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Clinical characteristics, bone mineral density and non-vertebral osteoporotic fracture outcomes among post-menopausal U.S. South Asian Women

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ABSTRACT

Purpose: There is limited data pertaining to osteoporotic fractures among North American women of South Asian (SA) descent. This study examines fracture incidence and risk factors among post-menopausal SA, Chinese and White women undergoing mineral density (BMD) testing within a large healthcare organization in Northern California.

Methods: Using data from a retrospective study of women aged 50–85 years with femoral neck BMD measured between 1997 and 2003, we identified a subset of women of SA race and an age-matched subgroup of Chinese (1:5) and White (1:10) women and examined rates of incident wrist, humerus and hip fractures up to 10 years following BMD. Clinical and demographic risk factors were identified using health plan databases. Multivariable Cox regression analyses were conducted to examine predictors of incident fractures.

Results: The study cohort included 449 SA, 2245 Chinese and 4490 White women, with an average age of 58.4 ± 6.1 years. The prevalence of femoral neck osteoporosis was higher among SA (8.9%) compared to White (6.5%) women and tended to be lower than Chinese (11.9%) women. More SA (7.1%) and White (9.6%) women had prior fracture compared to Chinese women (4.5%) and racial differences in smoking, rheumatoid arthritis, glucocorticoid use and hormone replacement therapy were seen. During a median of 8.4 years follow-up, wrist fracture incidence was similar among SA and White women (286 and 303 per 100,000 person-years, respectively) but significantly lower among Chinese women (130 per 100,000 person-years). In multivariable analyses, lower BMD, prior fracture and White and SA race (compared to Chinese race), were associated with a higher relative rate of wrist fracture. Lower BMD, prior fracture, older age and White but not SA race were also associated with a higher relative rate of non-vertebral (wrist, humerus or hip) fractures.

Conclusions: Post-menopausal South Asian women differed from Chinese and White women with respect to prevalence of femoral neck osteoporosis, certain risk factors and site of osteoporotic fracture. These findings support the need for more studies examining fracture risk and outcomes specific to SA women residing in the U.S. to inform clinical decisions relevant to fracture risk.

Introduction

Osteoporosis is a major world health problem associated with significant morbidity and mortality. In developed countries, the lifetime probability of osteoporotic fractures for women at age 50 years is estimated to exceed 40% [1]. Rates of fragility fracture also differ depending on race/ethnicity and are typically higher among those of White race [2]. Worldwide, the number of osteoporotic fractures is expected to increase, particularly in Asian countries where more than half of all osteoporotic fractures are projected to occur by 2050 [3]. China and India are among the two largest Asian countries experiencing rapid economic growth. By 2013, India is predicted to have 36 million people suffering from osteoporosis, while China is predicted to have 286.6 million suffering from either osteoporosis or osteopenia by 2020 [3].

According to the U.S. Census Bureau, the U.S. Asian population has risen 43% to nearly 15 million within the past decade, constituting an important subgroup for ascertainment of osteoporosis outcomes. The majority of studies examining bone health among Asians have been conducted among women of East Asian descent, where lower bone mineral density (BMD) and lower rates of osteoporotic fracture compared with White women have been reported [2]. Several factors may be responsible for the variation by race, including smaller bone size, lower body weight and height, hip geometry, nutritional and lifestyle factors, and differences in rates of bone accrual and bone loss.

Compared to East Asian subgroups and Chinese women in particular, data pertaining to osteoporotic fractures among women of South Asian (SA) descent, whether in the U.S. or abroad, are limited. Examination of risk factors and BMD in selected cohorts demonstrate that post-menopausal SA women have lower BMD, reduced calcium intake

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and a greater prevalence of vitamin D deficiency [4,5]. Immigrant SA women tend to be shorter and thinner than their White counterparts, with lower rates of smoking and alcohol consumption [6]. Potential factors contributing to lower BMD in SA women include skin pigmentation, reduced sun exposure, low vitamin D, and smaller bone size when measured by dual energy X-ray absorptiometry [5]. However, because the relationship of BMD and fracture risk among SA women has not been carefully examined, the question of appropriate reference standards has been raised [5,7]. For instance, use of Indian-based reference standards from North and South Indian populations yields a much lower proportion of SA women diagnosed with osteopenia and osteoporosis compared to the use of White reference standards [7,8]. Currently, little guidance exists for the application of FRAX™ to assess fracture risk in Indian women residing in the U.S., particularly since the Asian FRAX™ algorithms are not derived from data in Asian Indians. In addition, there are no specific risk models for countries of the Indian subcontinent and the only SA subgroup for which there is a FRAX™ model are Indians residing in Singapore. A recent study conducted among native Sri Lankan women found that the FRAX™ U.S.–Caucasian tool had greater sensitivity and specificity in detecting prevalent fractures and identifying those needing interventions compared to the FRAX™ Chinese, Japanese and US–Asian tools [9].

Given the increasing burden of osteoporosis and the growing SA population within the U.S., there is an important need to better understand the variation in osteoporotic risk and fracture incidence among specific Asian subgroups. This study describes the clinical characteristics, femoral neck BMD and fracture outcomes among postmenopausal SA women residing in Northern California and compares these findings to an age-matched cohort of Chinese and White women.

Material and methods

Population cohort

Kaiser Permanente Northern California is a large integrated healthcare delivery system with more than 3.2 million members annually. The population is racially and ethnically diverse, with a significant proportion of the membership consisting of Asian race, similar to state demographics. For this study, we conducted analyses within a cohort of women aged 50–85 years who underwent BMD testing on a Hologic scanner (QDR 2000, 4500 or Delphi) during 1997–2003, selecting the first BMD measurement of the femoral neck obtained during this period [10]. Women without at least one year health plan membership prior to and following the scan date and those in whom BMD data were incomplete or not electronically accessible were excluded [10].

We utilized data from health plan race/ethnicity databases and the medical record to identify women of SA race, defined by Indian, Pakistani or Sri Lankan ancestry. Several algorithms were applied. First, we identified women based on "South Asian" classification in health plan demographic databases, with verification of SA status in the medical record for those women with a non-SA first and surname name. Next, we identified additional women of non-white race classification who had an SA surname and were identified as SA in the medical record. Finally, we included women with an SA surname and designated as "other Asian race" without more specific race information (99% of these also had an SA first name).

A comparison cohort of age-matched Chinese and White women was selected within this cohort using a 1:5 ratio for Chinese and 1:10 ratio for White women. Chinese and White women were identified by specific race in health plan demographic databases among those of Asian and White race in the BMD database.

Clinical factors and fracture outcomes

Information pertaining to chronic glucocorticoid exposure in the prior year (defined by a total cumulative glucocorticoid dose equivalent of at least 1825 mg prednisone which approximates a daily prednisone dose of 5 mg/day for one year), diagnosis of rheumatoid arthritis, secondary causes of bone loss (such as diabetes mellitus, malabsorption syndrome, chronic liver disease, and osteogenesis imperfecta), estrogen-based hormone replacement therapy, and oral bisphosphonate use (alendronate, risedronate, ibandronate) were identified using electronic hospital, ambulatory and pharmacy records as previously described [10]. Oral bisphosphonate treatment following the BMD scan was calculated based on pills dispensed and dosing interval, allowing for a gap of up to 60 days between prescriptions to determine a continuous treatment exposure window. Use of systemic estrogen-based hormone therapy during follow-up was determined based on the prescription days supply, allowing for a gap of up to 30 days to determine a continuous treatment exposure window.

History of fracture occurring after age 45 was determined from hospitalization and outpatient diagnoses up to 10 years prior to scan date using the International Classification of Diseases, 9th revision (ICD 9) codes 800–829, excluding open fractures, trauma-related fractures, and fractures of the fingers, toes, facial bones and skull, as these are usually not related to osteoporosis [10]. Incident fractures of the hip (ICD-9 820.0, 820.2 and 820.8, excluding open fractures and those associated with trauma), wrist (open or closed fracture of the distal radius or ulna, ICD-9 813.4 and 813.5) and humerus (ICD-9 812.0 and 812.2, excluding open fractures and distal humerus fractures) were determined using hospitalization and outpatient diagnoses during up to 10 years of follow-up. Principal hospital discharge diagnoses were required for hip fractures and principal hospitalization, emergency room and urgent care visits (or confirmed acute fracture during orthopedic or other ambulatory care visit) were required for wrist and humerus fractures. Non-vertebral osteoporotic fractures were classified as fractures of the hip, wrist and humerus.

Statistical analyses

Differences between subgroups were compared using the chi-squared or Fisher exact tests. Incident fracture rates with 95% confidence intervals were calculated per 100,000 person-years, with up to 10 years follow-up, end of membership or December 31, 2010, whichever occurred first. Multivariable Cox proportional hazard models were conducted to examine independent predictors of incident wrist and non-vertebral osteoporotic fractures. All analyses were performed using SAS 9.1 (SAS Institute, Cary, NC).

Results

We identified a total of 449 SA women (184 classified as SA based on designation of Asian race and both SA first name and SA surname) and an additional 2245 age-matched Chinese and 4490 age-matched White women, all of whom underwent femoral neck BMD measurement during 1997–2003. In contrast to the source cohort [10] where the average age was 62.8 ± 8.6 years, postmenopausal SA women undergoing BMD testing were on average four years younger (58.4 ± 6.1 years) and more than half (62.4%) were aged 50–59 years.

The demographic and clinical characteristics of the South Asian women in comparison to the Chinese and White women are shown in Table 1. Not surprisingly, a significantly greater proportion of White women (12.3%) reported smoking compared to both SA (2.2%) and Chinese (2.9%) groups. Nearly half of the White women were also receiving hormone therapy prior to the baseline BMD scan, a significantly greater proportion than SA and Chinese women. More than three quarters of women discontinued hormone treatment within the first five years of follow-up. The SA group had the highest percentage of women with rheumatoid arthritis (2.7%) and recent glucocorticoid exposure (2.9%). A greater proportion of Whites and SAs had prior fracture after age 45 (9.6% and 7.1% respectively) compared to Chinese women (4.5%). Similar variation by race was seen for osteoporosis in the femoral neck (defined by BMD $T \leq -2.5$ g/cm^2 based on National Health and Nutrition