population of that age class in 1999. Summation of the expected number of all classes was the expected total number in 1999, based on the number of fractures in 1985. If the incidence did not change from 1985 to 1999, the expected number of fractures in 1999 would be the same as the observed number in 1999.

Results

Number of hip fractures in 1999

A total of 1697 cervical or trochanteric fractures of the proximal femur occurred in 1999 (400 males and 1297 females), with a male-to-female ratio of 1:3.24 (Tables 2 and 3; Fig. 1). Ninety-four percent (1599) of all cervical or trochanteric fractures occurred in "the elderly population", who were more than 65 years of age, and 78% (1324) of all fractures occurred in the "advanced age group", over 75 years of age.

Table 2. Summary of cervical and trochanteric fractures in the proximal femur for people living in Niigata Prefecture, Japan, in 1999

	Number	Incidence[a]
Total number of fractures	1697	68.2
Sex		
Male	400	33.1
Female	1297	101.4
Male-to-female ratio	1:3.24	
Type of fracture		
Cervical	622	25.1
Trochanteric	1075	43.2
Cervical-to-trochanteric ratio	1:1.73	

[a] Number of fractures/100000 population per year

The overall incidence of the combined number of cervical and trochanteric fractures was 68.2 per 100000 population per year, with 33.1 for males, and 101.4 for females (Tables 2 and 3). The incidence of the combined number of cervical and trochanteric fractures in those over 65 years of age was 168.6 for men and 405.6 for women. The incidence in those more than 85 years of age increased to 628.4 for men and 1299.8 for women. There were 1075 trochanteric fractures (63.4%) and 622 cervical fractures (36.6%) (Table 2).

The average age of patients with cervical fractures was 75.5 years for men and 80.5 years for women. The average age of the patients with trochanteric fractures was 89.5 years for men and 82.2 years for women. The average age of the patients of both sexes with trochanteric fractures was significantly higher than the age of the patients with cervical fractures (Tables 2–4).

Secular change in the incidence of hip fractures from 1985 to 1999

The total number of cervical and trochanteric fractures (observed number) in Niigata Prefecture increased in every study year from 1985 to 1999 (Table 4) [2–4]. The number and percentage of those over 65 years of age increased each year, from 12.9% in 1985 to 20.7% in 1999 (Table 1).

Based on a reference year of 1985, the population was adjusted by age and sex. The expected total number of fractures in 1999 was 1200.2, with 269.3 for males and 930.9 for females (Table 5). The actual observed number of fractures was 1697, with 400 for men and 1297 for women (Table 2). The expected number of fractures in 1999 was significantly less than the actual numbers observed ($P < 0.05$) (Fig. 2). This indicates that the

Table 3. Age-specific number and incidence of cervical and trochanteric fractures of the proximal femur in 1999

	Males		Females		Total	
Age (years)	Number	Incidence	Number	Incidence	Number	Incidence
Incidence						
0–49	11	1.5	12	1.7	23	1.6
50–54	5	5.2	7	7.6	12	6.4
55–59	8	10	11	13.4	19	11.7
60–64	21	28.3	31	38.2	52	33.5
65–69	35	48.5	57	68.5	92	59.2
70–74	54	86.0	125	159.4	179	126.8
75–79	64	169.4	231	367.7	295	293.2
80–84	105	469.4	321	770.3	426	665.2
85+	97	628.4	502	1299.8	599	1108.0
Total	400	33.1	1297	101.4	1697	68.2
Over 65	358	168.6	1241	405.6	1599	308.8
Percentage	89.5		95.7		94.2	
Over 75	267	351.9	1057	736.4	1324	613.6
Percentage	66.8		81.5		78.0	

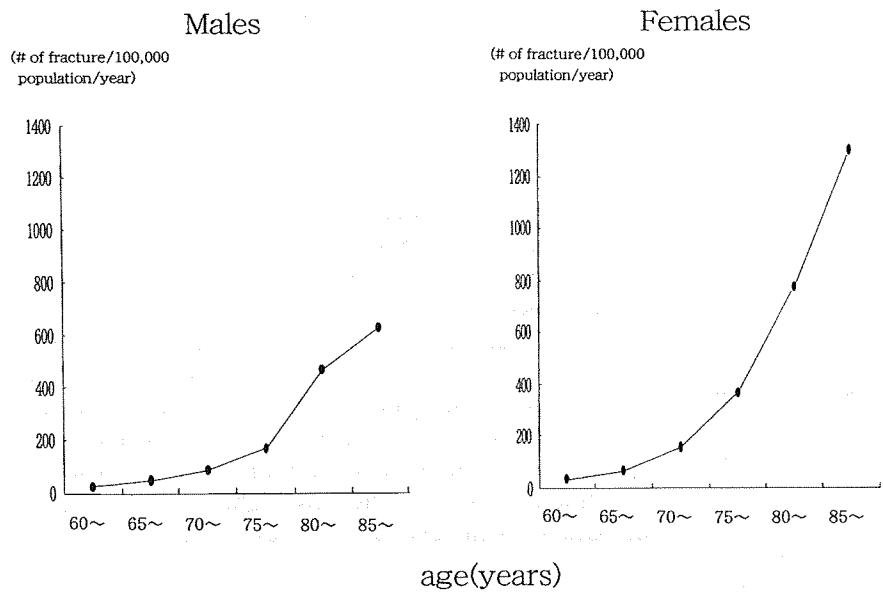

Fig. 1. Age-related incidence (/100000 population/year) of cervical and trochanteric fractures of the proximal femur

Table 4. Changes in the incidence of cervical and trochanteric fractures of the proximal femur in Niigata over the 5 study years

	1985	1987	1989	1994	1999
Total number of fractures	677	773	996	1468	1697
Male-to-female ratio	1:2.7	1:2.4	1:2.8	1:2.9	1:3.24
Average age (years)					
Males	67.5	70.4	71.4	74.4	75.5
Females	76.2	76.9	77.7	80.9	80.5
Raw incidence[a]	27.3	31.2	40.1	59.1	68.2

[a] Number of fractures/100000 population/year

Table 5. The number of fractures in 1985 and 1999 and expected number in 1999

Age class (years)	Fractures in 1985	Population in 1985	Incidence in 1985 (In)	Fractures in 1999	Population in 1999 (Pn)	Incidence in 1999	Expected no. (En) in 1999 (En = In*Pn/100000)
Male							
Under 60	46	1014251	4.6	24	923399	2.4	42.5
60–65	13	59464	21.9	21	74232	26.9	16.3
65–70	16	45379	35.3	35	72196	49.9	25.5
70–75	38	38231	102	54	62777	87.6	64
75–80	33	26673	127.5	64	37783	172.0	48.2
80–85	16	13243	120.8	105	22371	469.4	27.0
Over 85	17	5726	296.9	97	15437	628.4	45.8
Total	179	1202967	15.1	400	1208195	33.1	269.3
Female							
Under 60	34	1005077	3.5	30	892967	2.9	30.3
60–65	16	77113	20.8	31	81111	37.0	16.9
65–70	40	61258	65.3	57	83188	69.7	54.3
70–75	89	53227	167.2	125	78416	160.7	131.1
75–80	112	40320	280.3	231	62826	369.3	176.1
80–85	103	23042	451.4	321	41674	772.7	188.1
Over 85	104	12206	860.2	502	38622	1302.4	332.1
Total	498	1272243	39.5	1297	1278804	101.4	930.9
Both sexes							
Total	677	2475210	27.4	1697	2486999	68.2	1200.2

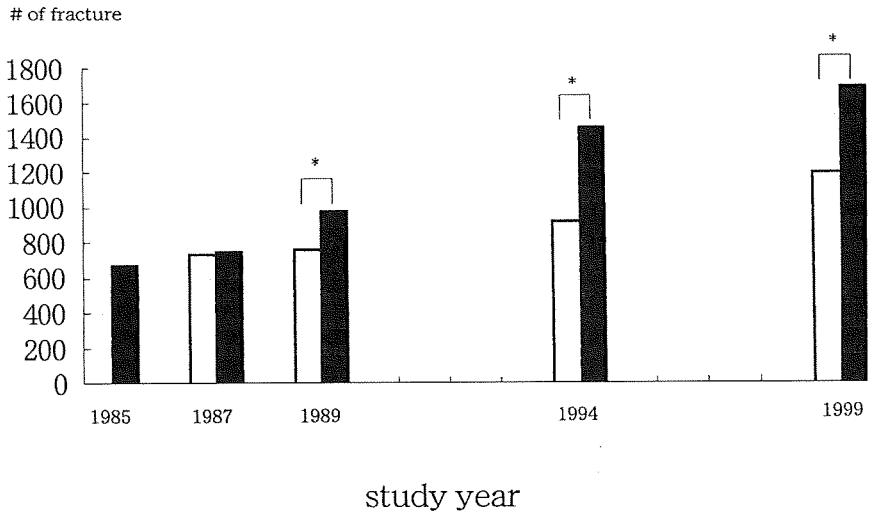

Fig. 2. The expected (*open columns*) and observed (*shaded columns*) numbers of cervical and trochanteric fractures in the 5 study years. $*P < 0.05$

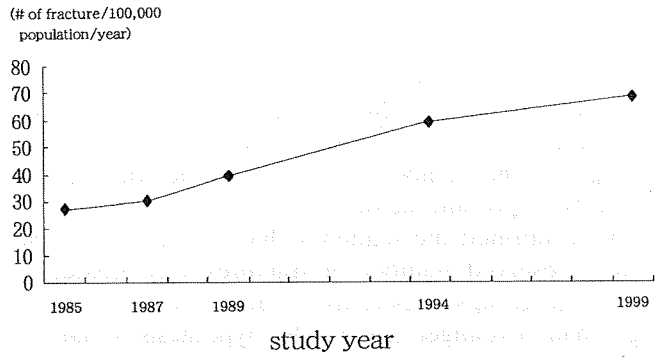

Fig. 3. Total incidence (/100000 population/year) of hip fractures in the 5 study years

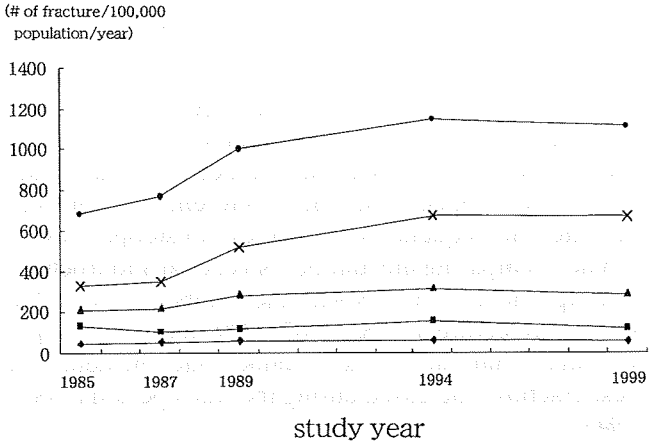

Fig. 4. The incidence (/100000 population/year) of hip fractures in patients over 65 years of age. *Closed circles*, Age 85 or more; *crosses*, age 80–84; *closed triangles*, age 75–79; *closed squares*, age 70–74; *closed diamonds*, age 65–69

incidence of patients with these fractures increased significantly from 1985 to 1999, on the basis of adjustment of the population composition.

The secular change of incidence was examined. There was a significant difference between 1985 and 1999, 1987 and 1999, and 1989 and 1999, but no significant difference was observed between 1994 and 1999. The rate increased from 1985 to 1989 and from 1989 to 1994, whereas, after that, the increasing rate of incidence from 1984 to 1994 went down slightly. In other words, the raw incidence of hip fractures increased from 1985 to 1999, while from 1994 to 1999, the increasing rate of incidence slowed down (Fig. 3). The incidence of hip fractures in people over 65 years of age slowed down, and in any age class of people over 65 years of age (elderly population) the incidence of hip fractures flattened or slightly decreased from 1994 to 1999 (Fig. 4).

Discussion

In this study, we determined the number of cervical and trochanteric fractures of the proximal femur in Niigata in 1999 by visiting all the hospitals with an orthopedic surgery department. However, some patients with hip fractures may have presented at other medical facilities without an orthopedic department, such as nursing homes or mental hospitals. Dohmae et al. [3] reported that patients with "neglected" hip fractures corresponded to only about 2% of the total number of fractures in Niigata Prefecture in the previous study. Because the present study was carried out using the same methodology as in 1989, it is believed that nearly all cases of hip fractures in Niigata Prefecture in 1999 were reliably included in this study, with low numbers of "neglected" patients.

The overall incidence of cervical and trochanteric fractures in Niigata prefecture in 1999 was 68.2 fractures per 100000 population per year (33.1 for men and 101.4 for women). The fracture incidence increased with age in the 5-year age groups. Because the incidence of hip fractures has been shown to be high in the elderly population, it has been reported that the incidence of these fractures is most likely related to senile osteoporosis [14] in the elderly population.

The use of long-acting sleeping drugs, visual difficulties, impaired physical capacity, altered cognitive function (failing muscle strength and poor balance) were risk factors for hip fractures [15,16].

The overall incidence of cervical fractures in this study was 25.1 (11.1 for men and 38.1 for women), and the overall incidence of trochanteric fractures was 43.2 (21.9 for men and 63.3 for women). It is well known that osteoporosis occurs more commonly in women than in men, and is more closely related to trochanteric fractures than to cervical fractures.

In the present study, the incidence of the combined number of cervical and trochanter fractures was greater in women than in men, and the number of trochanteric fractures was greater than the number of cervical fractures. It would appear that these differences result from the different frequencies or degrees of osteoporosis.

When comparing the number of cervical and trochanteric hip fractures in 1999 with the numbers reported in Niigata Prefecture in 1985, 1987, 1989, and 1994 [2–4], it is evident that the overall number and incidence of these fractures increased during the study period (1985–1994).

After computing the expected number of cervical or trochanteric fractures in 1999, adjusted with the age-related population in 1985, we compared this number with the observed number. Although the total expected number of fractures in 1999 was 1200.2, the observed number was 1697 (see Table 5). The observed number of fractures was higher than the expected number, indicating that the incidence of these fractures had been increasing from 1985 to 1999. This increase was evident in the total number of fractures, in both sexes, and in both types of fractures.

We also compared the secular change of incidence, between 1987 and 1999, 1989 and 1999, and 1994 and 1999, in the same manner. There was a significant difference between 1987 and 1999, and between 1989 and 1999, whereas between 1994 and 1999, there was no significant difference, in males only.

Kannus et al. [17] reported that the worldwide trend is for increasing incidence. Rogmark et al. [18] reported that the incidence of hip fractures increased. On the other hand, Levi [19] noted an incidence that was unchanged in Copenhagen, Denmark. Because of the decrease in the incidence of hip fractures in "the elderly population," the overall incidence of hip fractures has slowed down year by year. This suggests that the prevention of fractures for the elderly population (public information, including prevention and treatment for osteoporosis, etc) may be related to the above-mentioned results.

Many possible factors are responsible for the increase in the incidence of hip fractures [3,6,11,14,20–26]. In Niigata Prefecture, the age-related distribution of the population changed during the 14 years of the study period. The percentage of the elderly population (those over 65 years of age) within the overall population increased from 12.9% in 1985 to 20.7% in 1999. The incidence of cervical and trochanteric fractures was higher in the elderly group than in the younger age group. This increase in the elderly population may be one of the factors responsible for the increase in the incidence of hip fractures in Niigata.

Sernbo and Johnell [27] compared the Singh index of patients in the 1950s and 1980s, and suggested that the increase in the incidence of hip fractures was caused by a decrease in bone quality. Some changes in the degree (seriousness) of osteoporosis in the patients and some changes in the number of patients in the study group could be important factors.

We confirmed the tendency that an increase in the actual observed number of fractures was greater in older age groups (especially in those over 75 years of age) than in younger groups. Our hypothesis is that not only is there an increase in the elderly population but also there could be an increase in the weak (fragile) elderly population, and this can influence the increase in the number of fractures. It can be seen that the number of old people who lived in the 1940s increased (at the time, the elderly population, of over 75 years of age, were adolescents, during the period of insufficient food during World War II and the postwar period). As they were growing up through the age of puberty during this period, their bone density or quality may have been less than that of other age groups. Reid et al. [28] reported that nutrition in childhood played some part in the hip axis length and affected the incidence of hip fractures. Baker et al. [29] reported that the nutritional needs of children and adolescents for calcium influenced the development of osteoporosis in adulthood. In other words, each age group may have a particular bone strength. Making bones stronger during the early years and maintaining this strength in older age may be important measures in preventing fractures.

Epidemiological studies of cervical and trochanteric hip fractures were performed recently in other areas of Japan [11,12]. The age-specific incidences of fractures in Nagasaki and Tottori, Japan, were at nearly the same level as that in Niigata Prefecture [2–4]. In addition, the incidence of fractures in Japan was lower than the inci-

dence reported in Europe and the United States [30,31]. Hinton et al. [32] studied the geographic and sex- and age-related variations in the incidence of hip fractures from 1985 to 1987 in the United States. The regional variations in the incidence of hip fractures in the United States were greater than the regional difference in Japan [10–12,33,34].

Some previous studies have compared the bone mineral density of Japanese and Caucasians and reported that the degree of osteoporosis in Japanese was lower [9,10]. It was also reported that the incidence of spinal fractures was higher in Japanese than in Caucasians. Other authors reported that the incidence of hip fractures was related not only to osteoporosis but also to variations in the morphology of the proximal femur among races [30,35,36].

Brondy projected future trends in the population of the United States, and predicted that the number of hip fractures would increase as the percentage of elderly people in the population increased [21]. Recently, the ratio of the elderly population has been increasing year by year, and hip fractures have become a serious problem for our society [37–40].

The overall number of hip fractures in Niigata Prefecture increased from 1985 to 1999, but the ratio of increase in incidence slowed down from 1994 to 1999.

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ORIGINAL ARTICLE

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Incidence and outcome of osteoporotic fractures in 2004 in Sado City, Niigata Prefecture, Japan

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Abstract Osteoporotic fracture in elderly populations is increasing worldwide, but there are few data on the incidence and outcome of osteoporotic fractures, including upper extremity and vertebral fracture, during a certain period in a defined geographic area. The purpose of this study was to determine the incidence of osteoporotic fractures in a particular area: Sado City, Niigata Prefecture, Japan. From January to December 2004, osteoporotic fractures of the vertebra, hip, distal radius, and proximal humerus in Sado City were recorded. The incidence, age, gender, type of fracture (for hip fracture), right or left side (for distal radius, proximal humerus, and hip fracture), place of injury, cause of injury, outcome, hospitalization period, and patient status regarding taking of drugs for osteoporosis treatment were checked for each fracture. The incidence was calculated based on the whole population of Sado City. The incidence per 100000 population was 232.8, 121.4, 108.6, and 37.1 for fractures of the vertebra, hip, distal radius, and proximal humerus, respectively. The total incidence of these four kinds of fracture was 499.9 per 100000 persons per year. The average age at the time of injury was 81.4, 77.7, 75.7, and 60.2 years old for fractures of the hip, vertebra, proximal humerus, and distal radius, respectively. As the average age increased, the percentage of fractures that occurred indoors also increased; that is, a higher percentage of hip fractures occurred indoors, followed by fractures of the vertebra, proximal humerus, and distal radius. Most patients were not taking anti-osteoporosis drugs before fractures of the hip or vertebra. We determined the incidence of major osteoporotic fractures in 1 year in a defined geographic area. Our data showed that 81% of hip fracture patients also had a vertebral fracture and that the average age at the time of injury was higher for hip fractures than for vertebral fractures. Therefore, these results suggest that vertebral fracture leads to hip fracture, indicating that early fracture prevention and continuous prevention strategies through positive treatment are of importance in osteoporotic elderly people.

Key words vertebral fracture · hip fracture · proximal humerus fracture · distal radius fracture · incidence

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Introduction

Osteoporotic fractures, and especially vertebral and hip fractures, reduce quality of life (QOL) in elderly people because of associated pain, malposture, movement disability, and mental anxiety [1–4]. Knowledge of the descriptive epidemiology of the incidence and outcome of these fractures is important for prevention or reduction of such fractures. The aim of this study was to identify the incidence of fractures of the vertebra, hip, distal radius, and proximal humerus over a certain period in a population in a defined geographic area: Sado City, Niigata Prefecture, Japan.

Patients and methods

Study site

The study was carried out in Sado City, Japan. Sado City is located on Sado Island, and the population of the city and the island are equivalent. Sado Island is located in Niigata Prefecture on the Sea of Japan, at latitude 37°47′ N to 38°20′ N and longitude 138°12′ E to 138°34 E, situated north of the main Japanese island of Honshu. Sado Island has an area of 855 km^2, and the population of the island was 70011

(33418 males and 36593 females) as of June 30, 2004, of which 23787 (9603 males and 14184 females) (34%) were 65 years old and older. Tourism, fishing, and agriculture are the chief industries, and access to the island is only possible by sea or air. Immigration and emigration among the elderly people of the island are extremely low.

Subjects

We examined the occurrences of osteoporotic fractures of the vertebra, hip, distal radius, and proximal humerus on Sado Island from January to December 2004. Almost all patients with hip fractures visited one general hospital, where all cases of this type are concentrated and surgery for hip fractures is carried out. To obtain information on fractures of the vertebra, distal radius, and proximal humerus, we distributed questionnaires to four hospitals and five doctors' offices on the island, including the main orthopedics facility. Answers were obtained from three hospitals and three doctors' offices, comprising 94% of the number of beds allocated for orthopedics cases. Fractures that occurred in tourists were excluded from the data, and pathological fractures resulting from malignant tumor or other bone metabolic diseases were also excluded.

Methods

All fractures were examined by X-ray. For vertebral fractures, lateral spinal radiographs were examined and the fractures were defined as wedge, biconcave, and compound (Fig. 1) based on the dimensions of the vertebral body and diagnostic criteria issued by the Ministry of Health and Welfare and widely used in Japan [5,6]. It was not necessarily easy to identify a new vertebral fracture, but patients who visited the hospital for symptoms such as back pain for the first time and were judged to have a vertebral fracture by the orthopedic doctor based on X-ray and physical examination were considered to be new fracture cases (an incident of fracture: clinical fracture). Asymptomatic older fractures (prevalent fracture) discovered accidentally by X-ray were excluded from the data. The incidence, age, gender, type of fracture (for hip fracture), right or left side (for distal radius, proximal humerus, and hip fracture), place of injury, cause of injury, outcome, hospitalization period, and patient status regarding taking of anti-osteoporosis drugs were checked for each fracture. The incidence rates were calculated based on the whole population of Sado City. Incidence rates adjusted to the entire population of Japan in 2005 were also calculated.

Statistical analysis

A chi-square test for goodness of fit was used to evaluate the difference in numbers of right and left side fractures (for distal radius and proximal humerus fractures). The analysis was performed using Microsoft Excel for Windows.

Results

Vertebral fracture

There were 163 cases of vertebral fracture (45 males and 118 females), a male-to-female ratio of 1:2.6 (Table 1). The overall incidence was 232.8 per 100000 population per year, which was the highest incidence among the four kinds of fractures. With adjustment for the Japanese population, the incidence was 138.4. The average age at the time of injury was 77.7 years old, with a range of 18 to 97 years old.

Hip fracture

There were 85 cases of hip fracture (20 males and 65 females), a male-to-female ratio of 1:3.3. The overall incidence was 121.4 per 100000 population per year. Adjusted for the Japanese population, the incidence was 69.8. The

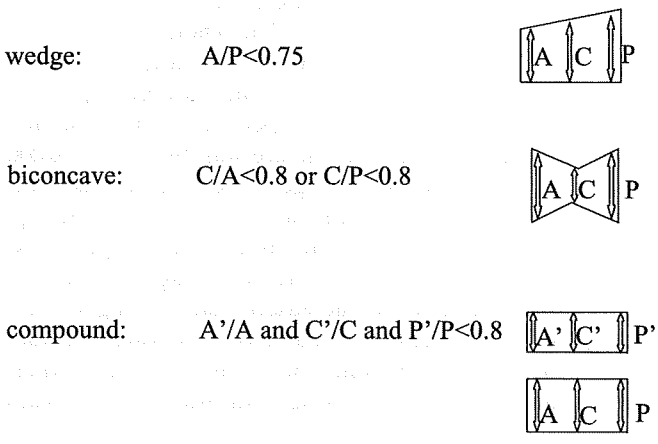

Fig. 1. Diagnostic criteria for vertebral fracture. (From [5, 6])

Table 1. Number and incidence of each fracture in Sado City in 2004

Site	Number of fractures (male, female)	Male-to-female ratio	Mean age (years)	Incidence (per 100000 person-year)	Adjusted for Japanese population (2005)
Vertebra	163 (45, 118)	1:2.6	77.7 ± 11.8 (18–97)	232.8	138.4
Hip	85 (20, 65)	1:3.3	81.4 ± 11.0 (42–104)	121.4	69.8
Distal radius	76[a] (18, 57)	1:3.2	60.2 ± 24.6 (8–91)	108.6	76.9
Proximal humerus	26 (3, 23)	1:7.7	75.7 ± 16.2 (15–92)	37.1	37.3
Total	350 (86, 263)	1:3.1	—	499.9	322.4

[a] One patient of unknown gender

cervical-to-trochanteric ratio was 1:1.30 [7]. The right hip was fractured in 47 patients and the left hip in 38 patients. The average age was 81.4 years old, which was the highest among the four kinds of fractures, with a range of 18 to 97 years old. Of 44 random hip fracture patients for whom we were able to examine a spinal X-ray, 81.8% (36 of 44) also had a vertebral fracture [7].

Distal radius fracture

There were 76 cases of fracture of the distal radius (18 males and 57 females, with 1 case of unknown gender): a male-to-female ratio of 1:3.2. The incidence per 100000 population per year was 108.6 [8]. Adjusted for the Japanese population, the incidence was 76.9. Thirty-four fractures occurred on the right side and 42 on the left side. The average age at the time of injury was 60.2 years old, with a range of 8 to 91 years old.

Proximal humerus fracture

There were 26 cases of fracture of the proximal humerus (3 males and 23 females), a male-to-female ratio of 1:7.7. The incidence per 100000 population per year was 37.1 [8]. Adjusted for the Japanese population, the incidence was 37.3. Nine fractures occurred on the right side, 16 on the left, and 1 occurred bilaterally. The average age at the time of injury was 75.7 years old, with a range of 15 to 92 years old.

Overall incidence of fracture

Incidences for the four kinds of fractures are shown in Table 1. We identified 350 fractures, including the vertebra, hip, distal radius, and proximal humerus, giving a total incidence of these fractures of 499.9 per 100000 population per year. The average age at the time of injury was highest for fractures of the hip (81.4 years old), followed by the vertebra (77.7 years old), proximal humerus (75.7 years old), and distal radius (60.2 years old). The incidence of each fracture by age is shown in Fig. 2: fractures of the vertebra, hip, and proximal humerus steeply increased in the seventies or eighties. A similar increase in incidence for fractures of the distal radius was not observed. The incidence of each fracture and the average age for males and females are also shown in Table 2: both the incidence and age at the time of injury were higher in females for all fractures.

The incidences of each fracture by age in males and females are shown in Fig. 3. These data show a peak in fractures of the distal radius in the male teens, whereas the incidence of fracture gradually rose in females with age and then decreased after the seventies. Very few fractures of the proximal humerus occurred in males, whereas a peak was present in the nineties in women. For vertebral fractures, the incidence gradually increased from the sixties and reached a peak in the nineties, without a large gender difference. The incidence of hip fractures began to increase from the seventies, with an exponential increase in women.

Place and cause of injury

The location in which each fracture occurred is shown in Fig. 4. Outdoor injuries were most common for fractures of the distal radius, followed by the proximal humerus, vertebra, and hip. Based on data for each kind of fracture, as the average age at the time of injury increased a greater percentage of injuries occurred indoors (Fig. 4). As shown in Fig. 5, the most common cause of injury was a fall, but there were many divergent causes of vertebral fracture.

Hospitalization and outcome after discharge

The average period of hospitalization and the places to which hospitalized patients were discharged are shown in

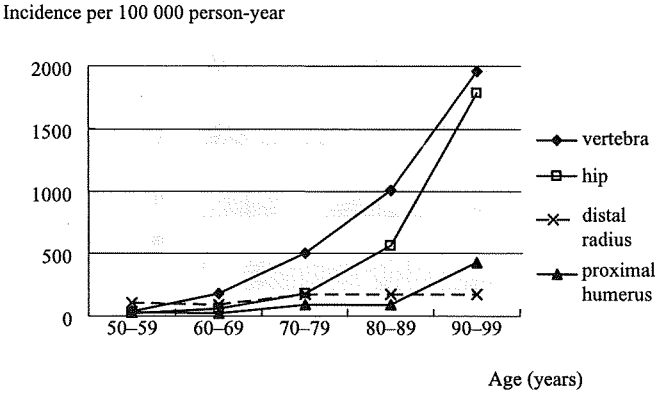

Fig. 2. Incidence of each type of fracture by age in years

Table 2. Incidence of each fracture in men and women

Site	Males			Females		
	Number of fractures	Incidence (per 100000 person-year)	Mean age (years)	Number of fractures	Incidence (per 100000 person-year)	Mean age (years)
Vertebra	45	134.7	75.0 ± 13.7 (18–96)	118	322.5	78.7 ± 10.9 (19–97)
Hip	20	59.8	75.2 ± 15.9 (42–94)	65	177.6	83.3 ± 8.2 (56–101)
Distal radius	18	53.9	36.0 ± 27.7 (8–82)	57	155.8	69.1 ± 16.7 (11–91)
Proximal humerus	3	9.0	57.3 ± 36.7 (15–79)	23	62.9	78.2 ± 11.2 (56–92)
Total	86	257.3	—	263	718.7	—

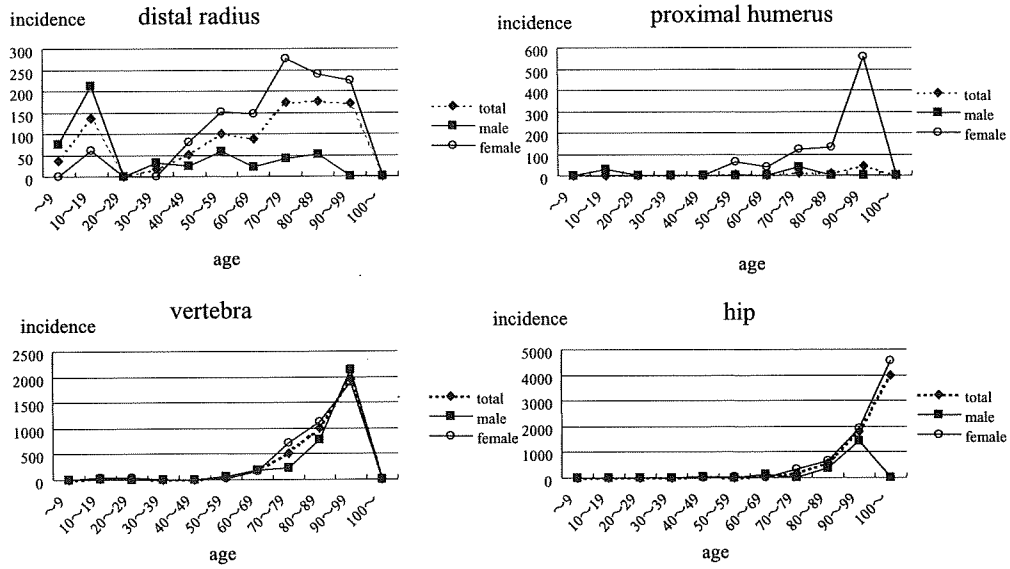

Fig. 3. Incidence of each type of fracture by age in years for males and females

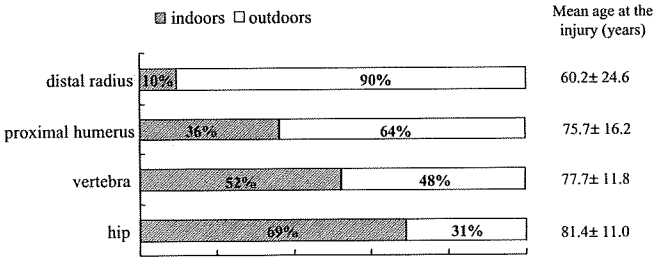

Fig. 4. Place where injury occurred, by each type of fracture: indoors or outdoors

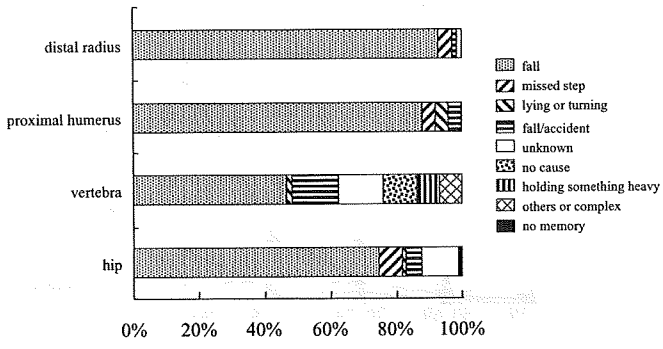

Fig. 5. Cause of injury leading to fracture

Fig. 6. Of patients with a fracture of a vertebra, 87% were discharged to home, whereas only 55% of patients with a hip fracture were discharged to home and 36% were transferred or discharged to a nursing home. The average hospitalization period was 30.5 days for a hip fracture and 20.4 days for a vertebral fracture.

Drugs taken before injury

The percentage of patients taking agents for osteoporosis before the injury is shown in Fig. 7. In most cases of hip and vertebral fractures, the patients did not take any anti-osteoporosis medicine before the injury occurred.

Discussion

The key aspect of the study was to examine all major osteoporosis-related fractures over a defined period of time in a limited area. Our results showed that there were 350 fractures (499.9 fractures per 100000 population per year), including fractures of the vertebra, hip, distal radius, and proximal humerus, in Sado City in 2004. Vertebral fractures were most common, followed by fractures of the hip, distal radius, and proximal humerus; for the last three fractures, this order is similar to those found in past surveys in Japan [9–12]. Concerning vertebral fractures, previous surveys of the Japanese population have found an incidence of 4000 per 100000 person-years (PY) for women in their seventies and 8400 per 100000 PY for women in their eighties [13]. A study in Europe found an incidence of 920–977 per 100000 PY for women of all ages [14]. Our survey showed an incidence of 322.5 per 100000 PY for all women and 1117 per 100000 PY for women in their eighties. Therefore, our incidence rate was lower than those found in previous studies, which may be because the survey was carried out in hospital subjects only, and some patients with a vertebral fracture may not consult with a hospital or clinic. Further examination of this issue is needed; however, it seems likely that vertebral fracture has a higher incidence than other kinds of osteoporotic fractures. Furthermore, we found that most hip fracture patients already had a vertebral fracture, suggesting that patients with a vertebral compression fracture have a high risk of a subsequent hip fracture. We note that previous data suggest that the Japanese population have a similar or greater number of vertebral fractures and fewer fractures of the long bone (including the hip and upper extremities) compared to European and American Caucasian populations [6,10,15–17].

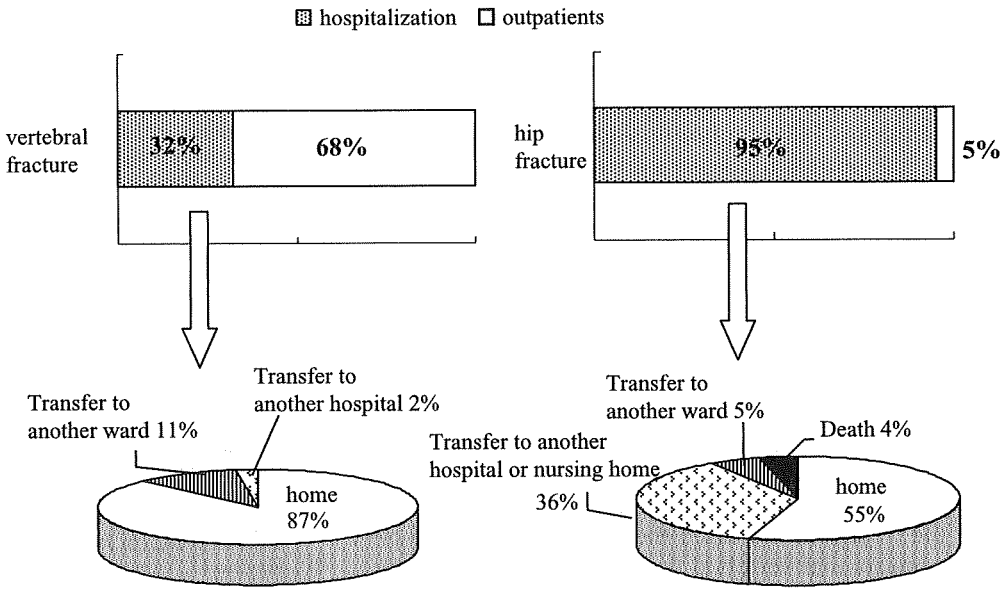

Fig. 6. Outcome of hospitalized patients after discharge. Average hospitalization period in the orthopedic ward was 20.4 ± 10.3 days for vertebral fractures and 30.5 ± 15.9 days for hip fractures

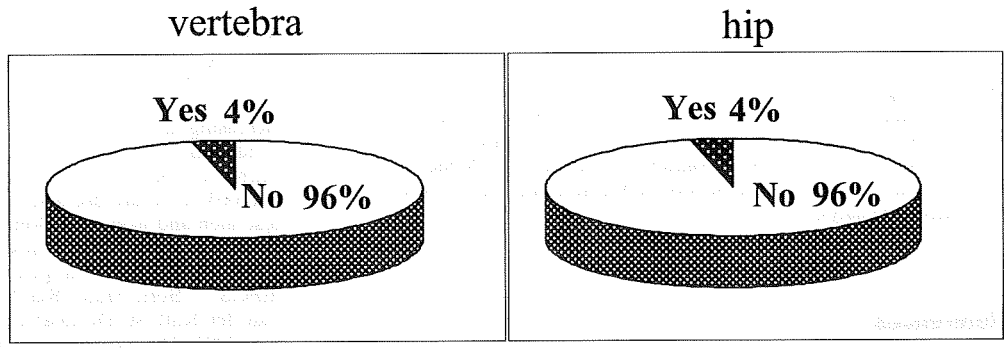

Fig. 7. Most patients who suffered vertebral or hip fracture had not taken anti-osteoporosis drugs before injury

Morita et al. [11] reported that the incidence of hip fractures in Niigata Prefecture in 1999 was 68.2 per 100000 PY, which was double the rate in 1985. In the current study, the incidence in Sado City was higher than all previous reports in Niigata Prefecture (Table 1). Therefore, hip fracture incidence appears to have increased since 1999, perhaps because the proportion of aged persons has increased more in Sado City than in Niigata Prefecture overall. The incidence of fracture of the distal radius in women in our study was lower than that found in Tottori Prefecture in 1995 (211.4 per 100000 PY) [10], but our incidence of proximal humerus fracture was higher than that in the earlier study (47.9 per 100000 PY) [10]. The mean age for injury of the proximal humerus is higher than that of the distal radius, which also suggests that the high aging rate in Sado City (34.0%) might account for these observations.

Our results indicated that the incidence of distal radius fracture increased for people in their fifties onward, but that there was no upward trend in incidence after the eighties (see Fig. 3), possibly because physical activity in the fifties to seventies leads to a higher rate of fracture of the distal radius, whereas reduced physical activity in people above 80 years of age tends to decrease the incidence of this fracture. Fracture of the distal radius may also occur more frequently in younger persons because such people are more likely to use a hand to protect against a fall, whereas elderly people might hit a hip or shoulder joint directly under such circumstances, thereby accounting for the higher incidence of fractures of the hip or proximal humerus in older people. However, the number of fractures of the radius or humerus was very small in males, and so this argument might not apply to men. The peak incidence of fracture of the distal radius occurred in teenagers in males, which we speculate is mainly the result of accidents.

There were more left-side fractures of both the distal radius and proximal humerus, compared to the right side, although the difference was not significant (distal radius, $P = 0.358795$; proximal humerus, $P = 0.161513$). Previous studies have reported similar results [10,18], and it has been suggested that dextral individuals are predisposed to injury on the opposite side as a consequence of environmental factors, or that there is decreased hand coordination of the left hand relative to the right in right-hand-dominant people [18]. The dominant hand was not checked in the current study, but most of the Japanese population are right handed; therefore, the larger number of left-side fractures is consistent with the expected data.

Injury while indoors was most common for fractures of the hip, followed by the vertebra, proximal humerus, and distal radius. The age at the time of injury decreased in a similar order; that is, the average age was highest for fractures of the hip. Injury indoors tended to increase with age, making it important to focus on prevention of slight falls or injury indoors in elderly people. About half the patients with a hip fracture were able to be discharged to their home. Both physical exercise by rehabilitation and maintenance and practical use of social welfare resources are important to increase the percentage of patients who can return home after hospitalization.

Drugs for osteoporosis were not taken before injury in most cases of hip and vertebral fractures. A past investigation performed on Sado Island indicated that the incidence of hip fracture significantly decreases with vitamin D treatment, compared with a nontreatment group, and that stopping the treatment increased the risk of hip fracture [19]. As it appears that vertebral fracture leads to hip fracture, fracture prevention from an early stage by treatment with drugs should be carried out to reduce the chance of this series of fractures, and preventive treatment should be further encouraged in osteoporotic elderly people.

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MINI REVIEW

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Serum 25-OHD insufficiency as a risk factor for hip fracture

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Abstract The aging population and an increasing number of hip fractures worldwide have made prevention of hip fractures a matter of importance. The prevalence of hypovitaminosis D in patients with acute hip fracture has been reported widely in recent years, and the vitamin D nutritional status in such reports is usually evaluated based on serum 25-hydroxyvitamin D (25-OHD). The aim of this article is to review the relationship of serum 25-OHD and osteoporotic fracture and the prevalence of 25-OHD insufficiency in patients with hip fracture, including assessment of nutritional status, oral status, activity, and dementia. We conclude that the serum 25-OHD level may be a useful index for risk of hip fracture in elderly people.

Key words 25-hydroxyvitamin D · intact PTH · hip fracture · number of remaining teeth · activity · dementia

25-OHD insufficiency and hip fracture

The number of cases of hip fracture has been increasing with the aging of societies worldwide, and methods for prevention of hip fracture are therefore of value. Vitamin D is an important nutrient for bone health and is a regulator of calcium metabolism. Vitamin D nutritional status is evaluated by measuring serum 25-hydroxyvitamin D (25-OHD), and 25-OHD insufficiency may occur in elderly people because of malnutrition, dementia, and inactivity leading to decreased exposure to sunlight. Serum 25-OHD insufficiency leads to an increase in parathyroid hormone (PTH) levels (secondary hyperparathyroidism), resulting in bone loss [1] and leading to hip fracture and decreased activities of daily living (ADL) or quality of life (QOL). Subclinical 25-OHD insufficiency is also considered to be a risk factor for osteoporotic hip fracture in elderly people [2–4] (Fig. 1). Hollis [5] reported that the normal range of 25-OHD is 32–100 ng/ml, and other studies performed in the United States and Australia [6,7] have shown that a serum 25-OHD level of at least 15–20 ng/ml is needed to achieve optimum PTH levels. Therefore, we defined a 25-OHD level of less than 20 ng/ml as vitamin D insufficiency (Fig. 2); we note that vitamin D deficiency defined as a 25-OHD of less than 5 ng/ml causes osteomalacia/rickets [8,9].

Serum 25-OHD status in hip fracture patients: the Sado study

In the United States, a serum 25-OHD level lower than 12 ng/ml was observed in 50% of women with osteoporotic hip fractures [4], and in Italy this value was found to be 13.5%, with 21.6% of patients having a serum 25-OHD level less than 20 ng/ml [3]. We compared the serum 25-OHD level in hip fracture patients with that in non-hip fracture control subjects over 1 year in the elderly population on Sado Island, Niigata, Japan (total population, 70 011; 34% were 65 years old and older); these data showed that the serum 25-OHD level was significantly lower in the hip fracture patients [10]. In addition to checking the 25-OHD levels and determining other laboratory data, we collected serum and urine samples at admission and also examined changes in the levels of serum 25-OHD in acute hip fracture patients at another general hospital in Niigata City [11]. Although the sample size was small ($n = 12$), serum 25-OHD did not show large changes (less than ±10%)

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during hip fracture healing, in comparison with the levels of other biochemical markers.

In the Sado study, 62% of 50 hip fracture patients had vitamin D insufficiency, which was defined as a serum 25-OHD concentration less than 20 ng/ml (Fig. 3). The average serum 25-OHD concentration was 17.8 ng/ml in hip-fracture patients and 25.8 ng/ml in non-hip fracture controls [10]; the mean for the patient population was lower than the recent mean value of 20.9 ng/ml reported for nonosteoporotic Japanese women more than 70 years of age [12]. In an age-matched comparative analysis, serum 25-OHD (means of 16.6 ng/ml and 22.0 ng/ml in hip fracture patients and controls, respectively) and albumin (3.6 g/l and 4.0 g/l, respectively) were significantly lower and intact PTH (45.8 pg/ml and 35.8 pg/ml, respectively) was significantly higher in the hip fracture patients [10]. In addition, the serum PTH level was not elevated (<65 pg/ml) in about 80% of hip fracture patients with 25-OHD insufficiency (see Fig. 3). Chapuy et al. [13] have reported that low serum 25-OHD does not always lead to an increase in serum PTH, and Sahota et al. [14,15] suggested that a slight reduction in serum calcium and a substantial decrease in $1,25\text{-}(OH)_2D$ may be partly related to the failure of the parathyroid gland to mount an adequate PTH response; however, the mechanisms underlying the PTH response remain unclear, and the cutoff for definition of an elevated PTH level requires further examination. A better understanding of the mechanism of serum 25-OHD and intact PTH and their relationship to bone metabolism is important for prevention of osteoporotic fractures and development of individualized treatment.

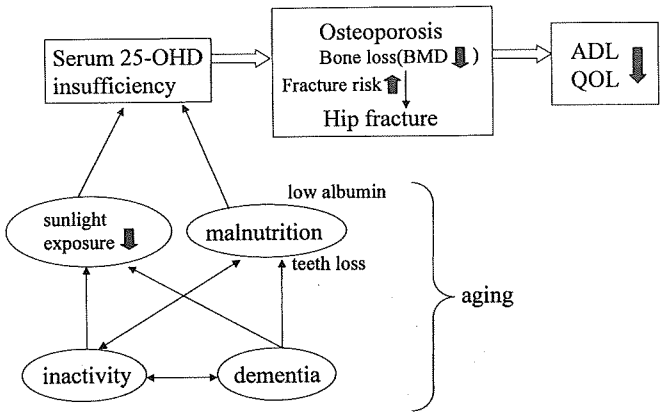

Fig. 1. Schema for the risk of fracture resulting from 25-hydroxyvitamin D (25-OHD) insufficiency and related factors. *BMD*, bone mineral density; *ADL*, activities of daily living; *QOL*, quality of life

25-OHD insufficiency	<20ng/mL
	osteoporosis (osteopenia, fragile bone)
25-OHD deficiency	<5ng/mL
	rickets, osteomalacia
	bone mineralization problems

Fig. 2. 25-OHD insufficiency and deficiency

Regarding the relationship of serum 25-OHD and the number of remaining teeth, for which the average is 6.3 in hip fracture patients and 8.9 in controls, there was no significant difference between the hip fracture group and the control group. However, a significant negative correlation between age and number of teeth was found ($\alpha = -0.45$, $P < -0.01$) [10] and a significant correlation between 25-OHD and number of teeth ($\alpha = 0.20$, $P < 0.05$) was also observed. It appears likely that the number of remaining teeth is mainly influenced by age; however, Krall et al. [16] have suggested that intake levels of calcium and vitamin D have a beneficial effect on tooth retention, which suggests a mutually beneficial relationship between the status of the oral cavity and nutritional status.

We also examined the relationship of the severity of dementia and physical activity level with serum 25-OHD in hip fracture patients, using a classification based on the criteria of the long-term care insurance system developed by the Ministry of Health, Labor and Welfare of Japan [17,18]. The mean 25-OHD level was highest, at more than 20 ng/ml,

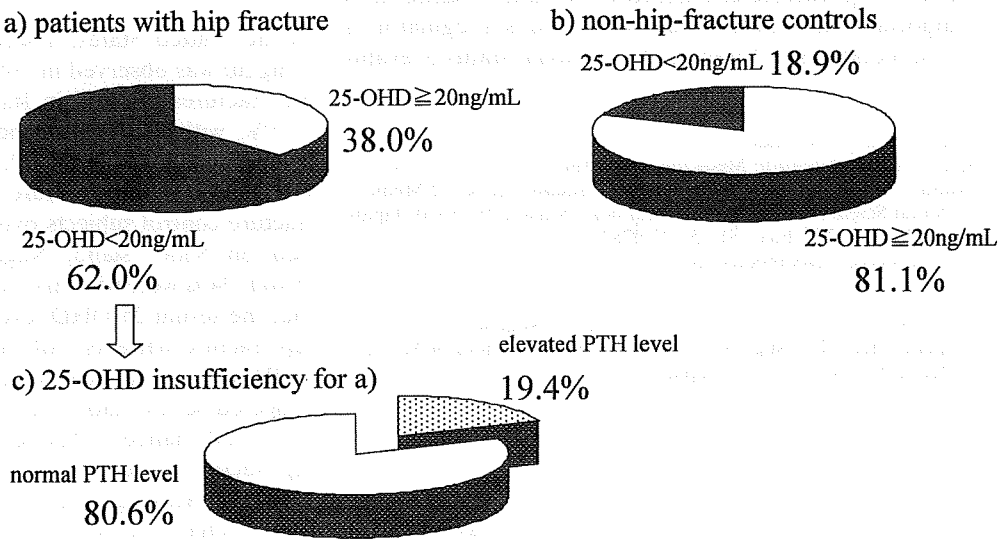

Fig. 3. Percentages of patients with 25-OHD insufficiency and elevated parathyroid hormone (*PTH*). In patients with hip fracture, 62.0% (31 of 50) had serum 25-OHD levels <20 ng/ml (**a**). In non-hip fracture controls, 18.9% (10 of 53) had serum 25-OHD levels <20 ng/ml (**b**). In hip fracture patients with low 25-OHD, 19.4% (6 of 31) had elevated PTH levels (>65 pg/ml) (**c**). (From [9])

Table 1. Relationship between dementia level and mean serum 25-hydroxyvitamin D (25-OHD)

Dementia level		25-OHD	*P* value
↓	Independent		
	I	↓	$P < 0.05$*
↓	II		
Severe	III–IV	Lower	

*Kruskal-Wallis test

in the independent (based on dementia level) group, and then tended to decrease as the degree of dementia progressed ($P < 0.05$) (Table 1). Sato et al. [19] reported that serum 25-OHD levels are significantly decreased in Alzheimer disease (AD) patients, and that vitamin D deficiency is more common among AD patients. They also reported that AD patients with lower bone mineral density (BMD) and low serum 25-OHD concentrations have an increased risk of hip fracture [20].

We have also examined the relationship between physical activity level and serum 25-OHD in hip fracture patients [10]. The mean level of 25-OHD was more than 20 ng/ml in the group assessed to be independent, and tended to decrease as the degree of activity decreased. Bischoff-Ferrari et al. [21] reported that 25-OHD concentrations between 40 and 94 nmol/l are associated with better musculoskeletal function in the lower extremities, and Di Monaco et al. [22] found a significant positive correlation between serum 25-OHD_3 and Barthel index score in hip fracture patients. Nakamura et al. [23,24] reported that elderly people requiring care at home have a high risk of hypovitaminosis D, and their low serum 25-OHD levels are mainly associated with low ADL levels. Therefore, although the relationships among dementia, activity level, and 25-OHD are not completely clear, decreased exposure to sunlight, decreased vitamin D production in the skin, and malnutrition appear to be of importance. Overall, these results suggest that dementia, decreased activity, and vitamin D deficiency are mutually associated and carry a high risk for hip fracture.

Summary and conclusion

Vitamin D insufficiency is prevalent in hip fracture patients and is associated with the status of the oral cavity, nutritional status, recognition function, and physical activity levels. Although these conditions are not caused by vitamin D insufficiency alone, we suggest that a good vitamin D status will reduce fragility in elderly people. The serum PTH level was not elevated in about 80% of hip fracture patients with 25-OHD insufficiency, but the mechanism of this observation remains unclear. Therefore, accumulation of more data linking 25-OHD, intact PTH, and hip fracture is required; this information should lead to better prevention of hip fracture in at-risk individuals and improved treatment of hip fracture and osteoporosis.

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ORIGINAL ARTICLE

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Risk factors for vertebral fracture in menopausal or postmenopausal Japanese women with rheumatoid arthritis: a cross-sectional and longitudinal study

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Abstract The occurrence of vertebral fracture was examined cross-sectionally and longitudinally over a 4-year interval in 117 menopausal and postmenopausal Japanese women with rheumatoid arthritis (RA), whose ages ranged from 50 to 64 years. Patients treated with bisphosphonate were excluded. Vertebral fracture was diagnosed by lateral thoracic and lumbar spine radiography at the start and end of a 4-year period. Bone mineral density (BMD) at L2–L4 according to dual-energy X-ray absorptiometry (DXA), the administration of corticosteroids or methotrexate, and urinary excretion of N-telopeptide of type I collagen (NTx) were also recorded. In the cross-sectional study, the prevalence of vertebral fracture in the initial radiographs of RA patients was 21%, while it was 5% in healthy age-matched controls. Among RA patients treated with corticosteroids, 33% had vertebral fracture, which was a significantly higher prevalence than that in RA patients without steroid administration. In the longitudinal study, vertebral fracture prevalence was also increased in patients more than 60 years old. RA patients having steroid treatment and a BMD/YAM (young adult mean) ratio below 70% had higher risk of vertebral fracture than patients with a BMD/YAM ratio of 70%–80%, which in turn exceeded the risk with a BMD of 80% or more. No adverse effect of low-dose methotrexate on vertebral fracture was found. Urinary NTx was high in RA patients, as reported previously, and did not differ between patients with or without new fracture after 4 years. In conclusion, Japanese RA patients more than 60 years old who were treated with corticosteroid or had a BMD below 80% had high risk of vertebral fracture.

Key words rheumatoid arthritis · vertebral fracture · steroid administration · postmenopausal age · longitudinal study design

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Introduction

Joint surgery using a prosthesis improves the performance of activities of daily living (ADL) and quality of life (QOL) in appropriately selected patients with rheumatoid arthritis (RA). Evidence of generalized osteoporosis has been reported in RA patients [1–12]. Osteoporosis in terms of reduced bone mineral density (BMD) is well known, but the clinically important end-point of osteoporosis is fracture. For example, symptomatic vertebral compression fracture is a significant problem which compromises both ADL and QOL. Recent reports concerning vertebral fracture in RA indicated that corticosteroid use significantly increased the risk of fracture [1–3,13]. Kanis et al. [2] reported an international metaanalysis concerning prior corticosteroid use and fracture risk, but Japanese data were not included. Reports by de Nijs et al. [13] and Ørstavik et al. [3] dealt with patients in Europe. In primary osteoporosis, the incidence of cervical and trochanteric fractures of the proximal femur was shown to be lower in Japan than in Europe and the United States [14,15]. We performed the present cross-sectional and longitudinal study to determine the incidence and risk factors for vertebral fracture in menopausal and postmenopausal Japanese women with RA.

The cross-sectional part of the present study involved a comparison of the radiographically demonstrated prevalence of vertebral fracture in RA patients with that in age-matched menopausal and postmenopausal women without RA. We then longitudinally examined how many RA

patients with or without glucocorticoid therapy sustained a new vertebral fracture during a 4-year period.

Patients and methods

Cross-sectional study

We examined 117 menopausal and postmenopausal women who fulfilled the revised 1987 RA criteria of the American College of Rheumatology [16], and who were treated in our RA outpatient clinic between September and November 1998. Patients treated with bisphosphonate were excluded, while those treated with vitamin D or vitamin K were included. No patients represented class 4 of the Steinbroker classification; most were in class 2. The ages of the 117 patients were as follows: 50–54 years (designated group A), 32 patients; 55–59 years (group B), 35 patients; 60–64 years (group C), 50 patients. The healthy control group consisted of 62 women who had been admitted to the hospital for a comprehensive osteoporosis evaluation (mean age ± SD, 57.4 ± 4.5 years). No difference in age was evident between RA patients and healthy controls.

Vertebral fracture was diagnosed from lateral radiographs of the thoracic and lumbar spine. Such a fracture was considered to have occurred when either the ratio of the height at the center of a vertebra (C) to the height at the anterior portion of the vertebra (A), or the ratio of C to the posterior portion of the vertebra (P), was less than 0.8, or when A/P was less than 0.75 [17]. This cross-sectional examination of 117 RA patients for vertebral fractures was carried out in 1998.

Longitudinal study

We followed up the 117 RA patients until 2002. Four patients died, while another became bedridden because of cerebral infarction. These five patients were excluded from the longitudinal analyses. In 2002, we reassessed vertebral fractures radiographically by the method used in 1998. As part of the longitudinal study, BMD at L2–L4 was determined in 1998 by dual-energy X-ray absorptiometry (DXA; Hologic QTR 2000, Waltham, MA, USA).

Treatments with corticosteroid and/or methotrexate (MTX) were recorded, as were the results of assays for N-telopeptide of type I collagen (NTx) in urine.

Statistical analysis

The results are expressed as the mean ± SD. To compare numerical data not normally distributed, a Mann–Whitney U test was used. When the distributions were normal and the variances approximately equal, the differences between means were compared by Student's t test. For categorical data comparisons, a χ^2 test was used. Differences were considered to be significant when P was below 0.05. We computed 95% confidence intervals (CI) for differences between means, and for odds ratios for paired data. Cut-off values were defined as the value at which subjects with vertebral fracture were distinguished with optimal sensitivity and specificity from those without vertebral fracture.

Results

Cross-sectional study (Table 1)

In 1998, vertebral fracture was detected in 25 RA patients among 117. The 117 RA patients included 55 receiving an oral steroid (6.0 ± 2.4 mg prednisolone daily). Among these, the 18 (33%) who had a vertebral fracture received 7.1 ± 3.1 mg prednisolone per day, compared with 5.4 ± 1.8 mg prednisolone per day in the 37 steroid-treated RA patients without vertebral fracture. This difference in dose between prednisolone-treated RA patients with and without a vertebral fracture was significant ($P < 0.05$). Fractures were found in 7 of 62 RA patients without oral steroid therapy (11%). The odds ratio for vertebral fracture associated with steroid administration compared with no steroid administration was 3.82 (95% CI, 3.01–4.85). In relation to the dose of prednisolone, the odds ratio for vertebral fracture associated with a daily dose of 5 mg or higher compared with less than 5 mg daily was 3.80 (95% CI, 3.03–4.76); that associated with a daily dose of 7.5 mg or higher compared with less than 7.5 mg daily was 4.34 (95% CI, 3.21–5.86). On the other hand, 3 of 62 healthy controls had a vertebral fracture (5%). Thus, the difference in the prevalence of vertebral fracture was significant between RA patients considered overall and healthy control subjects ($P < 0.05$), but was not significant between RA patients who did not have oral treatment with a steroid and the controls.

Table 1. Prevalence of vertebral fracture in 117 RA patients and 62 healthy control subjects in 1998

	No. of subjects	Age (years)	Prevalence of vertebral fracture
RA patients	117	58.0 ± 4.6	25 (21%)*
Steroid (+)	55	58.6 ± 4.4	18 (33%)**
Steroid (–)	62	57.4 ± 4.8	7 (11%)
Healthy controls	62	57.4 ± 4.5	3 (5%)*,**

There were no age differences between these groups
*,**Designated pairs compared; finding $P < 0.05$

Longitudinal study

We radiographically evaluated 112 RA patients for vertebral fracture in 1998 as part of the cross-sectional RA group above, and again in 2002. Four patients began oral steroid therapy between 1998 and 2002; these were considered as steroid-treated patients in the longitudinal study.

Patients with vertebral fractures in 2002 vs 1998, by age-defined group and therapy

In age-group A, 19 patients who received no steroid included none with a vertebral fracture in 1998 (0%) and 1 in 2002 (5%). Two patients began oral steroid therapy during 1998–2002, but did not sustain an additional vertebral fracture. Among 11 group-A patients receiving oral prednisolone (6.0 ± 2.3 mg daily) in 1998, 3 had a fracture in 1998 (27%); this increased to 4 by 2002 (36%). In age-group B, 2 of 21 patients with no steroid had a fracture in 1998 (10%), and this had increased to 6 by 2002 (29%). Among 12 patients in group B receiving oral prednisolone (5.5 ± 1.0 mg daily), 2 had a fracture in 1998 (17%), and this had increased to 3 by 2002 (25%). In age-group C, 4 of 21 patients with no steroid had a fracture in 1998 (19%), and this had increased to 7 by 2002 (33%). Two group-C patients began oral steroid therapy between 1998 and 2002, but did not sustain an additional vertebral fracture. Among 28 group-C patients receiving oral prednisolone (6.1 ± 2.8 mg daily), 12 had a fracture in 1998 (43%); this had increased to 21 by 2002 (75%; Table 2).

The fracture rate between 1998 and 2002 was analyzed in terms of age in 89 RA patients with no vertebral fracture in 1998. Sensitivity and specificity for vertebral fracture were calculated for each age, yielding a cut-off value of 59 years (Fig. 1).

Occurrence of new vertebral fractures in patients with preexisting fracture in 1998

In group A, no patient receiving no steroid had a preexisting fracture. Among group-A patients with oral steroid therapy, 3 had a fracture at the 1998 baseline, 1 of whom had sustained a fracture in another vertebra by 2002. In group B, 2 patients with no steroid had a fracture at baseline, while none showed a new fracture in 2002. Among group-B patients receiving an oral steroid, 2 had fractures at baseline, including 1 with a new fracture in another vertebra by 2002. In group C, among patients with no steroid, 4 had a fracture at baseline, while none had a new fracture by 2002. Group-C patients with oral steroid therapy included 12 with fractures at baseline, 6 of whom had a new fracture in another vertebra by 2002 (Table 3). Steroid administration increased the risk of new vertebral fractures in patients with a preexisting fracture ($P < 0.05$).

Influence of BMD and steroid administration on the risk of a first vertebral fracture during a 4-year period

Patients with no fracture in 1998 who were reevaluated in 2002 were divided into three groups according to their BMD relative to the young adult mean (YAM). Among patients with a BMD/YAM below 70%, 10 had prednisolone therapy (5.6 ± 1.9 mg daily), while 7 of these 10 had a vertebral fracture by 2002 (70%). Eight patients in this BMD range receiving no steroid included 3 with a vertebral fracture by 2002 (38%). Among patients with a BMD/YAM between 70% and 80%, 8 patients received prednisolone (4.6 ± 0.88 mg daily), with 3 showing a vertebral fracture by 2002 (38%). Among 12 patients in this BMD range with no steroid, 2 had a vertebral fracture by 2002 (18%). Among patients with a BMD/YAM of at least 80%, 19 patients received prednisolone (5.7 ± 1.9 mg daily), with 1 of 19 having a vertebral fracture by 2002 (5.3%). Of 32 patients in this BMD range with no steroid therapy, 3 patients had a vertebral fracture by 2002 (9.4%; Table 4).

The fracture rate was analyzed in terms of BMD/YAM (%) in RA patients treated with corticosteroid during a 4-year period. Sensitivity and specificity for BMD–YAM in predicting vertebral fracture were plotted for each 1% BMD/YAM increment. The cut-off value was 73%–74% of patients (Fig. 2).

Table 2. Vertebral fracture prevalence in 1998 and 2002

Age in 1998 (years)	Steroid	No.	Fracture (+)	
			1998	2002
Group A: 50–54	(–)	19	0 (0%)*	1 (5%)**
	(+)	11	3 (27%)*	4 (36%)**
Group B: 55–59	(–)	21	2 (10%)	6 (29%)
	(+)	12	2 (17%)	3 (25%)
Group C: 60–64	(–)	21	4 (19%)	7 (33%)#
	(+)	28	12 (43%)	21 (75%)#

Only 112 patients were evaluated (5 were excluded because of death or their bedridden state). Two group A patients and 2 group C patients began oral steroid therapy between 1998 and 2002; these patients did not sustain an additional vertebral fracture

*,**,# Designated pairs compared; finding $P < 0.05$

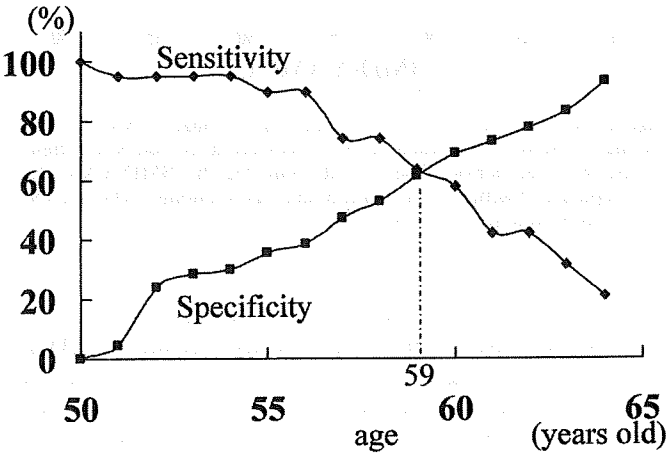

Fig. 1. Determination of a cut-off value for the age predicting a first vertebral fracture in RA patients during a 4-year period. The cut-off value for the age that best separates fracture from nonfracture cases among patients with RA was 59 years

Table 3. New vertebral fractures among patients with a fracture 4 years previously

Age in 1998 (years)	Steroid	No. with a vertebral fracture	No. with an additional vertebral fracture in 2002
Group A: 50–54	(–)	0	0
	(+)	3	1
Group B: 55–59	(–)	2	0
	(+)	2	1
Group C: 60–64	(–)	4	0
	(+)	12	6

Steroid administration increased the risk of new vertebral fractures in patients with a preexisting fracture ($P < 0.05$)

Table 4. BMD/YAM in 1998 according to fracture incidence in 2002

BMD/YAM (%)	1998 Fracture (–)	2002 Fracture (+)
<70%		
Steroid (+)	10	7 (70%)
Steroid (–)	8	3 (38%)
70%–80%		
Steroid (+)	8	3 (38%)
Steroid (–)	12	2 (18%)
≦80%		
Steroid (+)	19	1 (5%)
Steroid (–)	32	3 (9%)

BMD, bone mineral density; YAM, young adult mean

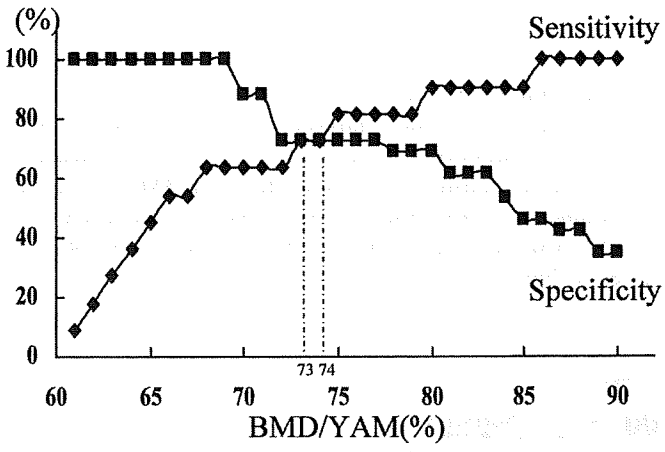

Fig. 2. Determination of a cut-off value for the BMD/YAM (%) predicting a first vertebral fracture in corticosteroid-treated RA patients during a 4-year period. The cut-off value for the BMD/YAM that best separates fracture from nonfracture cases among corticosteroid-treated RA patients was 73%–74%

The occurrence of new vertebral fractures between 1998 and 2002 was also examined specifically in relation to BMD in patients receiving no oral steroid. Of patients who had no fracture in 1998, 16% had a new vertebral fracture in 2002; their BMD/YAM was 76% ± 14% in 1998. The BMD/YAM of patients who did not have a new fracture in the 4-year period was 88% ± 16% in 1998. The BMD/YAM in patients who had a new vertebral fracture during the 4 years was significantly lower than that in patients who had no fracture.

Table 5. The odds ratio for the occurrence of new vertebral fractures between 1998 and 2002 associated with BMD/YAM (%) in patients receiving no oral steroid

BMD/YAM (%) in 1998	Odds ratio	95% CI
65	6.14	0.74–51.32
66	14.33	2.74–75.09
67	14.33	2.74–75.09
68	25.80	5.61–118.61
69	6.00	2.72–13.25
70	4.68	2.22–9.85
71	4.68	2.22–9.85
72	3.17	1.59–6.32
73	4.50	2.37–8.53
74	3.40	1.83–6.30
75	5.00	2.63–9.50
76	4.44	2.36–8.39
77	3.57	1.91–6.67
78	3.57	1.91–6.67
79	3.57	1.91–6.67
80	3.22	1.73–6.00

CI, confidence interval

The odds ratio for the occurrence of a new vertebral fracture between 1998 and 2002 associated with a BMD/YAM (%) in patients receiving no oral steroid was computed for each 1% BMD/YAM increment (Table 5). The odds ratio for vertebral fracture associated with a BMD/YAM (%) of 68% or higher compared with less than 68% was 25.80 (95% CI, 5.61–118.61). In RA patients receiving no oral steroid, a BMD/YAM below 69% indicates risk for vertebral fracture, as was suggested for primary osteoporosis.

Influence of steroid and/or MTX administration on vertebral fracture risk

Table 6 gives the fracture risk in patients treated with steroid and/or MTX in 1998. In 1998, 24 RA patients had treatment with oral prednisolone (5.6 ± 2.3 mg daily) plus MTX. In that year, 31 RA patients received oral prednisolone (6.3 ± 2.5 mg daily) without MTX. RA patients receiving MTX but no oral steroid numbered 22, while 35 RA patients had neither oral steroid nor MTX. There were no age differences between steroid (+) MTX (+), steroid (+) MTX (–), and steroid (–) MTX (+) groups, while MTX (–) steroid (–) patients were younger than the others. In steroid (+) MTX (+) patients, the prevalence of vertebral fracture