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ORIGINAL ARTICLE

Ethnic difference of clinical vertebral fracture risk

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Abstract
Summary Vertebral fractures are the most common osteoporotic fractures. Data on the vertebral fracture risk in Asia remain sparse. This study observed that Hong Kong Chinese and Japanese populations have a less dramatic increase in hip fracture rates associated with age than Caucasians, but the vertebral fracture rates were higher, resulting in a high vertebral-to-hip fracture ratio. As a result, estimation of the absolute fracture risk for Asians may need to be readjusted for the higher clinical vertebral fracture rate.

Introduction Vertebral fractures are the most common osteoporotic fractures. Data on the vertebral fracture risk in Asia remain sparse. The aim of this study was to report the incidence of clinical vertebral fractures among the Chinese and to compare the vertebral-to-hip fracture risk to other ethnic groups.

Methods Four thousand, three hundred eighty-six community-dwelling Southern Chinese subjects (2,302 women and 1,810 men) aged 50 or above were recruited in the Hong Kong Osteoporosis Study since 1995. Baseline demographic characteristics and medical history were obtained. Subjects were followed annually for fracture outcomes with a structured questionnaire and verified by the computerized patient information system of the Hospital Authority of the Hong Kong Government. Only non-traumatic incident hip fractures and clinical vertebral fractures that received medical attention were included in the analysis. The incidence rates of clinical vertebral fractures and hip fractures were determined and compared to the published data of Swedish Caucasian and Japanese populations.

Results The mean age at baseline was 62±8.2 years for women and 68±10.3 years for men. The average duration of follow-up was 4.0±2.8 (range, 1 to 14) years for a total of 14,733 person-years for the whole cohort. The incidence rate for vertebral fracture was 194/100,000 person-years in men and 508/100,000 person-years in women, respectively. For subjects above the age of 65, the clinical vertebral fracture and hip fracture rates were 299/100,000 and 332/100,000 person-years, respectively, in men, and 594/100,000 and 379/100,000 person-years, respectively, in women. Hong Kong Chinese and Japanese populations

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have a less dramatic increase in hip fracture rates associated with age than Caucasians. At the age of 65 or above, the hip fracture rates for Asian (Hong Kong Chinese and Japanese) men and women were less than half of that in Caucasians, but the vertebral fracture rate was higher in Asians, resulting in a high vertebral-to-hip fracture ratio.
Conclusions The incidences of vertebral and hip fractures, as well as the vertebral-to-hip fracture ratios vary in Asians and Caucasians. Estimation of the absolute fracture risk for Asians may need to be readjusted for the higher clinical vertebral fracture rate.

Keywords Asian · Chinese · Fracture incidence · Osteoporosis · Vertebral fracture

Introduction

Osteoporosis is a disease associated with decreased bone mass and bone strength and leads to increased fracture risk. Osteoporosis has become a major public health concern in the past decade due to the high prevalence and health care costs associated with it. Vertebral fractures, despite being the most common osteoporotic fracture, accounting for nearly 50% of all osteoporotic fractures, have received little attention compared to hip fractures. Data on the epidemiology of vertebral fractures in Asia remain sparse [1]. It has been shown that both symptomatic and asymptomatic vertebral fractures are predictors of future osteoporotic fractures [2] and are associated with physical deformity, as well as reduced mobility and quality of life [3, 4], and increased mortality [5, 6].

Unfortunately, obtaining accurate information on vertebral fracture is made difficult by the variable presentation of symptoms and the lack of a gold standard for the definition of vertebral fracture. Although vertebral fractures typically present with back pain, height loss and kyphosis, up to 75% of vertebral fractures were not diagnosed clinically due to the absence of specific symptoms in some cases and the difficulty in determining the cause of these physical symptoms [7]. Numerous methods were developed to help objectively identify morphometric vertebral fractures. The more important ones include the quantitative methods of measuring vertebral body height on radiographs [8, 9], as well as the semi-quantitative method proposed by Genant et al. [10]. These assessments use different cut-offs to define the presence of a vertebral fracture, and the reference for comparison of vertebral height could either be the individual's adjacent vertebral body or the mean of a reference population. These variations affected the sensitivity and specificity of the assessments resulting in high false-negative and false-positive rates and also created a considerable discordance of results in assessing the prevalence and incidence of vertebral fractures [11–13]. Also, vertebral fractures can also be confused with normal variants in vertebral shape or other end-plate deformities caused by other diseases Therefore, the exclusion of other vertebral deformities in order to make a correct diagnosis of vertebral fracture can only be accomplished by visual inspection and expert interpretation of the radiograph [14].

The lack of a gold standard for a definition of vertebral fracture makes it difficult to assess the true incidence of vertebral fractures. Previous cross-sectional and retrospective studies have suggested a similar prevalence of vertebral fracture in Asians and Caucasians [15–19] despite their lower hip fracture rates [20]. The World Health Organization (WHO) developed fracture risk assessment algorithms (FRAX®) to provide 10-year probabilities of hip fracture and major osteoporotic fracture (clinical spine, hip, humerus and forearm) based on a clinical risk factor profile and country-specific fracture and death incidence. The most complete models available are from the UK, Sweden, Japan and the US since the epidemiology of the relevant fractures is established [21]. However, the FRAX® models for some other countries (France, Spain, Italy, Turkey, Mainland China Hong Kong, etc.) are based on hip fracture risk alone due to the lack of ethnic-specific data and use assumptions, i.e. the site of fracture ratios observed from the Swedish population, to derive the relevant risk functions for other major fractures including vertebral fractures [22]. The objectives of this study were (1) to report the incidence rates of clinical vertebral and hip fractures in a prospective cohort of Chinese men and women, (2) to compare the clinical vertebral and hip fracture rates with those of other ethnic groups, and (3) to evaluate whether a fracture prediction model that assumes a universal spine-to-hip fracture ratio may be biased.

Methods

Hong Kong

This is the first prospective study of clinical vertebral fracture in an Asian population and is a part of the prospective Hong Kong Osteoporosis Study in which community-dwelling Southern Chinese men and women aged 50 or above were recruited from health fairs held in various districts in Hong Kong since 1995 [19, 23]. Baseline demographic data including anthropometric measurements, low-trauma fracture history after the age of 45 years, age at menopause and the use of hormone replacement therapy, medical history and symptoms associated with clinical vertebral fractures were obtained using a structured questionnaire at baseline. Subjects with conditions associated with vertebral deformity, including

osteomalacia, Paget's disease, Scheuermann's disease, hyperparathyroidism, renal bone disease and malignancy with bone metastasis, were excluded. Information on symptoms associated with vertebral fractures was also collected, including difficulty in bending forward, kyphosis (occiput-to-wall >0 cm and/or gap between the costal margin and iliac crest <3 fingerbreadths), low back pain and height loss more than 2 cm since the age of 25 years. These data were collected from interviews conducted by a trained research assistant.

All subjects were followed annually via telephone interviews using a structured questionnaire for assessment of the clinical outcome of incident fractures, falls, hospitalization, use of anti-osteoporotic medications, living status and functional status. Subjects who commenced anti-osteoporosis medication prior to the occurrence of a primary fracture were excluded. Medical history and incident fractures were verified with the computerized patient information system of the Hospital Authority of the Hong Kong Government. For this study, only non-traumatic incident hip fractures and clinical vertebral fractures were included in the analysis. Hip fractures were defined as having a diagnosis coded as International Classification of Disease, Tenth Revision (ICD-10) S72.0-S72.2 (fracture of the femoral neck, intertrochanteric, trochanteric, or subtrochanteric), and clinical vertebral fractures were identified in subjects who received medical attention from a physician with a diagnosis coded as ICD-10S22.0-S22.1 (fracture of the thoracic vertebra/multiple thoracic vertebrae), S32.0 or S32.7 (fracture of the lumbar vertebra/multiple lumbar vertebrae). Pathological fractures or fractures caused by traffic accidents or falls from standing heights were excluded. The study was approved by the Institutional Review Board of the University of Hong Kong and the Hong Kong West Clusters Hospital of the Hospital Authority.

Japan

The hip and clinical vertebral fracture incidence rates for the Japanese were obtained from previously published data used to develop the Japanese version of FRAX® [24]. The hip fracture incidence rate was based on data from a census study in Tottori Prefecture, Japan, in 1994 [25]. The incidence of vertebral fracture was based on data obtained from the Adult Health Study in Hiroshima, Japan [26]. Participants were followed through biennial medical examination including radiology assessments since the establishment of the study in 1958. A total of 2,613 subjects (763 men and 1,593 women) who attended at least two follow-up examinations in 1994 to 2000 were included in the analysis. An incident morphometric vertebral fracture was diagnosed by lateral and posterior–anterior chest and spinal X-rays using the semi-quantitative assessment [12], in which a decrease of at least 20% in height of any vertebral body from initial reading to the end of the study was defined as a morphometric vertebral fracture. Since the incidence of clinical vertebral fracture was not known in Japan, the ratio of clinical fracture to morphometric fracture incidence was assumed to be the same in Japan as it was for Sweden when the Japanese version of FRAX® was developed, i.e. 30% of morphometric vertebral fractures were assumed as clinical fractures [24, 27].

Sweden

The incidence rates of hip and clinical vertebral fractures for Swedish Caucasians were also obtained from a previously published study by Kanis et al., in which all incident fractures, including hip fractures (1991) and clinical vertebral fractures (1993 and 1994) were identified from files at the Department of Diagnostic Radiology in Malmo, Sweden, for the relevant year. Only vertebral fractures that came to clinical attention were captured, and subjects who previously sustained a fracture of the same type were excluded from analysis. The annual incidences of hip and clinical vertebral fractures were calculated for men and women by age [28].

Statistical analyses

Baseline characteristics of the Chinese subjects are expressed in means±SD for continuous variables and in percentage for categorical variables. Time to incident hip or vertebral fractures was calculated according to the date of X-ray reports or physician's consultations when the diagnosis was made. The average follow-up period for all subjects was 4.0±2.8 (range, 1 to 14) years, with a total follow-up of 14,733 patient-years. Subjects who had received anti-osteoporosis medication after sustaining a fracture during the follow-up period or those who deceased at the time of analysis were analysed up to their time of treatment initiation or last contact time point. Incidence rates were reported as rate per 100,000 person-years. The incidence rates of vertebral and hip fractures were compared to the published data from Japan and Sweden. Vertebral-to-hip fracture ratios were used to demonstrate the proportion of vertebral fractures in relation to hip fractures in different populations.

Results

A total of 4,116 Southern Chinese subjects (2,302 women and 1,810 men) aged 50 or above were included in the analysis. The mean age at baseline was 62±8.2 years for

women and 68±10.3 years for men. Of the women, 37.2% and 63.4% of men were above the age of 65 years. Baseline demographic information and characteristics are shown in Table 1. Of the men, 55.5% and 72.1% of women reported having difficulty bending forward, kyphosis, low back pain and/or height loss >2 cm since the age of 25. However, only 2.7% of men and 5.5% of women reported a history of past clinical vertebral fracture.

Two hundred and sixty-seven subjects had died at the time of analysis (77 women and 190 men), and 353 patients (333 women and 19 men) received anti-osteoporosis medication after sustaining a fracture during the follow-up period. The data for these subjects were analysed up to their last contact time point or time of treatment initiation, respectively. During the follow-up period, 57 clinical vertebral fractures and 34 incident hip fractures were reported (11 vertebral fractures and 10 new hip fractures in men; 46 vertebral fractures and 24 new hip fractures in women). The incidence for vertebral fractures was 194 per 100,000 person-years in men and 508 per 100,000 in women (overall female/male ratio=2.6:1), and the incidence for hip fractures was 176 per 100,000 person-years in men and 265 per 100,000 person-years in women (female/male ratio=1.5:1). Table 2 shows the incidence rates of clinical vertebral and hip fractures according to sex and age groups. Both clinical vertebral and hip fracture incidences increased exponentially with increasing age in both sexes. Men aged 50–55 years had a fracture incidence of 50 per 100,000 person-years for the vertebra and 10 per 100,000 for the hip versus men aged 85 years and above who have a vertebral fracture incidence of 954 per 100,000 person-years and a hip fracture incidence of 477 per 100,000 person-years. Similarly, incidences of vertebral and hip fracture increase from 219 and 16 per 100,000 person-years in women 50 years of age to 2,689 and 1,377 per 100,000 person-years, respectively, at age 85. Overall, men older than 65 years have a vertebral fracture incidence of 299 per 100,000 person-years and hip fracture incidence of 332 per 100,000 person-years, and the overall incidence of vertebral and hip fractures for women older than 65 years were 594 per 100,000 person-years and 379 per 100,000 person-years, respectively.

The fracture incidence of Chinese subjects was compared to those of the Swedish and Japanese populations. The incidence rates of hip fractures in Caucasian men and women rose exponentially with age, whereas the rise was near linear for vertebral fractures. In contrast, for Asian women in Hong Kong and Japan, the incidence rate for vertebral fractures rose exponentially with age, whereas the rise was near linear for hip fractures. In Asian men, both the incidence rates of vertebral and hip fractures rose near linearly with age. The hip fracture incidences in Hong Kong men and women were similar to those of Japan but much lower than those of the Caucasian population in Sweden. For example, the hip fracture rates for Hong Kong men and women aged 65 to 69 years old were only 49% and 33%, respectively, of those of the Caucasian men and women in the same age group. However, the incidence of vertebral fractures in Asian men was similar to that of Caucasian men; and Asian women have a much higher

Table 1 Clinical characteristic of the study population (Mean±SD)

	Men (n=1,810)	Women (n=2,302)
Years of follow-up (mean±SD (range))	3.5±2.9 (1–14)	4.7±2.6 (1–14)
Age (year)	68±10.3 (50–99)	62±8.2 (50–91)
Height (cm)	164.6±6.5	152.7±6.0
Weight (kg)	62.9±10.3	55.3±9.1
Body mass index (kg/m^2)	28.1±8.4	23.7±3.7
Number of postmenopausal women	–	2,229 (96%)
Age at menopause (year)	–	49.5±4.0
Current or history of hormone replacement therapy	–	217 (9.4%)
Difficulty bending forward	185 (10.2%)	365 (15.8%)
Kyphosis	78 (4.3%)	126 (5.5%)
Low back pain	510 (28.2%)	1,336 (58.0%)
Height loss >2 cm since 25 years old	442 (24.4%)	854 (37.1%)
Have at least one of the above symptoms	1,004 (55.5%)	1,660 (72.1%)
History of clinical vertebral fracture	48 (2.7%)	126 (5.5%)
History of hip fracture	24 (1.7%)	31 (1.3%)
Incident clinical vertebral fracture at follow-up	11 (0.6%)	46 (2.0%)
Incident hip fracture at follow-up	10 (0.6%)	24 (1.0%)

Table 2 Incidence (per 100,000 person-years) of hip and clinical vertebral fracture according to sex and age groups

Fracture site and age group	Men	Women	F/M
Hip			
50–54	10	16	1.6
55–59	21	31	1.5
60–64	46	57	1.2
65–69	99	103	1.0
70–74	215	273	1.3
75–79	348	527	1.5
80–84	602	1,059	1.8
85+	477	1,377	2.9
Vertebral			
50–54	50	219	4.4
55–59	111	313	2.8
60–64	165	516	3.1
65–69	95	564	5.9
70–74	226	874	3.9
75–79	450	1,205	2.7
80–84	594	2,119	3.6
85+	954	2,689	2.8

vertebral fracture incidence than Caucasian women (Fig. 1a and b). Among older women aged 80 or above, the incidence of vertebral fracture in Asians almost doubled to that of Swedish Caucasian women.

The spine-to-hip fracture ratios also differed between different Asians and Caucasians. Although vertebral fractures occur with a higher incidence earlier in life than hip fractures in both Asians and Caucasians, Asians have a much higher spine-to-hip fracture ratio than Caucasians, meaning vertebral fractures have a higher proportion to hip fractures in Asians than in Caucasians, especially among subjects younger than 65 years (Table 3).

Discussion

Vertebral fractures are the most common type of osteoporotic fractures, and they are well known as an independent predictor of future osteoporotic fractures, including both vertebral and non-vertebral fractures [22]. However, reports about the incidence of vertebral fracture are scant because of the discrepancies in the definition of vertebral fracture and the difficulties in recognizing them clinically. A

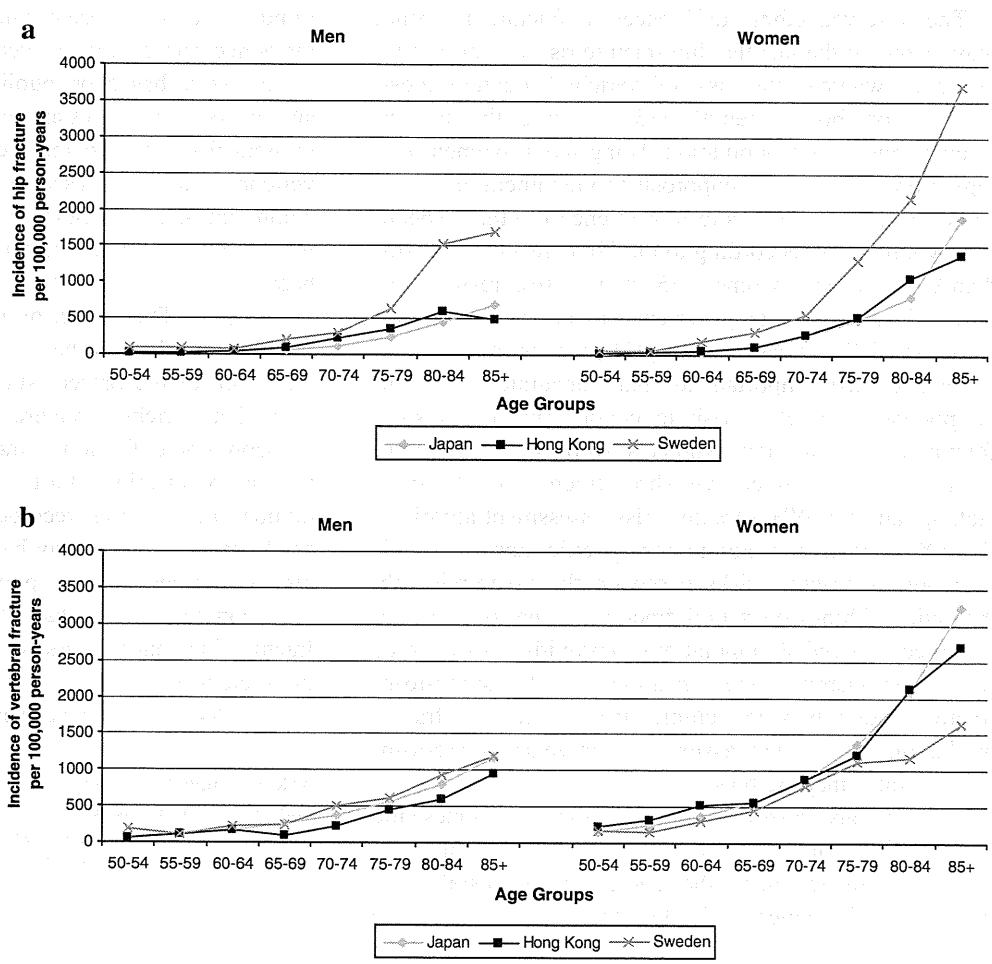

Fig. 1 Age-specific incidence rates (per 100,000 person-years) in Hong Kong compared to Japanese and Swedish Caucasians for hip fracture (**a**) and clinical vertebral fracture (**b**)

Table 3 Age- and sex-specific clinical vertebral-to-hip fracture ratio in Hong Kong compared to Japanese and Swedish Caucasians

	Men			Women		
Age group	Japan [24]	Hong Kong	Sweden [28]	Japan [24]	Hong Kong	Sweden [28]
50–54	3.9	5.0	2.2	N/A[a]	13.7	2.6
55–59	7.1	5.3	1.4	4.7	10.1	2.9
60–64	2.8	3.6	3.2	8.9	9.1	1.6
65–69	4.1	1.0	1.2	6.3	5.5	1.4
70–74	3.5	1.1	1.7	3.4	3.2	1.4
75–79	2.3	1.3	1.0	2.8	2.3	0.8
80–84	1.8	1.0	0.6	2.6	2.0	0.5
85+	1.7	2.0	0.7	1.7	1.1	0.4

[a] Clinical vertebral-to-hip fracture ratio for Japanese women aged 50–54 was not available since the hip fracture incidence for this group was zero

previous study has shown that the postmenopausal women in Hong Kong, Beijing and Taiwan have a similar prevalence of morphometric vertebral fracture as Caucasian women in the USA and Europe (about 25% in all regions), in contrast to the marked worldwide variations in the prevalence of hip fractures [21]. The present study further confirmed that, although the risk of hip fractures in Asians was low, Asian men do have a vertebral fracture risk similar to Caucasian men, and Asian women have an even higher clinical vertebral fracture risk than Caucasian women.

The observed ethnic differences in fracture incidences may be due to the fact that hip fracture risk was affected by fall risk, whereas the risk of vertebral fracture mostly depends on bone strength [13]. Despite the low hip fracture rate in our population, Hong Kong women had a higher prevalence of osteoporosis (bone mineral density T-score≤ -2.5 at any one site in reference to ethnic-specific peak young mean according to the ISCD recommendation) than US Caucasian women (35.8% vs. 20%, respectively) [29, 30] and a similar prevalence of about 6% in Hong Kong and US Caucasian men [31]. In view of the ethnic differences, it is important to obtain accurate information on population fracture risk to characterize the absolute fracture risk of individual subjects. At present, information on the risk of clinical vertebral fracture in Asians is lacking, and the WHO fracture risk assessment algorithms (FRAX®) estimated population-specific absolute major osteoporotic fracture risks based on the assumption that the ratio of hip-to-vertebral fracture is the same as that observed in Swedish populations to provide. However, our study demonstrated the variations of the spine-to-hip fracture ratios between ethnic groups; thus, a fracture prediction model that assumes a universal spine-to-hip fracture ratio may be biased.

Our previous prospective study on Southern Chinese men over 50 years old has shown that the FRAX® algorithm seemed to overestimate the 10-year major osteoporotic fracture risk in subjects with low fracture risk, but underestimated the risk for high-risk groups [29]. Results from the current study raise a concern that a model that presumes a ratio of vertebral fractures to hip fractures in a Swedish population might underestimate the risk of vertebral fractures in Asians, resulting in a general underestimation of the absolute risk of major osteoporotic fracture.

Strengths of this study include the use of a community-based population to investigate the incidence rate of clinical vertebral fractures. All clinical vertebral fractures and hip fractures were confirmed by the medical record. A major limitation of the present study is that the comparisons to incidence rate of clinical vertebral fracture to other ethnic groups were based on published literatures, and the data among Asian countries are scanty. Japan is the only country in Asia that reported the incidence rate on morphometric vertebral fractures based on a radiographic survey in a community-based population. Also, the Japanese data used for comparison came from the early 1990s, and there has been some evidence that hip fracture rates are increasing in Asians [20]. The impact on the change in epidemiology of fracture in Asians has not been evaluated. Another drawback of the present study is that only the incidences of clinical vertebral fractures were reported due to the lack of a common definition of morphometric vertebral fractures in other publications. Furthermore, the sample size and the number of fractures recorded in the men's cohort were small, and this study may have underestimated the fracture rates in the general male population.

In conclusion, this study demonstrated that while the hip fracture incidence in Asians is lower than in Caucasians, the incidence of clinical vertebral fractures was at least as high in Asians as in Caucasians.

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Conflicts of interest None.

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ORIGINAL ARTICLE

Longitudinal change in hip fracture incidence after starting risedronate or raloxifene: an observational study

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Abstract This study examined patients' risk profiles and adherence to treatment in relation to the effect of risedronate and raloxifene on hip fracture incidence. Administrative billing data were used to follow two cohorts of women aged 65 and older after starting therapy with either risedronate ($n = 86{,}735$) or raloxifene ($n = 37{,}726$). The fracture risk profile was described using a 6-month history period before starting therapy. Effectiveness of each therapy was evaluated by comparing the incidence of hip fractures during the first 3 months with the subsequent 12 months among women adherent (medication possession ratio >80%) compared with those non-adherent to treatment. At the start of therapy, the raloxifene cohort was younger than the risedronate cohort (median age 73 vs. 76 years) and had fewer prior fractures ($p < 0.01$ for both). In the first 3 months of therapy, hip fracture incidence was lower in the raloxifene group (0.51 per 100 person-years) compared with the risedronate group (0.94 per 100 person-years). In the subsequent 12 months, the incidence of hip fractures decreased among patients adherent to the risedronate regimen [relative risk (RR) 0.70, 95% CI 0.59–0.84, $p < 0.01$] and did not change significantly among patients adherent to the raloxifene regimen (RR 1.02, 95% CI 0.73–1.44). In poorly adherent patients, neither drug decreased hip fracture risk. Risedronate treatment in adherent patients rapidly decreased the risk of hip fractures, whereas raloxifene treatment did not.

Keywords Bisphosphonate · Hip fracture · Osteoporosis · Raloxifene · Risedronate

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Introduction

Randomized controlled clinical trials are the gold standard for measuring the efficacy of a therapy. All osteoporosis drugs approved to treat postmenopausal osteoporosis have demonstrated reduction of vertebral fractures in placebo-controlled clinical trials. Observations from non-comparative trials suggest that some drugs may reduce the incidence of vertebral fractures more efficiently than others [1–3]. Moreover, evidence for a reduction of hip fractures exists for certain drugs, including risedronate, alendronate, and zoledronate, but not with ibandronate and raloxifene [1, 4]. These apparent differences may pertain to the mode of action and

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distribution of the various drugs, and/or to the clinical characteristics of patients included in the trials. Indeed, recent data suggest that anti-fracture efficacy of osteoporosis drugs may be greater in patients with a higher 10-year fracture probability [5, 6]. Adherence to therapy is another major contributor to drug efficacy. Subjects who maintain a medication possession ratio (MPR) of ≥80% during all the observation time are usually considered adherent to treatment, and in these circumstances a higher level of efficacy is achieved [7–15]. How drug efficacy, baseline fracture risk, and adherence to therapy combine to determine fracture risk reduction in clinical practice however remains to be investigated [16].

Because health data on millions of patients on osteoporosis therapies in real-world clinical practice have been collected through administrative billing, medical records, and registries, many recent observational studies have examined the effectiveness of osteoporosis therapies for reducing clinical fractures [7–15, 17–30]. Some of these studies support that the effectiveness in reducing clinical fractures, particularly hip fractures, in actual patients varies among drugs, in keeping with the respective clinical trials [20, 26, 27, 30]. In the current observational study using administrative billing data, we first sought to describe and compare the fracture risk profile of patients initiating a bisphosphonate (risedronate) and an estrogen agonist/antagonist (raloxifene) therapy. The fracture risk profile included factors known to affect the probability of fracture such as demographic characteristics, co-morbidities, concomitant medication use, and history of prior fractures. We next sought to observe the hip fracture incidence in these patients according to their level of adherence to therapy. For this analysis, we followed two cohorts of women aged 65 and older after starting either risedronate or raloxifene therapy. Within each cohort, the baseline hip fracture incidence was defined by the 3-month period after starting therapy. To assess if therapy resulted in a change in fracture incidence over time, the fracture incidence during the subsequent 12 months on treatment was compared to the baseline incidence (first 3 months on treatment) within each cohort among women adherent to therapy as well as those who were non-adherent. Given the observed differences in the fracture risk profile of patients initiating a bisphosphonate or a selective estrogen receptor modulator, we further explored the hip fracture incidence in a subgroup of risedronate patients whose risk profile was matched more closely to those receiving a selective estrogen receptor modulator and conversely how effective a selective estrogen receptor modulator would be for reducing hip fractures among patients with a risk profile closer to those receiving a bisphosphonate.

Materials and methods

Data source

Computerized records of administrative billing provide a convenient data source for studying filled prescription use and outcomes in large populations. Records include patient-level data concerning: (1) inpatient and outpatient services specified by diagnosis codes of the International Classification of Diseases, 9th revision, clinical modification (ICD-9-CM); (2) retail and mail-order pharmacy dispensations specified by national drug codes; and (3) demographic information including sex, age, and eligibility dates of health plan coverage. The data for this study, from January 2000 through December 2008, originated from two mutually exclusive sources: Ingenix® Lab/Rx (Eden Prairie, MN) and Thomson Reuters' MarketScan® (Ann Arbor, MI). During the study period, the average number of eligible enrollees was 13 million in MarketScan, representing multiple health plans, and 12 million in Ingenix, representing a single health plan. Geographically, one half of this population was located in the states of Michigan, California, Florida, Ohio, Georgia, and Texas, and one half in the other 44 states.

Study population

The study population was comprised of two cohorts—one starting risedronate (5 or 35 mg) and one starting raloxifene (60 mg) therapy. Study patients were entered on the date of their initial filled prescription between July 2000 and December 2007. Inclusion criteria were: (1) being women ages 65 and over to provide a study population similar in age to that of the randomized controlled trials and for which clinical fractures are likely to be related to osteoporosis [31]; (2) having at least 3 months of coverage in the data source after cohort entry to provide a minimum observation period; and (3) having no diagnosis of a malignant neoplasm (ICD-9-CM codes 140–208) or Paget's disease (731.0) within 6 months prior to and 3 months after cohort entry to maximize the probability that patients were being treated for either post-menopausal osteoporosis or glucocorticoid-induced osteoporosis. Further description of subject identification is provided in Table 1.

Outcome

After patients were identified, each was followed to identify the first new hip fracture. "Hip fracture" was defined by an inpatient diagnosis of a fracture at the hip (ICD-9-CM code 820, 733.14). "New" was defined as no evidence of hip fracture in the 6 months before cohort entry.

Table 1 Identification of the study population

Risedronate	
Number of women in data source with first use of risedronate 5 mg (daily) (NDC = 001490471) or risedronate 35 mg (weekly) (NDC = 001490472) between July 2000 and December 2007; aged 65 years and over	202,028
Exclude women with less than 6 months of enrollment data before first use of bisphosphonate	−69,475
Exclude women with less than 3 months of enrollment data after first use of bisphosphonate	−7,445
Exclude women with diagnosis of Paget's disease (ICD-9 731.0) during period 6 months before and 3 months after first use of bisphosphonate	−193
Exclude women with malignancy diagnoses (ICD-9 140–208) during period 6 months before and 3 months after first use of bisphosphonate	−14,762
Exclude women with any other use of another **bisphosphonate** form in 6 months before first use of bisphosphonate	−17,025
Exclude women with any use of any *raloxifene* form during period 6 months before and 3 months after first use of bisphosphonate	−6,393
Number of women in bisphosphonate cohort	86,735
Raloxifene	
Number of women in data source with first use of raloxifene 60 mg (daily) (NDC = 000024165) between July 2000 and December 2007; aged 65 years and over	125,139
Exclude women with less than 6 months of enrollment data before first use of raloxifene	−68,314
Exclude women with less than 3 months of enrollment data after first use of raloxifene	−2,616
Exclude women with diagnosis of Paget's disease (ICD-9 731.0) during period 6 months before and 3 months after first use of raloxifene	−30
Exclude women with malignancy diagnoses (ICD-9 140–208) during period 6 months before and 3 months after first use of raloxifene	−5,897
Exclude women with any other use of another **raloxifene** form in 6 months before first use of raloxifene	−4
Exclude women with any use of any *bisphosphonate* form during period 6 months before and 3 months after first use of raloxifene	−10,552
Number of women in raloxifene cohort	37,726

NDC National Drug Code

To increase the probability of only including osteoporotic-related fractures, we excluded likely traumatic fractures by eliminating diagnoses of an open fracture or of a documented cause of injury from a transportation accident (E codes E800–E848).

Risk factors

Risk factors for fracture, which may be confounding variables, include age, fracture history, glucocorticoid use, and diagnosis of rheumatoid arthritis. Age was at the year of cohort entry. Fracture history was any fracture diagnosis at the hip, wrist, humerus, clavicle, pelvis, leg, or vertebrae in the 6 months prior to cohort entry. Glucocorticoid use was receiving 450 mg prednisone-equivalent pills within ±90 days of cohort entry—an approximation of a daily dose of 5 mg prednisone for at least 90 days [32]. A diagnosis of rheumatoid arthritis was any inpatient or outpatient diagnosis (ICD-9-CM code 714.0) within 6 months before and 3 months after cohort entry. Risk factors not available in the data source included bone mineral density, body mass index, smoking, alcohol consumption, and family history of fracture.

Statistical analysis

To calculate change in hip fracture incidence within each therapy cohort, we used a method described previously [30]. Briefly, within each cohort, fracture incidence during the first 3 months of therapy (baseline period) was compared with the fracture incidence during the subsequent 12 months among patients adherent to treatment. Fracture incidence during the baseline period after starting an osteoporosis therapy likely reflects the fracture risk of the cohort independent of any drug effect (i.e., fracture reduction does not begin immediately after the start of therapy). For the calculation of hip fracture incidence during the baseline period, the denominator was the sum of observation time within a cohort during the 3 months, and the numerator was the number of patients within a cohort with a new hip fracture during the 3 months.

For the calculation of hip fracture incidence during the subsequent 12 months, the denominator included all observation time where patients maintained a MPR of at least 80% to filled prescriptions of risedronate (5 or 35 mg) or raloxifene (60 mg). The 80% level utilized for the MPR has been suggested to provide a high level of therapy

effectiveness for bisphosphonates [7–15, 21–25]. The MPR was calculated at 3-month intervals after cohort entry. Therefore, patients with an MPR of at least 80% at the end of 3 months were followed into the subsequent 3-month period. The same process was applied at the end of 6, 9, and 12 months. The numerator was the number of patients with a new hip fracture preceded by a MPR of at least 80%. A simple ratio was used to compare the incidence of fractures between the baseline and subsequent periods. Poisson regression was used to compute the 95% confidence intervals around the ratio.

Two additional analyses were completed to further evaluate the primary analysis. One analysis assessed if there was any change in the hip fracture incidence between the first 3 months of therapy and the subsequent period of 12 months of all observation time where patients had a MPR <80% (i.e., not adherent to treatment). A second analysis attempted to equate the fracture risk profile of the two cohorts by matching. A 1:1 match on year of age (ages 65–100), fracture history (yes or no), and estrogen therapy use (yes or no) was completed so the risedronate cohort matched the raloxifene cohort. Hence, the number of strata matched on was 144 (36 × 2 × 2). If the raloxifene cohort had more patients in a stratum than the risedronate cohort, there was a reduction in the number of risedronate matches (i.e., of the 37,726 raloxifene patients; 37,501 had a match in the risedronate cohort). If the risedronate cohort had more patients in a stratum than the raloxifene cohort, then a random sample of risedronate patients was selected. The results presented in the matched cohort reflect the average of three random samples.

Results

Characteristics of patients starting risedronate or raloxifene

The study population included women 65 years of age and older who entered into a cohort on the date of their initial prescription filling for risedronate 5 mg daily or 35 mg weekly ($n = 86{,}735$) or raloxifene 60 mg daily ($n = 37{,}726$) between July 2000 and December 2007. The data source provided a record of health care utilization for the entire 15-month study period after cohort entry for approximately 75% of each cohort. At cohort entry, the patients receiving risedronate were older, had more prior fractures, had greater use of glucocorticoids, and overall appeared to be at greater risk for hip fracture than patients receiving raloxifene (Table 2).

Table 2 Characteristics of patients starting therapy

Characteristics	Risedronate	Raloxifene
Number of women in cohort	86,735	37,726
Year of cohort entry (% cohort)		
2000–2002	14	43
2003–2005	69	44
2006–2007	17	13
Age at entry (cohort median)	76	73
Age 75 and over (% cohort)	53	38
Any clinical fracture in 6 months before entry (% cohort)	9	4
Glucocorticoid use within 3 months of entry (% cohort)	6	3
Rheumatoid arthritis diagnosis within 3 months of entry (% cohort)	3	2
Estrogen use within 3 months of entry (% cohort)	14	26
Documented osteoporosis diagnosis in 6 months before entry (% cohort)	40	28
Medical specialty seen closest to entry (% cohort)		
Internal medicine/family practice	55	49
Obstetrics/gynecology	4	9
Other/undetermined	41	42
Estimated 10-year probability of hip fracture at cohort entry, cohort median[a]	6.0	4.0

For every characteristic, there is a statistical difference ($p < 0.01$) between raloxifene and risedronate cohorts based upon chi-square test for dichotomous variables and Wilcoxon rank sum test for continuous variables

[a] To summarize the impact of the available risk factors, a partial FRAX™ analysis was used to obtain an estimate of the 10-year probability of hip fracture based on age, fracture history, glucocorticoid use, and rheumatoid arthritis diagnosis, and assuming a body mass index of 25 for all (160 cm and 64 kg) in Caucasian women from the United States [6]. Among all patients in the cohort, the median FRAX value was reported

Incidence of hip fractures during the baseline period

During the 3 months after starting therapy in both cohorts, the incidence of hip fractures was higher among those of older age, prior fracture history, and glucocorticoid use, and lower among those using estrogen therapy (Table 3). During these 3 months, patients receiving risedronate, for whom a higher proportion had these risk factors, had an incidence of hip fractures of 0.94 per 100 person-years, nearly twice as high ($p < 0.01$) as the incidence among

Table 3 Hip fracture incidence in the 3 months after cohort entry by baseline characteristics

Characteristics	Risedronate			Raloxifene		
	Women	Women with fracture	Annualized incidence per 100 women	Women	Women with fracture	Annualized incidence per 100 women
Complete cohort	86,735	204	0.9	37,726	48	0.5
Year of entry						
2000–2002	12,591	32	1.0	16,090	17	0.4
2003–2005	59,778	134	0.9	16,594	24	0.6
2006–2007	14,366	38	1.1	5,042	7	0.6
Age 65–74 years	40,830	37	0.4	23,287	13	0.2
Age 75 and over	45,905	167	1.5	14,439	35	1.0
Clinical fracture prior to entry	8,006	44	2.2	1,466	4	1.1
No clinical fracture	78,729	160	0.8	36,260	44	0.5
Glucocorticoid use	5,261	18	1.4	1,054	2	0.8
No use	81,474	186	0.9	36,672	46	0.5
Hormone therapy use	12,292	10	0.3	9,938	3	0.1
No use	74,443	194	1.0	27,788	45	0.6
Documented osteoporosis	34,764	93	1.1	10,637	21	0.8
No documentation	51,971	111	0.9	27,089	27	0.4
Medical specialty						
Internal medicine	47,508	130	1.1	18,495	28	0.6
Gynecology	3,977	1	0.1	3,349	3	0.4
Other	35,250	73	0.8	15,882	17	0.4
Ten-year hip fracture probability						
1.2–6.0%	45,067	29	0.3	25,698	15	0.2
6.1–34.0%	41,668	175	1.7	12,028	33	1.1

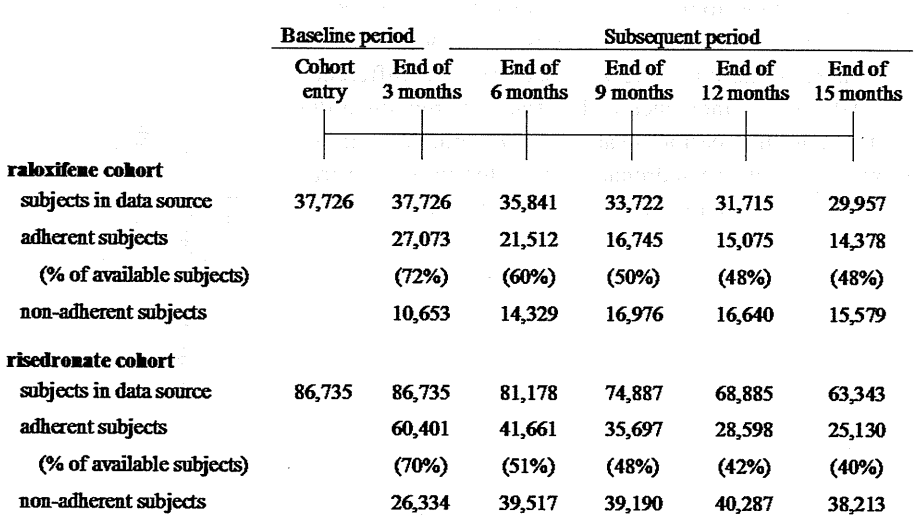

Fig. 1 Follow-up for measure of fracture incidence

those receiving raloxifene, which was 0.51 per 100 person-years.

Adherence to treatment

Patients with a MPR of at least 80% were considered to be treatment adherent and those with less than 80% MPR were considered to be non-adherent. At the end of the first 3 months, 72% of patients in the raloxifene cohort were adherent, while 70% of the patients were adherent in the risedronate cohort. These numbers continued to decrease during the subsequent 12-month period. At the end of the 15-month observation period, the percentage of patients adherent to treatment was 48% for raloxifene and 40% for risedronate (Fig. 1).

Incidence of hip fractures during the subsequent 12 months

In the subsequent 12 months compared to the baseline period, the incidence of hip fractures decreased among patients adherent to risedronate therapy (RR 0.70, 95% CI 0.59–0.84, $p < 0.01$), whereas no change was seen among patients adherent to raloxifene (RR 0.99, 95% CI 0.72–1.37). In contrast, among those patients not adhering to therapy, hip fracture incidence remained unchanged across the baseline period through the subsequent 12 months for both the risedronate and raloxifene cohorts (Table 4).

Matched analysis

To investigate the contribution of differences in baseline fracture risk between patients treated with risedronate or raloxifene (Table 1) in relation to the effectiveness of these drugs in reducing hip fractures, we attempted to match the risedronate cohort to the lower risk raloxifene cohort based on age, fracture history, and use of estrogen therapy. In this case, the resulting matching was incomplete as differences ($p < 0.01$) in the incidence of hip fractures remained during the baseline period (Table 5). Nevertheless, in the raloxifene-matched risedronate cohort, the initial hip fracture incidence decreased to 0.70 per 100 patient-years (from 0.94 per 100 patient-years in the overall risedronate cohort) (Table 4). In this relatively lower risk group, the incidence of hip fracture in the subsequent 12 months was still significantly reduced with risedronate therapy (Table 5).

Discussion

In this large, observational study of women aged 65 years and older initiating either risedronate or raloxifene therapy,

Table 4 Comparison of hip fracture incidence between baseline period and subsequent period

Cohort (number of patients)	Baseline period			Subsequent period			Ratio (95% CI) of fracture incidence for follow-up/baseline
	Initial 3 months after starting therapy			Subsequent 12 months after baseline period			
	Number patients with fracture	Person-years of observation	Fracture incidence per 100 person-years	Number patients with fracture	Person-years of observation	Fracture incidence per 100 person-years	
Raloxifene ($n = 37,726$)	48	9,432	0.51				
Adherent				102	19,594	0.52	1.02 (0.73–1.44)
Non-adherent				69	14,192	0.49	0.96 (0.66–1.38)
Risedronate ($n = 86,735$)	204	21,684	0.94				
Adherent				266	40,214	0.66	0.70 (0.59–0.84)
Non-adherent				316	34,787	0.91	0.97 (0.81–1.15)

Adherent defined as medication possession ratio of at least 80%

Non-adherent defined as medication possession ratio less than 80%

Table 5 Matched analysis (year of age, fracture history, estrogen use)

Cohort (number of patients)	Baseline period			Subsequent period			Ratio (95% CI) of fracture incidence for follow-up/ baseline
	Three-month period after starting therapy			Subsequent 1-year period adherent to therapy			
	Number subjects with fracture	Person-years of observation	Fracture incidence per 100 person-years	Number subjects with fracture	Person-years of observation	Fracture incidence per 100 person-years	
Raloxifene							
Complete cohort ($n = 37{,}726$)	48	9,432	0.51	102	19,594	0.52	1.02 (0.73–1.44)
Risedronate							
Matched cohort[a] ($n = 37{,}501$)	66	9,375	0.70	81	17,933	0.45	0.64 (0.46–0.89)
Risedronate							
Complete cohort ($n = 86{,}735$)	204	21,684	0.94	266	40,214	0.66	0.70 (0.59–0.84)
Raloxifene							
Matched cohort[b] ($n = 17{,}074$)	25	4,268	0.59	59	8,730	0.68	1.15 (0.72–1.84)

[a] A 1:1 match on year of age, fracture history (yes or no), and hormone replacement therapy use (yes or no) was completed so the risedronate cohort matched the raloxifene cohort. If the raloxifene cohort had more patients in a stratum than the risedronate cohort, there was a reduction in the number of risedronate matches (i.e., of the 37,726 raloxifene patients, 37,501 had a match in the risedronate cohort). If the risedronate cohort had more patients in a stratum than the raloxifene cohort, then a random sample of risedronate patients was selected. The numbers presented in the matched cohort reflect the average of three random samples

[b] A 1:5 match on year of age, fracture history (yes or no), and hormone replacement therapy use (yes or no) was completed so the raloxifene cohort matched the risedronate cohort. If the risedronate cohort had more than 5× patients in a stratum than the raloxifene cohort, there was a reduction in the number of raloxifene matches (i.e., of the 17,347 needed patients in the raloxifene group, 17,074 had a match in the risedronate cohort). If the raloxifene cohort had more patients in a stratum than 1/5 of the risedronate cohort, then a random sample of raloxifene patients was selected. The numbers presented in the matched cohort reflect the average of three random samples

we made three inquiries: (1) Were there any differences in the fracture risk profile at the time of initial prescription among these women? (2) How effective was each osteoporosis therapy in reducing hip fractures over time considering the adherence level? (3) What is the contribution of the baseline fracture risk to the effectiveness of these drugs in reducing hip fractures?

Consistent with prior observations [27, 33], we observed that patients receiving risedronate had more risk factors for fracture at the time of initial prescription than the population of patients receiving a selective estrogen receptor modulator. These observations suggest that physicians are selectively prescribing osteoporosis therapies based on their appreciation of the patients' risk profile and/or specialty. While these prescription patterns are likely clinically appropriate, selective prescribing creates a meaningful bias for any epidemiological study of drug effects. This bias, confounded by indication, results because the allocation of treatment is not randomized and the indication for treatment is related to the risk of future outcomes [34]. As a result, this bias may lead to a false interpretation of any comparison between treatment groups. While there is no one best way to manage this bias, we utilized a method in this study that makes a comparison within a population rather than between populations. A limitation of our method, which is a comparison in the fracture incidence during the first 3 months of therapy to the fracture incidence during the subsequent 12 months among patients adherent to treatment, is the presumption that fracture reduction does not begin immediately after therapy; consequently, the short baseline period after starting an osteoporosis therapy likely reflects the fracture risk of a cohort independent of any drug effect. One observation supporting this presumption includes changes in bone mineral density, a surrogate marker of therapeutic effect, whose least significant change may not be reached until at least 1 year on therapy [35]. Another supporting observation is that fracture reductions have not been noted earlier than 6 months after start of therapy within post hoc, pooled analysis of clinical trials [36, 37].

Based on our method of measuring effectiveness in this study, we observed that the patients receiving and adherent to risedronate had a reduction over time in the incidence of hip fractures, whereas the patients receiving and adherent to raloxifene had no reduction in hip fracture incidence. The strength of this observation is the consistency between these results and the results of clinical trials [1, 4] and another observational study [38]. Limitations of this observation include the limited availability of information to describe patients (e.g., no bone mineral density results), the inclusion of fracture outcomes not verified by medical charts, and the potential that differences in fracture risk profile at baseline between the risedronate and raloxifene populations may be linked to interpretation of results. In a recent study, McCloskey et al. [5] showed that the bisphosphonate clodronate was effective in women identified by the FRAX® tool (World Health Organization, Centre for Metabolic Bone Diseases, University of Sheffield, UK) to be at high risk even in the absence of bone mineral density information. Kanis et al. [6] showed that bazedoxifene, an estrogen angonist/antagonist, was effective at reducing vertebral and clinical fractures in postmenopausal women at high risk as assessed by FRAX. Thus, the observed differences in the present study may be partly due to the fracture risk profile at baseline.

To control for differences in fracture risk profile at baseline, we attempted to equate the risedronate and raloxifene populations on fracture risk at the time of initial prescription by matching on several major risk factors, including age, prior fracture, and use of estrogen therapy. However, even after matching on these risk factors, there remained significant differences in baseline fracture risk during the initial 3 months of therapy (i.e., matching did not fully control for differences between populations). It remains possible, therefore, that even modest differences in baseline fracture risk have an impact on the effectiveness of these therapies [6]. On the other hand, these results suggest that treating women at lower risk with risedronate might be more beneficial than treating them with raloxifene.

In conclusion, for this observational study of more than 100,000 patients receiving either risedronate or raloxifene, differences existed in the fracture risk profile of patients at the time of initial prescription between those starting different osteoporosis therapies. Among these patients, we found that adherence to risedronate therapy rapidly decreased the risk of hip fractures, whereas raloxifene prescribed to women at lesser fracture risk did not. Hence, cost-effective strategies to reduce the burden of clinical fractures should take into account both drug efficacy and baseline fracture risk.

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KNEE ARTHROPLASTY

Fall incidence and risk factors in patients after total knee arthroplasty

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Abstract
Purpose To prospectively investigate the relationship between physical function and falls among elderly patients who underwent total knee arthroplasty (TKA) and to determine the incidence of falls as well as their risk factors.
Methods A total of 108 patients (17 male, 91 female) over 60 years of age who underwent TKA were enrolled and who were living independently in community. 75 patients fulfilled our inclusion criteria and 74 (8 male, 66 female) of them agreed to participate. Baseline assessment (physical examination, physical performance tests, and self-administered questionnaire) were conducted between 6 and 12 months after the last arthroplasty and the follow-up assessment was performed 6 months after the baseline assessment. Monthly pre-stamped postcards were sent to assess the incidence of falls.
Results Of the 74 patients enrolled, 70 (94.6%) completed a 6-month prospective observation. 23 of 70 patients (32.9%) fell during the observational period. Postoperative range of knee flexion, ranges of knee flexion and extension and ankle plantar flexion were significantly lower in fallers than in non-fallers ($P = 0.016$, $P = 0.037$, $P = 0.014$, respectively). In the multivariate analysis, postoperative range of knee flexion (OR 0.277, 95%CI 0.088–0.869, $P = 0.028$) and ankle plantar flexion (OR 0.594, 95%CI 0.374–0.945, $P = 0.028$) were determined to be significant risk factors.
Conclusion Elderly people who underwent TKA are considered more likely to fall compared with healthy elderly people. For patients with limited knee flexion and ankle plantar flexion, improvement of ROM by exercise therapy and patient education regarding the prevention of falls and fractures are considered necessary.

Keywords Total knee arthroplasty · Falls · Physical function · Range of motion

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Introduction

Falls in the elderly have become a social problem. In particular, fragility fractures caused by falls in the elderly reduce their daily activity [1] and may lead to conditions requiring nursing care. Prevention of falls is therefore extremely important in allowing elderly people to continue to live independently.

Among the intrinsic risk factors for falls are deformed or painful joints. Age-related deformities of the knees, feet, or spine impair skeletal alignment and balance, thereby increasing the frequency of falls. Osteoarthritis (OA) in particular causes deformities of the knee joints and pain during walking, and has been reported to increase the risk of falls and fractures [2].

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The standard approach to the treatment of deformity and pain in the knee joint is total knee arthroplasty (TKA). TKA is a surgical intervention that eliminates pain and deformity and improves patients' quality of life (QOL). It results in stable outcomes [3] and was performed on approximately 680,000 patients in the USA in 2009 [4]. However, studies have demonstrated persistent deterioration in proprioception of the knee [5] and balance impairment [6] after TKA, and that among the elderly who underwent TKA, quadriceps torque was weaker and walking speed was lower compared with healthy counterparts [7, 8]. These findings suggest that physical functioning in the elderly declines after TKA. Moreover, supracondylar fractures of the femur were shown to occur in 0.3 to 2.5% of patients who underwent TKA [9–11], and delayed union or malunion have been reported after the surgical treatment of these fractures [12, 13]. Fractures around knee joints after TKA are thus a serious problem that impairs patients' activities of daily living (ADL) and QOL.

There are few surveys on falls and fractures after TKA. In 2009, Swinkels et al. [14] used a self-administered questionnaire to conduct a prospective study of the incidence of falls in 99 patients who underwent TKA, and showed that a preoperative history of falls and Geriatric Depression Scale (GDS) scores predicted postoperative occurrence of falls. In addition, Levinger et al. [15] identified impairment of lower limb proprioception and weakened knee extension strength as risk factors for falls during the early post-TKA period (within 4 months). However, there is not yet sufficient evidence on whether physical function after surgery is related to falls among the elderly after TKA.

Falls often occur due to impaired physical function and therefore, assessment of motor function [16] is essential when evaluating elderly patients with respect to their risk of falls for preventive purposes. Other risk factors for falls include changes in lower thoracic slope and knee joint angle [16], weakened lower limb muscles [17], kyphosis [18], and deformity of the foot [19]. Many elderly people who undergo TKA suffered from OA or rheumatoid arthritis (RA) before the surgery and therefore tend to exhibit the impairments mentioned above. For this reason, it is important to evaluate the physical functioning [20] of elderly patients who underwent TKA and clarify the risk factors for falls so as to minimize the postoperative incidence of falls and fractures and maintain QOL and ADL.

The present study was conducted to prospectively investigate the relationship between physical function and falls among elderly patients who underwent TKA and to determine the incidence of falls as well as their risk factors.

Patients and methods

Patients

Subjects included 108 patients (17 male, 91 female) over 60 years of age who underwent TKA at the Hakuai Hospital between January 2008 and December 2010, and who were living independently in community. Both bilateral and unilateral TKA patients were included. Their mean age was 75.8 ± 6.1 and their operations took place between 6 and 11 months before the enrollment. Patients were ineligible if they had cognitive impairment, mental disease, cerebrovascular disease, or Parkinson's disease. Seven patients were excluded as they did not meet the inclusion criteria. Another four were excluded due to the need for additional surgery and two due to hospital for fracture treatment. An additional 20 patients were excluded because they did not visit our hospital for follow-up. Thus, 75 patients fulfilled the inclusion criteria and 74 (8 male, 66 female) of them agreed to participate. The investigators provided written and verbal explanations of the study and obtained written consent from the subjects. The mean patient age was 75.7 ± 5.8 years old (range 60–88).

All surgeries were performed with a standard medial parapatellar approach by three orthopedists. The implants used were Scorpio (Stryker, USA) for 70 knees and LCS (DePuy, USA) for 4 knees. Early joint motion and weight bearing were encouraged during hospitalization and patients underwent rehabilitation for about 4 weeks according to the relevant clinical pathway. Postdischarge follow-up was planned for 1, 3, 6 months, and a year after surgery. Table 1 shows patients' preoperative characteristics and surgical information.

We assessed range of motion (ROM) of the knee (flexion, extension, range of flexion and extension) during the preoperative period and conducted the baseline assessment (physical examination, physical performance tests, and self-administered questionnaire) between 6 and 12 months after the last arthroplasty. Follow-up assessment was performed 6 months after the baseline assessment.

Fall assessment

A fall was defined as the subject unintentionally coming to rest on the floor or some lower level and not because of a major intrinsic event. In order to assess the incidence of falls we sent out monthly pre-stamped postcards. The postcard included the following questions: (a) Did you fall during the this month? (b) If you fell, did you fall once, twice, or more than three times? (c) If you fell, did you experience any fractures or injuries? Written reminders were sent if patients did not return their monthly postcard. Patients who completed the postcard incorrectly were contacted by telephone.