Bone Mineral Density in Residents of Care Facilities for the Aged and Effect of Pharmacotherapy

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ABSTRACT

Background Bone mineral densitometry has been proven to be a powerful tool for the diagnosis and treatment of osteoporosis, which is increasing with aging of the population, but opportunities to perform bone mineral densitometry in elderly facility residents, who are at a high risk of fracture, are scarce.

Methods We measured the bone mineral density in 315 residents of 5 care facilities for the aged in middle Tottori Prefecture from 2002 to 2006. We also evaluated residents of an elderly nursing home with a history of fragility fracture and those with osteoporosis who were administered risedronate for its therapeutic effect.

Results The bone mineral density was less than 70% of the young adult mean in 161 (51.1%) of the 315 subjects (aged 83.1 ± 7.8 years), 149 (57.8%) of the 258 women (83.9 ± 7.2 years), and 12 (21.1%) of the 57 men (79.8 ± 9.3 years). In the 13 subjects who were administered risedronate, the bone mineral density increased from 65.8 to 67.2% of the young adult mean from before to after the beginning of administration, but it decreased in the control group (n = 9). In those administered risedronate, the urinary level of N-telopeptide (a marker for bone resorption) began to decrease 3 months after the beginning of the administration and showed a significant decrease after 11 months (n = 8) compared with the control group. The mean pain score based on the visual analogue scale showed significant reduction in the risedronate group compared with the control group.

Conclusion The bone mineral density was low in the facility residents and was less than 70% of the young adult mean in 57.8% of women and in 21.1% of men, more frequently than expected. Bone resorption and osteoporotic pain were suppressed by risedronate in osteopenic patients in such care facility.

Key words bone mineral density; care facilities for the aged; osteoporosis; risedronate; young adult mean

In Japan, patients with osteoporosis are increasing annually with the rapid aging of the population.[1] Since fracture due to osteoporosis leads to serious disabilities and a decrease in the quality of life, which may even be fatal,[1] its management has emerged as an important social as well as medical issue.[2–4] Osteoporosis used to be understood simply as aging of bone, but, in the late 1980s, a few cohort studies involving local residents were also carried out in Japan, evaluating the incidence and effects of fracture due to osteoporosis, and indicating the importance of its prevention.[1] Moreover, the concept of evidence-based medicine proposed in the 1990s has also been adopted in the field of osteoporosis as a basic position of clinical medicine, and successive large-scale clinical trials with fracture as an endpoint have been conducted in Western countries since 1994. The spread of bone mineral analysis using a bone mineral analyzer and the availability of objective evaluation of the state of bone metabolism based on the measurements of bone metabolic markers have markedly contributed to this trend.[3] As a result, in 1998, the Working Group of the Osteoporosis Study Group, Ministry of Health, Labour and Welfare Comprehensive Research on Longevity evaluated and organized information concerning anti-osteoporosis medications from objective viewpoints on the basis of the concept of evidence-based medicine and prepared the Japanese Guidelines for the Prevention and Treatment of Osteoporosis.[3, 4] Thereafter, the necessity of the prevention and treatment of osteoporosis has become widely recognized, and the guidelines have also been revised and widely accepted.[4]

However, patients who can undergo bone mineral screening or measurement are limited to those who can visit departments such as the Departments of Orthopedics and Gynecology of a medical facility with

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Abbreviations: BMD, bone mineral density; NTX, cross-linked N telopeptide of type I collagen; VAS, visual analog scale; YAM, young adult mean

a bone mineral analyzer. The bone mineral density (BMD) has been shown to increase even in osteoporotic elderly people by making conscious efforts to walk,[5] and screening for osteoporosis is considered necessary for elderly care such as in long-term care facilities, in which many users are elderly people with a low activity level. The number of cases of hip fracture in Japan is estimated to exceed 120 thousand a year, about 10% of those who sustain the injury die within 1 year, and about 30% show declines in activities of daily living.[6] Also, skeletal deformities secondary to fracture cause a bedridden state or chronic lumbar pain, hump back, and a decrease in height, which impair activities of daily living and increase the necessity for long-term care.[7, 8]

Many residents of care facilities are elderly people at a constant risk of fracture associated with falling, etc., and its prevention is very important. The evaluation of factors related to the bone strength as well as lifestyle and living environment is necessary for the prevention of fracture. In this study, the prevalence of osteoporosis was investigated in residents of long-term care facilities in middle Tottori Prefecture and the effect of therapeutic intervention was evaluated in those who have few chances to be prescribed.

SUBJECTS AND METHODS

This study was carried out with approval (approval number 2301) by the Ethics Committee of Tottori University.

Prevalence of osteoporosis

The study was carried out between 2002 and 2006 in 315 who consented to cooperate in the study of 450 residents of 5 care facilities for the aged in middle Tottori Prefecture. The total capacity of 8 facilities were 572 in maximal number in the same district, residents of rest 3 facilities were not requested because of the lack of permission from the head of these facilities.

The BMD was measured using an ultrasound bone mineral densitometer (AOS-100NW, Hitachi-Aloka Medical, Tokyo, Japan) in the right calcaneus. This densitometer was convenient to use at care facilities for the aged, because it required a short time for measurement, permitted dry measurement without using water, and needed no special facility as it emitted no radiation.

For comparison of the BMD with middle-aged to elderly residents of the same area in middle Tottori Prefecture, it was also measured in those who underwent comprehensive health screening at Hospital A and consented to the measurement (using an ultrasound bone mineral densitometer, Benus III, Ishikawa Seisakusho, Hakusan, Japan).

In 1996, the Japanese Society for Bone and Mineral Research proposed diagnostic criteria for osteoporosis by taking the BMD into consideration, and set cutoff values at < 70% of the mean BMD of those aged 20 to 44 years (the young adult mean; YAM) for osteoporosis and 70 to 80% of the YAM for low BMD concerning Japanese women.[9] In the 2000 revision, the cutoff value for the diagnosis of osteoporosis was also evaluated for men, and it was concluded that about 70% of the YAM was appropriate for the discrimination of a high-risk group for fracture in men as well as women.[10] We adopted this criteria to detect the prevalence of osteoporosis in the residents of care facilities.

Effects of pharmacotherapy

The effects of pharmacotherapy were evaluated in the residents of a nursing home for the aged in middle Tottori Prefecture (Nursing Home B, one of 5 facilities). The BMD was measured using an ultrasound bone densitometer (AOS-100NW, Hitachi-Aloka Medical) in the right calcaneus. As a treatment, sodium risedronate (Benet, Takeda Pharmaceutical, Tokyo) was administered at 2.5 mg (once daily) to those with a history of fragility fracture and those with a BMD < 70% of YAM, and those who consented were followed up. Residents in Nursing Home B with same conditions as treated patients and those who consented to non-treatment were also followed up as the control. Risedronate is expected to reduce bone resorption[11, 12] and improve low back pain even in residents without vertebral fractures.[13]

Biological indices that specifically reflect bone metabolism have been confirmed to be useful as bone metabolic markers for the evaluation of bone turnover in bone remodeling, classification of disease types, and evaluation of therapeutic effects in metabolic bone disorders such as osteoporosis.[14–16] The measurement of the urinary levels of deoxypyridine and cross-linked N telopeptide of type I collagen (NTX) for osteoporosis began to be covered by insurance in December 1999. In this study, the urinary excretion of the bone resorption marker NTX was measured as an index of the therapeutic effect every 3 months for about 1 year. The measurement, commissioned to SRL (Tokyo, Japan), was carried out by enzyme-linked immunosorbent assay. For evaluation of the urinary NTX level, the value was corrected for the creatinine level [creatinine-corrected NTX level = (NTX concentration/creatinine concentration) × 11.3] in consideration of the effect of the renal function.

The number of fracture cases was investigated by preparing a check sheet and obtaining cooperation of the staff of Nursing Home B. As for physical findings,

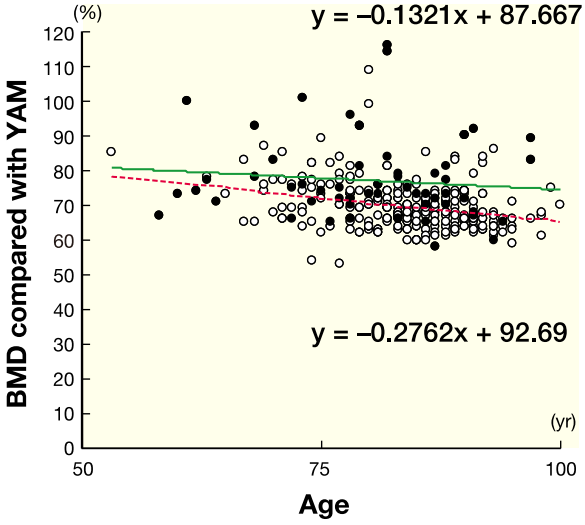

Fig. 1. BMD in facility residents. The BMD of the right calcaneus in 315 residents of 5 care facilities for the aged is expressed as the percentage of the YAM (vertical axis) and plotted against age (horizontal axis). In women (○), the approximation line is y = –0.2762x + 92.69 (solid line). In men (●), the approximation line is y = –0.1321x + 87.667 (dashed line). BMD, bone mineral density; YAM, young adult mean.

changes in the blood pressure were investigated using medical records. Pain was evaluated by quantification using Huskisson's visual analog scale[17] (VAS; 0 mm = no pain, 100 mm = worst pain possible).

Statistics

Data of the 2 groups were compared using Student's *t*-test.

RESULTS

Prevalence of osteoporosis

The 315 subjects consisted of 57 men (mean age: 79.8 ± 9.3 years, range: 58–97 years) and 258 women (83.9 ± 7.2 years, range: 53–100 years). The approximation curve of the relationship between the BMD as the percentage of the YAM and age was y = –0.2762x + 92.69 in women and y = –0.1321x + 87.667 in men (Fig. 1).

The BMD was < 70% of the YAM in 161 (51.5%) of the 315 subjects, 149 (57.8%) of the 258 women, and 12 (21.1%) of the 57 men. The percentage of those in whom the BMD was < 70% of the YAM was about 2.4-fold higher in women. As shown in the right of Fig. 2, in those who underwent comprehensive health screening at Hospital A, it was < 70% of the YAM in only 1 (1.1%) of all 91 subjects, 1 (1.3%) of the 78 women and none (0%) of the 13 men. The relationship between the BMD as the percentage of the YAM, the rate of BMD < 70% of the YAM and age are shown also in Table 1. The difference between the BMD in facility residents and in health screenees (control) is apparent even in the same age groups.

Effects of pharmacotherapy

In the subjects at Nursing Home B, the administration of sodium risedronate was recommended to 14 and initiated in 13 (2 men and 11 women with a mean age of 83.0 ± 5.3 years, range: 77–91 years). The patient's records showed that all patient had good compliance with their prescribed regimen. Fourteen similar residents (1 men and 13 women with a mean age of 87.6 ± 5.5 years, range: 83–100 years) who consented were allocated to the control. The BMD in the patients in whom it could be measured before and after the treatment (n = 6) was 65.8 and 67.2% of the YAM, respectively (Fig. 3). Its changing rate is +2.0 ± 2.0% in the treated subjects and –3.5 ± 2.2% in the controls (n = 9) (P = 0.06).

Of the patients administered sodium risedronate, urine samples could be obtained during the treatment period from 8. The urinary NTX level (creatinine-corrected) decreased significantly 3 and 11 months after the beginning of the administration compared with the pre-administration value and was significantly lower than in the control group after 11 months (Fig. 4).

During the observation period, no fracture occurred in the treated or control group. The mean pain score on the VAS decreased by 16.0 ± 5.8 mm in the treated group but showed slight decrease by 2.3 ± 4.1 mm in the control group. There is a significant difference between these values (P < 0.05).

The mean systolic blood pressure was 126.4 ± 4.1 mmHg before and 125.7 ± 4.5 mmHg after the administration in the treated group. In the control group,

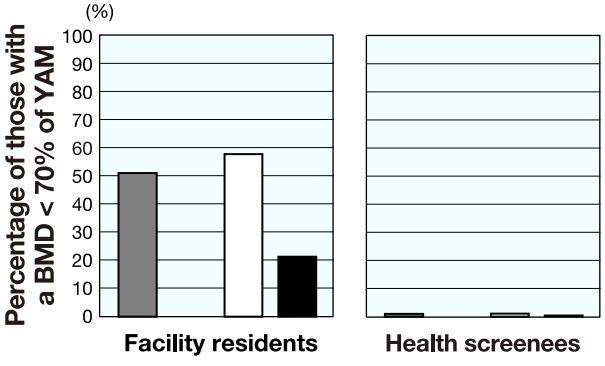

Fig. 2. Percentage of those with a BMD < 70% of the YAM in facility residents and health screenees. The left graph shows the percentages of those with a BMD < 70% of the YAM in all (51.1%, grey column), female (57.8%, white column) and male (21.1%, black column) facility residents. The right graph shows the percentages in all (1.1%), female (1.3%) and male (0%) health screenees. BMD, bone mineral density; YAM, young adult mean.

Table 1. BMD and number of those < 70%YAM by age group

		Age group (yr)						
		50–59	60–69	70–79	80–89	90–99	100–109	Total
Residents								
	Total number	2	15	74	155	68	1	315
	BMD (%YAM)	76 ± 12.7	77.8 ± 9.6*	73.3 ± 8.6*	69.9 ± 9.0	68.9 ± 7.3	70	
	< 70% YAM	1 (50%)	2 (13.3%)	26 (35.1%)	85 (54.8%)	47 (69.1%)	0 (0%)	
	Female	1	8	55	133	60	1	258
	BMD (%YAM)	85	75.1 ± 7.8*	71.8 ± 7.3	68.7 ± 7.5	68.1 ± 6.2	70	
	< 70%YAM	0 (0%)	2 (25%)	23 (41.8%)	81 (60.9%)	43 (71.7%)	0 (0%)	
	Male	1	7	19	22	8	0	57
	BMD (%YAM)	67	80.9 ± 11	77.7 ± 10.7	76.9 ± 13.7	74.5 ± 11.9		
	< 70%YAM	1 (100%)	0 (0%)	3 (15.8%)	4 (18.2%)	4 (50%)	0 (0%)	
Controls								
	Total number	40	4	3				47
	BMD (%YAM)	93.4 ± 12.9	93.4 ± 11.6	88.6 ± 3.1				
	< 70% YAM	1 (2.5%)	0 (0%)	0 (0%)				
	Female	34	4	1				39
	BMD (%YAM)	92.6 ± 12.9	93.4 ± 11.6	88.4				
	< 70% YAM	1 (2.9%)	0 (0%)	0 (0%)				
	Male	6	0	2				8
	BMD (%YAM)	97.8 ± 13.3	–	88.8 ± 4.3				
	< 70% YAM	0 (0%)	–	0 (0%)				

Residents: residents in 5 care facilities for the aged. Controls: health screenees at Hospital A.
< 70%YAM, number of subjects in whom the BMD is < 70% of the YAM; BMD (%YAM), bone mineral density as the percentage of the YAM (%YAM); YAM, young adult mean (age: 20–44 years).
*$P < 0.05$ compared with the values in control.

however, it had somewhat increased from 125.3 ± 4.6 mmHg to 132.3 ± 4.0 mmHg at the end of the observation period, without significant difference in changes between the 2 groups..

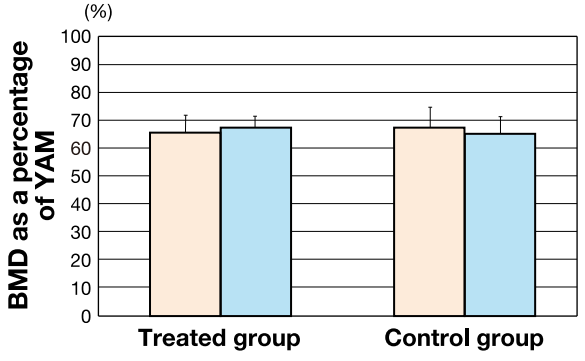

Fig. 3. Changes in the BMD as a percentage of the YAM between before and after the administration of sodium risedronate. The left bar graph shows the mean BMD as a percentage of the YAM in the risedronate-treated group before (left) and after (right) the administration ($n = 6$). The right graph shows the mean values in the control group before (left) and after (right) the same observation period ($n = 9$). Data are expressed as mean ± SEM. BMD, bone mineral density; YAM, young adult mean.

DISCUSSION

There are many reports describing the BMD in the elderly patients or elderly community residents. However, We have little knowledge about BMD of the aged in the care facilities especially in the Tottori Prefecture due to lack of chances to measurement. It is the first report concerning the BMD for such facility residents in Tottori prefecture. In the present study, we showed that the BMD was lower in older subjects, as was generally expected in the residents of 5 care facilities for the aged. Fujiwara et al. evaluated bone mineral densitometry data of 3,248 persons among the subjects of an epidemiological study selected from citizens of Hiroshima and Nagasaki Cities and reported, according to the diagnostic criteria of 1996, that the prevalence of osteoporosis was 24% (BMD in the lumbar vertebra) and 27% (BMD in the hip) in women aged 50 years and above.[18] In males aged 50 years and above, also, they reported that 3.2% were diagnosed with osteoporosis with a cutoff BMD of < 70% of the YAM (lumbar vertebra).[18] It was low in more women than men, showing a gender difference. Since a gender difference similar to that observed in this study has been reported in many previous regular studies,[19] Moreover, from the gender and age distribution of the prevalence of osteoporosis,

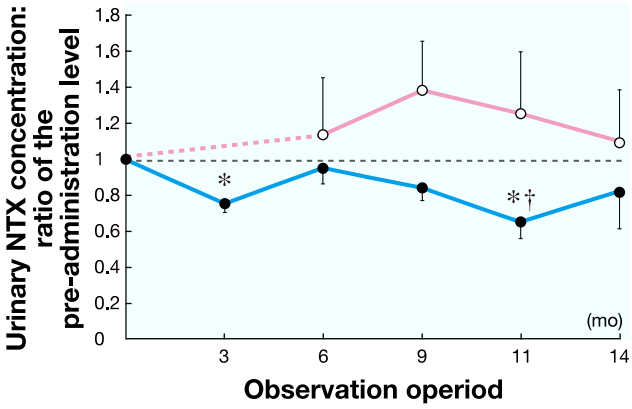

Fig. 4. Changes in the creatinine-corrected urinary cross-linked N telopeptide of type I collagen (NTX) level. Changes in the creatinine-corrected urinary NTX level after the administration of sodium risedronate at 2.5 mg are shown as a ratio of the value before administration (= 1). The values in the group administered sodium risedronate (●) showed significant decreases after 3 and 11 months (*) compared with the pre-administration value (n = 8). The values in the control group (○) also fluctuated but showed no significant change compared with the pre-administration value (n = 7). The urinary NTX concentration did not differ significantly between the risedronate-treated and control groups before the administration but differed significantly after 11-month administration (†). Data are expressed as mean ± SEM.

Yamamoto reported that the prevalence of osteoporosis was increasing with age in both men and women and that it was about 3-fold higher in women than in men.[20] In our study, also, the prevalence of osteoporosis in the facility residents was about 2.4-fold higher in women than in men. In our subjects, women were predominant, accounting for 81.9%. This may be related to very low bone mass of this study.

The percentage of those in whom the BMD of the lumbar vertebra was < 70% of the YAM among women aged 50 years and above, calculated from the population in 2000 estimated by the Ministry of Health, Labor and Welfare was reported to be 29.2%.[3] The percentage of those in whom the BMD of the calcaneus was < 70% of the YAM in women aged 50 years and above among the subjects of this study was about 57.8%, and this high frequency is suspected to be due to the presence of underlying diseases and the consequent low activity level. Yamazaki et al. reported that the BMD increases due to suppression of bone turnover in postmenopausal women regularly practicing outdoor walking compared with those with no such habit.[5] It has also been reported that the decrease in the BMD during a 10-year period was correlated with a decrease in activities of daily living in people aged 60 years and above.[21] Considering these reports, the low bone mass observed in our subjects may have been associated with a low activity level as a characteristic of the facility residents or combined effects of multiple factors. Concerning Western populations resembling the subjects of our study, there is also a report that osteoporosis was observed in 47% of the postmenopausal women (mean age: 79 ± 10 years) admitted to a nursing home who underwent BMD measurements.[22] Compared with this value, also, the prevalence of osteoporosis in our subjects (57.8%) was high.

However, the prevalence of osteoporosis was markedly lower in the health screenees than in the facility residents, probably because the health screenees were more active and younger. Therefore, to detect osteoporosis, it is considered necessary to screen those consulting for medical services other than a comprehensive health checkup. Also, as the subjects of this study were facility residents, investigation of, and comparison with, the elderly living at home are considered necessary.

Recently, a nation-wide survey in Japan revealed rapid increases in hip fracture over the last 10 years, and the necessity of treatment for osteoporosis and measures to prevent falls as well as appropriate treatment for hip fracture has been suggested.[23] In Japan, bisphosphonate is most widely known and studied among drugs for the treatment of osteoporosis.[1] Risedronate is a bisphosphonate which reduces resorption and bone turnover by inhibiting osteoclast activity. Risedronate has been shown to increase BMD and inhibit vertebral and hip fractures. Then, bisphosphonate preparations including sodium risedronate have been administered to patients with osteoporosis alone,[24] those with osteoporosis and vertebral fracture,[11, 12] and those after stroke,[25, 26] and their effectiveness for fracture prevention and cost-effectiveness have been evaluated. Among these studies, Ding et al.[27] reported that the cost-effectiveness of risedronate was poor in Japanese women aged 55 years or above and even those aged 70 years or above if they have no history of vertebral fracture. However, on the basis of the results of a survey of residents of various care facilities including homes for elderly people with dementia in the United Kingdom, Aspray et al.[28] contended that the risk of fracture at these facilities is ignored and that treatment is necessary. As far as we searched, effect of risedronate has not been examined in the residents in care facilities except for hospitalized disabled patients after stroke in Japan.[25] In this regard, it appears reasonable that patients who consented were treated at our study in care facilities for prevention against new fracture, and reduction of pain[13] concerning low bone mass.

There is a report that bisphosphonate increases the BMD but its preventive effect on postmenopausal fracture is insufficient without sufficient drug compliance,[29]

and a significant correlation between the compliance with bisphosphonate therapy and risk of fracture has been noted.[30] Particularly, drug compliance is likely to be poor when patients are asymptomatic, as in osteoporosis, and marked compliance has been reported to be related to BMD measurement after the administration and being nursing home residents,[31] both of which applied to our subjects. In this study, as a result of checking the administration using a check sheet, compliance with the risedronate therapy was satisfactory. Therefore, while the BMD decreased by 3.5% of the YAM in the control group, it increased by 2% in the treated group, probably because of the effect of the administration.

A long time is needed to evaluate the fracture-preventive effect, which is the ultimate objective of treatment for osteoporosis, and the BMD and bone metabolic markers, which suggest the course of its changes, are monitored as short-term indices. Bone formation and bone resorption play key roles in maintaining the bone mass and quality. There are different markers of bone formation and resorption, and they are useful because their measurements by blood tests or urinalysis permit simple evaluation of the state of bone metabolism.[16] If bone turnover is enhanced, aggressive treatment is considered necessary, because not only is the decrease in the BMD accelerated, but also the risk of fracture is increased regardless of the BMD.[32] Human bone is composed primarily of calcium phosphate and type I collagen, and if bone is decomposed by osteoclasts, NTX, a degradation product of type I collagen, is excreted into blood and, then, urine. Therefore, the degree of bone decomposition can be evaluated by measuring urinary NTX, and the urinary NTX level is used for the diagnosis of osteoporosis and its responses to treatment.[15, 16] The urinary NTX level, which reflects bone resorption, has been reported to be inversely correlated with the BMD, to be reduced by antiresorptive therapies, and to be more sensitive than the serum NTX level.[33] While the BMD is an index representing the results of past bone metabolism, the NTX level represents the present degree of bone resorption and predicts decreases in the BMD in the near future.[15] Thus, people with a high NTX level are considered to reach a high-risk zone for fracture earlier than those with about the same BMD but a low NTX level.[15] Therefore, people with a low bone mass and low NTX, in particular, may require more aggressive treatment. In treating osteoporosis or reducing the risk of fracture, a bone turnover marker is considered to be significant as an intermediate endpoint in an early period of treatment before changes in the BMD become clear.[34] Eastel et al.[35] reported not only that early changes in the bone-turnover marker level were predictive of changes in the BMD, but also that changes in the urinary NTX level 3 to 6 months after the beginning of treatment with risedronate, etc., were correlated with decreases in the risk of vertebral fracture. In this study, the creatinine-corrected urinary NTX level decreased in the group treated with sodium risedronate, suggesting that the drug suppressed bone turnover and reduced the risk of fracture.

Since the administration of sodium risedronate had been reported to be useful for improving the quality of life[24] as well as preventing spinal fracture and the recurrence of femoral fracture,[36] similar effects were expected in this study. Indeed, the significant difference between the decrease in the pain score in the control group and in the treated group may have been due to improvement of pain induced by osteoporosis or disorders associated with a low bone mass. However, no fracture was observed during the observation period in the treated or control group. This is considered to be related to the small number of subjects and short observation period.

The systolic blood pressure was slightly increased in the control group. This increase in the systolic blood pressure may be related to a decrease in the BMD. This is because reports that a low Ca intake and decrease in the BMD associated with Ca loss were related to an elevation of the blood pressure[37–39] and an increase in the arterial stiffness was correlated with a decrease in the BMD in hypertensive patients[40] suggest a relationship between a decrease in the BMD and an elevation of the blood pressure. However, as there is also a report that the BMD was not associated with hypertension,[41] further evaluation is necessary.

There are some limitations to our investigation. First, in this study, we used the criteria proposed in the diagnostic guideline 2000[10] to diagnose the osteoporosis because this survey had been planned and performed between 2002 and 2006. In the 2012 revision of the guideline,[42] for the definite diagnosis of osteoporosis, ultrasound bone mineral densitometry determined to be not appropriate. Second, the number of residents is too small, and especially to detect a pharmacological effect on the prevention of the bone fracture, the observation period is too short.

The authors declare no conflict of interest.

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