

Vitamin D and intact PTH status in patients with hip fracture

M. Sakuma · N. Endo · T. Oinuma · T. Hayami ·
E. Endo · T. Yazawa · K. Watanabe · S. Watanabe

Received: 21 October 2005 / Accepted: 3 May 2006 / Published online: 28 July 2006
© International Osteoporosis Foundation and National Osteoporosis Foundation 2006

Abstract

Introduction The prevalence of hypovitaminosis D in patients with acute hip fracture was examined in a population on Sado Island in Japan. There were 85 cases of hip fracture among this population in 2004, giving an overall incidence of hip fracture of 121.4 per 100,000 population per year. This study included 50 of the 85 cases, and these cases were defined as the hip fracture group. Patients older than 70 years without established osteoporosis who were admitted to the hospital on the island during almost the same period for treatment of an orthopedic condition other than a hip fracture were defined as the control group.

Materials and methods The levels of serum 25-hydroxyvitamin D (25-OHD), intact parathyroid hormone (intact PTH), alkaline phosphatase (ALP), albumin, and the number of remaining teeth were examined in each group.

In the hip fracture group, serum calcium, serum phosphorus, urine N-terminal cross-linking telopeptide of type I collagen (NTx), bone mineral density (BMD) of the nonfractured hip, the presence of a vertebral fracture on X-ray, severity of dementia, and physical activity level were also examined.

Results Both the serum 25-OHD and serum albumin levels were significantly lower in patients with hip fracture than in controls, and the intact PTH level was significantly higher in patients with hip fracture. The number of remaining teeth was correlated with age, and was also significantly correlated with 25-OHD. In the hip fracture group, 62% of the subjects had hypovitaminosis D (25-OHD <20 ng/ml) and one-fifth of cases with hypovitaminosis D showed elevated PTH levels (>65 pg/ml). On the other hand, in the control group, hypovitaminosis D occurred in 18.9% of the subjects, and only one case showed elevated PTH. The serum 25-OHD level showed a decrease as the severity of dementia progressed and the activity level decreased.

Conclusion Our results indicate that about two-thirds (62%) of hip fracture patients had vitamin D insufficiency, suggesting that this condition may be closely associated with hip fracture in elderly people. Therefore, the serum 25-OHD level may be a useful index for the risk of hip fracture in elderly people.

M. Sakuma (✉) · N. Endo
Division of Rehabilitation Medicine,
Department of Community Preventive Medicine,
Niigata University Graduate School of Medical
and Dental Sciences,
1-757 Asahimachi dori,
Niigata 951-8510, Japan
e-mail: msakuma@med.niigata-u.ac.jp

N. Endo · T. Hayami · S. Watanabe
Division of Orthopedic Surgery,
Department of Regenerative and Transplant Medicine,
Niigata University Graduate School of Medical
and Dental Sciences,
Niigata, Japan

T. Oinuma · E. Endo · T. Yazawa · K. Watanabe
Department of Orthopedic Surgery, Sado General Hospital,
Sado, Japan

Keywords 25-OHD · Activity · Dementia · Hip fracture ·
Intact PTH · Number of remaining teeth

Introduction

The number of cases of hip fracture has been increasing with the aging of societies worldwide, and methods for the

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 deficiency leads to an increase in PTH levels, resulting in bone loss [1], and subclinical vitamin D deficiency is considered to be a risk factor for osteoporotic hip fracture in the elderly [2–4]. The aim of this study was to examine whether osteoporotic patients with hip fracture have lower levels of serum 25-hydroxyvitamin D (25-OHD) compared to non-osteoporotic cases, based on a study of the elderly population of a particular Japanese geographical area (Sado Island). The number of remaining teeth, dementia, and physical activity level were also examined in the study.

Patients and methods

Study site

This study was carried out on Sado Island, Japan. Sado Island is located in Niigata Prefecture in 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 km² and the population of the island was 70,011 as of 30 June 2004, of which 23,787 (34%) were 65 years old and older. There were 1,754.5 h of daylight on the island during 2004. Tourism, fishing, and agriculture are the chief industries, and access to the island is only by ferry or airplane. Immigration and emigration among the elderly people of the island is extremely low.

Subjects

From January to December 2004, 85 patients (20 males and 65 females) visited the general hospital on Sado Island because of an acute hip fracture. All the patients lived on the island. Of the 85 patients, 81 (20 males and 61 females) were admitted to the hospital. Of these 81 patients, 2 were excluded from the study because they had a traumatic fracture, rather than an osteoporotic fracture. Patients with a generally poor medical condition and those who were immediately moved to another ward for treatment of an internal disease were also excluded from the study. After these exclusions, 50 remaining fracture patients (9 males and 41 females, 61–101 years old, average age: 82.6 years old) were included in the study. A control group was selected from patients who were admitted to the same general hospital with various orthopedic conditions from July to December 2004: 53 patients over 70 years old (25 males and 28 females, 70–96 years old, average age: 77.2 years old) with no clinical evidence of osteoporotic

fractures were included in the control group. The patients (or their family if the patient had dementia) were informed of the nature of the study and consent was obtained from each participant.

Serum 25-OHD, intact parathyroid hormone (intact PTH), albumin, alkaline phosphatase (ALP), and the number of remaining teeth were checked at the time of admission. The number of remaining teeth was counted macroscopically by the examiner. Since a lack of teeth might be related to poor nutritional status and hypovitaminosis D, the relationship between the number of remaining teeth and the level of serum 25-OHD was also examined.

In patients with hip fracture, serum calcium, serum phosphorus, urine N-terminal cross-linking telopeptide of type I collagen (NTx), and the bone mineral density (BMD) of the nonfractured hip were measured, and the presence of vertebral fractures was determined by X-ray. In addition, the severity of dementia and the activity level before fracture were checked, using the criteria of the long-term care insurance system of the Japanese Ministry of Health, Labour and Welfare.

Serum, urine, and BMD measurements

Blood samples were collected at the time of admission. Serum calcium, serum phosphorus, serum albumin, and serum ALP were determined using standard methods. Serum calcium was adjusted for the albumin concentration [adjusted calcium (mg/dl) = calcium – albumin (g/dl) + 4.0] [5]. The serum creatinine, aspartate aminotransferase, and alanine aminotransferase levels were checked to examine liver and renal function. Intact PTH was measured by the chemiluminescence immunoassay (CLIA) method (Nichols Institute Diagnostics, San Clemente, CA, USA), in which intact PTH molecules are detected; the normal range is 10–65 pg/ml [6, 7]. We note that Segersten et al. [8] have suggested that the upper limit of the normal range for PTH may be too high; however, LeBoff et al. [4] used a value of 65 pg/ml, and we also chose 65 pg/ml as the upper limit of the normal range for intact PTH.

The serum 25-OHD level was measured by an enzyme-linked immunosorbent assay (ELISA) using a kit supplied by DiaSorin (Stillwater, MN, USA). A serum 25-OHD level of at least 15–20 ng/ml is needed to achieve optimum PTH levels, based on several reports. Hence, Hollis et al. [9] reported that the normal range of 25-OHD was 32–100 ng/ml and that a concentration of less than 10 ng/ml indicated a vitamin D-deficient state. Other studies performed in the US and Australia [10, 11] show that a serum 25-OHD level of at least 15–20 ng/ml is needed to achieve optimum PTH levels, and therefore we defined a 25-OHD level of less than 20 ng/ml as vitamin D

insufficiency. The value obtained at admission (from the day the fracture occurred until a few days later) was used as the serum 25-OHD level. The urine NTx assay was performed using the Osteomark NTx ELISA kit (Inverness Medical Professional Diagnostics, Princeton, NJ, USA).

BMD of the nonfractured hip was measured using a dual-energy X-ray absorptiometry (DXA) scan (Hologic 4500A, Bedford, MA, USA). The presence of vertebral fractures was also checked using the X-ray scan.

Severity of dementia and physical activity level

The severity of dementia was classified according to the criteria of the long-term care insurance system developed by the Japanese Ministry of Health, Labour and Welfare [12, 13], in which the severity of dementia is rated from I to IV, and M, as follows: I, some dementia, but independent in almost all daily activities in the community; II, symptoms and actions that impair daily activities or difficulty with mutual understanding, but independent with some attention; III, symptoms and actions that impair daily activities or difficulty with mutual understanding and requires care; IV, frequent symptoms and actions that impair daily activities or severe difficulty with mutual understanding and always require care; and M, a very severe case with extremely disruptive behavior, for which special medical care is required (in the current study no patients were in the M category). These standards were approved by the Japanese Ministry of Health, Labour and Welfare in 1993 [12, 13].

Physical activity level was also evaluated using the standards of the long-term care insurance system of Japan that are used to assess the degree of independence of disabled elderly people. These standards comprise four categories: J, some disabilities, but independent in activities of daily life; A, housebound, needing partial assistance only in outdoor activities; B, chairbound, needing partial assistance in indoor activities; and C, bedridden, dependent for most daily activities. These standards were approved by the Japanese Ministry of Health, Labour and Welfare in 1991 [12, 13] and are used generally in medical institutions in Japan.

The relationships of the serum 25-OHD level with the severity of dementia and the physical activity level were also determined.

Statistical analysis

Data are expressed as means±SD. Comparison between the two groups was performed using a Mann-Whitney U test, and correlations were examined using Spearman's rank correlation test. Regarding the dementia and activity level, a comparison among groups was performed using a Kruskal-

Wallis test. Analysis was performed using StatView for Windows software (version 5.0).

Results

There were 85 cases of hip fracture on Sado Island in 2004, giving an overall incidence of 121.4 per 100,000 population per year. The male-to-female ratio was 1:3.25, and the cervical-to-trochanteric ratio was 1:1.30 (Table 1). Of the patients, 65.8% (25 of 38 cases) were classified as "osteoporotic" on the basis of WHO criteria, which defines osteoporosis as BMD below 2.5 standard deviations (SD) of the mean BMD for young adults [14]. Of the 85 patients, a group of 50 patients with hip fracture were judged eligible for the study and were compared with a group of 53 patients with other orthopedic diseases. All patients had normal renal function, based on a serum creatinine level within the normal range, and none of the patients had serum calcium and phosphorus levels consistent with a diagnosis of primary hyperparathyroidism or osteomalacia. The characteristics of the hip fracture patients are shown in Table 1. The average hip total BMD of the hip fracture group was 0.513 g/cm², and 81% of the patients had vertebral fractures (Table 1).

Table 1 Laboratory data for patients with hip fracture (*n*=50)

Variables	Male+female (<i>n</i> =50)	Male (<i>n</i> =9)	Female (<i>n</i> =41)
Serum calcium (mg/ml)	9.5±0.5	9.5±0.3	9.5±0.6
Serum phosphorus (mg/ml)	3.2±0.6	2.8±0.7	3.3±0.5
Urine NTx (nmol BCE/nmol Cr)	106.2±62.4	95.7±84.0	108.8±57.3
Hip BMD (g/cm ²)			
Total area	0.513±0.1	0.634±0.09	0.485±0.17
Neck	0.456±0.1	0.557±0.08	0.427±0.14
Trochanter	0.359±0.1	0.473±0.07	0.327±0.15
Intertrochanter	0.583±0.2	0.739±0.11	0.539±0.20
Ward's	0.218±0.1	0.270±0.88	0.203±0.13
Classified as osteoporotic on the basis of WHO criteria (%) ^a	65.8	57.1	67.7
Patients with vertebral fracture (%) ^b	81.8	62.5	86.1
Ratio of cervical to trochanter fractures	1:1.30	1:0.80	1:1.93

^aHip total BMD ≤−2.5: 38 patients were examined; 12 patients (2 males and 10 females) were not examined because there was no opportunity for a DXA examination

^b44 patients were examined; 6 patients (1 male and 5 females) were not examined because there was no opportunity for an X-ray examination

Table 2 Characteristics of patients in the study

Variables	Patients with hip fracture (<i>n</i> =50, 9 males and 41 females)	Non-hip fracture controls (<i>n</i> =53, 25 males and 28 females)	<i>p</i> value
Age range (years)	61–101	70–96	–
Average (years)	82.6±8.7	77.2±5.3	<0.01
Albumin (g/l)	3.53±0.5	3.97±0.5	<0.01
ALP (IU/l)	311.0±226	250.0±99.8	<0.05
25-OHD (ng/ml)	17.8±22.2	25.8±7.4	<0.01
Intact PTH (pg/ml)	45.1±22.2	31.4±18.3	<0.01
Number of remaining teeth	6.1±8.6	10.1±9.9	<0.05

Further characteristics of the patients in the study are shown in Table 2. Serum albumin levels were significantly lower ($p<0.0001$) in patients with hip fractures than in patients without hip fractures, and the hip fracture group had higher serum ALP levels, significantly lower serum 25-OHD levels ($p<0.0001$), and significantly higher intact PTH levels ($p<0.001$) compared to the control group. The number of remaining teeth in the hip fracture group was significantly fewer than in the control group (Table 2).

Because there was a significant difference in age and gender between the hip fracture group and the control group, a subgroup analysis was performed with adjustments for age and gender. There were 13 patients (2 males and 11 females) aged more than 90 years in the hip fracture group and there was 1 male only aged more than 90 years in the control group. There was no significant difference in age between the groups for subjects aged less than 90 years;

Table 3 Sub-group analysis of women aged less than 90 years

Variables	Patients with hip fracture (<i>n</i> =30)	Non-hip fracture controls (<i>n</i> =28)	<i>p</i> value
Age range 67–88 (years)		70–87	–
Average (years)	79.9±5.4	77.5±4.8	n.s.
Albumin (g/l)	3.6±0.5	4.0±0.5	<0.05
ALP (IU/l)	309.0±281	255.3±112	n.s.
25-OHD (ng/ml)	16.6±6.3	22.0±6.0	<0.01
Intact PTH (pg/ml)	45.8±20.4	35.8±22.8	<0.05
Number of remaining teeth	6.3±8.9	8.9±9.5	n.s.

therefore, a subgroup analysis was performed for women of less than 90 years of age in the hip fracture group ($n=30$, average age: 79.9 years old, range: 67–88 years old) and the control group ($n=28$, average age: 77.5 years old, range: 70–87 years old) (Table 3). Significant differences in albumin, 25-OHD, and intact PTH levels persisted in the subgroup analysis, but there was no significant difference in ALP level or in the number of teeth.

Correlations were also examined in the total population ($n=103$, 50 hip fracture patients and 53 controls) (Table 4): albumin was significantly inversely correlated with age ($r=-0.22$, $p<0.05$) and positively correlated with 25-OHD ($r=0.35$, $p<0.05$); 25-OHD was significantly inversely correlated with age ($r=-0.24$, $p<0.05$) and intact PTH ($r=-0.40$, $p<0.01$); and number of teeth was significantly inversely correlated with age ($r=-0.45$, $p<0.01$) and positively correlated with 25-OHD ($r=0.20$, $p<0.05$) (Table 4).

In hip fracture patients ($n=50$, 9 males and 41 females), intact PTH was significantly correlated with phosphorus ($r=0.31$, $p<0.05$) and NTx was significantly inversely correlated with 25-OHD ($r=-0.44$, $p<0.01$) (Table 5). In addition, BMD was significantly negatively correlated with age ($r=-0.53$, $p<0.01$) and NTx ($r=-0.52$, $p<0.01$), and number of teeth was significantly negatively correlated with age ($r=-0.48$, $p<0.01$) and BMD ($r=-0.42$, $p<0.01$). The relationships between intact PTH and 25-OHD level in patients with hip fracture ($n=50$) and in control subjects ($n=53$) are shown in Fig. 1. In the controls, there was a significant negative correlation between the intact PTH and 25-OHD levels (Fig. 1a, $R^2=0.127$), but this was not found in the hip fracture patients (Fig. 1b). In patients with hip fracture, 62.0% (31 of 50) had serum 25-OHD levels of less than 20 ng/ml, whereas in non-hip fracture patients, only 18.9% (10 of 53) had 25-OHD levels of less than 20 ng/ml.

Table 4 Correlation matrix for age, serum albumin, serum ALP, serum 25-OHD, serum intact PTH, and number of remaining teeth in the total population (fracture group and control group, $n=103$, 69 females and 34 males)

Variables	Albumin	ALP	25-OHD	Intact PTH	Number of remaining teeth
Age	-0.22*	0.10	-0.24*	0.19	-0.45**
Albumin	–	-0.11	0.35*	-0.06	0.18
ALP	–	–	-0.08	0.15	0.10
25-OHD	–	–	–	-0.40**	0.20*
Intact PTH	–	–	–	–	-0.17
Number of remaining teeth	–	–	–	–	–

* $p<0.05$; ** $p<0.01$

Table 5 Correlation matrix for age, serum calcium, serum phosphorus, serum ALP, serum 25-OHD, serum intact PTH, urine NTx, BMD of the femoral neck, and number of teeth in patients with hip fracture ($n=50$, 9 males and females)

Variables	Calcium	Phosphorus	Albumin	ALP	25-OHD	Intact PTH	NTx	BMD	Number of teeth
Age	0.10	-0.10	-0.19	0.07	0.08	0.06	0.08	-0.53*	-0.48*
Calcium	-	0.10	-0.22	0.18	0.04	0.16	0.04	-0.28	-0.17
Phosphorus	-	-	0.06	-0.15	-0.05	0.31**	-0.10	0.11	-0.10
Albumin	-	-	-	-0.24	0.03	0.19	-0.31	0.18	0.04
ALP	-	-	-	-	0.01	0.18	0.14	0.02	0.19
25-OHD	-	-	-	-	-	-0.17	-0.44*	0.30	0.23
Intact PTH	-	-	-	-	-	-	-0.12	-0.04	-0.05
NTx	-	-	-	-	-	-	-	-0.52*	-0.03
BMD	-	-	-	-	-	-	-	-	-0.42*
Number of teeth	-	-	-	-	-	-	-	-	-

* $p<0.01$; ** $p<0.05$

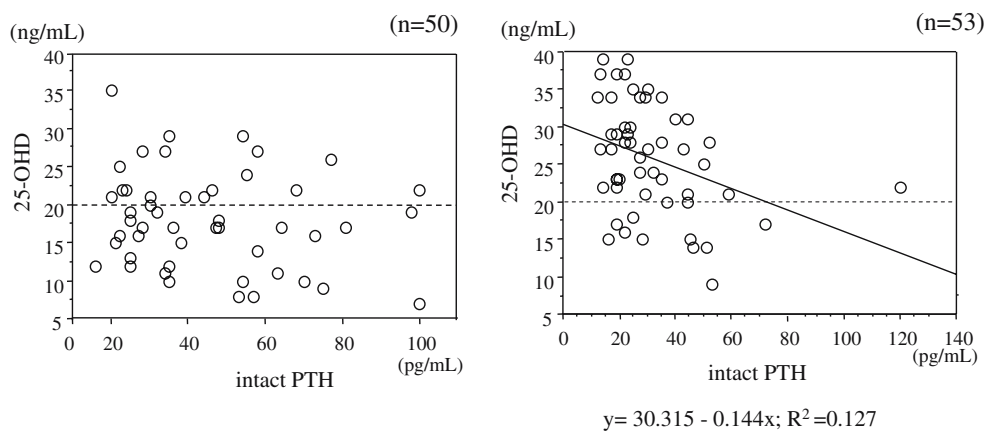
The hip fracture patients were also classified into two categories based on the level of 25-OHD: a hypovitaminosis group with 25-OHD <20 ng/ml and a normovitaminosis group with 25-OHD ≥ 20 ng/ml. NTx was significantly higher in patients with a lower level of 25-OHD (<20 ng/ml) (Table 6), but significant differences were not observed for other items in the 25-OHD subgroup analysis.

The relationship between dementia level and serum 25-OHD in the hip fracture patients ($n=50$) is shown in Fig. 2. The mean 25-OHD level was highest, at more than 20 ng/ml, in the normal (based on dementia level) group and then tended to decrease as the degree of dementia progressed ($p<0.05$). The relationship between physical activity level and serum 25-OHD in the hip fracture patients is shown in Fig. 3. The mean level of 25-OHD reached a level of more than 20 ng/ml in the group assessed to be independent and then tended to decrease as the degree of activity decreased.

Discussion

Our data show that the serum albumin level was significantly lower in the hip fracture group compared to the control group (Tables 2 and 3), consistent with the study of Thiebaud et al. [15], in which low albumin was also reported to be an important risk factor for hip fracture. The 25-OHD level was also significantly lower and the intact PTH level was significantly higher in the hip fracture group, also consistent with previously reported results [3, 4]. In the US, a serum 25-OHD level lower than 12 ng/ml was observed in 50% of women with osteoporotic hip fractures [4]. In Italy this value was found to be 13.5%, and 21.6% of patients had a serum 25-OHD level less than 20 ng/ml [3]. Our data show that 26% of the hip fracture patients (13 of 50) had a serum 25-OHD level of less than 12 ng/ml and 62% (31 of 50) had a level of less than 20 ng/ml; these percentages were higher than in the study performed in Italy, but lower than the study in the US. We note that intake of fishery products is very common on Sado Island, but despite these habits, vitamin D insufficiency was observed in patients with hip fracture. ALP was significantly higher

Fig. 1 Relationship between serum intact PTH and 25-OHD levels. **a** Patients with hip fracture. **b** Non-hip fracture controls. Of 50 patients with hip fracture, 31 (62.0%) had serum 25-OHD levels <20 ng/ml (**a**). Of 53 non-hip fracture controls, 10 (18.9%) had serum 25-OHD levels <20 ng/ml (**b**)



a) Patients with hip fracture

b) Non-hip fracture controls

Table 6 Characteristics of patients with hip fracture grouped according to 25-OHD

Variables	25-OHD <20 ng/ml (n=31, 5 males and 26 females)	25-OHD ≥20 ng/ml (n=19, 4 males and 15 females)	p value
Age range (years)	61–101	66–97	–
Average (years)	81.7±9.0	84.2±8.3	n.s.
Cervical-to-trochanter ratio	1:1.81	1:1.38	
Intact PTH (pg/ml)	46.7±22.6	42.5±21.7	n.s.
Calcium (mg/ml)	9.54±0.5	9.44±0.5	n.s.
Phosphorus (mg/ml)	3.30±0.5	3.05±0.7	n.s.
Albumin (g/l)	3.51±0.5	3.55±0.5	n.s.
ALP (IU/l)	320.0±278.4	296.4±100.9	n.s.
NTx (nmol BCE/nmol Cr)	117.6±60.7	84.3±61.9	<0.05
Number of remaining teeth	5.6±8.5	7.0±8.8	n.s.
Hip BMD (g/cm ²)			
Total area	0.490±0.171	0.551±0.164	n.s.
Neck	0.435±0.128	0.497±0.155	n.s.
Trochanter	0.344±0.166	0.381±0.129	n.s.
Intertrochanter	0.570±0.218	0.610±0.187	n.s.
Ward's	0.186±0.116	0.263±0.129	n.s.

and the number of teeth was significantly lower in the hip fracture group. However, since there were no significant differences in these items in a subgroup analysis in women less than 90 years old, the influence of age on ALP and number of teeth appeared to be significant.

Regarding the number of remaining teeth, there was no significant difference between the hip fracture group and the control group, but a strong correlation between age and the number of teeth was found. However, a significant correlation between 25-OHD and the number of teeth was

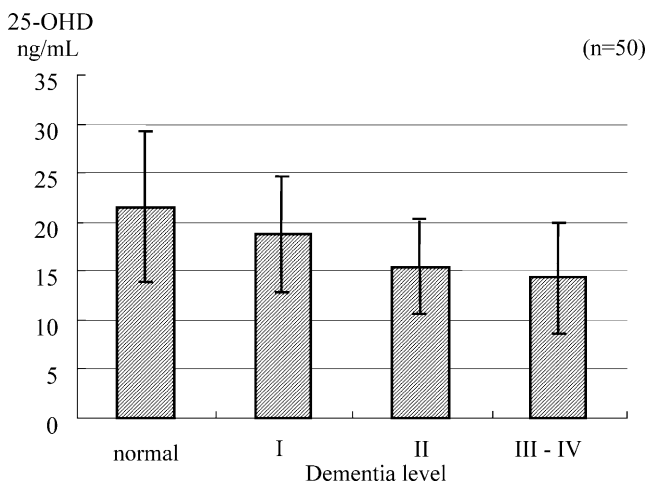


Fig. 2 Relationship between dementia level and 25-OHD in patients with hip fracture ($p<0.05$) (mean±SD)

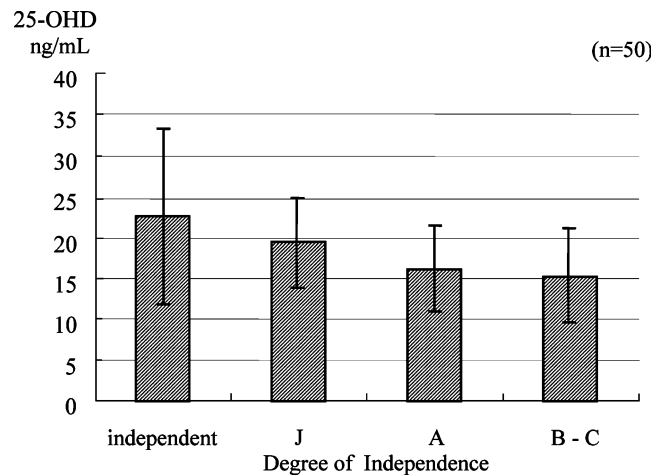


Fig. 3 Relationship between serum 25-OHD and degree of independence in patients with hip fracture (n.s.) (mean±SD)

also observed (Table 4). Bollen et al. [16] reported that the number of teeth is not influenced by fracture state, whereas Krall et al. [17] have suggested that intake levels of calcium and vitamin D have a beneficial effect on tooth retention. It appears likely that the number of remaining teeth is mainly influenced by age and is not necessarily associated with fracture directly, but may be associated with serum 25-OHD levels. The significant correlation between the number of teeth and BMD was mainly related to age (Table 5).

Regarding the relationship between intact PTH and 25-OHD levels, although intact PTH was significantly correlated with 25-OHD in the control group ($r^2=0.127$) (Fig. 1), no such correlation was found in the hip fracture group. When the 25-OHD level becomes insufficient, the intact PTH level generally rises. However, of the 31 patients in the current study with a low 25-OHD level, only a few (6 of 31) had an elevated PTH level (>65 pg/ml). Chapuy et al. [18] have reported that low serum 25-OHD does not always lead to an increase in serum PTH, and Sahota et al. [19] suggested that a slight reduction in serum calcium and a substantial decrease in 1,25-(OH)₂D levels may be partly related to the failure of the parathyroid gland to mount an adequate PTH response. In addition, the cutoff for definition of an elevated PTH level may require further examination.

The relationship of dementia level with 25-OHD indicated a tendency for the 25-OHD level to decrease as dementia progressed (Fig. 2). Sato et al. [20] reported that serum 25-OHD levels are significantly decreased in Alzheimer disease patients and that vitamin D deficiency due to sunlight deprivation and malnutrition contributes significantly to reduced BMD. The relationship of activity level with 25-OHD also indicated a tendency for the 25-OHD level to decrease as the activity level decreased (Fig. 3). Bishoff-Ferrari et al. [21] have reported that 25-OHD concentrations between 40 and

94 nmol/l are associated with better musculoskeletal function in the lower extremities, and Monaco et al. [22] reported a significant positive correlation between serum 25-OHD₃ and Barthel Index score in hip fracture patients.

Overall, our results suggest that dementia, decreased activity, and vitamin D deficiency are mutually associated and carry a high risk of hip fracture. In particular, of the patients with hip fracture in the current study, two-thirds had vitamin D deficiency. Since aging of the population is progressing and cases of hip fracture are likely to increase in number, we conclude that determination of the level of serum 25-OHD in elderly patients is of value, because vitamin D deficiency is a risk factor for hip fracture.

Acknowledgements This study was performed with the permission of the Ethical Review Board of Sado General Hospital. The authors gratefully acknowledge all the staff at Sado General Hospital for their support in the collection of patient data. We acknowledge Teijin Pharma Limited and SRL Inc. for measurements of laboratory data.

References

- Garnero P, Sornay-Rendu E, Chapuy MC, Delmas PD (1996) Increased bone turnover in late postmenopausal women is a major determinant of osteoporosis. *J Bone Miner Res* 11(3):337–349
- Cumming RG, Klineberg RJ (1994) Case-control study of risk factors for hip fractures in the elderly. *Am J Epidemiol* 139:493–503
- Nuti R, Martini G, Valenti R, Gambera D, Gennari L, Salvadori S, Avanzati A (2004) Vitamin D status and bone turnover in women with acute hip fracture. *Clin Orthop Relat Res* 422:208–213. DOI 10.1097/01.blo.0000129163.97988.06
- LeBoff MS, Kohlmeier L, Hurwitz S, Franklin J, Wright J, Glowacki J (1999) Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA* 281(16):1505–1511
- Payne RB, Little AJ, Williams RB, Milner JR (1973) Interpretation of serum calcium in patients with abnormal serum proteins. *Br Med J* 4:643–646
- Omote M, Nakagawa K, Matsushima H, Yasui T (1997) Evaluation of chemiluminescence immunoassay kit “Lumico PTH” and “Lumico ACTH”. *Jpn J Med Pharm Sci* 38(4):805–812
- Paudian MR, Segre GV, Sherrard D, Potts JT, Lavigne JR, Carlton EI (1983) Immunoradiometric assay for intact PTH: a new generation of PTH assay for assessment of parathyroid function. *Nichols Institute Reference Laboratories* 60-712-204:1–7
- Segersten U, Correa P, Hewison M, Hellman P, Dralle H, Carling T, Akerstrom G, Westin G (2002) 25-hydroxyvitamin D(3)-1α-hydroxylase expression in normal and pathological parathyroid glands. *J Clin Endocrinol Metab* 87(6):2967–2972
- Hollis BW (2005) Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. *J Nutr* 135:317–322
- Malabanan A, Veronikis E, Holick MF (1998) Redefining vitamin D insufficiency. *Lancet* 351:805–806
- Need AG, Horowitz M, Morris HA, Nordin BC (2000) Vitamin D status: effects on parathyroid hormone and 1,25-dihydroxyvitamin D in postmenopausal women. *Am J Clin Nutr* 71:1577–1581
- Sato S, Demura S, Minami M, Kasuga K (2002) Longitudinal assessment of ADL ability of partially dependent elderly people: examining the utility of the index and characteristics of longitudinal change in ADL ability. *J Physiol Anthropol Appl Human Sci* 21(4):179–187
- Arai Y, Zarit SH, Kumamoto K, Takeda A (2003) Are there inequities in the assessment of dementia under Japan’s LTC insurance system? *Int J Geriatr Psychiatry* 18(4):346–352
- Kanis JA, WHO Study Group (1994) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. *Osteoporos Int* 4:368–381
- Thiebaud D, Burckhardt P, Costanza M, Slutskis D, Gilliard D, Quinodoz F, Jacquet AF, Bumand B (1997) Importance of albumin, 25(OH)-vitamin D and IGFBP-3 as risk factors in elderly women and men with hip fracture. *Osteoporos Int* 7:457–462. DOI 10.1007/s001980050033
- Bollen AM, Taguchi A, Hujuel PP, Hollender LG (2004) Number of teeth and residual alveolar ridge height in subjects with a history of self-reported osteoporotic fractures. *Osteoporos Int* 15(12):970–974. DOI 10.1007/s00198-004-1695-1
- Krall EA, Wehler C, Garcia RI, Harris SS, Dawson-Hughes B (2001) Calcium and vitamin D supplements reduce tooth loss in the elderly. *Am J Med* 11(6):452–456
- Chapuy MC, Preziosi P, Maamer M, Arnaud S, Galan P, Hercberg S, Meunier PJ (1997) Prevalence of vitamin D insufficiency in an adult normal population. *Osteoporos Int* 7(5):439–443. DOI 10.1007/s001980050030
- Sahota O, Gaynor K, Harwood RH, Hosking D (2001) Hypovitaminosis D and ‘functional hypoparathyroidism’—the NoNoF (Nottingham Neck of Femur) study. *Age Ageing* 30:467–472
- Sato Y, Asoh T, Oizumi K (1998) High prevalence of vitamin D deficiency and reduced bone mass in elderly women with Alzheimer’s disease. *Bone* 23(6):555–557
- Bischoff-Ferrari HA, Dietrich T, Orav EJ, Hu FB, Zhang Y, Karlson EW, Dawson-Hughes B (2004) Higher 25-hydroxyvitamin D concentrations are associated with better lower-extremity function in both active and inactive persons aged > or =60 y. *Am J Clin Nutr* 80:752–758
- Di Monaco M, Vallero F, Monaco R, Manutino F, Cavanna A (2005) Serum levels of 25-hydroxyvitamin D and functional recovery after hip fracture. *Arch Phys Med Rehabil* 86:64–68