)
- Undetectable	62 (81.5)
ART-related risk factor	
Currently using ART (%)	105 (47.5)

ART=anti-retroviral therapy; SD=standard deviations

Table 2. Characteristic of persons with HIV and persons without HIV (n=221)

Variable	HIV status		P value
	HIV (+) (n=107)	HIV (-) (n=114)	
Sex, male (%)	64 (59.8)	38 (33.3)	<0.001
Age (years) (mean) (SD)	37.6 (11.8)	45.4 (14.4)	<0.001
Body weight (kg) (mean + SD)	56.7 (9.7)	56.9 (13.1)	0.910
Body height (cm) (mean + SD)	160.9 (16.7)	157.7 (8.2)	0.071
Marital status			<0.001
Not married	55 (51.4)	16 (14.1)	
Married	42 (39.3)	86 (75.4)	
Divorced	10 (9.3)	12 (10.5)	
Fracture history (%)	4 (3.7)	8 (7%)	0.282
Parental hip fracture history (%)	38 (35.5)	25 (21.9)	0.025
Smoking (%)	12 (11.2)	7 (6.1)	0.179
Glucocorticoid use (%)	29 (27.1)	34 (29.8)	0.654
Rheumatoid Arthritis (%)	19 (24.7)	22 (29.3)	0.518
Alcohol abuse (%)	9 (8.4)	3 (2.6)	0.058

SD=standard deviations

Table 3. Major Osteoporotic Fracture risk and the related factors among persons with HIV and persons without HIV (n=221)

Characteristic	MOF score (%)		P value
	HIV	non HIV	
Overall	3.1 (1.9)	2.7 (2.3)	
Sex			.250
Male	2.8 (1.6)	2.5 (2.1)	
Female	3.4 (2.4)	2.8 (2.4)	
Fracture history			.002
Yes	3.5 (1.3)	5.3 (4.3)	
No	3.0 (2.0)	2.5 (1.9)	
Parents' hip fracture history			.933
Yes	3.4 (1.8)	2.1 (1.5)	
No	2.8 (2.1)	2.9 (2.4)	
Smoking			<.001
Yes	4.6 (1.7)	4.6 (1.7)	
No	2.8 (1.9)	2.7 (2.1)	
Glucocorticoid used			.017
Yes	3.7 (2.3)	3.1 (2.1)	
No	2.7 (1.8)	2.6 (2.4)	
Arthritis rheumatoid			.641
Yes	2.8 (1.5)	2.7 (2.3)	
No	5.9 (4.7)	2.7 (2.3)	
Alcohol used			.308
Yes	2.4 (1.8)	6.7 (2.7)	
No	3.0 (2.0)	2.6 (2.2)	

HIV=human immunodeficiency virus; MOF=major osteoporotic fracture; HF=hip fracture

who agreed to participate were enrolled in the study. During the data collection, the privacy of the subjects was maintained. Those who decided to stop their participation were allowed without any consequences.

Results

Demographics

The characteristics of the participants showed more than half were male participants (n=102, 46.2%) with a mean age of 41.6 (13.8) years (Table 1). The mean body weight was 56.9 (11.8) kg, while the body height was 157.6 (16.9) cm. Most of the participants were married (n=128, 57.9%). The number of participants with HIV was 107 (48.4%), while the those without HIV were 114 (51.6%). There were only 12 (5.4%) participants reported having a fracture history, and 63 participants (28.5%) had parents' hip fracture history. Only 19 participants (8.6%) were a smoker, while 63 (28.5%) were on glucocorticoid therapy. Related to the comorbidity, 41 participants (27.0%) had Rheumatoid Arthritis. For HIV related factors, among the fifty-five tested participants, most of the participants (n=44, 80.0%)

showed undetectable viral load. For the antiretroviral therapy (ART) related factors, among the persons with HIV, most participants (n=105, 98.1%) were on ART.

The characteristic of participants with HIV and participants without HIV is showed in Table 2. The male proportion in the HIV group were higher (59.8%) than in the non-HIV group (33.3%). For the age, the participant in the HIV group were younger (mean age of 37.6 years) than in the non-HIV group (mean age of 45.4 years). For the body weight, both group were similar (56.7 kg vs 56.9 kg). Non HIV group were mostly married (75.4%), while the married participants in the HIV group were only 39.3%.

Major Osteoporotic Fracture risk among persons with HIV and persons without HIV

For the 10-year probability of major osteoporotic fractures (MOF), overall, the mean score among participants with HIV with fracture history showed significantly higher scores than those without history (3.5 vs 3.0) (Table 3). Among participants without HIV, those with fracture history scored higher than those without (5.3 vs 3.5). Compared with persons

Table 4. Hip Fracture risk and the related factors among HIV and non-HIV (n=221)

Characteristic	HF		P value
	HIV	middle-age non-HIV	
Overall	0.5 (0.5)	0.6 (0.9)	
Sex			.577
Male	0.4 (0.5)	0.6 (1.0)	
Female	0.5 (0.7)	0.6 (0.9)	
Fracture history			.351
Yes	0.3 (0.3)	0.9 (1.7)	
No	0.4 (0.5)	0.6 (0.9)	
Parents' hip fracture history			.754
Yes	0.6 (0.5)	0.4 (0.8)	
No	0.4 (0.5)	0.6 (1.0)	
Smoking			.002
Yes	0.8 (0.6)	1.6 (1.9)	
No	0.4 (0.6)	0.5 (0.9)	
Glucocorticoid used			.087
Yes	0.6 (0.4)	0.7 (1.2)	
No	0.4 (0.6)	0.5 (0.8)	
Arthritis rheumatoid			.054
Yes	0.4 (0.4)	0.8 (1.5)	
No	1.4 (1.5)	0.6 (0.9)	
Alcohol used			.184
Yes	0.4 (0.5)	2.23 (1.6)	
No	0.4 (0.6)	0.6 (0.9)	

HIV=human immunodeficiency virus; HF=hip fracture

without HIV, persons with HIV with fracture history showed lower scores (3.5 vs 5.3). Furthermore, among persons with HIV, those who were smokers showed significantly higher scores than non-smoker participants (4.6 vs 2.8). Among participants without HIV, the smoker participants also showed higher scores than the non-smokers. Regarding the medical treatment, among persons with HIV, those who had undergone glucocorticoid use showed higher scores than those who had not (3.7 vs 2.7). Among the persons without HIV, the participants with glucocorticoid use also showed higher scores than those who were not (3.1 vs. 2.6).

Hip fracture risk among persons with HIV and persons without HIV

For the 10-year probability of hip fractures (HF), among persons with HIV, the smoker participants showed higher scores than the non-smokers (0.8 vs 0.4) (Table 4). Among the participants without HIV, the smoker participants also showed higher score than those without history (1.6 vs 0.5). Compared to the persons without HIV who were smoking, the smokers persons with HIV group showed a lower score (0.8 vs 1.6).

Discussion

The study showed the various fracture risk scores according to the related factors. The primary finding of this study was that the 10-year risk of both major osteoporotic fractures (MOFs) and hip fractures (HFs) was predominantly higher among persons with HIV who exhibited several risk factors, including a history of fractures, parental history of hip fractures, smoking behavior, and glucocorticoid use. In contrast, HIV-related factors such as antiretroviral therapy (ART) duration, tenofovir disoproxil fumarate (TDF) exposure, and a history of drug and alcohol abuse were not associated with an increased risk of MOFs or hip fractures. Our earlier study in 2020 found that the factors affecting 10-year fracture risk among HIV-infected persons included age, fracture history, and HCV coinfection (Pramukti, Lindayani, et al., 2020; Pramukti Liu et al., 2020). Similar factors were found in another two studies explaining how traditional factors play an important role in affecting the fracture risk among persons with HIV (Gedmintas et al., 2017; Jiang et al., 2013).

When comparing between persons with HIV and persons without HIV group, the present study

findings suggested that the persons without HIV with fracture history showed a higher MOF score than HIV group. This difference may be due to the different age ranges among the two groups. In earlier studies, age has been found as a significant risk factor affecting fracture risk among HIV and non-HIV, as the non-HIV group is consisted of participants with older age than the HIV group (Pramukti et al., 2020; Ye et al., 2024). Furthermore, fracture history among the older population may affect their fracture risk more than the younger population (Honkanen et al., 1997; Ye et al., 2024).

Another possible risk factor for persons with HIV having fracture was associated with smoking behavior. Our study showed the same major osteoporotic fracture score between smokers with HIV and smokers in the non-HIV group. However, for the hip fracture, the middle-aged HIV group showed a higher score, which indicates smokers who are older in the general population may be at higher risk compared to smokers who are younger in the HIV population. This finding may be relevant to the previous study stating that a combination of smoking behavior and older age may affect a higher fracture risk than a smoker in the HIV population (Olofsson et al., 2005).

The use of glucocorticoid is also common among persons with HIV and may affect the fracture risk. In our study, persons with HIV with glucocorticoid use showed a higher major osteoporotic fracture risk than the non-HIV with glucocorticoid use. It indicates that the use of glucocorticoids among the HIV population may impact more fracture risk than among the middle-aged persons without HIV. This finding is relevant to a previous study which found that persons with HIV undergoing protease inhibitors may affect their bone loss (Moran et al., 2016).

Strengths and limitations of the study

Our study compared the fracture risk between persons with HIV and persons without HIV. Several limitations were found in this study. First, the different age ranges between HIV and non-HIV groups may be found as the confounding factor. However, the new finding on how the two factors, including HIV disease and older age, affect the fracture risk and the large sample size employed may overcome the limitation found. Furthermore, the multi-center used in this study design may improve the sample's representativeness and the finding of generalizability. Another limitation in this study is that the estimation of fracture risk did not consider bone mineral density (BMD) measurement in the laboratory. Therefore, it may affect the fracture risk score. However, FRAX™ is also reliable when calculating the fracture risk without the BMD data. In addition, the large sample size included may overcome the limitation.

Nursing Implication

This study predicted the fracture risk among persons with HIV persons as the vulnerable population for

10 years. The finding may be beneficial as the baseline data to determine the health promotion program in the nursing care, particularly among HIV populations. In addition, as the findings found how the risk differs in different groups, it may be beneficial for determining the specific program related to fracture prevention among those groups.

Conclusions

The 10-year fracture risk was elevated in persons with HIV who presented with multiple factors, such as a history of fractures, smoking behavior, and glucocorticoid use, compared to persons without HIV. Further investigation using multivariate regression analysis is necessary to confirm the specific factors associated with an increased fracture risk.

Declaration of Interest

There was no conflict of interest in this study

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None

Data Availability

None

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