Correspondence

Table 1. Sensitivity and Specificity of the FRAX Algorithm to Identify Human Immunodeficiency Virus (HIV)–Infected Patients with Low Bone Mineral Density (BMD)

Basis of FRAX score, fracture risk	No. of patients with low BMD	No. of patients with normal BMD
CRFs only		
Above intermediate IT	7	3
Below intermediate IT	25	15
Sensitivity or specificity, %[a]	22	83
CRFs and HIV infection		
Above intermediate IT	12	4
Below intermediate IT	20	14
Sensitivity or specificity, %[a]	37.5	77

NOTE. Results of a 2×2 contingency analysis to evaluate the sensitivity and specificity of the FRAX algorithm, computed on the basis of classic risk factors (CRFs) alone and by considering HIV infection as a secondary cause of osteoporosis. Low BMD was defined as a T score or a Z score of <-1. Data are no. of patients, unless otherwise indicated. IT, intervention threshold (defined by the National Osteoporosis Guideline Group).

[a] Sensitivity for patients with low BMD and specificity for patients with normal BMD.

Use of the FRAX Equation as First-Line Screening of Bone Metabolism Alteration in the HIV-Infected Population

To the Editor—We read with interest the article by Calmy et al [1], who investigated bone mineral density (BMD) in the human immunodeficiency virus (HIV)–infected population. To our knowledge, this paper provides the first evaluation of the 10-year fracture risk in HIV-positive patients through use of the FRAX equation.

FRAX is a computer-based algorithm that provides the 10-year probability of fractures in men and women on the basis of classic risk factors (CRFs) alone or by integration of CRFs with BMD, which is measured by dual-energy x-ray absorptiometry (DXA) [2]. After the assessment of fracture risk by use of CRFs alone, the patient can be classified to be at low, intermediate, or high risk, on the basis of thresholds defined by the National Osteoporosis Guideline Group. According to these guidelines, patients at low risk have no indication for further analysis, patients at intermediate risk should have their BMD measured and reassess the risk to evaluate the opportunity for treatment, and patients at high risk should be considered directly for treatment with or without BMD assessment [3, 4].

On the basis of this evidence, the FRAX algorithm has been proposed as a screening tool for HIV-positive patients to identify those who have increased clinical risk of fractures, for whom BMD measurement is strongly recommended [5].

In their interesting paper, Calmy et al [1] comparatively calculated the FRAX score, computed with and without BMD, for 153 HIV-infected adults and evaluated whether the latter score, based on CRFs alone, might have the power to identify HIV-positive patients with reduced BMD. The authors failed to detect differences in the CRF-based FRAX score between patients with normal BMD and patients with low BMD; they concluded that the CRF-based FRAX score does not discriminate between patients with osteopenia and those without osteopenia and thus provides very limited usefulness as screening tool in the HIV-positive population.

We would like to share our experience with the use of the FRAX score in a cohort of 50 HIV-infected individuals aged $\geqslant 40$ years. We selected all patients with an available DXA analysis and evaluated whether the measurement of the CRF-based FRAX score could have been useful in the identification of patients who were candidates for BMD assessment, which in turn would have optimized the use of DXA analysis.

We interviewed all patients to specifically address the risk factors that are included in the FRAX algorithm and calculated the FRAX score at the time of DXA analysis. We evaluated whether the intermediate threshold of the FRAX score, defined as the limit above which DXA is recommended, was indeed able to properly identify patients with low BMD, defined as a T score of <-1 or a Z score of <-1 for patients <50 years old and premenopausal women.

Of 32 patients with low BMD, only 7 had a FRAX score above the intermediate threshold, with a sensitivity of 22%; of 18 patients with normal BMD, 15 had a FRAX score below the intermediate threshold, with a specificity of 83% (Table 1). If osteoporosis (defined as a T score or a Z score of <-2.5) was considered to be the endpoint, instead of low BMD, then the sensitivity increased to 37%.

The low sensitivity of the FRAX score in identifying patients with osteopenia and/or osteoporosis may be explained by the inclusion of only classic, HIV-independent risk factors, despite the evidence

that both HIV infection and highly active antiretroviral therapy significantly increase the risk of low BMD [6]. Moreover, given the HIV-driven hyperactivated, proinflammatory setting, we agree with the model proposed by Calmy et al [1], which considers HIV infection to be an independent risk factor to be integrated in the FRAX score.

Accordingly, and also in consideration of recent European guidelines [5], we performed the same analysis with HIV infection included as risk factor. Of 32 patients with low BMD, 12 had a FRAX score above the intermediate threshold, with a sensitivity of 37.5%; of 18 patients with normal BMD, 14 had a FRAX score below the intermediate threshold, with a specificity of 77% (Table 1). Considering osteoporosis as the endpoint increased the sensitivity of the FRAX score to 62%.

Our results confirm that the FRAX score, when used on the basis of CRFs alone to select HIV-positive patients who should undergo DXA analysis, underestimates the proportion of patients with osteopenia and/or osteoporosis. Even the introduction of HIV infection as secondary cause of osteoporosis does not significantly change the ability of the FRAX score to correctly indicate HIV-positive patients who should undergo DXA testing. Larger studies are warranted to evaluate the most appropriate exploitation of the FRAX score among HIV-infected individuals, and further efforts should address the evaluation of the relative weight of classic risk factors compared with HIV-related risk factors in the emergence of osteopenia and osteoporosis among HIV-infected patients.

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