

A significant decrease in the incidence of vertebral fractures and the safety of the drug were consistently observed during the 5-year treatment with bazedoxifene.

Calcitonin derivatives

Calcitonin is a bone resorption inhibitor acting directly on osteoclasts and pre-osteoclasts to control their functions. Calcitonin also relieves pain via the central serotonergic system, and therefore its derivatives may be the first choice to obtain pain relief and improves QOL in the early phase after the occurrence of osteoporotic fractures or in patients with postural distortion associated with vertebral fractures.

There are some reports on the effect of calcitonin derivatives on BMD and vertebral fracture (Fig. 13a) [16], but none on non-vertebral or proximal femoral fractures.

Some randomized clinical trials and systematic reviews revealed significant reductions in the severity of pain associated with ADLs 1 to 4 weeks after calcitonin was started (Fig. 13b) [17]. In terms of QOL, improvement in SF-36 scores, pain relief, and improved ADLs, and an enhanced effect of rehabilitation in patients who had a total hip replacement after proximal femoral fracture was reported.

Outside of Japan, intra-nasal formulations of calcitonin derivatives are used primarily, and a preventive effect on fractures and beneficial effect on pain was observed. However, the increased risk of cancer was reported from the European Medical Association (EMA) in patients treated with calcitonin and intra-nasal calcitonin was withdrawn from the European market.

Although antibodies might be produced after injection of calcitonin derivatives, they do not influence the effect of

calcitonin and are not involved in the side effects of calcitonin derivatives. Therefore, patient monitoring is not needed.

Teriparatide (recombinant human parathyroid hormone)

Unlike bone-resorption inhibitors, intermittent administration of teriparatide (a recombinant form) as a daily subcutaneous injection specifically increases serum P1NP, a bone formation marker, indicating promotion of bone remodeling followed by the formation of bone tissue.

Teriparatide, given as a daily subcutaneous injection, is recommended in patients at high risk of fractures such as patients who have had a fracture(s) while being treated with a bisphosphonate or SERM, elderly patients with multiple vertebral fractures or proximal femoral fractures, or patients with significantly reduced BMD. The combination of teriparatide with an oral bisphosphonate is not recommended.

Teriparatide increases BMD at the lumbar vertebrae and proximal femur, and reduces vertebral and non-vertebral fracture. The incidence of a radial fracture is reduced with teriparatide, while the apparent BMD of the radius is slightly decreased in association with the formation of new bone matrix, and the external diameter of the radius is increased. A meta-analysis revealed that teriparatide reduces low back pain.

Teriparatide (a recombinant form) approved in Japan is self-injected daily at home, after instruction by physicians or nurses. The total dosing period is limited to 24 months. After 24 months of treatment with teriparatide, adequate treatment with a bone-resorption inhibitor is recommended to maintain the bone strength.

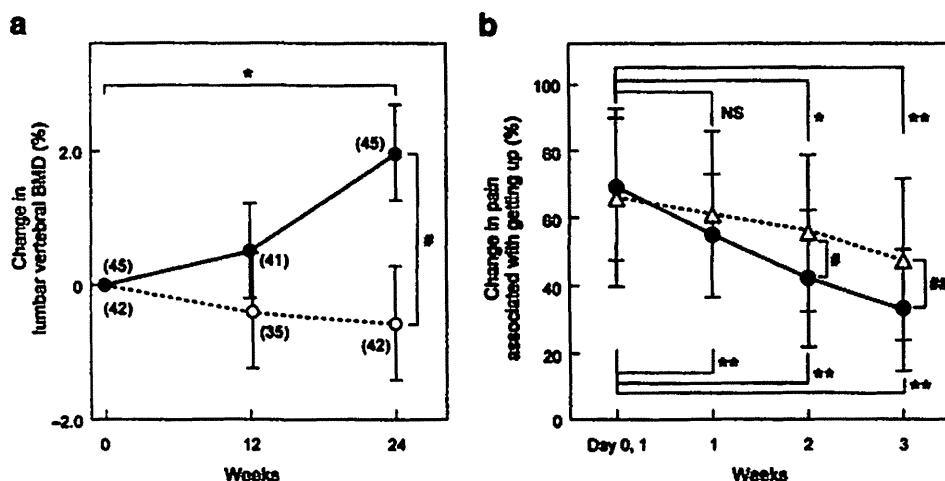


Fig. 13 Effect of elcatonin on BMD and pain associated with vertebral fracture. **a** Percent change in lumbar spine BMD. *Solid line* is elcatonin (20 units per week) with 0.6 g calcium lactate and *broken line* is control (calcium lactate only). Data are mean \pm SE. Numerals in parentheses denote number of patients. Comparison within groups: Student's paired *t*-test, #*p*<0.05; between groups: Student's unpaired *t*-test, **p*<0.05.

Orimo H [16] (Copyright© 1996 Springer Science + Business Media BV). **b** Percent change in pain associated with getting up evaluated with visual analog scale (VAS). *Solid line* is elcatonin (20 units per week, *n*=44) and *broken line* is control (untreated, *n*=42). Two-way repeated-measures ANOVA, **p*<0.05, ***p*<0.01, *NS* not significant. Mann-Whitney *U* test, #*p*<0.05, ##*p*<0.01 (Nakano [17])

Combination therapy

Osteoporosis is a multifactorial disease, thus combination therapy with agents with different mechanisms of action is considered reasonable. However, the efficacy of combination therapy lacks evidence at this time.

The Adequate Treatment of Osteoporosis (A-TOP) Research Group was authorized in the year 2000 by the Japan Society of Osteoporosis and assisted by the Public Health Research Foundation to obtain clinical evidence regarding osteoporosis treatment. It conducted a clinical trial comparing monotherapy with alendronate, a new bisphosphonate at the time, and combination therapy with alendronate and alfacalcidol, an active vitamin D₃ derivative developed in Japan (Japanese Osteoporosis Intervention Trial: JOINT-02). The incidence of vertebral fracture was significantly reduced in the combination therapy group during the first 6 months of treatment, and in both subgroups of patients with multiple vertebral fractures and grade 3 vertebral fractures by semiquantitative assessment during the 2-year treatment period (Fig. 14) [18]. The incidence of non-vertebral fracture (weight-bearing bones) was also significantly reduced in the combination therapy group. Based on these results, combination therapy with alendronate and an active vitamin D₃ derivative is recommended for the prevention of incident vertebral and non-vertebral fracture in patients at a high risk of fracture.

Secondary osteoporosis

Osteoporosis secondary to other diseases

Secondary osteoporosis is defined as decreased BMD and deteriorated bone quality (pathologic state specific to osteoporosis) having one or more causes in addition to genetic

factors, lifestyle, menopause, and aging. Secondary osteoporosis that is caused by a disease, such as hyperparathyroidism, can be improved by treating the underlying disease.

Hyperparathyroidism can be classified into either primary hyperparathyroidism, a disorder of the parathyroid itself, or secondary hyperparathyroidism, a pathological state secondary to other disorders, such as chronic kidney disease or vitamin D deficiency/depletion. In both types of hyperparathyroidism, excessively secreted parathyroid hormone promotes bone turnover and consequently decreases the BMD, resulting in an increased fracture risk. However, the therapeutic strategies employed for each type are entirely different. Primary hyperparathyroidism is treated mainly by parathyroidectomy, and there is no evidence regarding pharmacologic treatment. Secondary hyperparathyroidism improves with treatment of its underlying disease. Hyperparathyroidism secondary to CKD should be treated in accordance with the Japanese Evidence-based Practice Guideline for the Treatment of CKD.

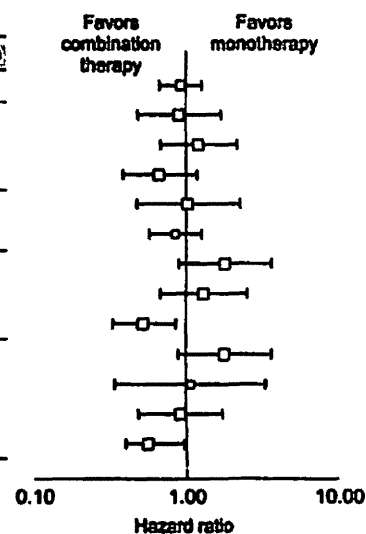
In rheumatoid arthritis, bone resorption increases and BMD decreases because of several factors, including activation of inflammatory cytokines, immobility, and use of glucocorticoids. Consequently, the fracture risk increases. Infliximab, an anti-TNF agent used to treat rheumatoid arthritis, increases BMD in patients with osteoporosis secondary to rheumatoid arthritis. Among the useful therapeutic medications for osteoporosis, bisphosphonates reduce fracture risk.

Osteoporosis secondary to lifestyle-related diseases

In recent years, it was demonstrated that bone metabolism is influenced by some atherosclerosis-inducing disorders such as diabetes mellitus, dyslipidemia, hypertension, and chronic kidney disease. In particular, osteoporosis caused by diabetes mellitus or CKD is established as "osteoporosis secondary to

Fig. 14 Efficacy of combination therapy with alendronate and active vitamin D₃ on vertebral fracture. *HR* hazard ratio of incident vertebral fracture, *CI* confidence interval (Orimo [18] (Copyright© 2011 Informa Plc.))

Factors	n	HR	95% CI	p value
All randomized	2016	0.89	0.64–1.25	0.51
Age (years)	<75	0.87	0.47–1.63	0.67
	75≤<80	1.19	0.67–2.13	0.54
25(OH)vitamin D (ng/mL)	80≤	0.68	0.38–1.16	0.15
	<20	1.02	0.47–2.24	0.96
Number of prevalent vertebral fracture	20≤	0.84	0.57–1.23	0.36
	0	1.73	0.85–3.55	0.13
	1	1.28	0.66–2.47	0.48
Maximum grade of prevalent vertebral fracture	2≤	0.51	0.32–0.84	0.01
	0	1.74	0.85–3.55	0.13
	1	1.04	0.33–3.21	0.96
	2	0.89	0.48–1.71	0.72
	3	0.55	0.38–0.94	0.03



lifestyle-related diseases”, bringing it special attention within secondary osteoporosis. A vigorous assessment for osteoporosis is recommended in patients with these diseases.

Osteoporosis secondary to lifestyle-related diseases is mainly associated with deterioration in bone quality, whereas BMD is relatively well-preserved in most cases. Therefore, therapeutic intervention in patients with diabetes mellitus or CKD should be started as soon as “decreased bone mass” is identified, in accordance with the diagnostic criteria of osteoporosis.

The main cause of deterioration in bone quality in these patients is thought to be altered cross-links among the collagen molecules in bone tissue (nonphysiological collagen cross-links, i.e., advanced glycation endproducts) due to an increase in oxidative stress and acceleration of glycation.

While the therapeutic modality has not been established yet, the benefit of alendronate, risedronate, raloxifene, and parathyroid hormone derivatives has been reported in large clinical trials. Pentosidine is likely to be a marker for bone quality and is expected to be an index of the fracture risk.

Treatment-related osteoporosis

Glucocorticoid agents and sex hormone lowering therapy are important causes of treatment-related osteoporosis.

Systemically administrated glucocorticoid decreases bone mass and increases fracture risk, thus 50 % of patients under long-term treatment with glucocorticoids suffer from osteoporosis. In general, patients taking glucocorticoids at doses of 5 mg (prednisolone equivalent) or more per day for 3 months or more should be assessed for bone mass and the need for osteoporosis treatment. Moreover, it is recommended to start treatment at higher BMD values than those used in the criteria for treatment of primary osteoporosis. In Japan, a revision of the 2004 “Guidelines on the management and treatment of corticosteroid-induced osteoporosis” is being developed.

Even though guidelines currently recommend bisphosphonates for the treatment of glucocorticoid-induced osteoporosis, generally they are not recommended for women intending to become pregnant. Although teriparatide is expected to increase bone mass, it is indicated only for “osteoporosis with a high risk of fractures”.

Endocrine therapy (sex hormone lowering therapy) for breast cancer and prostate cancer decreases BMD. Bisphosphonates can improve BMD in these patients, but there is no evidence yet about its ability to reduce fracture risk.

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Conflicts of interest None.

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Interrelationship of oral health status, swallowing function, nutritional status, and cognitive ability with activities of daily living in Japanese elderly people receiving home care services due to physical disabilities

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Abstract – Objectives: Malnutrition and cognitive impairment lead to declines in activities of daily living (ADL). Nutritional status and cognitive ability have been shown to correlate with oral health status and swallowing function. However, the complex relationship among the factors that affect decline in ADL is not understood. We examined direct and indirect relationships among oral health status, swallowing function, nutritional status, cognitive ability, and ADL in Japanese elderly people living at home and receiving home care services because of physical disabilities. **Methods:** Participants were 286 subjects aged 60 years and older (mean age, 84.5 ± 7.9 years) living at home and receiving home care services. Oral health status (the number of teeth and wearing dentures) was assessed, and swallowing function was examined using cervical auscultation. Additionally, ADL, cognitive ability, and nutritional status were assessed using the Barthel Index, the Clinical Dementia Rating Scale, and the Mini Nutritional Assessment-Short Form, respectively. Path analysis was used to test pathways from these factors to ADL. **Results:** The mean number of teeth present in the participants was 8.6 ± 9.9 (edentates, 40.6%). Dysphagia, malnutrition, and severe cognitive impairment were found in 31.1%, 14.0%, and 21.3% of the participants, respectively. Path analysis indicated that poor oral health status and cognitive impairment had a direct effect on denture wearing, and the consequent dysphagia, in addition to cognitive impairment, was positively associated with malnutrition. Malnutrition as well as dysphagia and cognitive impairment directly limited ADL. **Conclusions:** A lower number of teeth are positively related to swallowing dysfunction, whereas denture wearing contributes to recovery of swallowing function. Dysphagia, cognitive

Key words: activities of daily living; cognitive ability; elderly people with physical disabilities; nutritional status; oral health status

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impairment, and malnutrition directly and indirectly decreased ADL in elderly people living at home and receiving home nursing care. The findings suggest that preventing tooth loss and encouraging denture wearing when teeth are lost may indirectly contribute to maintaining or improving ADL, mediated by recovery of swallowing function and nutritional status.

In almost every country, the proportion of older people is increasing relative to younger age groups (1). Especially in Japan, the population is aging rapidly because of dramatic reductions in early mortality and declines in fertility. Indeed, the population aged 65 years old and older in Japan accounts for 23% of the total population in 2011 (2), and this percentage is the highest in the world. As the number of elderly people increases, so does the number of those requiring long-term nursing care, such as those who are bedridden and suffering from dementia (3).

Since 2000, nursing services supporting the daily lives of elderly individuals who require long-term care because of physical disability have been provided through the social insurance system enacted in Long-term Care Insurance Act in Japan (4). In this system, applicants for services are classified into five grades according to the severity of their physical disability, and the amount of nursing care service provided is determined by grade (5). The number of elderly receiving long-term care based on this act was about 4 million in 2010 according to a report by Japanese Ministry of Health, Labour and Welfare (6). Another report showed that 29% of elderly Japanese requiring long-term care deteriorated as measured by the grade of care service needed, and 23% of them died within 2 years (7). For elderly people receiving nursing care, further deterioration in their ability to conduct activities of daily living (ADL) such as bathing, dressing, and walking is an important concern.

Previous studies have suggested that malnutrition and cognitive impairment can lead to deterioration in ADL (8, 9), and malnutrition has been associated with cognitive impairment in elderly people (8). Moreover, nutrition and cognitive function have also been shown to correlate with oral health status (10, 11) and swallowing function (12, 13). However, these studies focused on direct relationships between bivariate. We need to also take into account that decline in ADL is affected by complex direct and indirect interactions among multiple factors. That is, it is not enough to analyze an association incorporating multiple factors as independent variables to show comprehensively how these risk factors affect deterioration in ADL.

Furthermore, most studies about the effects of oral condition on malnutrition and decline in ADL have been limited to elderly people in nursing homes and hospitals (11–13); few studies have examined these associations in elderly people living at home. In Japan, about 3 million people received home care services, and about 1 million people received facility services, such as at a nursing home, via long-term care insurance in 2010 (5, 14). In the United States, because of social trends toward reduced nursing home use, the number of disabled elderly people needing home care support has increased (15). Considering the growing number of aged people and the inevitable subsequent increase in the number who will require long-term nursing care in most developed countries, an increase in the number of elderly people requiring home care is expected to be a major issue in modern societies worldwide. Therefore, it is useful to investigate the many factors leading to a decline in ADL among elderly people living at home.

In the present study, we examined the direct and indirect effects of oral health status, including number of teeth and denture wearing, swallowing function, nutritional status, and cognitive ability, on ADL in Japanese elderly people living at home and receiving home care services because of physical disabilities. We hypothesized the following: (i) cognitive impairment leads to eating difficulties (e.g., difficulty chewing food, difficulty swallowing food), and these difficulties impair nutritional status (16); (ii) oral health status affects eating difficulties (17); (iii) cognitive impairment affects oral health status (18), or, conversely, oral health status affects cognitive impairment (19); (iv) cognitive impairment and malnutrition lead to a decline in ADL (9) (Fig. 1). The conceptual model was proposed, based on empirical evidence.

Materials and methods

Study setting and study population

This cross-sectional study was undertaken in two mid-sized municipalities in Fukuoka prefecture (western Japan) between November 2010 and

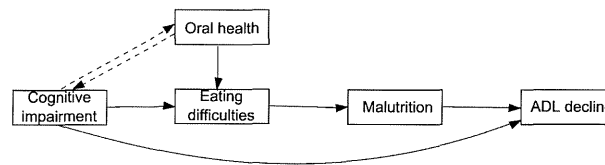


Fig. 1. The conceptual model. Dotted lines indicate paths explored the direction in this study.

February 2011. The study population comprised 337 participants aged 60 years or older who were living at home and using an in-home long-term care support center that coordinates home care services such as home nursing care, visiting rehabilitation, visiting bathing service, day service, and day care (rehabilitation) by service providers. Of these, 51 participants with missing data were excluded. Finally, 286 participants (75 men, 211 women) were included.

The study was approved by Kyushu University Institutional Review Board for Clinical Research. We obtained participants' or their family members' consent, as required for approval by the review board.

Assessment of oral health status and swallowing function

Oral health status and swallowing function were assessed by qualified dental hygienists. Oral health status was assessed by recording the number of teeth and denture wearing.

Swallowing function was examined by cervical auscultation, a non-invasive method of listening with a stethoscope to the sounds of swallowing 3 ml of water during the pharyngeal phase, following the method of Zenner et al. (20) with minor modifications. When breath sounds after swallowing material were clear, we evaluated swallowing function as normal. When stridor, coughing, or throat clearing was heard after swallowing material or when swallowing was repeated, we evaluated this as impaired swallowing function (i.e., dysphagia).

Measurement of ADL, cognitive ability, and nutritional status

Participant's ADL, cognitive ability, and nutritional status were recorded by a nurse or a care worker at the in-home long-term care support center. ADL was assessed using the Barthel Index, which covers all aspects of self-care independence in daily living activities such as transfer, walking stairs, toilet use, dressing, feeding, and bathing (21). A total score of 100 points indicates complete self-sufficiency, whereas a score of zero indicates that the person is completely dependent (21).

Cognitive ability was assessed using the Clinical Dementia Rating (CDR). CDR status was assigned according to the presence or absence of dementia and, if present, its severity (none, questionable or very mild, mild, moderate, or severe cognitive impairment), as described previously (22).

Nutritional status was evaluated using the Mini Nutritional Assessment-Short Form (MNA-SF) (23). The MNA-SF has the option of using calf circumference when body mass index is not available because of a bedridden and immobile state. Nutritional status was defined in three classifications by the MNA-SF: 0–7 points = malnourished; 8–11 points = at risk of malnutrition, and 12–14 points = well nourished.

Comorbid conditions

We assessed comorbidity with the Charlson comorbidity index (24, 25), which provides a weighted score for a participant's comorbidities taking into account how many of 19 predefined comorbid conditions an individual has, because elderly people generally live with multiple diseases, and the presence of comorbidities has a negative effect on both physical and cognitive function (26).

Statistical analysis

Bivariate associations between oral health status and swallowing function, nutritional status, cognitive ability, ADL, or confounding variables such as age, gender, and comorbid conditions were tested with the chi-square or ANOVA test. Oral health status was categorized as 20 or more teeth with dentures; 20 or more teeth without dentures; 10 to 19 teeth with dentures; 10 to 19 teeth without dentures; 0 to 9 teeth with dentures; or 0 to 9 teeth without dentures. A P value < 0.05 was considered to indicate statistical significance. The SPSS software (ver. 19.0 for Windows; IBM SPSS Japan, Tokyo, Japan) was used for data analyses.

To test the hypothesis, we conducted path analysis using the M-plus statistical package (27). Path analysis can be used instead of several separate regressions to examine mediating effects within a single model (28). Additionally, path analysis allows testing of causal relationships among a set

of observed variables (29). We tested the hypothesized model using path analysis (Fig. 2). The model examined the interactive effects of nine constructs. We hypothesized that cognitive ability and nutrition status directly affect ADL. We also hypothesized that the number of teeth, denture wearing, and cognitive ability precede swallowing function. Additionally, the number of teeth, denture wearing, and swallowing function precede nutrition status. Considering the association between cognitive ability and oral health status, it is possible that cognitive impairment affects oral health status (18) or, conversely, that oral health status affects cognitive impairment (19). We tested alternative path models each with different directionalities among the number of teeth, denture wearing, and cognitive ability. We adjusted for age, gender, and comorbid condition.

Data used in this study included both continuous and dichotomous variables. Thus, the path model was analyzed using weighted least-squares mean and variance adjustment estimation (WLSMV). WLSMV uses a diagonal weight matrix with robust standard errors and mean- and variance-adjusted chi-square test statistics (27). We used a significance level of $P < 0.05$ for the regression coefficients. The degree of correspondence between the hypothesized models and the actual data was assessed with a goodness-of-fit test. Criteria for the goodness-of-fit test include a comparative fit index (CFI), a Tucker-Lewis index (TLI), a root-mean-square error of approximation (RMSEA), and the weighted root-mean-square residual (WRMR). Values of >0.95 for the CFI, >0.95 for the TLI, <0.06 for the RMSEA, and

<0.90 for the WRMR are considered to indicate a good fit of the data to the model (27) (30).

Statistical power was considered for this analysis. In path analysis, sample sizes of around 150 to 200 are more desirable (31). With an alpha level of 0.05 and 286 subjects, it is estimated that the statistical power for this study reached 0.95.

Results

The participants were 75 men and 211 women. The age of the study population ranged from 61 to 104, and the mean age \pm SD was 84.5 ± 7.9 years (79.1 ± 7.9 years for men and 86.4 ± 6.9 years for women). The mean number of teeth present was 8.6 ± 9.9 , and 40.6% of participants were edentulous, while the mean number of teeth present was 14.4 ± 8.9 in 170 dentate subjects. The proportion of participants who did not visit a dental clinic was 75.9%.

Activities of daily living, cognitive ability, and nutritional status according to different categories of oral health status (including number of teeth, denture wearing), and swallowing function are presented in Tables 1 and 2. Subjects having 0 to 19 teeth and no dentures showed lower levels of ADL, cognitive function, and nutritional status than did those who had more than 20 teeth or who wore dentures. Subjects with dysphagia had lower ADL, more severe cognitive impairment, and more malnutrition than those with normal swallowing (Table 3).

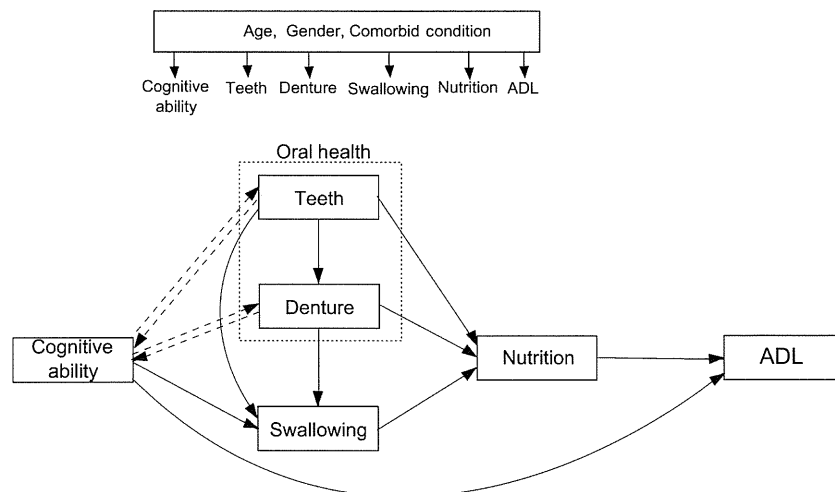


Fig. 2. The hypothesized model. The model consists of nine observed variables including confounding variables such as age, gender and comorbid conditions. Dotted lines indicate paths explored the direction in this study.

Table 1. Functional ability, cognitive function, and nutritional status according to the number of teeth [n (%)]

Variable	0–9 teeth (n = 179)	11–19 teeth (n = 48)	≥ 20 teeth (n = 59)	Total	P value
Age, mean ± SD	86.4 ± 7.1	82.8 ± 7.2	80.0 ± 8.5	84.5 ± 7.9	<0.001
Female	144 (80.4)	33 (68.8)	34 (57.6)	211 (71.3)	0.002
Dysphagia	57 (31.8)	16 (33.3)	16 (27.1)	89 (31.1)	0.743
Functional ability (Barthel Index), mean ± SD	57.2 ± 26.7	59.8 ± 28.4	62.1 ± 30.2	58.6 ± 27.7	0.467
Nutritional status (MNA-SF), mean ± SD	10.2 ± 2.1	9.7 ± 2.4	10.3 ± 2.6	10.1 ± 2.2	0.361
Nutrition status category					0.311
Normal (12–14)	52 (29.1)	13 (27.1)	23 (39.0)	88 (30.8)	
Risk of malnutrition (8–11)	105 (58.7)	25 (52.1)	28 (47.5)	158 (55.2)	
Malnutrition (0–7)	22 (12.3)	10 (20.8)	8 (13.6)	40 (14.0)	
Cognitive function (CDR)					0.262
None/Questionable	48 (26.8)	11 (22.9)	23 (39.0)	82 (28.6)	
Mild/Moderate	90 (50.3)	25 (52.1)	28 (47.5)	143 (50.0)	
Severe	41 (22.9)	12 (25.0)	8 (13.6)	61 (21.3)	
Comorbid condition (Charlson Comorbidity Index), mean ± SD	1.3 ± 1.1	1.5 ± 1.2	1.7 ± 1.3	1.4 ± 1.2	0.100

SD, standard deviation.

Table 2. Functional ability, cognitive function, and nutritional status according to oral health status [n (%)]

Variable	0–9 teeth, no denture (n = 26)	0–9 teeth with denture (n = 153)	10–19 teeth, no denture (n = 18)	10–19 teeth with denture (n = 30)	≥ 20 teeth, no denture (n = 49)	≥ 20 teeth with denture (n = 10)	P value
Age, mean ± SD	88.5 ± 6.6	86.1 ± 7.2	81.8 ± 7.5	83.3 ± 7.1	78.4 ± 8.2	87.6 ± 5.4	<0.001
Female	19 (73.1)	125 (81.7)	12 (66.7)	21 (70.0)	26 (53.1)	8 (80.0)	0.005
Dysphagia	15 (57.7)	42 (27.5)	7 (38.9)	9 (30.0)	13 (26.5)	2 (20.0)	0.061
Functional ability (Barthel Index), mean ± SD	38.1 ± 29.6	60.4 ± 24.8	53.9 ± 28.6	63.3 ± 28.2	59.8 ± 30.3	73.5 ± 28.0	0.001
Nutritional status (MNA-SF), mean ± SD	9.2 ± 2.1	10.4 ± 2.0	9.3 ± 2.4	10.0 ± 2.4	10.1 ± 2.8	11.4 ± 1.2	0.041
Nutritional status category							0.313
Normal (12–14)	4 (15.4)	48 (31.4)	4 (22.2)	9 (30.0)	18 (36.7)	5 (50.0)	
Risk of malnutrition (8–11)	16 (61.5)	89 (58.2)	10 (55.6)	15 (50.0)	23 (46.9)	5 (50.0)	
Malnutrition (0–7)	6 (23.1)	16 (10.5)	4 (22.2)	6 (20.0)	8 (16.3)	0 (0.0)	
Cognitive function (CDR)							0.038
None/Questionable	4 (15.4)	44 (28.8)	3 (16.7)	8 (26.7)	17 (34.7)	6 (60.0)	
Mild/Moderate	10 (38.5)	80 (52.3)	9 (50.0)	16 (53.3)	25 (51.0)	3 (30.0)	
Severe	12 (46.2)	29 (19.0)	6 (33.3)	6 (20.0)	7 (14.3)	1 (10.0)	
Comorbid condition (Charlson Comorbidity Index), mean ± SD	1.3 ± 0.9	1.3 ± 1.2	1.1 ± 0.5	1.7 ± 1.4	1.7 ± 1.4	1.6 ± 1.3	0.151

SD, standard deviation.

Path analysis

First, we estimated an initial model with all hypothesized pathways corresponding to the estimated variables directly or indirectly affecting ADL. Then, some insignificant paths were eliminated, and others who showed significant bivariate correlations were added while confirming the

model-fit indices. A final model was then estimated with only statistically significant paths retained. The final model was a fairly good fit [χ^2 (14) = 19.805; P = 0.136; CFI = 0.972; TLI = 0.945; WRWR = 0.571; RMSEA = 0.038 (0.001 to 0.074)]. Figure 3 shows parameter estimates for the final path model. The model showed the following

Table 3. Activities of daily living, cognitive ability, and nutrition status with or without dysphagia [n (%)]

Variable	Dysphagia (n = 89)	Normal (n = 197)	P value
Age, mean ± SD	84.5 ± 8.6	84.5 ± 7.5	0.991
Female	55 (61.8)	156 (79.2)	0.002
ADL (Barthel Index), mean ± SD	42.8 ± 28.3	65.8 ± 24.3	<0.001
Nutritional status (MNA-SF), mean ± SD	9.3 ± 2.3	10.5 ± 2.1	<0.001
Nutritional status category			<0.001
Normal (12–14)	16 (18.0)	72 (36.5)	
Risk of malnutrition (8–11)	52 (58.4)	106 (53.8)	
Malnutrition (0–7)	21 (23.6)	19 (9.6)	
Cognitive impairment (CDR)			<0.001
None/Questionable	32 (36.0)	60 (30.5)	
Mild/Moderate	35 (39.3)	108 (54.8)	
Severe	22 (24.7)	29 (14.7)	
Comorbid condition (Charlson Comorbidity Index), mean ± SD	1.4 ± 1.1	1.4 ± 1.2	0.976

SD, standard deviation.

significant direct paths: (i) ones from ‘Age’ and ‘Gender’ to ‘Teeth’; that is, increasing age decreased the number of remaining teeth [β

(standardized coefficient) = -0.36] and females had fewer teeth than males ($\beta = -0.14$); (ii) one from ‘Teeth’ to ‘Denture’; fewer teeth led to wearing denture ($\beta = -0.79$); (iii) one from ‘Teeth’ and ‘Denture’ to ‘Swallowing’; having many teeth and wearing dentures promoted normal swallowing function ($\beta = 0.78, 0.81$, respectively); (iv) one from ‘Gender’ to ‘Swallowing’; female tended to have normal swallowing function ($\beta = 0.22$); (v) one from ‘Cognitive Ability’ to ‘Denture’ and ‘Nutrition’; a high level of cognitive ability led directly to wearing dentures and better nutritional status ($\beta = 0.23$ and 0.34 , respectively); (vi) one from ‘Swallowing’ to ‘Nutrition’; normal swallowing function promoted normal nutritional status ($\beta = 0.25$); (vii) ones from ‘Swallowing’, ‘Cognitive Ability’, and ‘Nutrition’ to ‘ADL’; normal swallowing function, a high level of cognitive ability, and normal nutritional status resulted in a higher level of ADL ($\beta = 0.33, 0.26$, and 0.35 , respectively); (viii) one from ‘Comorbid Condition’ to ‘ADL’; severer comorbid condition caused a lower level of ADL ($\beta = -0.10$); and (ix) double-headed arrows among ‘Age’, ‘Gender’, ‘Comorbid Condition’, and ‘Cognitive Ability’; age was correlated with cognitive ability, gender, and comorbid conditions. On the other hand, the number of teeth and denture wearing were not directly associated with either nutritional status or ADL.

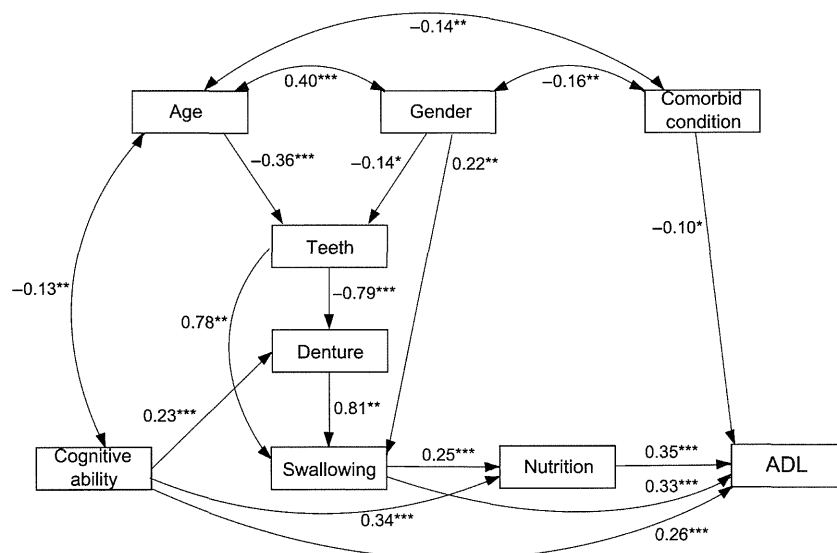


Fig. 3. The final model. Double-headed arrows indicate covariance. All significant values (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$) indicate standardized coefficients. Continuous variables are ‘Age’, ‘Comorbid Conditions’ (Charlson Comorbidity Index), ‘Nutrition’ (MNA-SF), ‘Teeth’, and ‘ADL’ (Barthel Index). Categorical or ordered variables are ‘Gender’ (1 = male, 2 = female), ‘Dentures’ (0 = not wearing, 1 = wearing), ‘Swallowing’ (0 = dysphagia, 1 = normal swallowing function) and ‘Cognitive Ability’ (1 = severe cognitive impairment, 2 = moderate, 3 = mild, 4 = questionable, 5 = none).

Discussion

This study showed the complex pathway from cognitive ability and oral health status via swallowing function and nutritional status to ADL in aged Japanese people living at home and receiving home care, using path analysis. To the best of the authors' knowledge, this is first study to show the interaction between multiple factors leading to a decline in ADL. Path analysis is an analytical technique that allows the testing of causal models using cross-sectional data. Possible pathways leading to ADL decline, based on our findings and those of previous studies, are as follows. Having fewer teeth leads to wearing dentures, but severe cognitive impairment disrupts denture wearing because of problems in accessing dental care; chewing difficulties resulting from having fewer teeth and no dentures can lead to dysphagia; dysphagia impairs the ability of elderly people to consume adequate amounts of food to meet their nutritional needs, leading to malnutrition (16); cognitive impairment, in turn, causes potential problems related to the inability to eat or to lack of access to food (32), hence leading to malnutrition. Swallowing function, cognitive ability, and nutritional status had direct effects on ADL. This finding agrees with previous studies in elderly people (9, 13). Malnutrition and cognitive impairment are associated with poor muscle strength and reduced physical performance (33), leading to disability, which reduces the ability to perform the basic activities of daily living. Although the effect of oral health status on ADL was indirect in this study, we cannot ignore it because of the moderate association between oral health status and swallowing function. Understanding various factors related to deterioration in ADL among these subjects would contribute to considering a multilateral approach for maintaining ADL in elderly people who are living at home.

The results of the present study suggested that oral health status, as measured by indicators such as the number of teeth and denture wearing, had a direct effect on swallowing function. A previous study reported that laryngeal penetration, usually because of neuromuscular disorder, occurs with much greater frequency in edentulous elderly people who are not wearing dentures than in those who dentulous (34). In our study, when the effect of denture wearing on swallowing function in edentulous persons was examined, 10 of 15 edentates (66.7%) without dentures showed dysphagia, whereas 29 of 101 edentates (28.7%) wearing dentures did.

Tamura et al. described that wearing dentures and keeping the appropriate mandible position and proper occlusion were important for smooth swallowing in elderly individuals (35). Additionally, loss of occlusal support and loss of mandibular stopping by occlusion may disturb the coordination of swallowing function (34).

In this study, we did not find a statistically significant association between oral health status and nutritional status in the path analysis. This finding conflicts with those of previous studies (11, 12). There may be at least two reasons that oral health status was not associated with nutritional status in the present study. First, our path model included some factors related to nutritional status, such as oral health status, swallowing function, cognitive ability, and ADL. However, previous studies (11, 12) that demonstrated an association between oral health status and nutritional status failed to incorporate these factors into their analyses. Probably, because factors other than oral health status more strongly affect nutritional status, the relationship would be less obvious in our study. Second, even when elderly people do not have enough teeth, do not wear dentures, and do not chew satisfactorily, food preparation by a caregiver may make food easy to chew and thereby prevent nutritional deterioration. Nutritional status was related to swallowing function, but not to oral health status, in this study, suggesting that swallowing function may have a greater direct effect than chewing ability on malnutrition. However, there was an association between swallowing function and oral health status in our study, and oral health status may still indirectly influence nutritional status.

Our results suggest that maintaining or improving oral health status and swallowing function indirectly or directly contribute to preventing a decline in ADL in elderly people who require home care. Yoneyama et al. (36) reported that oral care reduced febrile days and the risk of pneumonia in older patients receiving nursing care. These findings indicate that dental interventions, such as provision of dentures, treatment for dental caries or periodontal disease, professional oral care, swallowing training, and oral care training for caregivers, have a beneficial indirect effect on general health in those requiring long-term nursing care. However, our results also showed that 75.9% of participants had not received dental treatment; many elderly people requiring home care have difficulty in gaining access to professional dental care. Further efforts are needed to develop a long-term

care system or community system that provides ready access to dental services.

Our study had some limitations. Using path analysis, our study made causal inferences about the relationships among various factors related to ADL; however, the cross-sectional design means that we cannot rule out reverse causation. Further longitudinal study is needed to examine a temporal relationship. Second, we did not incorporate sociological factors, such as socioeconomic status and education level, into this study. Several studies have reported a relationship between sociological factors and oral health status, ADL, cognitive ability, and nutritional status (9, 37–39). ADLs are associated with psychosocial factors (9). Because sociological factors and psychosocial factors were considered to have more indirect effects on ADL than oral health status, cognitive ability, and nutritional status, we did not gather this information in this survey. Third, we did not assess the prevalence of specific oral diseases such as dental caries and periodontal disease. Finally, we recruited the subjects using an in-home long-term care support center in two midsized municipalities in Japan. Our sample may limit the ability to extrapolate our findings to all Japanese elderly people. Caution is warranted in generalizing our findings to the rest of the Japanese population.

In conclusion, based on the present study, we propose a potential causal pathway by which oral health status directly affects swallowing function, and dysphagia, cognitive impairment, and malnutrition directly or indirectly affect ADL in elderly people living at home and receiving home nursing care. These findings suggest that maintaining the number of teeth from a younger age and wearing dentures when teeth are lost may indirectly reduce malnutrition and subsequent ADL decline in these people.

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ORIGINAL ARTICLE: EPIDEMIOLOGY,
CLINICAL PRACTICE AND HEALTH**Relationship between nutrition status and dental occlusion
in community-dwelling frail elderly people**

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Aim: This study aimed to determine the risk of malnutrition in some communities where the frail elderly receive public long-term care insurance. We also clarified the dental problems in those at risk of malnutrition.

Methods: A total of 716 frail elderly who lived in eight cities in Japan (240 males and 476 females with a mean age of 83.2 ± 8.6 years) were divided into three groups according to Mini Nutritional Assessment short form results: well nourished, at risk of malnutrition and malnourished. They were also divided into three groups in terms of remaining teeth occlusion and denture occlusion: group A, natural dentition with adequate function; group B, partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws; and group C, functionally inadequate occlusion with no dentures. The relationship between nutrition status and dental occlusion was evaluated using logistic regression analysis with sex, age, activities of daily living and cognitive function as covariates.

Results: The number of participants in each of the groups was as follows: 251 well nourished, 370 at risk of malnutrition and 95 malnourished. When they were divided into just two groups, (i) well nourished and (ii) at risk of malnutrition plus malnourished, in order to study malnutrition risk factors, there were significant relationships between their nutritious status and sex, Barthel index, and occlusion.

Conclusion: This large-scale cross-sectional survey showed that loss of natural teeth occlusion was a risk factor for malnutrition among community-dwelling frail elderly. **Geriatr Gerontol Int 2013; 13: 50–54.**

Keywords: frail elderly people, Mini Nutritional Assessment short form, nutrition, occlusion.

Introduction

The intake of nutrients from daily meals is the foundation of life. Low nutrition decreases the immunological defenses, reduces physical functions, and can be a direct or indirect cause of morbidity and mortality among the elderly.^{1,2} It has been reported that 1–15% of outpatients and 15–60% of the institutionalized elderly suffer from protein-energy malnutrition (PEM),³ suggesting that the condition of elderly at risk of malnutrition should be investigated and improved without delay.

Several screening methods are available for determining malnutrition, but the use of a questionnaire is a simpler and more convenient method for a large-scale survey.⁴ Especially, The Mini Nutritional Assessment short form (MNA-SF) has been highly utilized worldwide, and its sensitivity and specificity have already been shown.^{5,6}

The present study evaluated the malnutrition risk for community-dwelling frail elderly receiving public long-term homecare insurance in Japan using the MNA-SF to determine whether dental occlusion might influence the risk of malnutrition.

Methods

The participants were 716 elderly individuals living at home and receiving public long-term care insurance services (240 males and 476 females with a mean age of

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83.2 ± 8.6 years) in eight prefectures in Japan (Tokyo, Fukushima, Kanagawa, Yamanashi, Shizuoka, Niigata, Fukuoka and Okinawa). Their malnutrition risk was evaluated using the MNA-SF, and also age, sex and underlying medical problems using the Charlson index⁷ were determined. In addition, activities of daily living (ADL) and cognitive function were evaluated using the Barthel index⁸ and the Clinical Dementia Rating,⁹ respectively, based on information from caregivers or care managers. This evaluation also determined one of the living environment factors, whether or not living alone.

The participants received oral examinations by a dentist or dental hygienist at home or at the day care facility they usually used, and molar occlusion was classified into the following three groups according to edentulous condition and denture-wearing status:

- Group A, natural dentition with adequate function
- Group B, partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws
- Group C, functionally inadequate occlusion with no dentures

Swallowing function was evaluated using a stethoscope to determine whether cervical auscultation of swallowing sounds was normal or abnormal.¹⁰ Before the examination, the dentist and dental hygienist in charge were instructed about the cervical auscultation method.

The participants were divided into three groups according to the result of the MNA-SF: (i) well-nourished; (ii) at risk of malnutrition; and (iii) malnourished. The relationship between participants' general condition and oral status was analyzed using the χ^2 -test and one-way ANOVA. In addition, participants were also divided into two groups: (i) well-nourished; and (ii) at risk of malnutrition or malnourished. Logistic regression analysis was carried out to study the significant risk factors influencing malnutrition. Participants were also divided into two groups according to whether they were:

(i) well-nourished *plus* those at risk of malnutrition; and (ii) malnourished. Logistic regression analysis was carried out to clarify the characteristics of malnourished subjects. PASW Statistics 18 (IBM, Tokyo, Japan) was used for statistical analysis with the significance level set at 95%.

Results

The MNA-SF showed the following: 251 individuals (94 males and 157 females) were well nourished, 370 (120 males and 250 females) were at risk of malnutrition and 95 (26 males and 69 females) were malnourished. Table 1 shows the general condition of participants, number of missing teeth and number of remaining teeth roots among those without occlusion according to nutrition group. The number of participants who lived alone by nutrition group was 30 in the well-nourished group (17.9%), 29 in the at risk of malnutrition group (14.0%) and 16 in the malnourished group (28.6%; $P < 0.05$).

The number of participants by occlusal relationship was 174 in group A (80 males and 94 females with a mean age of 78.7 ± 9.0 years), 421 in group B (120 males and 301 females with a mean age of 84.6 ± 8.0 years) and 121 in group C (40 males and 81 females with a mean age of 84.9 ± 7.7 years), which indicated that there was a significant correlation between occlusal relationship and nutrition status ($P < 0.05$; Fig. 1).

Cervical auscultation showed that the 516 participants exhibited normal swallowing sounds (151 males and 365 females with a mean age of 82.8 ± 8.4 years) and 200 had abnormal swallowing sounds (89 males and 111 females with a mean age of 84.0 ± 9.0 years). There was a significant relationship between normal swallowing sounds and nutrition status ($P < 0.05$, Fig. 2).

The results of the logistic regression analysis showed a significant relationship between malnutrition risk and sex, Barthel index, and occlusal relationship (Table 2).

Table 1 General condition and the number of missing teeth by nutrition group

	Well nourished	At risk of malnutrition	Malnourished
Age	81.9 ± 8.6	83.9 ± 8.3*	83.8 ± 9.3
Charlson index	1.4 ± 1.5	1.6 ± 1.4	1.8 ± 1.4**
Barthel index	77.1 ± 20.8	57.2 ± 27.8*	34.3 ± 28.6***
Clinical dementia rating	0.8 ± 0.9	1.2 ± 1.0*	1.4 ± 1.1**
No. missing teeth	20.2 ± 10.6	22.4 ± 9.8*	21.2 ± 9.6
No. remaining teeth root	0.9 ± 2.2	1.7 ± 3.3*	2.3 ± 4.0**
No. occlusal group (group A/B/C)	80/145/26	66/232/72	28/44/23 [†]
No. swallowing sounds (normal/abnormal)	208/43	262/108	46/49 [†]

One-way ANOVA and Games-Howell pairwise comparison test were used for parametric variables. * $P < 0.05$, well-nourished versus at risk of malnutrition; ** $P < 0.05$, well nourished versus malnourished; *** $P < 0.05$, at risk of malnutrition versus malnourished. [†]The χ^2 -test was used for non-parametric variables (<0.05).

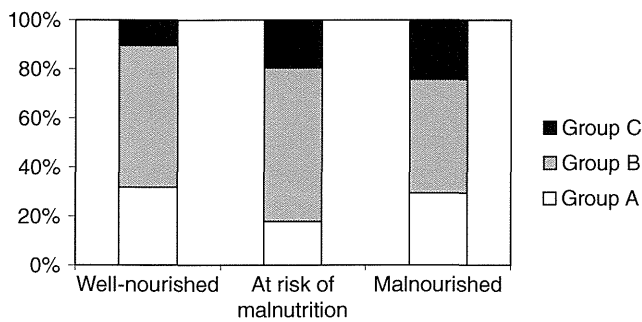


Figure 1 Relationship between nutrition and occlusion (χ^2 -test, $P < 0.05$). Group A: natural dentition with adequate function. Group B: partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws. Group C: functionally inadequate occlusion with no dentures.

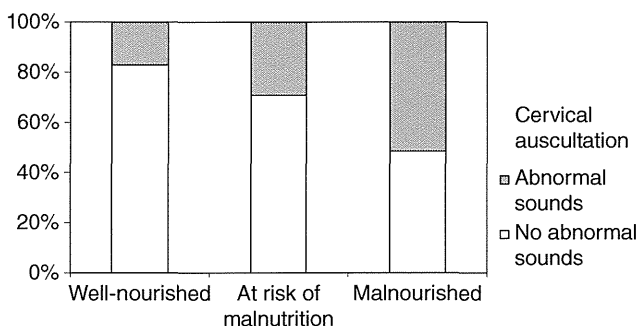


Figure 2 Relationship between nutrition and abnormal swallowing sounds detected by cervical auscultation (χ^2 -test, $P < 0.05$).

A significant relationship was also observed between malnutrition and Barthel index, abnormal swallowing sounds by cervical auscultation, and living alone (Table 3).

Discussion

The results of the present study showed that the number of frail elderly with malnutrition was 13.3% (95), which is nearly in agreement with the results of a previous study carried out in Japan.¹¹ Furthermore, the number of the participants at risk of malnutrition, including those in the at risk of malnutrition and malnourished groups was 64.9% (465), which surprisingly exceeded 50% of the participants. This result shows that improvement in the nutrition status of frail elderly living in home care needs to be urgently addressed.

The Barthel index was the significant factor documenting both malnutrition risk and malnourishment in the present study. Many researchers agree that there is a

relationship between physical function and nutrition status.¹² It might be concluded that individuals whose daily activity is limited tend to avoid shopping for food items, resulting in nutritional disturbance.

In addition to the Barthel index, sex was found to be a significant factor influencing malnutrition risk. The present study showed that older females had a 1.845-fold greater malnutrition risk than older males (95% CI 1.121–3.036), which agreed with the results of a previous study that showed that older females were more likely to develop nutritional disturbance, both obesity and malnutrition.¹³

Furthermore, occlusal status was significantly related to malnutrition risk. The group C individuals (functionally inadequate occlusion with no dentures) had a 3.189-fold greater malnutrition risk than group A (natural dentition with adequate function; 95% CI 1.437–7.080). Chewing efficiency, for example, the rate of breakdown of food during mastication, is clearly correlated with features of the dentition, such as number of posterior teeth and occlusal relationships.¹⁴ The most pronounced difference in intake involves hard-to-chew foods, such as vegetables and some fruits, therefore tooth loss affects elements of nutritional intake, such as dietary fiber and vitamins.¹⁵ These micronutrients are the key element in maintaining good nutrition, which suggests that lack of such food might result in greater malnutrition risk.

In addition, group B (partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws) had a 1.704-fold greater malnutrition risk than group A (95% CI 1.013–2.864). Previous studies have shown that individuals who have lost natural molar contacts consume lesser amounts of hard-to-chew foods, such as vegetables and fruits, even though they use their dentures during food intake.¹⁶ Our findings in the present study support the view that denture use is not sufficient to compensate for natural teeth. Recently, Bradbury *et al.* showed that food instruction encourages an increase in the consumption of vitamins and minerals among new denture wearers.¹⁷ In general, denture treatment has not usually included in such dietary intervention. Future studies will be required to identify the effect of dietary intervention on the prevention of malnutrition in denture users.

In contrast, there was no significant relationship between malnourishment and occlusion in frail elderly participants. There were significant relationships between malnutrition and Barthel index, abnormal swallowing sounds detected by cervical auscultation, and living alone. These results suggest that malnourished elderly have already developed dysphagia resulting in dietary modification;¹⁸ therefore, their malnutrition might be less influenced by a proper occlusal relationship. A vicious cycle, in which decreased ability to

Table 2 Items significantly involved in malnutrition risk

	B	Standard deviation	Wald	P-value	Exp (B)	95% Confidence interval	
Sex	0.612	0.254	5.803	0.016	1.845	1.121	3.036
Age	-0.001	0.015	0.006	0.939	0.999	0.971	1.028
Charlson index	0.089	0.082	1.168	0.280	1.093	0.930	1.284
Barthel index	-0.036	0.005	43.381	0.000	0.965	0.955	0.975
Clinical Dementia Rating	0.156	0.140	1.251	0.263	1.169	0.889	1.537
Swallowing sounds	0.482	0.297	2.627	0.105	1.619	0.904	2.900
Occlusal relationship (a) group A <i>vs</i> group B	0.533	0.265	4.039	0.044	1.704	1.013	2.864
Occlusal relationship (b) group A <i>vs</i> group C	1.160	0.407	8.125	0.004	3.189	1.437	7.080
Living alone	0.353	0.301	1.380	0.240	1.424	0.790	2.567
Constant	1.701	1.265	1.807	0.179	5.479		

The participants were divided into two groups according to their nutrition status: (i) a well-nourished group; and (ii) a group that included those at risk of malnutrition and malnourished. Group A, natural dentition with adequate function; group B, partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws; group C, functionally inadequate occlusion with no dentures.

Table 3 Items significantly involved in malnutrition

	B	Standard deviation	Wald	P-value	Exp (B)	95% Confidence interval	
Sex	0.613	0.388	2.501	0.114	1.846	0.864	3.947
Age	-0.002	0.021	0.007	0.933	0.998	0.958	1.040
Charlson Index	0.014	0.104	0.019	0.891	1.014	0.827	1.244
Barthel Index	-0.035	0.007	27.940	0.000	0.966	0.953	0.978
Clinical Dementia Rating	-0.072	0.178	0.165	0.685	0.930	0.657	1.318
Swallowing sounds	1.060	0.340	9.684	0.002	2.885	1.480	5.623
Occlusal relationship (a) group A <i>vs</i> group B	-0.453	0.391	1.343	0.246	0.636	0.295	1.368
Occlusal relationship (b) group A <i>vs</i> group C	-0.485	0.520	0.871	0.351	0.616	0.222	1.705
Living alone	1.461	0.403	13.143	0.000	4.312	1.957	9.502
Constant	-0.746	1.777	0.176	0.674	0.474		

Participants were divided into two groups according to their nutritious status: (i) a group of well-nourished individuals and those at risk of malnutrition; and (ii) a group of malnourished individuals. Group A, natural dentition with adequate function; group B, partially or fully edentulous, but maintaining functional occlusion with dentures in either or both jaws; group C, functionally inadequate occlusion with no dentures.

swallow food could accelerate malnutrition, was also considered. Elderly people who live alone are less likely to follow through with dietary modification,¹⁹ and it might lead to malnutrition regardless of occlusal status.

In conclusion, the present study, as well as previous studies, has shown that retaining the natural teeth plays an important role in the prevention of nutritional disturbance, and that early dental treatment in the elderly is important to protect their teeth and occlusion. Dietitians, as well as other care staff, should monitor oral

conditions, such as remaining teeth and occlusion, in the elderly in order to prevent malnutrition. We also suggest that all dentists enhance their skills and knowledge in the fields of swallowing function and nutritional guidance.

Acknowledgments

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Relationship Between Normal Serum Creatinine Concentration and Periodontal Disease in Japanese Middle-Aged Males

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Background: Periodontitis has been shown to be closely related to diabetes, which was recently found to be associated with lower serum creatinine. Conversely, several studies have suggested a positive relationship between periodontitis and abnormally high concentrations of serum creatinine associated with renal dysfunction, seemingly contradicting the above. This study evaluates periodontal status and serum levels of creatinine within the normal range to resolve this apparent contradiction.

Methods: A comprehensive health examination of 907 Japanese males, 49 to 59 years old, was performed from 2000 to 2002. A blood sample was collected from the antecubital vein after an overnight fast. The periodontal parameters were periodontal probing depth (PD) and clinical attachment loss (AL). We examined the association between serum creatinine concentration within the normal range and periodontal parameters.

Results: Serum creatinine concentration within the normal range was inversely correlated with mean PD and mean AL. In multivariate linear regression analyses, every 0.1-mg/dL increment in serum creatinine concentration was associated with a 0.064-mm decrease in both mean PD and mean AL ($P < 0.05$) after adjusting for confounding variables.

Conclusion: This study finds a significant inverse association between normal serum creatinine concentration and periodontal disease. *J Periodontol* 2013;84:94-99.

KEY WORDS

Creatinine; epidemiology; periodontal diseases; periodontitis.

Periodontal disease is a highly prevalent chronic inflammatory disease. Many studies have suggested that periodontal disease is closely related to several systemic diseases, such as cardiovascular disease and diabetes.¹⁻³ Among systemic diseases, diabetes has been manifestly confirmed as a major risk factor for periodontitis.⁴⁻⁶ Chronic subclinical inflammation plays an important role in the pathogenesis of type 2 diabetes, although the disease is influenced by multiple lifestyle-related factors. Recently, several studies have shown that lower serum creatinine levels may be a new risk factor for type 2 diabetes in non-diabetic Japanese males⁷ and white morbidly obese patients.⁸ Considering the above facts, periodontal disease may be associated with lower levels of serum creatinine.

In contrast, the serum creatinine concentrations of patients with renal dysfunction increase as a result of a reduction in creatinine clearance. High serum creatinine concentrations and glomerular filtration rates (GFRs) are often used as indicators of renal function in clinical practice.⁹ Some studies have demonstrated a relationship between periodontal disease and renal dysfunction, as evaluated by GFR and serum creatinine concentration in surveys in the United States.¹⁰⁻¹² Kshirsagar et al.¹⁰

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showed that patients with periodontal disease were more likely to have lower GFRs and subsequently elevated serum creatinine concentrations compared with those of individuals with healthy gingiva or gingivitis. These findings are inconsistent with the fact that lower serum creatinine level could be a new risk factor for type 2 diabetes and closely linked to periodontal disease. Therefore, in this study, we evaluate periodontal status and serum creatinine levels within the normal range among Japanese middle-aged males in an attempt to resolve this apparent contradiction. To our knowledge, no published study to date has examined the relationship between normal serum creatinine concentration and periodontal status.

MATERIALS AND METHODS

Study Population

More than 95% of the males enlisted in the Japan Self-Defense Force in Fukuoka, Japan, received a comprehensive health examination ≤ 5 years before retirement that included 5 days of admission to Japan Self-Defense Force Fukuoka Hospital. The examination was conducted as part of preretirement health care. A total of 1,123 males, 49 to 59 years old, were examined from January 2000 to March 2002. Of these, 182 participants who had < 20 teeth or who were not able to provide sufficient data were excluded because of difficulties in properly assessing their periodontal health. Because the purpose of this study is to examine the relationship between serum creatinine concentration within the normal range and periodontal status in individuals without renal dysfunction, we excluded 34 individuals with serum creatinine concentrations > 1.2 mg/dL or estimated GFR < 60 mL/min/1.73 m², as calculated from serum creatinine values using the revised equations for Japanese individuals.¹³ Thus, the final study sample consisted of 907 individuals. The individuals provided verbal consent to participate in this study. This study was conducted in accordance with the Helsinki Declaration, and the design and procedures were approved by the Japan Self-Defense Force Fukuoka Hospital and the Ground Staff Office.

Measurements

Oral examinations were performed by one dentist (MM) trained to perform a clinical examination of oral health status using a normal dental chair. Mesio-buccal and mid-buccal periodontal probing depth (PD) and clinical attachment loss (AL) were measured using a periodontal probe[†] in all remaining teeth except third molars, following the method described in the Third National Health and Nutrition Examination Survey.¹⁴ Examiner reliability was verified by intra-examiner calibration with a sample of volunteers; PD values showed 91.0% to 100%, and AL values showed

89.0% to 100% agreement (± 1 mm). κ values were 0.86 to 1.00 for PD and 0.84 to 1.00 for AL.

Each participant completed a self-administered questionnaire that assessed smoking history and toothbrushing habits, and an examiner (MM) verified the answers orally. Smoking history was quantified as pack-years by multiplying the number of cigarettes smoked per day by the number of years during which the participants had smoked. The frequency of toothbrushing was divided into three categories: 1) ≤ 1 times per day; 2) twice a day; and 3) ≥ 3 times per day.

A blood sample was collected from the antecubital vein after an overnight fast to determine lipid, glucose, and creatinine levels. The body mass index (BMI) was defined as weight (in kilograms) divided by the square of height (in meters).

Statistical Analyses

The mean PD and mean AL were used as dependent variables to reflect periodontal health status. Spearman correlation coefficient among each periodontal parameter and other variables were calculated. Simple and multivariate linear regression analyses were used to examine the relationship between serum creatinine concentration and each periodontal parameter. Variables for which the correlation coefficient was significant were entered into the multivariate models. Age and BMI were entered into the multivariate models unconditionally to control for the influence of physical constitution on the relationship between serum creatinine concentration and periodontal parameters. A value of $P < 0.05$ indicated statistical significance. Statistical analyses were performed using a software program.[‡]

RESULTS

Table 1 shows the Spearman correlation coefficients for the study variables. The number of teeth, smoking history, high-density lipoprotein cholesterol, and serum creatinine concentration were significantly correlated with both periodontal parameters, and toothbrushing frequency was significantly associated with mean PD.

A simple linear regression analysis identified a significant relationship between serum creatinine concentration and each periodontal parameter (Table 2). Table 3 shows the results of the multivariate linear regression analysis of each independent variable in relation to the periodontal parameters. Serum creatinine concentration was significantly inversely correlated with both periodontal parameters. Every 0.1-mg/dL increment in serum creatinine concentration was associated with a 0.064-mm decrease in both mean

[†] PCP-UINC 15, Hu-Friedly, Chicago, IL.

[‡] SPSS v.17.0, SPSS Japan, Tokyo, Japan.

Table 1.
Characteristics of Variables and Spearman Correlation Coefficients

	Median (quartile, third quartile)	Spearman Correlation Coefficient	
		Mean PD	Mean AL
Age (years)	52 (52, 53)	-0.029	-0.007
Mean PD (mm)	2.4 (2.0, 2.8)	—	0.77*
Mean AL (mm)	2.8 (2.3, 3.5)	0.77*	—
Number of teeth	27 (24, 28)	-0.22*	-0.35*
Smoking history (pack-years)	24.75 (7.5, 33)	0.24*	0.30*
Toothbrushing frequency (times/day)	2 (1, 2)	-0.12*	-0.019
BMI (kg/m ²)	23.7 (22.0, 25.7)	0.058	-0.020
Triglyceride (mg/dL)	119 (83, 173)	0.057	0.048
High-density lipoprotein cholesterol (mg/dL)	56 (46, 67)	-0.090*	-0.12*
Fasting plasma glucose (mg/dL)	98 (92, 106)	0.041	0.041
Systolic blood pressure (mmHg)	128 (120, 138)	0.029	0.003
Diastolic blood pressure (mmHg)	82 (76, 88)	0.021	-0.050
Serum creatinine concentration (mg/dL)	0.8 (0.8, 0.9)	-0.11*	-0.12*

— = not applicable.

* $P < 0.01$.

Table 2.
Parameter Estimates From Simple Linear Regression Models Evaluating Serum Creatinine Concentration in Relation to Periodontal Parameters

Independent Variable	Dependent Variable					
	Mean PD (mm)			Mean AL (mm)		
	Coefficient	SE	<i>P</i> Value	Coefficient	SE	<i>P</i> Value
Serum creatinine concentration (0.1 mg/dL)	-0.095	0.026	<0.001	-0.12	0.035	<0.001
Intercept	3.32	0.22	<0.001	4.08	0.23	<0.001

Mean PD $R^2 = 0.014$; mean AL $R^2 = 0.010$.

PD and mean AL ($P < 0.05$), after adjusting for other confounding variables.

DISCUSSION

In this study, we analyze the correlations between serum creatinine concentration within the normal range and periodontal parameters in Japanese middle-aged males. The results showed that serum creatinine concentration was significantly inversely related to both mean PD and mean AL.

Most serum creatinine is derived from skeletal muscle as a metabolite of creatine. Thus, normal se-

rum creatinine concentrations are proportional to muscle mass, which is an important target organ of insulin.¹⁵ One cohort study in non-diabetic Japanese males examining the relationship between serum creatinine concentrations within the normal range and the subsequent incidence of type 2 diabetes found that lower serum creatinine levels increased the risk for type 2 diabetes.⁷ This relationship remained when the analysis was stratified according to BMI. The authors thus suggested that low serum creatinine concentrations, suggestive of low lean body mass, may be