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SHORT COMMUNICATION

Racial/ethnic differences in hip and diaphyseal femur fractures

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Abstract
Summary Contemporary femur fracture rates were examined in northern California women and compared by race/ethnicity. During 2006–2012, hip fracture rates declined, but diaphyseal fracture rates increased, especially in Asians. Women with diaphyseal fracture were younger and more likely to be bisphosphonate-treated. These disparities in femur fracture should be further examined.
Introduction The epidemiology of diaphyseal femur fracture differs from proximal femur (hip) fracture, although few studies have examined demographic variations in the current era. This study examines contemporary differences in low-energy femur fracture by race/ethnicity in a large, diverse integrated health-care delivery system.
Methods The incidence of hip and diaphyseal fracture in northern California women aged ≥50 years old during 2006–2012 was examined. Hip (femoral neck and pertrochanteric) fractures were classified by hospital diagnosis codes, while diaphyseal (subtrochanteric and femoral shaft) fractures were further adjudicated based on radiologic findings. Demographic and clinical data were obtained from health plan databases. Fracture incidence was examined over time and by race/ethnicity.
Results There were 10,648 (97.3 %) hip and 300 (2.7 %) diaphyseal fractures among 10,493 women. The age-adjusted incidence of hip fracture fell from 281 to 240 per 100,000 women and was highest for white women. However, diaphyseal fracture rates increased over time, with a significant upward trend in Asians (9 to 27 per 100,000) who also had the highest rate of diaphyseal fracture. Women with diaphyseal fracture were younger than women with hip fracture, more likely to be of Asian race and to have received bisphosphonate drugs. Women with longer bisphosphonate treatment duration were also more likely to have a diaphyseal fracture, especially younger Asian women.
Conclusion During 2006 to 2012, hip fracture rates declined, but diaphyseal fracture rates increased, particularly among Asian women. The association of diaphyseal fracture and bisphosphonate therapy should be further investigated with examination of fracture pattern.

Keywords Asian · Femoral neck · Femoral shaft · Femur fracture · Hip fracture · Osteoporosis · Pertrochanter · Subtrochanter

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Introduction

Several population studies over the past two decades have examined rates of hip and diaphyseal femur fractures [1–4],

the latter including both subtrochanteric and femoral shaft fractures [5–7]. While diaphyseal fractures account for only a small proportion of fractures involving the femur, attention has increased following case reports of atypical fracture in women with prolonged bisphosphonate (BP) exposure [8–10]. Nieves and colleagues [2] found that the incidence of diaphyseal femur fracture remained stable among older US women between 1996–2006, while the incidence of typical hip fractures (femoral neck and pertrochanter) declined from 600 to 400 per 100,000 person-years during this same time period. Wang and Bhattacharyya [6] similarly reported declining rates of typical hip fracture from 1,020 to 697 per 100,000 during 1996–2007 temporally associated with rising use of BP drugs, but noted an increase in subtrochanteric fractures from 28 to 34 per 100,000 during 1999–2007. These findings, based on identification of fractures using coded hospital diagnoses, suggest that the epidemiology of hip and diaphyseal fractures is changing.

Using 2-year data from Kaiser Permanente Northern California (KPNC) with exclusion of peri-prosthetic and distal femur fractures, we previously found that about 3 % of femur fractures anatomically localize to the femoral diaphysis [11, 12]. Identification of diaphyseal fractures required radiologic review, as only 26 % of subtrochanteric-coded fractures were actually within the subtrochanteric region [11] defined according to Orthopedic Trauma Association (OTA) and modified *Arbeitsgemeinschaft fur Osteosynthesesfragen* (AO) criteria [13, 14]. Preliminary findings were also notable for a higher proportion of Asian women with diaphyseal fracture compared to hip fracture, where Asians also contributed the largest subset of women experiencing an atypical femur fracture [11, 12].

Using these same OTA criteria for subtrochanteric fracture, Ng and colleagues [5] observed an overall increase in non-hip femur fractures among Olmsted County Minnesota women, with an age-adjusted incidence of 20 per 100,000 in 1984–1995 rising to 29 per 100,000 in 1996–2007. This study, conducted in women mostly of white race [5], was among the first to examine longitudinal changes in the incidence of diaphyseal fractures, with anatomic fracture site adjudication based on radiologic review. However, few studies have examined racial/ethnic differences in diaphyseal femur fracture in the current era.

In the present study, we examined the incidence and temporal trend of hip and diaphyseal fracture within a diverse population of older women receiving care in KPNC during 2006–2012. We hypothesized that hip fracture rates would decrease and diaphyseal fracture rates would increase over the period of observation. We further hypothesized that postmenopausal women suffering these two types of fracture would differ by race/ethnicity.

Methods

Cohort identification

The source population for this study included KPNC, a large, integrated health-care delivery system with over 3 million members. Centralized electronic databases for hospitalization, ambulatory, pharmacy, radiology, and operative records have been maintained since 1995, with digital radiographic images since 2005. For this study, we identified women aged ≥50 years old with a principal hospital discharge diagnosis of femur fracture between January 1, 2006–December 31, 2012 at a KPNC hospital, based on the *International Classification of Diseases, Ninth Revision* (ICD-9) codes: *femoral neck* (820.0x, 820.8x), *pertrochanteric* (820.20, 820.21), *subtrochanteric* (820.22), and *femoral shaft* (821.0) fractures, not including open fractures (ICD-9 820.1x, 820.3x, 820.9x, 821.1x) and those associated with high-energy trauma (secondary ICD-9 diagnoses E800-848, N=195). The first qualifying femur fracture for each woman per calendar year was included, with fracture admissions to a non-KPNC hospital (and not transferred to a KPNC facility) excluded (N=676, 5.6 %). Femoral neck and pertrochanteric fractures were classified as *hip* fracture, and subtrochanteric and femoral shaft fractures were classified as *diaphyseal* fracture. These data include 2,865 previously reported femur fractures among KPNC women during 2007–2008 [11, 12].

Adjudication of subtrochanteric and femoral shaft fractures

Since a high concordance between ICD-9-coded diagnoses for femoral neck (96.1 %) and pertrochanter (94.7 %) fractures was previously established [11], anatomic assignment of these fractures was based on ICD-9-coded hospital discharge diagnoses. However, subtrochanteric and femoral shaft-coded fractures were classified after additional radiologic review by an orthopedic trauma surgeon (CDG) using OTA (modified AO) criteria as previously described [11, 14]. Subtrochanteric fractures were defined as fractures occurring within 5 cm distal to the lower border of the lesser trochanter [11]; femoral shaft fractures were defined as fractures occurring below the subtrochanter and up to but not including the supracondylar metaphyseal flare [12].

Demographic and clinical characteristics

Age at fracture (or on June 30 for the qualifying membership year for population denominator estimates) and self-reported race/ethnicity were classified based on health plan databases with assignment of race category and a separate Hispanic ethnicity indicator. Race/ethnicity was classified as non-Hispanic white, non-Hispanic black, Asian and Hispanic. Filipinas and other Asians who were assigned both Asian race

and Hispanic ethnicity (1 % of the cohort) were classified as Asian for these analyses. Oral BP exposure (alendronate, risedronate, and ibandronate) was examined using pharmacy databases with calculation of total treatment duration based on day supply and a 60-day allowable gap between prescriptions as previously described [12]. Recent oral BP exposure was defined as ≥2 filled prescriptions within 12 months prior to fracture.

Statistical analyses

Differences between women with hip versus diaphyseal fracture were compared using Student's *t* test (for age) or chi-square test (for racial/ethnic distribution and BP exposure category). The trend in proportion of diaphyseal fractures across increasing BP exposure category was examined using the Cochrane-Armitage test. The overall incidence of fracture (with 95 % confidence interval, CI) was examined by year based on the number of age-eligible KPNC female members within the calendar year, with rates adjusted for age using the 2010 U.S. Census Bureau standard population data [15]. Age-adjusted fracture incidence was also examined by race/ethnicity, excluding 4–6 % of the age-eligible KPNC female membership with unknown race and 4 % with other/multiple races. Trends in age-adjusted fracture incidence were examined using generalized estimating equations to account for repeated measurements from the same subjects over time and to derive valid standard errors; trends were estimated with the slope of a weighted linear regression of fracture incidence (overall or by race) on the year counter with weights defined by 2010 census age distributions. Racial/ethnic differences in age-adjusted fracture incidence for 2012 were examined using linear combinations of the coefficients of a saturated linear regression of fracture incidence on both race and age group. All analyses were conducted using SAS version 9.3 (Cary, NC), and a p value of <0.05 was considered statistically significant.

Results

We initially identified 11,192 qualifying femur fractures among 10,682 women aged ≥50 years during 2006–2012. There were 244 fractures (207 peri-prosthetic, 17 distal femur, 5 greater/lesser trochanter only, and 15 indeterminate fractures) subsequently excluded after radiologic review. Consistent with prior observations [12], peri-prosthetic fractures accounted for nearly half (45.4 %) of all femoral shaft-coded fractures. Furthermore, the majority of subtrochanteric-coded fractures (70.4 %) were reclassified to hip (mostly pertrochanteric) fracture after radiologic review.

The analytic dataset included 10,948 femur fractures among 10,493 women. Most fractures (97.3 %) were localized to the femoral neck and pertrochanter, with the remaining 2.7 % occurring in the femoral diaphysis [11]. Only 6.6 % of fractures occurred in women aged 50–64 years, while over half (65.0 %) occurred in women aged ≥80 years. Women experiencing a diaphyseal fracture were significantly younger compared to those experiencing hip fracture (75.5±10.6 vs. 81.6±9.4 years old, respectively, $p<0.001$). The racial/ethnic distribution for women with hip fracture was 81.2 % white, 2.9 % black, 6.5 % Hispanic, 5.4 % Asian, and 3.9 % of other or unknown race, significantly different ($p<0.001$) from the distribution of women with diaphyseal fracture, where less than half were white and more than one third were Asian (47.7 % white, 4.7 % black, 8.3 % Hispanic, 34.7 % Asian, and 4.7 % of other/unknown race).

Among women with either type of femur fracture, 35.7 % had evidence of prior (oral) BP exposure, with a median treatment duration of 1.4 years (interquartile range 0.4–4.0 years) at the first qualifying fracture. Among the 3,745 women with oral BP exposure before fracture, 662 (17.7 %) had received BP for 5 or more years and 1,444 (38.6 %) received at least two prescriptions within the 1 year prior to fracture. The remaining 64.3 % with femur fracture were BP treatment-naïve. Table 1 shows the distribution of fracture site by age, race/ethnicity, and prior BP exposure. Women with diaphyseal fracture were more likely to have recent BP exposure compared to those with hip fracture ($p<0.01$ overall and within each age-race group), with differences especially striking among women of Asian race where approximately 80 % of Asians with diaphyseal fracture received BP within the prior year compared to less than 20 % of Asians with hip fracture (Table 1, recent BP). Increasing BP duration was also associated with a greater proportion of fractures occurring in the femoral diaphysis, primarily in younger women and those of Asian race (Table 1, diaphyseal proportion). In contrast, a very low proportion of women naïve to BP experienced diaphyseal fracture (95–99 % of fractures in women naïve to BP occurred in the hip).

During the 7-year observation period, the annual age-adjusted incidence of hip fracture fell from 281 to 240 per 100,000 women ($p<0.001$ for trend), largely reflecting the reduction in hip fractures among women of white race (Fig. 1). The percent reduction in hip fractures among women aged ≥80 years was similar (1,506 to 1,299 per 100,000 women) to the entire cohort. In contrast, the age-adjusted incidence of diaphyseal femur fracture increased from 3 to 8 per 100,000 during 2006–2012 ($p<0.001$ for trend), with a significant increase in diaphyseal fracture incidence among Asian women (9 to 27 per 100,000, $p<0.01$ for trend; Fig. 1, peak incidence 37 per 100,000 in 2011). When these analyses were restricted to the subset of women aged 50–79 years old, rates of hip fracture were relatively stable except for modest

Table 1 Age, race, and bisphosphonate (BP) exposure in women with femur fracture. Mean ± standard deviation and column percentages provided

Femur fractures in women aged 50–79 years old (*N*=3,717)											
	All women (*N*=3,717)		White (*N*=2,871)			Asian (*N*=299)			Other non-white (*N*=547)		
	Hip *N*=3,541	Diaphysis *N*=176	Hip *N*=2,802	Diaphysis *N*=69	Diaphyseal proportion by BP[a]	Hip *N*=228	Diaphysis *N*=71	Diaphyseal proportion by BP[a]	Hip *N*=511	Diaphysis *N*=36	Diaphyseal proportion by BP[a]
Age (years)	71.1±7.0	68.6±7.0*	71.1±7.0	67.5±7.3*		71.4±7.1	69.3±6.2*		71.2±7.1	69.3±7.6	
BP duration											
None	2,465 (69.6 %)	58 (32.9 %)	1,941 (69.3 %)	30 (43.5 %)	0.02	163 (71.5 %)	9 (12.7 %)	0.05	361 (70.7 %)	19 (52.8 %)	0.05
<3.0 years	781 (22.1 %)	29 (16.5 %)	628 (22.4 %)	10 (14.5 %)	0.02	38 (16.7 %)	12 (16.9 %)	0.24	115 (22.5 %)	7 (19.4 %)	0.06
3–4.9 years	142 (4.0 %)	22 (12.5 %)	105 (3.7 %)	8 (11.6 %)	0.07	18 (7.9 %)	12 (16.9 %)	0.40	19 (3.7 %)	2 (5.6 %)	0.10
≥5.0 years	153 (4.3 %)	67 (38.1 %)	128 (4.6 %)	21 (30.4 %)	0.14	9 (3.9 %)	38 (53.5 %)	0.81	16 (3.1 %)	8 (22.2 %)	0.33
Recent BP[b]	403 (11.4 %)	104 (59.1 %)*	312 (11.1 %)	32 (46.4 %)*	0.09	34 (14.9 %)	58 (81.7 %)*	0.63	57 (11.2 %)	14 (38.9 %)*	0.20
Femur fractures in women aged ≥80 years old (*N*=6,776)											
	All women (*N*=6,776)		White (*N*=5,538)			Asian (*N*=361)			Other non-white (*N*=877)		
	Hip *N*=6,665	Diaphysis *N*=111	Hip *N*=5,471	Diaphysis *N*=67	Diaphyseal proportion by BP[a]	Hip *N*=333	Diaphysis *N*=28	Diaphyseal proportion by BP[a]	Hip *N*=861	Diaphysis *N*=16	Diaphyseal proportion by BP[a]
Age (years)	87.0±4.7	86.2±5.1	87.0±4.7	86.6±5.4		86.4±4.5	84.5±3.7*		86.8±4.7	87.6±5.7	
BP duration											
None	4,188 (62.8 %)	37 (33.3 %)	3,448 (63.0 %)	26 (38.8 %)	0.01	194 (58.3 %)	4 (14.3 %)	0.02	546 (63.4 %)	7 (43.8 %)	0.01
<3.0 years	1,692 (25.4 %)	26 (23.4 %)	1,368 (25.0 %)	17 (25.4 %)	0.01	86 (25.8 %)	4 (14.3 %)	0.04	238 (27.6 %)	5 (31.2 %)	0.02
3–4.9 years	377 (5.7 %)	14 (12.6 %)	314 (5.7 %)	9 (13.4 %)	0.03	23 (6.9 %)	5 (17.9 %)	0.18	40 (4.7 %)	0	0
≥5.0 years	408 (6.1 %)	34 (30.6 %)	341 (6.2 %)	15 (22.4 %)	0.04	30 (9.0 %)	15 (53.6 %)	0.33	37 (4.3 %)	4 (25.0 %)	0.10
Recent BP[b]	882 (13.2 %)	55 (49.6 %)*	702 (12.8 %)	27 (40.3 %)*	0.04	61 (18.3 %)	22 (78.6 %)*	0.27	119 (13.8 %)	6 (37.5 %)*	0.05

*$p<0.05$ comparing hip versus diaphysis

[a] Proportion of diaphyseal fractures (among femur fractures) by BP duration. The trend test was significant across increasing BP duration category ($p<0.05$)

[b] Recent BP=2 BP prescriptions in the year prior to fracture

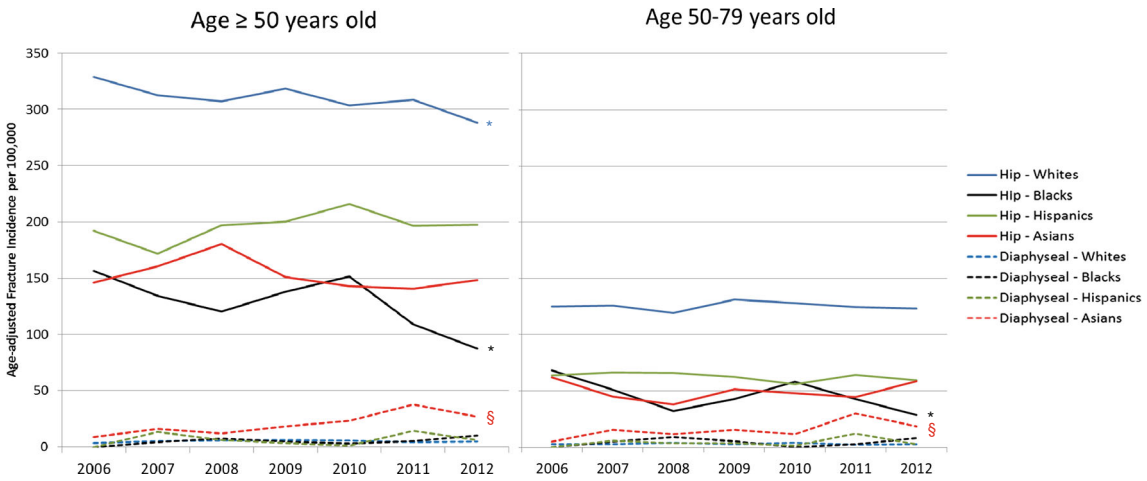

Fig. 1 Annual age-adjusted incidence of hip and diaphyseal fracture by race/ethnicity. *Significant downward trend in proximal hip fracture incidence over time for white women ($p<0.01$) and black women ($p<0.05$). §Significant upward trend in diaphyseal fracture incidence over time for Asian women ($p<0.01$)

declining rates in black women. However, an upward trend in diaphyseal fracture incidence remained for Asian women in this younger age category.

In 2012, the age-adjusted incidence of hip fracture was highest among white women (288 per 100,000), followed by Hispanic (198), Asian (148), and black (87) women (per 100,000, $p<0.05$ for all comparisons). In contrast, the age-adjusted incidence (per 100,000) of diaphyseal fractures was highest among Asian women (27) compared to black (10), Hispanic (6), and white (5) women ($p<0.001$ comparing Asians to other race/ethnicities, with no significant differences among blacks, Hispanics, and whites). For the subset of women aged 50–79 years old, the age-adjusted incidence of hip fracture was only 3-fold higher than that of diaphyseal fracture for Asian women, whereas the incidence of hip fracture exceeded that of diaphyseal fracture by more than 40-fold for white women (59 hip and 19 diaphyseal fractures per 100,000 Asian women; 123 hip and 3 diaphyseal fractures per 100,000 white women).

Discussion

This study examined contemporary trends in femur fracture in a diverse multiethnic population of older US women and found significant racial/ethnic differences in hip and diaphyseal femur fracture. Consistent with our prior analyses of data drawn from 2007–2008 [11, 12], most fractures occurred in the hip, with only 3 % localizing to the femoral diaphysis after anatomic assignment. During the 7-year period of observation from 2006–2012, a decline in the age-adjusted incidence of hip fractures was evident. In contrast, there was an increase in diaphyseal fracture incidence, with a strong upward trend evident in Asian women.

Other US studies have demonstrated declining incidence of hip fracture in older women [2, 6], variously ascribed to increasing use of BP drugs for osteoporosis [6], other interventions for fracture prevention, and secular trends in bone mineral density [16]. Adams et al. [1] examined a similar health-care delivery system in Southern California during 1997–2006 and reported a 15 % decline in the incidence of hip fracture which they attributed in part to implementation of an interdisciplinary osteoporosis management and fracture prevention program. Data from older Medicare beneficiaries between 2000 and 2009 also demonstrate declining rates of hip fracture among white women, with nonsignificant declines in blacks and Asians and minimal change in Hispanic women [17]. While earlier increases in hip fracture have been observed in California Hispanics, with a near doubling of fracture incidence between 1983 and 2000 [18], differences during the period of 2006–2012 were not seen for the Hispanic women in our study. We were unable to examine trends based on specific Hispanic origin, although the majority of current California Hispanics are of Mexican origin.

Fewer studies have examined diaphyseal fracture rates in the contemporary era. Investigators using ICD-9-coded diagnoses to identify diaphyseal fractures in large-population studies found that the incidence of diaphyseal femur fractures was stable or slightly increasing [2, 6]. In Olmsted County, Minnesota, the incidence of radiographically confirmed non-hip femur fractures rose from 41 per 100,000 during 1984–1995 to 76 per 100,000 during 1996–2007 among largely white women aged 60 years and older [5]. Our study found an increase in the incidence of diaphyseal fracture, in part due to considerably higher rates of diaphyseal fractures among Asian women. Within our fracture cohort, an association between increasing length of BP exposure and greater proportion experiencing diaphyseal fractures was also seen, particularly among younger Asian women.

Why would Asian women be more likely to suffer diaphyseal fracture than their counterparts? The type of femur fracture occurring in Asians may relate to femur geometry, BP therapy, treatment adherence and persistence, or unique unknown physiologic and/or genetic factors. In addition to preliminary data from KPNC [12], two large population studies from Sweden and southern California [19, 20] reported an association of atypical femoral diaphysis fracture with increasing length of BP exposure. Data from Kaiser Permanente Southern California also noted a large proportion of Asians (49.3 %) among cases of atypical fracture [20], similar to early findings from KPNC [12].

One of the strengths of our study is the inclusion of a large ethnically diverse urban and suburban patient population within an integrated health-care delivery system where centralized electronic databases of femur fracture events are available, including digital radiologic images since 2005 and pharmacy records since 1995. Thus, we were able to examine both hip and diaphyseal fracture incidence over time, including differences by race/ethnicity and the relationship of fracture site and BP exposure. However, these data included only fractures managed within KPNC hospitals and did not encompass the small percentage of women with femur fracture (5.6 %) who received care at non-KPNC hospitals only. Furthermore, we cannot exclude the possibility of changing patterns in femur fracture coding over time and rare miscoding of diaphyseal fractures, although this would be unlikely to substantively affect reported trends. Finally, because our analyses primarily focused on patterns in fracture incidence rather than underlying causal factors, we did not investigate other clinical risk factors and associated comorbidities that might impact fracture risk. Future steps include examination of atypical fractures, as well as differences in BP adherence and persistence by race/ethnicity.

In summary, while overall hip fracture rates have declined especially among white women, we observed an increase in diaphyseal fracture rates, most notable among Asian women. These findings suggest that there may be important racial disparities in femur fracture that should be considered when weighing the risks and benefits of long-term osteoporosis management.

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