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Changes in metacarpal bone mineral density with age and menopause using computed X-ray densitometry in Japanese women: Cross-sectional and longitudinal study

YUICHIRO KATO[1], KAZUKO ISHIKAWA-TAKATA[1], KYOKO YASAKU[2], YAYOI OKAWA[3], OSAMU KAWAKAMI[3], & TOSHIKI OHTA[3]

[1]*Division of Health Promotion and Exercise, National Institute of Health and Nutrition, Shinjuku, Tokyo, Japan,* [2]*Department of Nutrition and Dietetics, Kamakura Women's University, Kamakura, Kanagawa, Japan, and* [3]*National Center for Geriatrics and Gerontology, Obu, Aichi, Japan*

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Abstract

Background: Bone mineral density (BMD) loss with age and menopause is widely accepted in elderly women. However, only a few studies have utilized a multiple regression model that includes physical characteristics to assess comprehensive lifetime changes in BMD.

Objective: A prospective study was conducted to characterize the normal patterns in metacarpal BMD changes in Japanese women, and to assess the applicability of a fitting model using cross-sectional data compared with longitudinal variability.

Subjects and methods: The study consisted of 5422 healthy women in cross-sectional data and a 1-year follow-up of 359 women. The metacarpal BMD was measured by computed X-ray densitometry. Multiple linear and nonlinear regression analyses were performed in cross-sectional subjects. Nonparametric analysis was used to compare percentage rates of BMD changes between actual and estimated values.

Results: The cross-sectional data showed that the best-fit equation was a nonlinear change model using the variables of age and height in premenopausal women, and years since menopause (YSM), age and height in postmenopausal women. The results of longitudinal data indicated the following. In premenopausal women, the actual BMD changes were greater in the 30–39 age group than the 20–29 age group and were less in the 50–59 group than the 40–49 group. The rates of annual change in BMD between the actual value and estimated value by change model were very similar. In postmenopausal women, the actual changes in BMD indicated that the rapid rate of reduction observed was over 3% at 0–5 YSM and 1.5% at 6–10 YSM, and thereafter showed a slower rate of decline at 11 YSM. The change model represented the trend of actual change in BMD for postmenopausal women, whereas the rates of estimated BMD loss underestimated the actual changes at 1–10 YSM.

Conclusion: The change model for premenopausal women using cross-sectional data is beneficial in evaluating the actual metacarpal BMD variability, whereas that for postmenopausal women is insufficient in estimating the longitudinal BMD variability.

Correspondence: Kazuko Ishikawa-Takata, Division of Health Promotion and Exercise, National Institute of Health and Nutrition, 1-23-1 Toyama, Shinjuku, Tokyo 162-8636, Japan. E-mail: kazu@nih.go.jp

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Introduction

Bone mineral density (BMD) is the most important measurable determinant of bone health status and osteoporotic fracture (Melton et al. 1988; Christiansen 1993). In healthy humans, the onset of age-related BMD loss occurs generally during the fourth decade of life and continues into extreme old age (Nuti and Martini 1993; Nakamura et al. 2000; Lu et al. 2001; Warming et al. 2002). The pattern of age-related change in BMD is a significant issue for quality of life in elderly populations, especially in women.

The decline in ovarian function that occurs with menopause is the most significant factor linked to BMD loss in women (Luisetto et al. 1993; Bjarnason et al. 1995; Warming et al. 2002). Therefore, numerous studies concerning the changes in BMD and menopause have classified women into pre- and postmenopausal groups. However, these studies used data from narrow intervals (Hansen 1994; Bjarnason et al. 1995; Goto et al. 1996), sometimes showing no continuity between the age groups (Matsumoto et al. 1994), and made a comparison of different skeletal sites (Gallagher et al. 1987; Heaney et al. 1997). In these cases, the general patterns of age-related BMD change are neither referenced nor delineated.

To estimate the BMD loss with age, previous studies have applied a simple linear model that failed to consider the menopausal factor (Seo et al. 1994; Löfman et al. 1997; Maggio et al. 1997; Nakamura et al. 2000). In addition, physical characteristics such as height and weight have been generally associated with BMD changes in many cross-sectional studies (Gallagher et al. 1987; Mazess et al. 1987; Nuti and Martini 1993; Seo et al. 1994; Heaney et al. 1997; Melton et al. 2000; Nakamura et al. 2000). However, there are only a few studies in the literature that utilize a multiple regression model that includes physical characteristics to assess comprehensive lifetime changes in BMD (Gallagher et al. 1987; Nuti and Martini 1993). Therefore, there is a need for more information about changes in BMD with age and menopause that includes physical characteristics.

Since there is a wide range of BMD measuring techniques and skeletal sites in current use, the pattern of change in BMD for each measuring technique and site is still under development (Lu et al. 2001). Computed X-ray densitometry (CXD) is a method for measuring metacarpal BMD, an index of cortical bone volume, and has the advantages of technical ease and feasibility at low cost (Derisquebourg et al. 1994; Matsumoto et al. 1994; Seo et al. 1994). The purpose of the present study was to characterize the best-fitting model of normal difference in metacarpal BMD for pre- and postmenopausal women. We measured metacarpal BMD using CXD in 5422 healthy Japanese women. Furthermore, we performed a 1-year follow-up study of 359 subjects to determine whether the prospective change model corresponded to the actual BMD changes.

Materials and Methods

Subjects

A total of 8807 women were recruited from the general population in eight communities of Japan. They were Japanese females aged 18–85 years and were invited by publicity in each community to a measurement of BMD and a health assessment at community

health care centers in 1994–1996. Of these, 3365 subjects were excluded because they had a disease or received treatment known to affect bone metabolism or because their menstruation status was interrupted by operations or medications. The final study sample consisted of 5442 healthy women (aged 20–78 years); 3142 were premenopausal and 2280 were postmenopausal. Such a large sample enabled us to obtain normative data and to identify the patterns of differences in BMD with age and menopause. We also randomly selected samples for the longitudinal study and enrolled 359 women (aged 21–70 years) who agreed to participate in a 1-year follow-up survey; 185 were premenopausal, 14 were perimenopausal, and 160 were postmenopausal. In longitudinal data, premenopausal women were divided into decade-age groups, and postmenopausal women were classified into three groups: 1–5 years since menopause (YSM), 6–10 YSM, and 11–15 YSM.

This study was approved by the Ethics Committee of the National Institute of Health and Nutrition, Japan. Subjects gave written informed consent for joining the study and permission for our use of BMD data for evaluation.

The measurement variables included chronological age, menstruation status, age at menopause, height, and weight. Body mass index (BMI) was calculated as weight/height^2 (in kg m^{-2}). Absence of menstruation lasting more than half a year was taken as an age at menopause and was checked by community nurses. Perimenopausals were defined as those who had their menopause during the 1-year follow-up in longitudinal study.

BMD measurement

BMD of the second metacarpal was measured by CXD (Bonalyzer, Teijin, Tokyo, Japan). This procedure provides an anterior–posterior radiographic view in comparison with the density of an aluminum step wedge (20 steps, 1 mm step^{-1}) as a standard (Matsumoto et al. 1994). The diagram of the quantity of absorbed light was converted to 256-grayscale digital data. The computer automatically calculated the metacarpal BMD on the basis of the gradation patterns on the aluminum step wedge. BMD was expressed as the thickness of an aluminum equivalent (mm Al). The precision error of this instrument was within 0.7% according to the manufacturer's standard. The reproducibility of CXD *in vivo* were 0.3–1.2% coefficient of variation (CV) in short-term and 0.2–0.8% CV in midterm (Matsumoto et al. 1994).

Statistical analysis

The differences in BMD with age for premenopausals was analyzed by simple and polynomial regression in cross-sectional data. The differences in BMD with reference to both age and YSM for postmenopausals were analyzed by simple and polynomial regression in cross-sectional data separately. The difference in each correlation coefficient was determined by the following formula:

$$z = (Z_1 - Z_2)/\sqrt{[1/(n_1 - 3) + 1/(n_2 - 3)]} \quad (1)$$

$$Z_i = \ln[(1 + r_i)/(1 - r_i)]/2 \quad (2)$$

where z represents standardized distribution, r is the correlation coefficient, and n is the number of samples. The suitable model was chosen.

Table I. BMD and physical characteristics in cross-sectional population.

Groups	*n*	Age (years)	Height (cm)	Weight (kg)	BMI ($kg\,m^{-2}$)	BMD (mm Al)
20–29*	365	26.5 ± 2.4	157.9 ± 5.1	50.9 ± 7.1	20.38 ± 2.52	2.710 ± 0.220
30–39*	1395	35.1 ± 2.9	157.3 ± 5.0	52.4 ± 7.1	21.18 ± 2.77	2.738 ± 0.216
40–49	1181	45.1 ± 3.0	156.2 ± 5.1	52.7 ± 7.0	21.63 ± 2.73	2.741 ± 0.253
Premenopause	1064	44.8 ± 2.9	156.3 ± 5.1	52.8 ± 7.0	21.64 ± 2.71	2.756 ± 0.249
Postmenopause	117	48.1 ± 1.7	155.5 ± 4.7	52.0 ± 7.4	21.51 ± 2.92	2.605 ± 0.248
50–59	1495	54.9 ± 3.1	153.8 ± 4.9	52.2 ± 7.0	22.06 ± 2.80	2.485 ± 0.300
Premenopause	291	52.0 ± 2.7	153.9 ± 4.8	52.8 ± 6.7	22.28 ± 2.78	2.668 ± 0.268
Postmenopause	1204	55.6 ± 2.7	153.7 ± 4.9	52.0 ± 7.0	22.00 ± 2.81	2.441 ± 0.290
60–69	969	63.0 ± 2.2	152.8 ± 5.0	52.1 ± 7.4	22.33 ± 3.01	2.254 ± 0.267
Premenopause	31	62.9 ± 2.2	151.6 ± 4.6	52.9 ± 8.1	23.04 ± 3.58	2.194 ± 0.285
Postmenopause	938	63.0 ± 2.2	152.8 ± 5.0	52.1 ± 7.3	22.31 ± 2.99	2.256 ± 0.266
70–78**	21	72.7 ± 2.2	149.1 ± 6.0	50.2 ± 8.0	22.52 ± 2.75	2.127 ± 0.220

Values are means ± SD; *premenopausal women; **postmenopausal women.

To estimate the prospective BMD change models in both pre- and postmenopausal women, stepwise regression techniques were used with age, YSM (when fitting for postmenopausals), height, weight and BMI as independent variables on the basis of the chosen model.

The annual percentage rates of BMD changes were calculated from longitudinal data. The predicted BMD in a particular individual was obtained using the change model at their baseline and 1 year after. The predicted annual rates of BMD changes were computed based on these values. To assess the validity of the change models calculated from stepwise regression in cross-sectional data, nonparametric analysis was used to compare actual percentage rates of BMD changes with predicted percentage rates of BMD changes within each group. The significance level was set at 0.05.

Results

Differences in BMD: Cross-sectional design

The BMD and physical characteristics of the cross-sectional population for each age group are shown in Table I. The recalled age at menopause was 50.4 ± 3.3 years. Height and BMI were correlated with age ($r = -0.353$, $p < 0.001$; and $r = 0.193$, $p < 0.001$), respectively. No correlation between weight and age was found. The BMD was significantly higher in the 40–49 age groups, and thereafter was significantly lower by 22.4% in the over 70 age group ($F(5,5416) = 574.9$, $p < 0.001$). Significant differences in BMD between pre- and postmenopausal women were observed both in the 40–49 and 50–59 age groups ($t(1117) = 6.26$, $p < 0.001$; and $t(1492) = 12.14$, $p < 0.001$), respectively. There was no significant difference that in the 60 year age group.

To analyze the pattern of age-related BMD differences for premenopausal women, we applied various regression analyses for the relationship between BMD and age. The simple and polynomial regression equations significantly fit the observed BMD differences (Figure 1). A significant difference was observed in the correlation coefficients between the two regression equations. Therefore, the suitable equation was a nonlinear-change model used to evaluate the age-related BMD differences for premenopausal women.

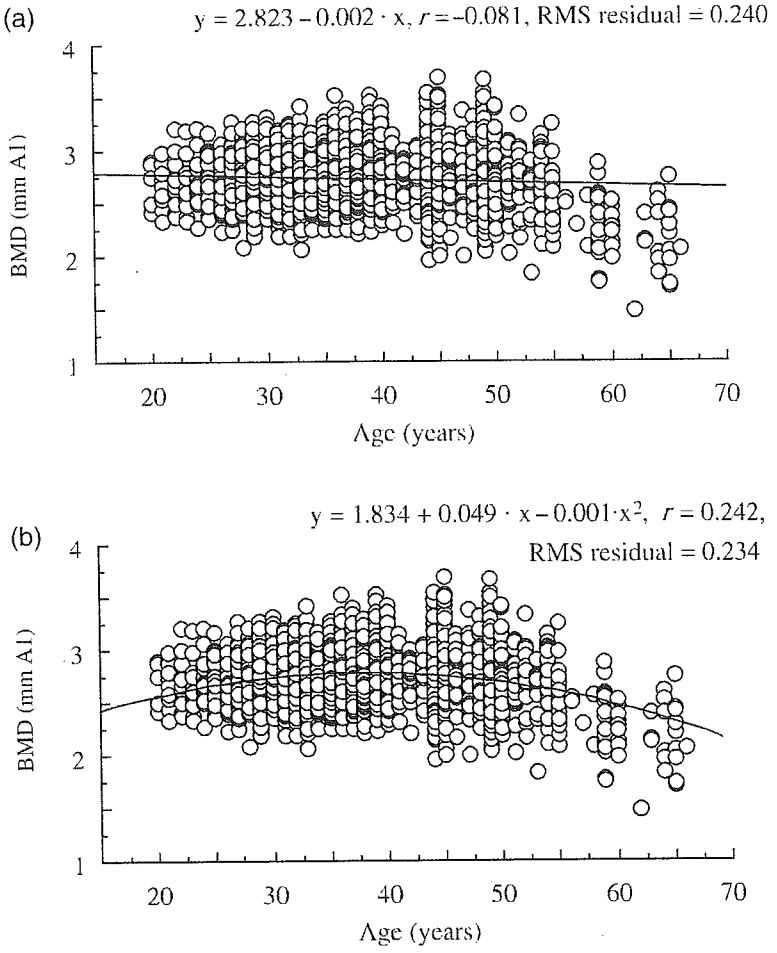

Figure 1. Relationship between BMD and age in premenopausal women as a function of simple (a) and polynomial (b) regression.

In the postmenopausal women, we examined various regression analyses for the relationship between BMD vs. age and YSM (Figure 2). As the result of a comparison of correlation coefficients among each regression, it was not found whether a nonlinear or linear function was suitable for postmenopausal women. In the nonlinear functions as determined by polynomial regression, overall partial coefficients of the YSM were significantly related to BMD, while a partial coefficient of age for the binomial variable was not significant. Therefore, the BMD of postmenopausal women plotted against the YSM instead of age is used hereafter. No significant regressions were obtained from the logarithm or exponential-function models.

In order to establish a prospective-change model of BMD both in pre- and postmenopausal women, we performed a stepwise regression analysis with age, YSM, height, weight, and BMI as independent variables. Table II shows the best-fit equations for the nonlinear and linear change models. For premenopausal women, the nonlinear-change model was applied for age as a binomial variable. For postmenopausal women, linear- and nonlinear-change models were used as well as a later model that included YSM as a binomial variable.

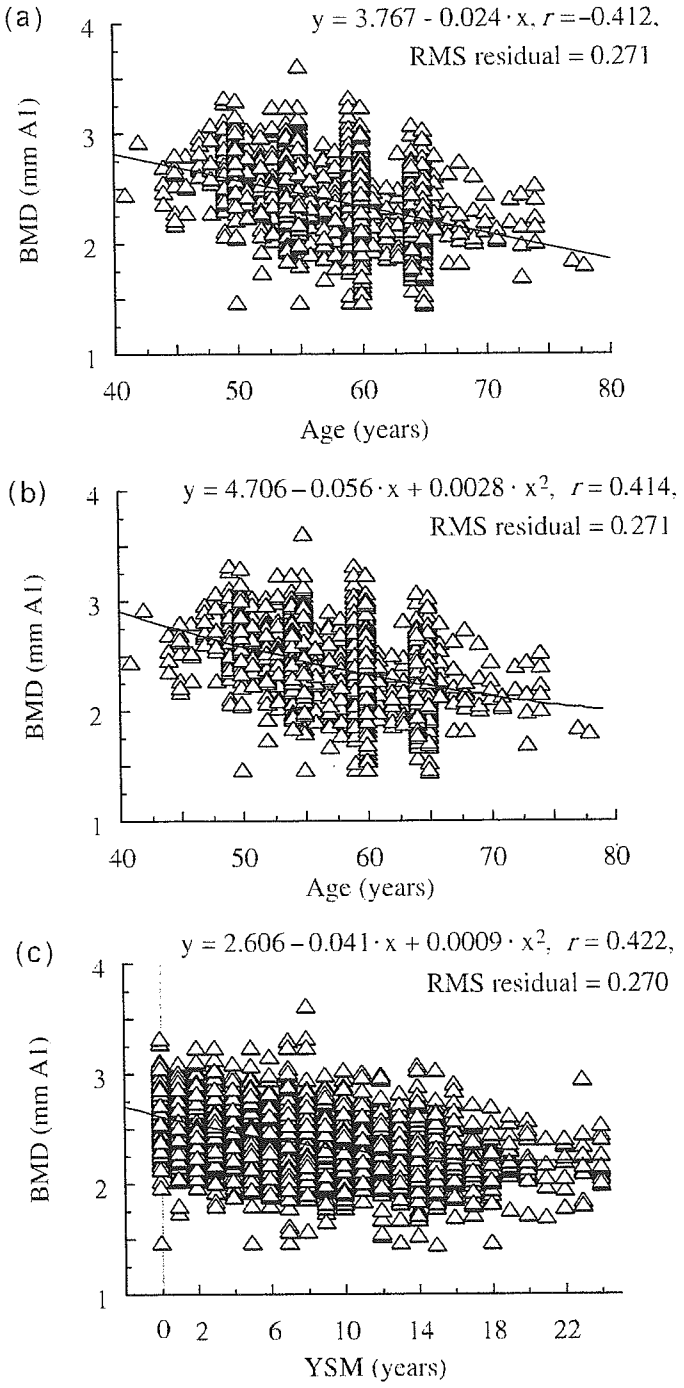

Figure 2. Relationship between BMD *vs.* age and years since menopause (YSM) in postmenopausal women. Simple regression for BMD with age (a). Polynomial regression for BMD with age (b) and with YSM (c).

Table II. Best-fit equations expressing BMD in cross-sectional population.

	Equation	*r*	RMS residual
Premenopause	$BMD = 1.0841 - 0.0006 \cdot age^2 + 0.0481 \cdot age + 0.0048 \cdot height$	0.262	0.233
Postmenopause			
Nonlinear	$BMD = 2.4388 + 0.0008 \cdot YSM^2 - 0.0277 \cdot YSM - 0.0115 \cdot age + 0.0055 \cdot height$	0.446	0.266
Linear	$BMD = 2.3908 - 0.0136 \cdot age - 0.0117 \cdot YSM + 0.0005 \cdot height + 0.005 \cdot BMI$	0.438	0.268

BMD, bone mineral density (mm Al); YSM, years since menopause; BMI, body mass index; RMS, root mean square.

Changes in BMD: Longitudinal design

The longitudinal data represented in Table III contains the means and standard deviations of BMD and physical characteristics at the baseline and 1-year follow-up. In premenopausal women, the BMD of the 40-year age group significantly decreased by 0.9% ($t(78) = 2.80$, $p < 0.01$), whereas the other age groups showed no BMD loss. In perimenopausal women, we found a statistically significant decrease of 3.2% ($t(13) = 2.78$, $p < 0.05$). In postmenopausal women, the BMD of the 1–5 and 6–10 YSM groups significantly decreased by 3.5% and 1.52% ($t(64) = 6.78$, $p < 0.001$; and $t(47) = 3.51$, $p < 0.001$), respectively. No significant BMD reduction was observed in the 11–15 YSM group.

Validity of change model

The annual percentage changes in BMD between the actual and predicted values of the longitudinal population are shown in Table IV. To compare the difference between the actual and predicted values in premenopausal women, the Wilcoxon signed-rank test was applied. The results showed no significant differences in any of the age groups.

In peri- and postmenopausal women, the Friedman test was used to compare the difference between the actual and predicted values for each of the YSM groups. Significant differences were found in all the groups: perimenopause, 1–5 YSM, 6–10 YSM, and 11–15 YSM ($\chi^2(2, n = 14) = 10.86$, $p < 0.01$; $\chi^2(2, n = 65) = 47.66$, $p < 0.001$; $\chi^2(2, n = 48) = 12.04$, $p < 0.01$; and $\chi^2(2, n = 47) = 17.53$, $p < 0.001$), respectively. A *post hoc* Steel–Dwass test showed that actual bone reductions were significantly underestimated by the nonlinear- and linear-change models at 1–5 YSM and 6–10 YSM, whereas the nonlinear-change model provided a closer estimate to the actual BMD changes (Table IV). In addition, the annual percentage rates of BMD loss with YSM decreased significantly both in actual and estimated values from the nonlinear equation ($F(3,170) = 7.47$, $p < 0.001$; and $F(3,170) = 24.00$, $p < 0.001$), whereas they increased significantly in values estimated from the linear equation ($F(3,170) = 4.99$, $p < 0.01$).

Discussion

We found, in both cross-sectional and longitudinal data, that the BMD for premenopausal women increased slowly until age 40 and fell gradually after that. It is suggested that the changes in the metacarpal BMD of premenopausal women are characterized by three

Table III. BMD and physical characteristics of follow-up subjects at baseline and 1 year after.

Groups	n	Height (cm)		Weight (kg)		BMI ($kg\,m^{-2}$)		BMD (mm Al)	
		Baseline	1 year	Baseline	1 year	Baseline	1 year	Baseline	1 year
Premenopause									
20–29†	21	158.6 ± 6.5	158.8 ± 6.5	53.5 ± 6.8	53.0 ± 7.2	18.44 ± 7.94	19.11 ± 6.72	2.639 ± 0.195	2.656 ± 0.179
30–39†	75	159.0 ± 4.6	159.1 ± 4.6	51.4 ± 6.5	52.0 ± 6.7**	15.57 ± 9.12	16.51 ± 8.67	2.700 ± 0.217	2.714 ± 0.243
40–49†	79	154.8 ± 5.3	154.8 ± 5.4	53.9 ± 6.7	54.0 ± 6.7	22.50 ± 2.65	22.43 ± 2.63	2.754 ± 0.194	2.728 ± 0.195***
50–59†	10	153.8 ± 2.3	152.8 ± 2.5	55.7 ± 8.7	55.9 ± 8.8	23.55 ± 3.67	23.96 ± 3.77	2.686 ± 0.189	2.676 ± 0.183
Perimenopause									
YSM 0	14	154.2 ± 5.9	154.2 ± 6.2	50.6 ± 6.8	51.4 ± 7.1*	21.25 ± 2.36	21.58 ± 2.46*	2.845 ± 0.220	2.751 ± 0.190*
Postmenopause									
YSM 1–5	65	153.7 ± 4.7	153.7 ± 4.6	53.5 ± 6.6	53.8 ± 6.4	22.66 ± 2.72	22.78 ± 2.51	2.560 ± 0.264	2.468 ± 0.252***
YSM 6–10	48	152.9 ± 5.5	153.0 ± 5.7	53.2 ± 6.9	53.1 ± 6.9	22.75 ± 2.85	22.79 ± 2.77	2.370 ± 0.251	2.333 ± 0.247***
YSM 11–15	47	151.9 ± 4.4	151.7 ± 4.3	52.0 ± 7.4	52.4 ± 7.4	22.52 ± 3.14	22.77 ± 3.16	2.245 ± 0.208	2.234 ± 0.212

Values are means ± SD; †Age at baseline; YSM, years since menopause. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, baseline vs. 1 year.

Table IV. Annual changes in BMD (%) between actual and predicted values in longitudinal population.

Groups	*n*	Actual	Nonlinear	Linear
Premenopause				
20–29†	21	0.75 ± 3.45	0.61 ± 0.16	–
30–39†	75	0.48 ± 3.78	0.25 ± 0.16	–
40–49†	79	−0.88 ± 2.88	−0.26 ± 0.20	–
50–59†	10	−0.33 ± 2.88	−0.69 ± 0.58	–
Perimenopause				
YSM 0	14	−3.17 ± 4.57	−1.47 ± 0.17	−0.92 ± 0.16[c]
Postmenopause				
YSM 1–5	65	−3.50 ± 3.86	−1.32 ± 0.26[a]	−0.97 ± 0.18[b,c]
YSM 6–10	48	−1.52 ± 3.24	−1.08 ± 0.19[a]	−1.02 ± 0.15[b]
YSM 11–15	47	−0.46 ± 3.12	−0.89 ± 0.52	−1.11 ± 0.33[c]

Values are means ± SD. †Age at baseline; BMD, bone mineral density; YSM, years since menopause. Significant differences between actual vs. nonlinear-model[a]; Actual vs. linear-model[b]; Nonlinear- vs. linear-models[c].

distinct phases: an initial increase in adolescence, stabilization at maturity, and a decline in old age. This pattern of changes in BMD is in agreement with previous research which measured the distal forearm (Nakamura et al. 2000), hand (Malkin et al. 2002), and metacarpal BMD (Matsumoto et al. 1994). Our main result for premenopausal women showed that the nonlinear-change model using the square of age, age and height as variables was beneficial in evaluating the actual metacarpal BMD variability. The fitted nonlinear function for age-related BMD changes is consistent with a previous study that found that the quadratic equation for age was best fitted to the forearm BMD changes in premenopausal women using a large sample (Luisetto et al. 1993). Although other studies have observed that BMD loss in the distal forearm is not age-related for premenopausal Caucasian women (Nuti and Martini 1993; Hansen 1994; Löfman et al. 1997), they only examined a relatively small sample size.

For postmenopausal women, regression analyses of cross-sectional data obtained two models of BMD variabilities with linear and nonlinear functions, and these depended on both YSM and age (see Table II). Most of the research examining postmenopausal women has shown BMD reduction occurring in conjunction with YSM (Gallagher et al. 1987; Bjarnason et al. 1995; Hansen et al. 1995; Warming et al. 2002). However, those studies used either YSM or age as a variable for the regression function to assess BMD differences. Nuti and Martini (1993), who applied multiple regression analysis, showed that BMD differences were affected by both YSM and age in healthy postmenopausal women. Therefore, it is valid to estimate the metacarpal BMD change model that is associated with both YSM and age.

In comparing the absolute changes in BMD with the predicted changes from longitudinal data by two prospective models, we found that the nonlinear-change model using the square of YSM, YSM, age and height as variables was adequate to estimate actual metacarpal BMD reduction rather than the linear-change model. Additionally, the annual percentage rates of BMD loss for the perimenopausal and 1–5 YSM groups were 3.2% and 3.5%, respectively. These rates were more than double the 1.5% of the 6–10 YSM group. This finding was similar to those in previous studies. Hansen et al. (1995) have shown in a 15-year follow-up study that the annual rates of decrease in forearm bone mineral content were around 3% the first 3 years after menopause and continued at around 1% until 15 YSM. Gallagher et al. (1987) have indicated that BMD loss occurs

as a logarithmic rather than a linear function, and that the annual rate of bone loss in the second postmenopausal year was 3.4%, 1.7% in the fourth year, and 0.8% in the ninth year. These studies support that the nonlinear function utilizing YSM is suitable in evaluating in metacarpal BMD loss for postmenopausals.

The present nonlinear-change model in BMD for postmenopausal women was able to express the decreasing trend of annual percentage rates, whereas this change model underestimated rates 10 years after menopause. Warming et al. (2002) compared the 2-year changes in BMD estimated from cross-sectional data with the actual longitudinal changes. They showed an agreement for the first decade after menopause, and disagreement for the period beyond 10 YSM, but chose to show only the simpler linear regression for age-related changes. In contrast, Melton et al. (2000) indicated that the cross-sectional data underestimated the bone loss actually observed longitudinally at the distal forearm site. In addition, some studies have indicated that a rapid rate of bone loss is observed in about one in three women within their early postmenopausal years (Hui et al. 1990; Nordin et al. 1993; Ross et al. 1994). In a cross-sectional study it is difficult to identify the determinants of individual changes if a rapid rate of bone loss occurs in a short period. As a consequence, the rates of BMD loss predicted by the change model underestimate the longitudinal rates of rapid bone loss. It is suggested that longitudinal data are needed to improve the evaluation of BMD variability in postmenopausal women. In addition, the present longitudinal study has limitation in terms of sample size, given that the follow-up subjects represented only 7% of the cross-sectional population. Further investigation with sufficiently larger samples must be undertaken to delineate more precisely the changes in BMD at different stages of life.

With regard to physical characteristics, stepwise regression analysis showed that the BMD differences were related to height in change models for pre- and postmenopausal women. There is also evidence of age- and height-related forearm BMD loss in healthy women (Seo et al. 1994; Melton et al. 2000). However, it remains unclear whether this relationship was due to an actual reduction in height over time or to an effect of secular changes. Although weight is well known to be a major determinant of bone mass (Nuti and Martini 1993), our results show that it has not been used as an independent variable in any change model. Since the metacarpal bone is a non-weight bearing site, it is likely that a mechanical-load effect is precluded.

Conclusion

We found nonlinear-change models reflect BMD variabilities using age and height as variables in premenopausal women, and YSM, age and height in postmenopausal women. Our results indicated that the change model for premenopausal women might be useful for the estimation of individual BMD changes, but that the change model for postmenopausal women underestimated the actual rates of BMD loss in groups under 10 YSM. Further longitudinal studies will be needed to address the issue of long-term variability in the individual rate of bone loss for postmenopausal women.

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Résumé. *Arrière plan:* On accepte communément que les femmes âgées aient connu une perte de densité minérale osseuse (DMO) avec l'âge et la ménopause, cependant seulement

un petit nombre d'études ont utilisé un modèle de régression multiple, qui inclut des caractéristiques physiques afin de suivre de manière adéquate les changements de DMO au cours de la vie
Objectif: Une étude prospective a été menée afin de caractériser les modalités normales du changement de la DMO métacarpienne chez les femmes japonaises et pour estimer la possibilité d'appliquer un modèle d'ajustement utilisant des données transversales comparées avec la variabilité longitudinale.
Sujets et méthodes: L'étude consiste en sonnées transversales de 5422 femmes en bonne santé et d'un suivi d'un an pour 359 femmes. La DMO métacarpienne a été mesurée par densitométrie radiographique calculée par ordinateur. Des analyses de régression linéaires multiples et non linéaires, ont été effectuées sur les données transversales. Une analyse non paramétrique a été utilisée pour comparer les pourcentages de changement de DMO entre valeurs estimées et valeurs observées.
Résultats: Les données transversales indiquent que la meilleure équation ajustée est un modèle non linéaire employant les variables d'âge et de stature des femmes avant la ménopause, les années depuis la ménopause (ADM) et l'âge et la stature après la ménopause. Les résultats des données longitudinales indiquent qu'avant la ménopause, le changement en DMO est plus élevé dans le groupe d'âge 30–39 ans que dans le groupe d'âge 20–29 ans et ceux-ci sont inférieurs aux valeurs de des groupes 40–49 et 50–59 ans. Les taux annuels de changement de DMO que ce soit par les valeurs mesurées ou par les valeurs estimées sont similaires. Chez les femmes ménopausées, les changements en DMO observés indiquent que le rapide taux de réduction est supérieur à 3% entre 0 et 5 ans après la ménopause, puis de 1,5% entre 6 et 10 ans après la ménopause et décline à un rythme plus lent à partir de 11 ans après la ménopause. Le modèle de changement coïncide avec les changements en DMO observés chez les femmes ménopausées, tandis que les taux de perte de DMO du modèle sous estiment les changements effectifs entre 1 et 10 ans après la ménopause.

Zusammenfassung. *Hintergrund:* Es ist allgemein bekannt, dass bei älteren Frauen die Knochendichte (bone mineral density, BMD) im Alter und mit der Menopause abnimmt. Allerdings haben nur wenige Studien ein multiples Regressionsmodell benutzt, das körperliche Merkmale einschließt, um die komplexen Änderungen der Knochendichte im Verlauf des Lebens zu erfassen.
Ziel: Es wurde eine prospektive Studie durchgeführt, um das normale Muster von Mittelhandknochendichte-Änderungen bei Japanischen Frauen zu charakterisieren und um unter vergleichender Verwendung von Quer- und Längsschnittsdaten die Anwendbarkeit eines rechnerischen Anpassungsmodells zu prüfen.
Probanden und Methoden: Die Studie umfasste Querschnittsdaten von 5422 gesunden Frauen und eine Einjahres-Nachuntersuchung von 359 Frauen. Die Mittelhandknochendichte wurde radiologisch mittels Rechner-Densitometrie gemessen. Multiple lineare und nicht-lineare Regressionsanalysen wurden an den Querschnittsdaten durchgeführt. Eine nicht-parametrische Analyse wurde benutzt, um die prozentuale Veränderung der Knochendichte zwischen tatsächlich gemessenen und geschätzten Werten zu vergleichen.
Ergebnisse: Die Querschnittsdaten zeigten, dass die beste rechnerische Anpassung durch ein nicht-lineares Modell unter Verwendung der Variablen Alter und Körperhöhe bei Frauen vor der Menopause erzielt wurde, und unter Verwendung der Variablen Jahren seit der Menopause (years since menopause, YSM), Alter und Körperhöhe bei Frauen nach der Menopause. Die Ergebnisse der longitudinalen Daten zeigten folgendes. Bei Frauen vor der Menopause waren die tatsächlichen Knochendichteänderungen in der Gruppe

der 30–39-jährigen größer als in der Gruppe der 20–29-jährigen und geringer in der Gruppe der 50–59-jährigen als in der der 40–49-jährigen. Das prozentuale Ausmaß der jährlichen Veränderung der Knochendichte zwischen den tatsächlich gemessenen und den über das Anpassungsmodell geschätzten Werten war sehr ähnlich. Bei Frauen nach der Menopause zeigten die tatsächlich gemessenen Veränderungen der Knochendichte, dass die beobachtbare Abnahmerate der Knochendichte 0 bis 5 Jahre nach der Menopause größer als 3% war, 6 bis 10 Jahre nach der Menopause 1,5% betrug, und erst 11 Jahre nach Menopause langsamer wurde. Das rechnerische Anpassungsmodell zeigte zwar den Trend der tatsächlichen Knochendichteänderung bei Frauen nach der Menopause, unterschätzte allerdings die tatsächlichen Knochendichteänderungen in den ersten 10 Jahren nach der Menopause.

Resumen. *Antecedentes*: La pérdida de densidad mineral ósea (BMD) con la edad y en la menopausia está ampliamente reconocida en las mujeres ancianas. Sin embargo, muy pocos estudios han utilizado un modelo de regresión múltiple que tuviera en cuenta características físicas para evaluar los cambios globales que se producen lo largo de la vida en la BMD.
Objetivo: Se realizó un estudio prospectivo para caracterizar los patrones normales de cambio en la BMD de los metacarpos en mujeres japonesas y para estimar la aplicabilidad de un modelo ajustado, utilizando datos transversales comparados con la variabilidad longitudinal.
Sujetos y métodos: Se obtuvieron datos transversales de 5422 mujeres sanas y se realizó un seguimiento de 359 mujeres durante 1 año. La BMD de los metacarpos se determinó mediante densitometría de rayos X computerizada. Se realizaron análisis de regresión lineal y no lineal múltiple en los sujetos de la muestra transversal. Se utilizó un análisis no paramétrico para comparar las tasas porcentuales de los cambios en la BMD entre los valores reales y los estimados.
Resultados: Los datos transversales mostraron que la ecuación con el mejor ajuste era un modelo de cambio no lineal, que usaba como variables la edad y la estatura en las mujeres premenopaúsicas, y los años que habían transcurrido desde la menopausia (YSM), así como la edad y la estatura, en las mujeres postmenopaúsicas. Los resultados de los datos longitudinales indicaron lo siguiente: en las mujeres premenopaúsicas, los cambios reales en la BMD fueron mayores en el grupo de 30–39 años de edad que en el de 20–29 años, y menores en el grupo de 50–59 años que en el de 40–49. Las tasas de cambio anual de la BMD entre el valor real y el estimado por el modelo de cambio eran muy similares. En las mujeres postmenopaúsicas, los cambios reales en la BMD indicaban que la rápida tasa de reducción observada era superior al 3% a los 0–5 YSM y del 1,5% a los 6–10 YSM; posteriormente, mostraban una menor tasa de disminución a los 11 YSM. El modelo de cambio representaba la tendencia del cambio real en la BMD en las mujeres postmenopaúsicas, mientras que las tasas estimadas de pérdida de la BMD subestimaban los verdaderos cambios a los 1–10 YSM.

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ORIGINAL ARTICLE

Two new potent and convenient predictors of mortality in older nursing home residents in Japan

Orie Tajima,[1,4] Eiichi Nagura,[1] Kazuko Ishikawa-Takata[2] and Toshiki Ohta[3]

[1]Chubu National Hospital, [3]Chubu National Hospital, National Institute for Longevity Sciences, and [4]Nagoya University Graduate School of Medicine, Aichi and [2]Division of Health Promotion and Exercise, National Institute of Health and Nutrition, Tokyo, Japan

Background: Malnourishment is closely connected with poor health outcomes in frail elderly. However, the relative importance of specific nutritional predictors of mortality remains unclear in the Japanese population. We investigated the potent nutritional factors associated with mortality from nutritional assessments of three parameters in Japanese frail elderly.

Methods: Ninety residents in a nursing home in Japan, aged 65 and over (18 men, 72 women; mean age 82.2 ± 8.0 years) were enrolled in a 38-month follow-up study. The eligibility condition for analysis was having lived at the nursing home for more than 30 days, so three participants were excluded. Three nutritional parameters, which included: anthropometric measurements (body mass index, mid-arm circumference, triceps skinfold thickness and calf circumference); serum markers (albumin, total protein, prealbumin, retinol binding protein and total cholesterol); and food intake, were assessed. After categorizing each putative factor according to tertile distribution, risk of mortality was analyzed using Cox proportional hazard models.

Results: At the end of the 38-month follow-up period, 29 participants had died. After adjustment for gender, age, clinical status, and functional status, three indicators (i.e. mid-arm circumference, triceps skinfold thickness and lipid intake) showed a significant relationship with mortality. When all of the putative factors were included in a stepwise procedure, mid-arm circumference and lipid intake were significantly associated with adjusted mortality.

Conclusion: Among institutionalized Japanese frail elderly, lower levels of mid-arm circumference and lipid intake could potently predict an increased risk of mortality. These two indicators may be useful for many kinds of assessments and intervention for the improvement of health conditions in Japanese frail elderly.

Keywords: Japanese frail elderly, lipid intake, malnourishment, mid-arm circumference, risk of mortality.

Introduction

Malnourishment and functional disability are closely connected with poor health outcomes in elderly persons.[1–3] Biochemical markers signifying severe malnutrition, such as hypoalbuminemia and hypocholesterolemia, increase the mortality risk in nursing home residents.[2,4–6] Malnourishment, which was assessed by

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Correspondence: Orie Tajima, PhD., Department of Biological Chemistry, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya Aichi 466–0065, Japan. Email: onak@med.nagoya-u.ac.jp

anthropometric parameters, including body mass index, weight change, and mid-arm circumference, is reported adversely affect mortality in the frail elderly.[6–9] Among elderly patients with moderate diseases, it is suggested that low food intake is negatively related to 28-month survival.[10] Although malnourishment can be assessed using various parameters,[11] the relative importance of specific nutritional indicators remains unclear. Additionally, few studies have been carried out by concomitantly analyzing the physical parameters and food intake as nutritional predictors of mortality in the frail elderly.[10]

In Japan in 2001, the proportion of the population older than 65 years of age was estimated to be 18.0%.[12] With the rapidly growing number of elderly, there will be a greater need for the care of frail elderly, especially institutionalized people with a high risk of malnutrition. However, there is a paucity of literature about the contribution of nutritional factors to survival in Japanese frail elderly.

The purpose of this study is to investigate the potent nutritional factors associated with mortality based on the nutritional assessment of three parameters, including anthropometric measurements, biochemical markers and food intake. For this purpose, we monitored 38-month survival in a sample of Japanese frail elderly people.

Methods

Participants

Ninety residents in a nursing home in Aichi Prefecture, Japan, aged 65 and over (18 men, 72 women; mean age 82.2 ± 8.0 years), were enrolled in this study with their informed consent and/or that of their guardians. The eligibility for analysis was having lived in the nursing home for more than 30 days.

Protocol

The project was approved by the ethical committee of National Chubu Hospital. Baseline assessment of three nutritional parameters, including anthropometric measurements (body mass index, mid-arm circumference, triceps skinfold thickness, and calf circumference), serum markers (albumin, total protein, prealbumin, retinol binding protein, and total cholesterol) and food intake, were investigated in December, 2000. Nonfasting blood samples were obtained from each subject 3 h after breakfast. Using standardized methods, mid-arm circumference, triceps skinfold thickness and calf circumference were measured by the same physician. The measurements of the arm were made on the nondominant or the nonparetic side for the subjects who have had a cerebro-vascular accident. The dietary intake history of the subjects, based on the menu provided in the nursing home, was investigated by a trained dietitian by interview with the resident and considering additional dietary supplements from the subjects or their carers. On the basis of the dietary history for one month before the anthropometric and biological measurements, the 24-h intake of energy and macronutrients (protein, lipid and carbohydrate) was estimated and calculated as a mean value. Also, additional information on subjects' health status, including number of diseases, number of currently administered drugs and functional status based on the level of care, were examined. Functional status was classified into independent (able to ambulate with or without use of an supportive device), partly dependent (requiring a wheelchair for ambulation) and dependent (usually bedridden).

Data analysis

Mortality data on the date and cause of death were collected over a 38-month follow-up period. For each subject, a time to event and a status variable were created. The status variable indicated whether the event was death or the last follow-up. The relation between each putative nutritional factor and mortality was analyzed using Cox proportional hazard models by computing relative risks and 95% confidence intervals (95% CI). Risk of mortality was assessed and categorized (high, medium or low) according to the tertile distribution of each indicator. Nutrient variables were coded with dummy variables, the reference category being a high level. In order to determine the adjusted association between nutritional indicators and survival, multivariable analyses were also performed by controlling for individual characteristics as confounding factors, including gender, age, disease, drugs and functional status.

Furthermore, the strongest combination of nutritional predictors of survival for the frail elderly was identified. After forcing individual characteristics into a Cox regression model, the stepwise procedure was performed to select significant predictors from all of the putative nutritional parameters examined. Adjusted survival curves were then generated based on the estimated cumulative survivorship functions by the Cox regression model for specific sets of covariate values.

An SPSS statistical package (Statistical Product and Service Solution) was used for all analyses, and statistical significance was established at $P < 0.05$.

Results

Three participants were excluded from the analysis because they had been admitted to the nursing home less than 30 days before the baseline measurements were taken. The remaining participants were followed-up over a 38-month period in the institution. The

characteristics of the eligible 87 frail elderly are shown in Table 1. The study population consisted of 17 men and 70 women with an average age of 82.5 ± 7.8 years (range 66–101 years). Almost all of them (97.7%) had some medical problems, including dementia (52.9%), hypertension (26.4%), anemia (26.4%), heart disease (13.8%) and arthritis (6.9%). The subjects had an average 1263 kcal/day of energy intake (men 1412 ± 309 kcal/day, women 1229 ± 324 kcal/day). The proportion of those calories among macronutrients was as follows: 15.5% proteins, 20.7% lipids and 63.8% carbohydrates. The cutoff point for each nutrient indicator was established by its tertile distribution (Table 2).

At the end of the 38-month follow-up period, 29 participants (six men, 23 women) had died, amounting to a cumulative annual death rate of 0.11 per year. The main causes of death in the subjects under study were cardiovascular disease (41.4%) and infection (31.8%). Table 3 presents both unadjusted and adjusted relative risks of death for each nutritional factor we studied. Univariate analysis revealed significant associations with 38-month mortality for all anthropometric measurements, including body mass index, mid-arm circumference, triceps skinfold thickness and calf circumference. Albumin, total protein and prealbumin were independently detected as a significant serum risk factor. Also, low food intake was related to increased risk of mortality in the frail elderly subjects. However, individual factors confounded the associations between each nutrient variable and the mortality risk. After adjustment for gender, age, clinical status and functional status, three indicators, mid-arm circumference, triceps skinfold thickness and lipid intake, showed significant relationships with 38-month mortality (Table 3).

To select the strongest nutritional predictors for survival in frail elderly, the 12 putative nutrient variables we studied were included in a stepwise procedure with the forcing model of the confounding factors (individual characteristics). This Cox regression model demonstrated that mid-arm circumference and low lipid intake are significantly associated with 38-month mortality in the frail elderly (Table 4). Survivorship functions of mid-arm circumference and lipid intake levels after adjustment for the confounding factors are depicted graphically in Fig. 1.

Discussion

The anthropometric characteristics of Japanese nursing home residents we studied seemed to be smaller than

Table 1 Baseline characteristics of subjects (n = 87)

	Mean – SD	% (n)
Individual characteristics		
Gender female	NA	80.5 (70)
Age in years	82.5–7.8	NA
Diseases, n (range)	2.9–1.3 (0–6)	NA
Drugs, n (range)	3.6–2.5 (0–10)	NA
Functional status		
Independent	NA	37.9 (33)
Partly dependent	NA	26.4 (23)
Bedridden	NA	35.6 (31)
Nutritional status		
Anthropometric measurements		
Body mass index, kg/m^2	18.9–4.0	NA
Mid-arm circumference, cm	22.2–3.5	NA
Triceps skinfold thickness, mm	12.5–7.3	NA
Calf circumference, cm	26.0–4.6	NA
Serum markers		
Albumin, g/dL	3.8–0.5	NA
Total protein, g/dL	6.5–0.6	NA
Prealbumin, mg/dL	20.4–5.8	NA
Retinol binding protein, mg/dL	3.1–1.3	NA
Total cholesterol, mg/dL	191.9–37.7	NA
Food intake		
Energy, kcal/day	1263.3–327.7	NA
Protein, g/day	49.0–11.7	NA
Lipids, g/day	29.1–7.5	NA
Carbohydrate, g/day	195.7–54.2	NA

Table 2 Tertiles of nutritional indicators

	Low	Medium	High
Anthropometric measurements			
Body mass index, kg/m^2			
Cutoff	≤ 16.5	16.6–20.1	≥ 20.2
Mean (SD)	14.6 (1.4)	18.7 (1.0)	23.4 (2.6)
Mid-arm circumference, cm			
Cutoff	≤ 20.0	20.1–23.4	≥ 23.5
Mean (SD)	18.2 (1.4)	22.0 (0.7)	25.8 (1.9)
Triceps skinfold thickness, mm			
Cutoff	≤ 8.0	8.1–14.9	≥ 15.0
Mean (SD)	5.2 (1.4)	11.2 (1.7)	21.6 (4.8)
Calf circumference, cm			
Cutoff	≤ 23.6	23.7–28.0	≥ 28.1
Mean (SD)	20.9 (1.9)	26.1 (1.5)	31.2 (2.3)
Serum markers			
Albumin, g/dL			
Cutoff	≤ 3.4	3.5–4.0	≥ 4.1
Mean (SD)	3.1 (0.3)	3.7 (0.2)	4.3 (0.2)
Total protein, g/dL			
Cutoff	≤ 6.3	6.4–6.8	≥ 6.9
Mean (SD)	5.9 (0.4)	6.6 (0.1)	7.2 (0.3)
Prealbumin, mg/dL			
Cutoff	≤ 17.7	17.8–22.4	≥ 22.5
Mean (SD)	14.1 (3.0)	20.2 (1.4)	26.9 (2.5)
Retinol binding protein, mg/dL			
Cutoff	≤ 2.3	2.4–3.3	≥ 3.4
Mean (SD)	1.8 (0.4)	(0.3)	4.6 (0.9)
Total cholesterol, mg/dL			
Cutoff	≤ 173.0	173.1–202.0	≥ 202.1
Mean (SD)	153.3 (14.6)	186.5 (8.9)	236.0 (22.2)
Food intake			
Protein, g/day			
Cutoff	≤ 41.4	41.5–56.3	≥ 56.4
Mean (SD)	36.7 (5.5)	47.7 (4.4)	62.9 (3.9)
Lipids, g/day			
Cutoff	≤ 25.0	25.1–33.0	≥ 33.1
Mean (SD)	21.6 (4.2)	28.6 (2.4)	37.8 (2.1)
Carbohydrate, g/day			
Cutoff	≤ 165.0	165.1–210.0	≥ 210.1
Mean (SD)	142.7 (24.8)	185.6 (12.4)	260.8 (29.1)

those of Canadian and European frail elderly populations.[9,10,13] Moreover, the quantity and proportion of macronutrients in daily food intake among our subjects differed from nursing home residents in Italy.[10] In addition, Japan has a relatively higher percentage of residents with a low level of activities of daily living (ADL) than their US and European counterparts.[14] Nevertheless, the values of biochemical markers for nutritional status in our subjects were consistent with those in European frail elderly.[10] The heterogeneity of physical or nutritional characteristics may therefore imply the importance of a population-specific indicator of nutritional status that could predict health-related outcomes or mortality. However, as in previous reports in European populations,[6,10] we demonstrated that univariate predictors of mortality included mid-arm circumference, triceps skinfold thickness and lipid intake after controlling for functional and other physical parameters.

It is evident that functional disability and malnourishment can be strongly connected with mortality in elderly persons.[1–3] Matsubayashi *et al.* have reported a

Table 3 Association of putative nutritional variables with survival for 38 months in nursing home residents

	Unadjusted Relative risk (95% CI)	*P*	Adjusted for confounders Relative risk (95% CI)	*P*
Anthropometric measurements				
Body mass index		0.007		0.147
Low	3.524 (1.376–9.023)	0.009	2.795 (0.823–9.496)	0.099
Medium	1.174 (0.394–3.496)	0.773	1.021 (0.324–3.217)	0.971
Mid-arm circumference		0.003		0.018
Low	7.707 (2.226–26.680)	0.001	8.404 (1.930–36.600)	0.005
Medium	3.345 (0.887–12.617)	0.075	3.569 (0.936–13.608)	0.062
Triceps skinfold thickness		0.011		0.045
Low	9.127 (2.071–40.216)	0.003	7.391 (1.501–36.403)	0.014
Medium	5.265 (1.153–24.048)	0.032	4.595 (0.944–22.357)	0.059
Calf circumference		0.030		0.406
Low	4.181 (1.374–12.719)	0.012	3.144 (0.587–16.832)	0.181
Medium	2.152 (0.648–7.148)	0.211	1.781 (0.442–7.178)	0.417
Serum markers				
Albumin		0.002		0.060
Low	5.478 (1.984–15.126)	0.001	3.709 (0.883–15.575)	0.073
Medium	2.171 (0.728–6.479)	0.165	1.304 (0.358–4.750)	0.687
Total protein		0.029		0.704
Low	3.557 (1.279–9.887)	0.015	1.611 (0.503–5.162)	0.422
Medium	1.668 (0.570–4.881)	0.350	1.211 (0.401–3.653)	0.734
Prealbumin		0.026		0.401
Low	2.802 (1.140–6.887)	0.025	1.701 (0.654–4.424)	0.276
Medium	1.046 (0.367–2.983)	0.933	0.965 (0.336–2.773)	0.947
Retinol binding protein		0.290		0.892
Low	1.983 (0.810–4.856)	0.134	1.233 (0.472–3.223)	0.669
Medium	1.033 (0.399–2.678)	0.946	1.037 (0.377–2.850)	0.944
Total cholesterol		0.159		0.136
Low	1.478 (0.648–3.374)	0.353	0.851 (0.333–2.175)	0.736
Medium	0.577 (0.210–1.588)	0.287	0.351 (0.115–1.073)	0.066
Food intake				
Protein		0.083		0.471
Low	3.221 (1.146–9.049)	0.026	2.025 (0.600–6.832)	0.256
Medium	2.129 (0.713–6.355)	0.176	2.038 (0.602–6.905)	0.253
Lipid		0.001		0.013
Low	7.479 (2.198–25.451)	0.001	6.972 (1.593–30.507)	0.010
Medium	2.414 (0.604–9.652)	0.213	2.522 (0.544–11.692)	0.237
Carbohydrate		0.027		0.148
Low	4.455 (1.464–13.558)	0.009	3.694 (0.889–15.347)	0.072
Medium	2.521 (0.776–8.186)	0.124	1.944 (0.505–7.475)	0.334

significant association between ADL dependency and death in community-dwelling elderly Japanese.[15] In our study of nursing home residents, the relative risks of mortality for partly dependent and dependent were 2.087 (95% CI; 0.724–6.017, $P = 0.173$) and 3.200 (95% CI; 1.240–8.254, $P = 0.016$), respectively, when univariately analyzed. This result supports previous findings that lower levels of functional status may increase the risk of mortality. However, forcing physical parameters, except for nutritional variables, into the Cox regression model did not remain the association between functional status and survival among nursing home elderly, suggesting that individual characteristics could be confounding factors.

Among the 12 putative nutritional indicators we studied, mid-arm circumference and low lipid intake were significant predictors of adjusted mortality among Japanese frail elderly. The reason why mid-arm circumference was more sensitive than BMI is unclear. Miller *et al.* reported a similar result, indicating that low corrected

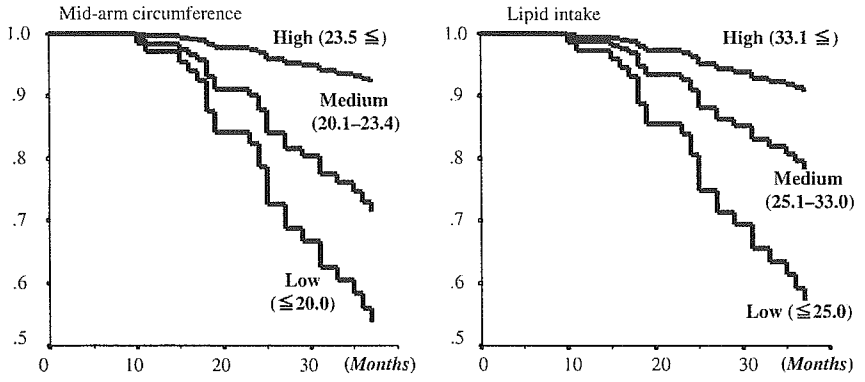

Figure 1 Survivorship functions of lipid intake levels after adjustment for gender, age, clinical and functional status. Survivorship functions are estimated by the Cox regression model for specific sets of covariate values, and the curves represent high (upper curve), medium (middle curve), and low (lower curve), respectively.

Table 4 Nutritional predictors of survival estimated by Cox regression model

	Relative risk (95% CI)	*P*
Individual characteristics†		
Gender, Female	0.351 (0.101–1.215)	0.098
Age, years	1.053 (0.990–1.120)	0.100
Disease, *n*	1.4635 (0.972–2.203)	0.068
Drugs, *n*	0.925 (0.773–1.107)	0.396
Functional status	0.333	
Independent	1.000	
Partly dependent	0.644 (0.179–2.310)	0.499
Bedridden	0.326 (0.070–1.511)	0.152
Nutritional indicators		
Mid-arm circumference		0.039
Low	7.707 (1.595–37.235)	0.011
Medium	4.184 (0.996–17.569)	0.055
Lipid intake		0.055
Low	5.710 (1.149–28.368)	0.033
Medium	2.506 (0.469–13.379)	0.283

†Forced into Cox regression model.

arm muscle area, calculated by mid-arm circumference and triceps skinfold thickness, increased the risk of mortality whereas BMI did not.[16] Age-related reductions in muscle mass are responsible for most of the loss of function in the arm.[17] Additionally, the relationship between mid-arm circumference and deterioration of physical function has been demonstrated.[15] It is plausible therefore that use of one's arm for daily living may result in the maintenance of arm circumference, and that arm mobility might be the most reliable indicator for ADL in predicting mortality in frail subjects.

Low lipid intake was detected as another strong predictor of mortality in our analyzed model. Previous studies suggested that malnutrition resulting from protein-energy deficiency could be associated with increased mortality,[18,19] but there is little direct evidence to support the association. Frisoni *et al.* revealed that decreasing food intake, especially of lipids and protein, was increasingly associated with mortality in frail nursing home patients.[10] They also suggested the relative importance of macronutrients in maintaining the health of frail elderly. Our finding supported the idea that lipid-energy intake as well as protein intake may play an important role in the treatment of malnutrition. Indeed, it is well known that lipid produces energy about two times greater than protein or carbohydrate, and consequently low lipid intake is considered to be an important factor in low energy intake. In the present investigation, the correlation between lipid intake and total energy was 0.818, and the correlation between lipid intake and protein intake was 0.861. These findings suggested that sufficient lipid intake implied sufficient intake of both protein and total energy.

Food intake reduction may impact on organ system functioning, thus directly contributing to poor health outcomes. Implementation of nutritional support will possibly improve survival in frail elderly, because the decrease in food intake could be an early sign of worsening health. In the data from the present study, the relative risk for mortality in frail elderly persons with low lipid intake, defined as less than 25 g/day by the tertile distribution, was about 5.7 times compared to those with high lipid intake. The recommended dietary allowance (RDA) for Japanese elderly (aged 70 or over) suggests that the basal metabolic energy is 1220 and 1010 kcal/day for men and women, respectively.[20] A rate of lipid to total energy of 20–25% is also recommended.[20] The lowest lipid/energy rate (20%) for basal metabolic energy in female elderly (1010 kcal/day) is equivalent to a lipid intake of 25 g/day. Therefore, the implication of our result is that a nutritional intervention strategy assuring more than 25 g/day of lipid intake be recommended so as to improve health conditions among Japanese frail elderly.

There are a few limitations in the present study. First, our sample consisted of only a relatively small number of frail nursing home residents, resulting in a poor statistical power with wide confidence intervals. Our observations must be confirmed in larger samples and in other frail elderly populations. It was difficult to