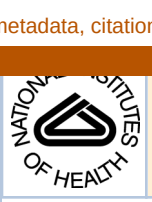

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Skeletal Health among African Americans with Recent Onset Rheumatoid Arthritis

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Abstract

Background—African Americans with rheumatoid arthritis (RA) may be at increased fracture risk. We applied the World Health Organization (WHO) fracture risk assessment tool (FRAX) and National Osteoporosis Foundation (NOF) guidelines to a cohort of African Americans with early RA to identify which patients were recommended for osteoporosis treatment.

Methods—Risk factors and bone mineral density (BMD) were assessed in acohort of African Americans with RA. The WHO FRAX tool estimated ten-year fracture risk. Patients were risk-stratified using FRAX without BMD to identify which individuals might be most efficiently targeted for BMD testing.

Results—Participants (n = 324) had a mean age of 51 years and included 81% women. There were no associations of RA disease characteristics with BMD. The proportion of patients recommended for osteoporosis treatment varied from 3% to 86%, depending on age and BMI. Ten-year fracture risk calculated with BMI only was generally the same or higher than fracture risk calculated with BMD; adding BMD data provided the most incremental value to risk assessment in patients 55–70 years of age with low/normal BMI and in those ≥ 70 years of age with BMI > 30 kg/m^2.

Conclusions—A high proportion of African Americans with RA were recommended for treatment under 2008 NOF guidelines. FRAX without BMD identified low risk patients accurately. Systematic application of FRAX to screen high risk groups such as RA patients may be used to target individuals for BMD testing and reduce the use of unnecessary tests and treatments.

Keywords

African Americans; osteoporosis; fracture risk; rheumatoid arthritis; FRAX

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Introduction

Osteoporosis is recognized as a major source of morbidity in rheumatoid arthritis (RA), with up to one-third of women with RA experiencing a fracture within five years of follow-up (1). Compared to others, RA patients are twice as likely to experience hip fracture (2) and more than four-times as likely to have vertebral deformities suggestive of fracture (3). The impact of hip fractures can be substantial, with approximately one-half of patients unable to walk without assistance and up to one-fourth requiring long-term nursing care (4). Likewise, vertebral compression fractures lead to significant declines in quality of life (5) resulting in both chronic pain and disability (6) and are associated with a more than four-fold increase in mortality (7).

Prior investigations of osteoporosis and bone mineral density (BMD) in RA have almost exclusively involved populations of European ancestry. The lack of such studies in African Americans represents an important knowledge gap given existing racial/ethnic disparities in osteoporosis treatment and fracture-related outcomes observed in this population (8–12). We have previously shown that African Americans at increased risk for fracture are far less likely than Caucasians to receive appropriate diagnostic tests in addition to preventive therapies including prescription osteoporosis medications (11).

Previously, the decision of whether to treat RA patients for osteoporosis has been based primarily on BMD T-scores measured using dual-energy x-ray absorptiometry (DXA) (13). Recent efforts have emphasized the role of absolute fracture risk assessment, particularly with the release of the World Health Organization (WHO) Fracture Risk Assessment Tool (FRAX™) (14). FRAX is an Internet-based tool that provides ten-year estimates of absolute risk of fracture for individual patients. FRAX estimates ten-year absolute risk for both hip fracture and major osteoporotic fracture, incorporating nine clinical risk factors and can be calculated with or without femoral neck BMD (14).

Recently released guidelines from the National Osteoporosis Foundation (NOF) incorporate FRAX (15) with osteoporosis treatment recommended if any one of the following criteria are met: 1) history of previous hip or vertebral fracture; 2) a T-score of ≤ −2.5 at the femoral neck, total hip or spine; 3) low BMD and FRAX ten-year absolute risk of hip fracture ≥ 3%; 4) low BMD and FRAX ten-year absolute risk of major osteoporotic fracture ≥ 20%. If patients do not have one of the clinical indications for osteoporosis treatment (e.g. prior fracture), FRAX without BMD could potentially identify lower versus higher risk patients on the basis of integrating clinical risk factor information. Some patients might then be targeted for further evaluation, including BMD testing. This two-step screening approach could potentially lead to a more efficient use of BMD testing resources.

The purpose of this analysis was to 1) evaluate relationships between RA disease features and BMD, and 2) to describe the proportion of African-American patients with early RA who would be recommended for treatment under the new NOF guidelines. To facilitate the latter evaluation, we used FRAX to estimate the absolute ten-year fracture risk. Furthermore, we sought to focus on patients that might be treated on the basis of exceeding the NOF fracture risk thresholds (ten-year risk of hip fracture ≥ 3% or major fracture risk ≥ 20%) to determine whether including BMD in the FRAX calculations impacted treatment decisions and if so, which patient factors influenced these differences.

Methods and Materials

Study subjects and clinical measures

Study subjects (n = 324) were participants in the Consortium for the Longitudinal Evaluation of African Americans with Early Rheumatoid Arthritis (CLEAR) (16,17), enrolled between October 2000 and July 2006. Participants self-reported African American race/ethnicity, satisfied the American College of Rheumatology (ACR) RA classification criteria (18), and had less than two years of disease duration (19). Baseline data were collected at enrollment and included medical history (e.g. medications, use of calcium/vitamin D supplementation), smoking history, alcohol use, and menopausal status for women. Measures of disease activity/severity included the Health Assessment Questionnaire (HAQ) disability index (20), pain (0–10 scale), rheumatoid nodules, tender joints (range 0–42), swollen joints (range 0–40), and the presence of radiographic erosions (a van der Heijde modified Sharp erosion score ≥ 1 (21)). At the time of this analysis, baseline radiographic scores were available for 183 of 324 patients.

BMD measurement

Femoral neck and lumbar spine (L1–L4, anterior-posterior) BMD was measured at enrollment using DXA (22). BMD was not measured on a small subset of patients due to the presence of either bilateral total hip replacements or other artifact interfering with either hip (n = 9) or vertebral measurements (n = 4). Because DXA machine type varied by site, BMD values were standardized to Hologic BMD (Hologic Inc., Bedford, MA) using published conversion equations (23).

Site-specific T-scores were calculated by subtracting peak referent BMD for Caucasian women from the patient's value and dividing the difference by the referent standard deviation. Z-scores were calculated using African American referent data specific to the participant's age-decile (peak referent BMD ages 20–29, 30–39 years, etc.). For the spine, we used the manufacturer's reference database (Hologic). For the hip, we used reference data from the Third National Health and Nutrition Examination Survey (NHANES-III) (24). Reduced BMD adjusted for age decile was defined as a Z-score ≤ −1.0. Osteopenia and osteoporosis were defined using the T-score thresholds established by the WHO for diagnosis in postmenopausal Caucasian women (25). Osteoporosis is defined as a BMD T-score ≥ 2.5 SD below the young adult mean in women. Osteopenia is defined as a BMD T-score between 1SD and 2.5 SD below this mean.

Laboratory measures

Laboratory measures were obtained from serum and plasma obtained at enrollment. Rheumatoid factor (RF-IgM, IU/ml, INOVA Diagnostics, USA), antibody to cyclic citrullinated peptide (anti-CCP, U/ml, Diastat, Axis-Shield Diagnostics Ltd., UK), N-telopeptide (NTX, nM BCE, Wampole Laboratories, USA) and bone specific alkaline phosphatase (BAP, U/L, Quidel Corp., USA) were measured using ELISA. Positive values for RF (≥ 9.5 IU/ml) and anti-CCP antibody (≥ 5 U/ml) were defined as previously reported (26). Elevations in NTX (pre-menopausal women > 19.0 nM BCE, post-menopausal women > 33.9 nM BCE, men > 24.2 nM BCE) and BAP (pre-menopausal women > 30.6 U/L, post-menopausal women > 43.4 U/L, men > 41.3 U/L) were defined using cutoffs provided by the manufacturers. High sensitivity C-reactive protein (hs-CRP, mg/L) was measured with an immunoturbidimetric assay on a Hitachi 917 autoanalyzer (Roche Diagnostics, USA), with the use of reagents and calibrators from Denka Seiken (Tokyo, Japan, normal < 3 mg/L). Plasma estradiol (pg/ml, Research Diagnostic Inc., USA) and 25-OH vitamin D (nmol/L, IDS, UK, insufficiency ≤ 37.5 nmol/L (27)) were measured using commercially available radioimmunoassay (RIA).

FRAX

Ten-year risk of hip fracture and major osteoporotic fracture were calculated using the WHO FRAX Tool (http://shef.ac.uk/FRAX) specific to U.S. African Americans (calculations completed October 25, 2008). FRAX incorporates the following clinical risk factors: age, gender, weight, height, previous fracture, parental history of hip fracture, current smoking status, glucocorticoid use, RA, other causes of secondary osteoporosis, alcohol use, and, if available femoral neck BMD (T-scores from men and women referent to Caucasian women). Excluding the 9 persons for whom femoral neck BMD was not available, all variables that are required for FRAX were measured in this population, except that parental history of hip fracture was not measured in this cohort and therefore was entered as "no" for all participants, and only information about clinical (but not radiographic) vertebral fractures was available. Additionally, CLEAR and FRAX did not ascertain alcohol use in the same way, and this variable was considered to be present if the subject reported 'regular alcohol use'. Parenthetically, the presence of other secondary causes of osteoporosis does not affect fracture risk estimates produced by the FRAX calculator if patients have RA. Ten-year absolute risk estimates for hip fracture and major osteoporotic fracture (hip, clinical vertebral, forearm/wrist, and humerus) were calculated for each individual with and without BMD.

Updated 2008 NOF treatment recommendations

We applied the 2008 NOF guidelines, as outlined in the introduction, to estimate the proportion of individuals that would be recommended for treatment, by age and BMI. Although we used T-scores referent to Caucasian women in FRAX calculations as recommended by the WHO, T-scores used in the remainder of the NOF recommendations were referent to gender-matched Caucasians (28).

We used FRAX with BMD to identify which patients met or exceeded a ten-year risk for hip fracture ≥ 3% or major fracture ≥ 20%. We then used FRAX to re-compute fracture risk after removing BMD information. The proportion of persons meeting the fracture risk threshold using FRAX with BMD compared to FRAX without BMD were considered, stratified by age (40–54, 55–69, and ≥ 70 years) and BMI (< 25, 25 to < 30 and ≥ 30 kg/m^2). The goal of this analysis was to determine whether it might be possible to identify groups of patients based upon age and BMI that were at such low (or high) risk for fracture based only on FRAX without BMD that obtaining BMD was unnecessary because it did not change whether or not they exceeded the NOF-specified fracture risk thresholds. Patients exceeding the risk thresholds under FRAX without BMD but who did not when using FRAX with BMD (or vice-versa) were considered 'discordant'. The number needed to screen (NNS) with DXA was computed for various age and BMI strata. The NNS is the number of persons that need to undergo DXA in order to find 1 discordant person. For this exploratory subanalysis and because we wished to focus on FRAX-computed fracture risk exclusively, other clinical criteria (e.g. prior hip fracture) that might make a patient recommended for treatment under the 2008 NOF guidelines were not considered.

Statistical analyses

Patient characteristics were summarized using means (± S.D.) and frequencies. Associations of patient characteristics with femoral neck and lumbar spine BMD were examined for each site using backwards stepwise multivariate linear regression ($p \leq 0.25$ required to enter model, $p \leq 0.05$ to remain). Gender and menopausal status were incorporated as a single variable so that pre-menopausal and post-menopausal women were compared to men as the referent group. Additional variables examined as determinants of BMD included age (years), BMI (< 25, 25–30, and > 30 kg/m^2), ever smoking, alcohol use, estradiol concentration, 25-OH vitamin D concentration and deficiency, hs-CRP concentration and elevation (≥ 3 mg/

L), HAQ score, disease duration, tender/swollen joint counts, pain score, presence of radiographic erosions, nodules, glucocorticoid use, and autoantibody status. All analyses were performed using SAS v9.1 (SAS Institute Inc., Cary, NC).

Results

Sociodemographic, health, and disease-specific characteristics of study participants are shown in Table 1. The cohort was predominantly female (81%) with an overall mean age of 51 years (median 51 years, range 21 to 86 years) and disease duration of just over one year. Approximately one-half of participants had a previous smoking history and approximately half met criteria for obesity (BMI > 30 kg/m^2). Approximately 80% had previously taken systemic glucocorticoids for their RA and approximately one-half were deficient in 25-OH vitamin D (≤ 37.5 nmol/L). The proportion of patients meeting T-score criteria for osteoporosis (T-score ≤ −2.5 at either the lumbar spine or femoral neck) was 4%. Reduced BMD (Z-score ≤ −1) was observed in approximately one-third (31%) of patients. Elevations in circulating NTX and BAP were observed in 9.2% and 9.6% of patients, respectively. Measures of RA disease activity suggested moderate to severe disease with mean HAQ score of 1.6 and mean tender and swollen joint counts of 6 and 12, respectively. A total of 70% were seropositive for RF-IgM and 61% were seropositive for anti-CCP antibody.

Results from multivariate analysis examining the association of patient factors with BMD are shown in Table 2. There were no associations of RA activity, severity, or erosions with BMD at either site on a univariate or multivariate level. Likewise, there were no associations of glucocorticoid use (ever use, daily or cumulative dose), 25-OH vitamin D (concentration or deficiency), or hs-CRP (concentration or elevation) with BMD. BMI was independently and positively associated with higher BMD values at both sites. In addition, increases in plasma estradiol concentration were associated with higher spine BMD while younger age and male gender were associated with increased femoral neck BMD.

The proportion of RA patients classified as ‘recommended for treatment’ based on 2008 NOF guidelines (as described in the introduction) is shown in Table 3. It varied dramatically by age and BMI, ranging from a low of 3% (age 40–55, BMI > 30) up to 86% (age > 70, BMI 25–30). Focusing exclusively on the ten-year hip fracture risk ≥ 3% or major fracture risk ≥ 20% calculated without BMD (and not any of the other NOF criteria), the proportion meeting either of these risk thresholds is shown in Figure 1 (top panel). This analysis was repeated using FRAX with BMD and shown in Figure 1, bottom panel. As shown, the proportion of people exceeding the 3%/20% fracture risk thresholds was generally higher using FRAX without BMD and varied substantially by age and BMI. Only 10% (n = 29) of people were “discordant” in crossing the hip fracture ≥ 3% or major fracture ≥ 20% thresholds when comparing results from FRAX with and without BMD (Figure). Among subjects with discordance, a majority of them had normal femoral neck T-scores (T-score > −1.0) while the remainder had femoral neck T-scores < −1.0 but > −2.0; none had osteoporosis. The number needed to screen (NNS) for DXA leading to identify 1 discordant person varied by age and BMI. Among persons older than 70, 2–3 individuals would need to be tested with DXA to identify 1 discordant person. For persons age 55–70, at least 4–6 individuals would need to be tested with DXA to identify 1 discordant person.

Discussion

Although the incidence of osteoporosis is lower in African Americans than Caucasians (29), African Americans experiencing fracture have substantially worse outcomes. Compared to Caucasians, African Americans suffering from hip fracture have substantially longer hospitalizations, are more likely to be non-ambulatory at the time of discharge (30), and

have higher mortality (9). Additionally, African Americans are less likely than Caucasians to receive the same degree of physical rehabilitation (31) or medical intervention following fracture (32), treatments shown to be effective in African Americans (33). In this population of African Americans with early RA, a majority of patients (approximately 80%) over the age of 70 years with normal or low BMI were recommended for treatment under the recently-revised NOF guidelines. For patients between 55 to 70 years of age, 8% to 36% of people were recommended for treatment, varying based upon BMI. We also found that using FRAX without BMD was an efficient approach to identifying people at low enough fracture risk based on clinical risk factors such that measuring BMD was not necessary.

The clinical variables included in FRAX can be collected in minutes with a simple questionnaire and may be available within many electronic health records to identify higher risk patients in a more systematic fashion. A strategy of 'case-finding' through the use of FRAX without BMD may be effective in targeting patients for additional evaluation (including DXA), a strategy that might be most feasible within large integrated health systems (i.e. Veterans Affairs, Kaiser Permanente). This strategy has the potential of reducing the racial/ethnic disparities that too often characterize osteoporosis management in African Americans (11,12).

It is likely that in the near future FRAX results will be incorporated as a component of DXA reports, assuming that the necessary data is collected by technicians performing these measurements. In the absence of routinely including FRAX results in DXA reports, there are currently several important operational issues to consider in using FRAX as part of day-to-day patient care. These logistical issues include the need for Internet access, the proprietary nature of the FRAX and the associated lack of transparency regarding the impact of the data elements used to estimate long term risk, and patient preferences regarding the 'risk threshold' that must be exceeded in order to accept prescription osteoporosis treatment.

Although BMD measurement with DXA has long served as the gold standard for fracture risk assessment, its inclusion in FRAX appears to have widely variable incremental yield among African American subjects with recent onset RA. In our study population, the addition of BMD data to the fracture risk estimate led to changes in risk assessment in as few as 10% of patients. DXA provided the greatest amount of incremental value in assessing fracture risk in patients 55–70 years of age with BMI < 30 kg/m^2, and among those ≥ 70 years of age with a BMI > 30 kg/m^2. In most cases of discordance, patients went from being above the fracture risk threshold of 3%/20% (computed under FRAX without BMD) to below the threshold under FRAX with BMD. Based on our results, a change in the FRAX risk assessment would occur for approximately 1 of every 3 patients over the age of 70 screened with DXA.

These results have important implications. In the absence of other clinical indications to treat osteoporosis (e.g. prior hip fracture), our results show that a 'do not treat' result based upon fracture risk could obviate the need for BMD measurement since its inclusion in the FRAX calculation is highly unlikely to change the risk assessment and corresponding treatment decision. On the other hand, DXA measurement in high-risk patients may lead to a change in treatment decision to not treat, and thus minimize exposure to potentially unnecessary treatments.

Although glucocorticoid use and measures of RA disease severity (e.g. rheumatoid factor positivity, radiographic erosions) have been potentially associated with RA-associated bone loss, these factors do not appear to significantly influence BMD in African Americans early in the course of RA. Thus, RA-related factors in this population should not be used to guide

BMD referral and do not appear to portend added risk beyond the RA diagnosis itself, at least early in the course of the disease.

There are limitations to this study. This study involved African American RA patients recruited from select centers in the Southeast U.S., limiting the generalizability of these findings. These results can not be extended to other disease states or other racial/ethnic populations, underscoring the need for additional study. Because this investigation involved patients with limited disease duration (and limited glucocorticoid exposure), it is possible that these results may not apply to African Americans with more longstanding RA. It may be reasonable, for instance, to obtain baseline BMD measurement in an otherwise 'low-risk' RA patient to guide the future management of glucocorticoid induced osteoporosis. We also recognize that the cohort was relatively young (mean age 51 years), and most treatment guidelines focus on post-menopausal women and older men. However, we included these younger populations since RA is a well established, independent risk factor for osteoporosis and fracture (34) and glucocorticoid induced osteoporosis (GIOP) management guidelines (35,36) pertain to younger patients (just as FRAX calculates fracture risk for individuals as young as 40 years of age). The high prevalence of overweight (76%) and obesity (51%) in this population impacted our results, decreasing the proportion of subjects recommended for osteoporosis treatment. However, it is important to recognize that prevalence rates of overweight/obesity in this study are similar to those from a recent national, population-based investigation of African Americans (37). Also, select risk factors (e.g. alcohol use) in this cohort were defined differently than in the WHO FRAX, and only lumbar spine and femoral neck BMD (but not total hip BMD) were available to identify osteoporosis based upon a T-score ≤ -2.5.

There are limitations to the FRAX and NOF guidelines worth noting. FRAX does not incorporate every clinical variable that may be important in fracture risk assessment (e.g. fall risk) and lacks information on dose-response relationships (e.g. glucocorticoid dose). Additionally, it is important to recognize that epidemiological studies of fracture risk in African Americans are scarce, and the accuracy of FRAX for fracture prediction in African Americans has not been validated. FRAX represents an important starting point in the complex task of risk assessment and fracture prevention but should not be regarded as a substitute for clinical judgment. Finally, only weak evidence exists that the benefit of bisphosphonates and other osteoporosis medications extends to persons with T-scores > -2.5 (i.e. osteopenia).

Despite its limitations, this study has notable strengths. This effort represents the single largest study to date of BMD and fracture risk assessment in African Americans with RA. With the exception of parental fracture history, all of the necessary data were available to allow for the calculation of ten-year fracture risk in this group. These data, coupled with standardized DXA data and detailed information on RA-specific disease characteristics, provided the unique opportunity to examine BMD status and promote improved fracture risk assessment and osteoporosis management in this unique and understudied population. We conclude that systematic application of FRAX to screen high risk groups, including African-Americans with RA, may be useful in targeting patients for BMD measurement and in the process reduce unnecessary testing and treatment in fracture prevention.

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The CLEAR Registry is an NIH-sponsored resource, with clinical data, DNA, and other biological samples available to approved users. Details on obtaining data or biological samples are available at the following website: http://www.dom.uab.edu/rheum/CLEAR%20home.htm.

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References

1. Michel BA, Bloch DA, Fries JF. Predictors of fractures in early rheumatoid arthritis. J Rheumatol. 1991; 18:804–808. [PubMed: 1895260]
2. Cooper C, Coupland C, Mitchell M. Rheumatoid arthritis, corticosteroid therapy and hip fracture. Ann Rheum Dis. 1995; 54:49–52. [PubMed: 7880122]
3. Baskan B, Sivas F, Alemdaroqlu E, Duran S, Ozoran K. Association of bone mineral density and vertebral deformity in patients with rheumatoid arthritis. Rheumatol Int. 2007; 27:579–584. [PubMed: 17287933]
4. Riggs B, Melton LI. The worldwide problem of osteoporosis: insights afforded by epidemiology. Bone. 1995; 17(suppl 5):505–511.
5. Silverman S, Mason J, Greenwald M, et al. Quality of life after osteoporotic vertebral fracture. Arthritis Rheum. 1993; 36 (abst):s122.
6. Silverman S. The clinical consequences of vertebral compression fracture. Bone. 1992; 13:s27–31. [PubMed: 1627411]
7. Jalava T, Sarna S, Pylkkanen L, et al. Association between vertebral fracture and increased mortality in osteoporotic patients. J Bone Min Res. 2003; 18:1254–1260.
8. Furstenberg A, Mezcy M. Differences in outcome between black and white elderly hip fracture patients. J Chronic Dis. 1987; 40:931–938. [PubMed: 3038943]
9. Jacobsen S, Goldberg J, Miles T, Brody J, Stiers W, Rimm A. Race and sex differences in mortality following fracture of the hip. Am J Public Health. 1992; 82:1147–1150. [PubMed: 1636840]
10. Kellie S, Brody J. Sex-specific and race-specific hip fracture rates. Am J Public Health. 1990; 80:326–328. [PubMed: 2305917]
11. Mikuls TR, Saag KG, George V, Mudano AS, Banerjee S. Racial disparities in the receipt of osteoporosis related healthcare among community-dwelling older women with arthritis and previous fracture. J Rheumatol. 2005; 32(5):870–5. [PubMed: 15868624]
12. Mudano AS, Casebeer L, Patino F, et al. Racial disparities in osteoporosis prevention in a managed care population. South Med J. 2003; 96(5):445–51. [PubMed: 12911182]
13. National Osteoporosis Foundation. Physician's guide to prevention and treatment of osteoporosis. Belle Mead (NJ): Excerpta Medica, Inc; 1999.
14. Kanis JA, Borgstrom F, De Laet C, et al. Assessment of fracture risk. Osteoporos Int. 2005; 16(6): 581–9. [PubMed: 15616758]

15. Dawson-Hughes B, Tosteson AN, Melton LJ 3rd, et al. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. Osteoporos Int. 2008; 19(4):449–58. [PubMed: 18292975]
16. Sokka T, Willoughby J, Yazici Y, Pincus T. Databases of patients with early rheumatoid arthritis in the USA. Clin Exp Rheumatol. 2003; 21 (Suppl 31):S146–153. [PubMed: 14969067]
17. Bridges SJ, Hughes L, Mikuls T, et al. Early rheumatoid arthritis in African-Americans: the CLEAR Registry. Clin Exp Rheumatol. 2003; 21 (Suppl 31):S138–145. [PubMed: 14969066]
18. Arnett F, Edworthy S, Bloch D, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum. 1988; 31:315–324. [PubMed: 3358796]
19. Bridges SL Jr, Hughes LB, Mikuls TR, et al. Early rheumatoid arthritis in African-Americans: the CLEAR registry. Clin Exp Rheumatol. 2003; 21 (5 Suppl 31):S138–145. [PubMed: 14969066]
20. Fries J, Spitz P, Kraines R, Holman H. Measurement of patient outcome in arthritis. Arthritis Rheum. 1980; 23:137–145. [PubMed: 7362664]
21. van der Heijde D. How to read radiographs according to the Sharp/van der Heijde method. J Rheumatol. 1999; 26:743–5. [PubMed: 10090194]
22. Mikuls TR, Saag KG, Curtis J, et al. Prevalence of osteoporosis and osteopenia among African Americans with early rheumatoid arthritis: the impact of ethnic-specific normative data. J Natl Med Assoc. 2005; 97:1155–1160. [PubMed: 16173331]
23. Genant H, Grampp S, Gluer C, et al. Universal standardization for dual X-absorptiometry: patient and phantom cross-calibration results. J Bone Miner Res. 1994; 9:1503–1514. [PubMed: 7817795]
24. Looker A, Wahner H, Dunn W, et al. Updated data on proximal femur bone mineral levels of US adults. Osteoporosis Int. 1998; 8:468–489.
25. Kanis J, Melton LI, Christiansen C, Johnston CJ, Khaltev N. Perspective: the diagnosis of osteoporosis. J Bone Miner Res. 1994; 9:1137–1141. [PubMed: 7976495]
26. Mikuls T, Holers VM, Parrish LA, et al. Anti-cyclic citrullinated peptide antibody and rheumatoid factor isotypes in African Americans with early rheumatoid arthritis. Arthritis Rheum. 2006; 54:3057–9. [PubMed: 16948136]
27. Nesby-O'Dell S, Scanlon K, Cogswell M, et al. Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: the third National Health and Nutrition Examination Survey, 1988–1994. Am J Clin Nutr. 2002; 76:187–192. [PubMed: 12081833]
28. Lewiecki EM, Watts NB, McClung MR, et al. Official positions of the international society for clinical densitometry. J Clin Endocrinol Metab. 2004; 89(8):3651–5. [PubMed: 15292281]
29. Silverman S, Madison R. Decreased incidence of hip fracture of Hispanics, Asians, and Blacks: California hospital discharge data. Am J Public Health. 1988; 78:1482–1483. [PubMed: 3177728]
30. Furstenberg A, Mezey M. Differences in outcome between black and white elderly hip fracture patients. J Chron dis. 1987; 40:931–938. [PubMed: 3038943]
31. Hoenig H, Rubenstein L, Kahn K. Rehabilitation after hip fracture - equal opportunity for all? Arch Phys Med Rehabil. 1996; 77:58–63. [PubMed: 8554475]
32. Mudano A, Casebeer L, Patino F, et al. Racial disparities in osteoporosis prevention in a managed care population. South Med J. 2003; 96:445–451. [PubMed: 12911182]
33. Bell N, Bilezikian J, Bone H, Kaur A, Maragato A, Santora A. Alendronate increases bone mass and reduces bone markers in postmenopausal African-American women. J Clin Endrocrinol Metab. 2002; 87:2792–2797.
34. Kanis JA, Johansson H, Oden A, et al. A meta-analysis of prior corticosteroid use and fracture risk. J Bone Miner Res. 2004; 19(6):893–9. [PubMed: 15125788]
35. American College of Rheumatology Ad Hoc Committee on Glucocorticoid-Induced Osteoporosis. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis: 2001 update. Arthritis Rheum. 2001; 44:1496–503. [PubMed: 11465699]
36. American College of Rheumatology Task Force on Osteoporosis Guidelines. Recommendations for the prevention and treatment of glucocorticoid-induced osteoporosis. Arthritis Rheum. 1996; 39:2022–9.

37. Yun S, Zhu BP, Black W, Brownson RC. A comparison of national estimates of obesity prevalence from the behavioral risk factor surveillance system and the National Health and Nutrition Examination Survey. Int J Obes (Lond). 2006; 30(1):164–70. [PubMed: 16231026]

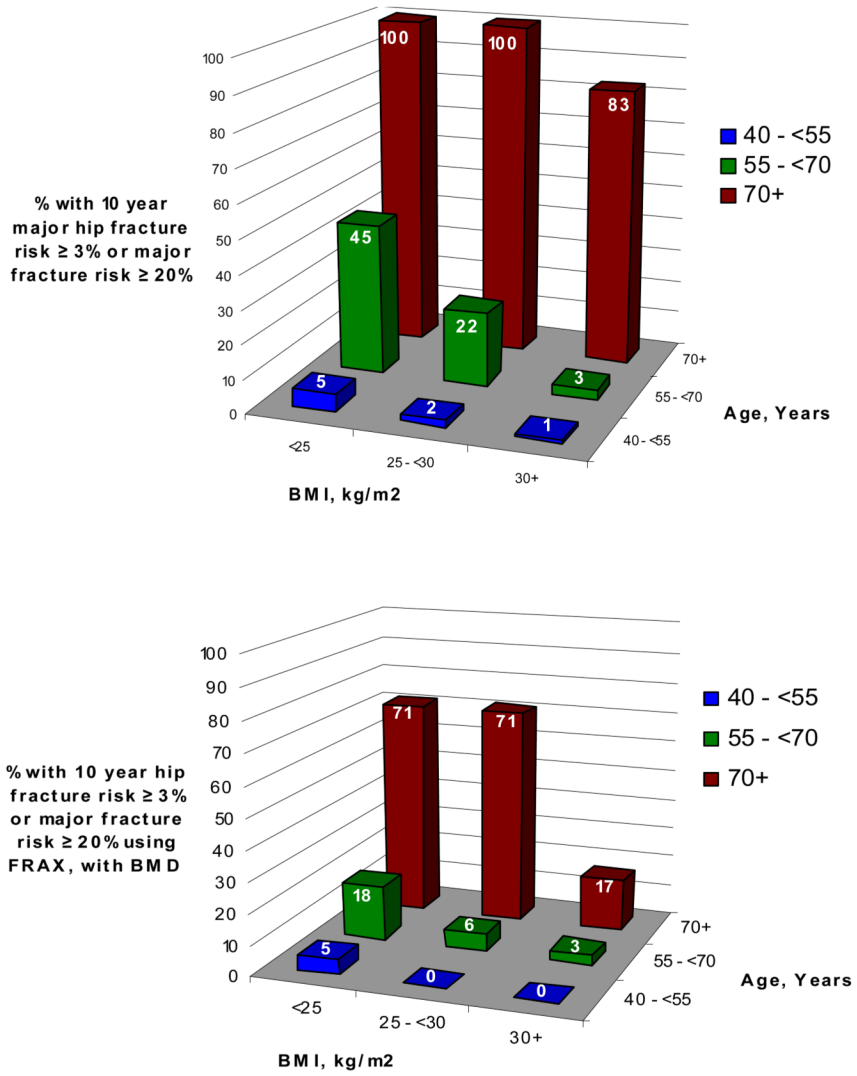

Figure 1.

The proportion of African American patients with recent-onset RA with hip fracture risk ≥ 3% or major osteoporotic fracture ≥ 20%. Estimates generated using WHO FRAX Tool without (top) and with (bottom) BMD data

Table 1

Characteristics of African American subjects with recent-onset rheumatoid arthritis (N = 324)

Characteristic	% or mean (SD)
Sociodemographics and anthropormetrics	
Age, years	51 (13)
Gender	
Men	19
Post-menopausal women	31
Pre-menopausal women	50
Body mass index (BMI), kg/m2	
< 25	22
25–30	27
> 30	51
Fracture-related risk factors and other determinants of bone health	
Prior fracture	
Hip	1.3
Clinical Vertebral	1.6
Other fracture	21
Ever glucocorticoid use	79
Glucocorticoid daily dose, mg prednisone	7.3 (7.2)
25-OH Vitamin D deficient (≤ 37.5 nM/L)	49
25-OH Vitamin D, nM/L	41 (16)
Estradiol, pg/ml	36 (35)
Vitamin D supplementation	15
Ever antiresorptive therapy	19
Calcium supplementation	42
Current alcohol use	17
Ever smoking	52
Bone Mineral Density (BMD) and bone turnover markers	
Femoral neck or lumbar spine T-score < −1.0*	29
Femoral neck or lumbar spine T-score < −2.5*	4
Femoral neck or lumbar spine Z-score < −1.0**	31
N-telopeptide (NTX), nM BCE‡	17 (6)
Elevated NTX	9.2
Bone specific alkaline phosphatase (BAP), U/L‡	26 (11)
Elevated BAP	9.6
RA Disease Characteristics	
Disease duration, months	13 (7)
Subcutaneous nodules	14
Anti-CCP antibody positive	61
Rheumatoid factor (IgM) positive	70

Characteristic	% or mean (SD)
Swollen joint count (0–40)	6 (7)
Tender joint count (0–42)	12 (11)
Pain (0–10)	6 (3)
hs-CRP (mg/L)	16 (42)
hs-CRP ≥ 3 mg/L	62
HAQ Disability Index score (0–3)	1.6 (0.9)

CCP = cyclic citrullinated peptide; hs-CRP = highly sensitive C-reactive protein; HAQ = Health Assessment Questionnaire

[*] BMD values standardized to Hologic machine (23)

[†] T-scores determined using referent normative data from Caucasian women; Z-scores sex-adjusted using African American referent database

[‡] Elevated serum levels of NTX: pre-menopausal women > 19.0 nM BCE, post-menopausal women > 33.9 nM BCE, men > 24.2 nM BCE; elevated serum levels of BAP: pre-menopausal women > 30.6 U/L, post-menopausal women > 43.4 U/L, men > 41.3 U/L

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Table 2

Univariate and multivariate associations of patient factors with bone mineral density (BMD, gm/cm^2) measurements of lumbar spine (L1–L4) and femoral neck among African Americans with recent-onset rheumatoid arthritis*

	Lumbar spine (L1-L4)		Femoral neck	
	Univariate B-coefficient (p-value)	**Multivariate B-coefficient (p-value)**	**Univariate B-coefficient (p-value)**	**Multivariate B-coefficient (p-value)**
Age, years	−0.003 (0.0006)	----	−0.005 (< 0.0001)	−0.005 (< 0.0001)
Gender/menopausal status				
Men	Referent	Referent	Referent	Referent
Premenopausal women	0.031 (0.27)	----	0.031 (0.18)	−0.063 (0.006)
Postmenopausal women	−0.016 (0.53)	----	−0.058 (0.009)	−0.057 (0.006)
Body mass index (BMI), kg/m2				
< 25	Referent	Referent	Referent	Referent
25–30	0.080 (0.003)	0.078 (0.007)	0.067 (0.004)	0.073 (0.0004)
> 30	0.137 (< 0.0001)	0.127 (< 0.0001)	0.128 (< 0.0001)	0.134 (< 0.0001)
Ever smoking	−0.016 (0.43)	----	−0.026 (0.12)	----
Current alcohol use	0.013 (0.62)	----	0.013 (0.57)	----
Estradiol, pg/ml	0.001 (0.001)	0.0007 (0.02)	0.001 (< 0.0001)	----
25-OH vitamin D deficiency	0.022 (0.30)	----	0.013 (0.50)	----
hs-CRP, mg/L	0.0002 (0.49)	----	0.0001 (0.55)	----
HAQ score (0–3)	0.009 (0.39)	----	0.007 (0.47)	----
Tender joint count	0.0006 (0.51)	----	0.0007 (0.32)	----
Swollen joint count	0.001 (0.37)	----	0.0005 (0.63)	----
RA disease duration	−0.0006 (0.65)	----	−0.0004 (0.72)	----
Ever glucocorticoid use	0.004 (0.88)	----	−0.0008 (0.97)	----
Calcium supplementation	0.001 (0.95)	----	−0.018 (0.28)	----
Pain (0–10)	0.007 (0.03)	0.008 (0.02)	0.008 (0.008)	----
Radiographic erosions	0.018 (0.53)	----	0.012 (0.61)	----
Nodules	−0.019 (0.50)	----	−0.023 (0.34)	----
Anti-CCP positive	−0.006 (0.79)	----	0.033 (0.08)	----
Rheumatoid factor (IgM) positive	0.010 (0.66)	----	0.045 (0.03)	----

	Lumbar spine (L1-L4)		Femoral neck	
	Univariate B-coefficient (p-value)	**Multivariate B-coefficient (p-value)**	**Univariate B-coefficient (p-value)**	**Multivariate B-coefficient (p-value)**
		R^2 = 0.14		**R^2 = 0.33**

*hs-CRP = high sensitivity C-reactive protein, HAQ = Health Assessment Questionnaire, CCP = cyclic citrullinated peptide; All factors entered into multivariable model with p-values ≤ 0.25 at univariate level with stepwise removal until all remaining p-values ≤ 0.05; Additional variables examined (all p-values > 0.25 at univariate level) included 25-OH vitamin D concentration, hs-CRP elevation, usual daily and cumulative glucocorticoid dose (prednisone equivalent); radiographic erosions based on van der Heijde modified Sharp erosion score ≥ 1 (n = 183)

Table 3

Proportion of African Americans with recent-onset rheumatoid arthritis that would be recommended for treatment under 2008 National Osteoporosis Foundation Guidelines, by age and body mass index, % (95% confidence interval)

Age, years	40–55	55–70	> 70
Body Mass Index, kg/m^2			
< **25**	5 (1, 18)	36 (17, 59)	71 (29, 96)
25–30	7 (1, 17)	11 (1, 35)	86 (42, 100)
> **30**	3 (1, 8)	8 (2, 20)	17 (2, 48)