in this study when skin reflection was below 10% (Na et al. 2001).

Muscle strength and power

Grip strength and leg extension power were measured. Grip strength was measured with a digital Smedley-type hand dynamometer (T.K.K.5401; Takei Scientific Instruments Co., Ltd, Niigata, Japan). The participants were told to adjust the device for hand comfort and fit and to place their arm in a relaxed, stationary position. Highest grip strength force of either right or left arm was used as representative grip strength.

Leg extension power was measured by Aneropress 3500 (Combi Wellness, Tokyo, Japan). Each participant was placed well back on a seat, the waist was fixed with a belt, and the knee joint angled at 90°. Isometric contractions lasted for 5 s each and were separated by 15-s rest intervals. Peak power was detected, calculated, and recorded in watts with a microcomputer. The highest measurement among five trials was recorded as "isometric strength performance." To reduce the bias related to differences in body mass, leg extension power was expressed as the peak of the leg power relative to body weight (W/kg).

Assessment of other variables

Depressive symptoms were assessed according to the Japanese version (Fukuda and Kobayashi 1973) of the Self-Rating Depression Scale (SDS). Participants were considered as depressive when SDS score was 45 or more (Fountoulakis et al. 2001). Blood pressure (BP) in the left upper arm was measured twice using an automatic device (YAMASU605P; Kenzmedico Co. Ltd., Saitama, Japan) following a 5-min rest in the sitting position. The mean values were used as the BP value.

Blood samples were drawn from the antecubital vein, with minimal tourniquet use, while the subjects were seated. Specimens were collected in siliconized vacuum glass tubes containing sodium fluoride for fasting blood glucose and no additives for lipid analyses. Fasting blood glucose concentration was measured by enzymatic methods (Eerotec, Tokyo, Japan). The triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) concentrations were measured by enzymatic methods using appropriate kits (Sekisui Medical, Tokyo, Japan).

Information on age, smoking status (never, former, or currently smoking), alcohol-drinking status (never, ≥1 day/week, or 7 days/week), occupation (desk work or non-desk work), history of physical illness and current medication use ("yes" or "no") of the participants were obtained from a questionnaire. The educational level was assessed by determining the last grade level and divided into two categories: less than college level or college-level and above. Levels of daily physical activity (PA) were estimated using the International Physical Activity Questionnaire (Japanese version) (Craig et al. 2003). PA was categorized into tertiles with similar numbers of individuals in each group (low, middle, or high). Total energy consumption and vitamin C intake were estimated using a brief self-administered diet history questionnaire (Sasaki 2005). A diagnosis of metabolic syndrome (MS) was defined according to the modified Japanese criteria [defined by the Japanese Society for the Study of Obesity (JASSO)] (Matsuzawa 2005).

Statistical analysis

All statistical analyses were performed using the SPSS 17.0 statistical software package for Windows (SPSS, Inc., Chicago, IL, USA).

In this study, because the distribution of all continuous variables, except for grip strength and systolic blood pressure, was not normal, the common logarithm was applied to normalize the data before statistical analysis. The Spearman rank correlation test was performed. ANCOVA was used to examine the relationships between skin AF and grip strength (analysis I, $n = 232$) or log-transformed leg extension power (analysis II, $n = 138$), adjusting for age and body mass index (model 1); all of the above parameters, in addition to PA, smoking status, drinking status, depressive symptoms, educational level, occupation, and total energy consumption, were used in model 2; all parameters in model 2 plus MS, diabetes, and kidney disease were used in model 3; and all parameters in model 3 plus vitamin C intake were used in model 4 (Fig. 1). ANCOVA was performed with the forced entry of all factors considered to be potential covariates. Bonferroni-corrected P values were used for comparisons between groups differing in skin AF. All P values for linear trends were calculated; all tests for statistical significance were two sided, and $P < 0.05$ was defined as statistically significant.

Results

The number of participants with skin reflection above 10% was 246 (47.5%), and the median (interquartile range) skin AF was 1.98 (1.78, 2.18) AU. The participant characteristics according to the tertiles of skin AF in analysis I are presented in Table 1. Subjects in the highest tertile of skin AF tended to be older and had a higher fasting glucose concentration (P for trend < 0.01 and 0.06, respectively); this group also had a higher percentage of current smokers compared with that in the lowest tertile (P for trend < 0.01). Otherwise, no

Table 1 Characteristics of the participants according to the tertiles of skin autofluorescence in analysis I ($n = 232$)

Range (unit, AU)	Tertiles of skin autofluorescence			P for trend[a]
	Low ($n = 78$) (1.28–1.84)	Middle ($n = 77$) (1.84–2.09)	High ($n = 77$) (2.09–4.44)	
Age (years)	40.0 (35.0, 51.0)	45.0 (38.0, 57.0)	52.0 (40.0, 58.5)	<0.01
BMI (kg/m)	23.7 (22.1, 25.7)	23.7 (21.8, 25.9)	23.6 (21.7, 26.2)	0.89
Waist circumference (cm)	84.0 (77.8, 91.0)	86.0 (79.5, 90.5)	85.0 (80.0, 91.5)	0.29
SBP (mmHg)	130.0 (120.0, 137.3)	129.0 (116.0, 139.0)	130.0 (120.0, 142.0)	0.42
DBP (mmHg)	80.0 (74.0, 90.0)	80.0 (76.0, 88.5)	84.0 (74.0, 90.0)	0.44
Fasting blood glucose (mg/dl)	92.0 (88.8, 97.5)	93.0 (88.0, 100.0)	95.0 (88.5, 103.5)	0.06
TG (mg/dl)	110.5 (69.5, 153.5)	141.0 (79.5, 198.5)	131.0 (86.0, 186.5)	0.09
LDL (mg/dl)	120.0 (93.0, 139.0)	121.0 (95.0, 133.0)	122.0 (109.0, 144.5)	0.21
HDL (mg/dl)	53.0 (45.5, 63.3)	50.0 (42.5, 59.0)	52.0 (42.5, 56.5)	0.15
Total energy intake (kcal/d)	1910.9 (1599.7, 2409.1)	1806.8 (1569.9, 2201.5)	1747.7 (1416.0, 2267.8)	0.39
Vitamin C intake ([mg/d]/2000 kcal)	84.0 (61.4, 121.9)	93.8 (73.1, 128.6)	95.9 (66.7, 126.4)	0.72
High PA (%, median values: 48.0 METs·h/week)	43.6	28.6	40.3	0.09
Middle PA (%, median values: 12.1 METs·h/week)	39.7	46.8	36.4	0.05
Smoking status				
Current (%)	29.5	40.3	49.4	0.04
Former (%)	12.8	20.8	10.4	0.17
Drinking status				
7 drinks/week (%)	28.2	29.9	23.4	0.64
≥1 drinks/week (%)	59.0	54.5	58.4	0.83
Depressive symptoms (SDS ≥ 45, %)	30.8	31.2	29.9	0.98
Education (≥college, %)	43.6	35.1	40.3	0.55
Desk work (%)	87.2	74.0	77.9	0.12
Diabetes (%)	6.4	10.4	9.1	0.67
Kidney disease (%)	2.6	1.3	6.5	0.23
MS (JASSO, %)	20.5	24.7	27.3	0.61

Data are medians (interquartile range) or proportions

AU arbitrary units, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *LDL* low-density lipoprotein cholesterol, *HDL* high-density lipoprotein-cholesterol, *PA* physical activity, *SDS* self-rating depression scale, *MS* metabolic syndrome, *JASSO* Japanese Society for the Study of Obesity

[a] Analysis of variance or logistic regression

significant differences were observed among the tertiles of skin AF. In Fig. 2a, outlier (skin AF = 4.44 A.U.) was a person with both diabetes and kidney disease, and skin AF correlated with age ($r = 0.31$, $P < 0.01$).

Table 2 shows the relationship of skin AF tertiles to grip strength. In the final multivariate models, the adjusted means [95% confidence interval (CI)] of the grip strength across the tertiles of skin AF was 44.5 (43.2, 45.9) kg for the lowest tertile, 42.0 (40.6, 43.3) kg for the middle tertile, and 41.7 (40.3, 43.1) kg for the highest tertile (P for trend < 0.01). The adjusted mean grip strength was 6.3% lower for the highest tertile of skin AF than for the lowest tertile of skin AF (Bonferroni-corrected P value = 0.01).

To assess the relationship between skin AF tertiles and leg extension power, we performed an additional analysis (analysis II) that excluded those subjects who did not undergo the leg extension power test ($n = 138$). Table 3 shows the participant characteristics according to tertiles of skin AF in analysis II. In analysis II, subjects in the highest tertile of skin AF were older and had higher fasting glucose concentrations compared with those in the lowest tertile (P for trend < 0.01 and 0.02, respectively). Although no significant difference was observed in the percentage of current smokers, the prevalence of diabetes in the highest tertile of skin AF tended to be higher than that of the lowest tertile (P for trend = 0.05). In the Spearman rank correlation test, skin AF correlated with age ($r = 0.34$, $P < 0.01$) (Fig. 2b).

Table 4 shows the relationship of the tertiles of skin AF with leg extension power. In the final multivariate models, the adjusted geometric mean (95% CI) of log-transformed leg extension power across the tertiles of skin AF was 17.8

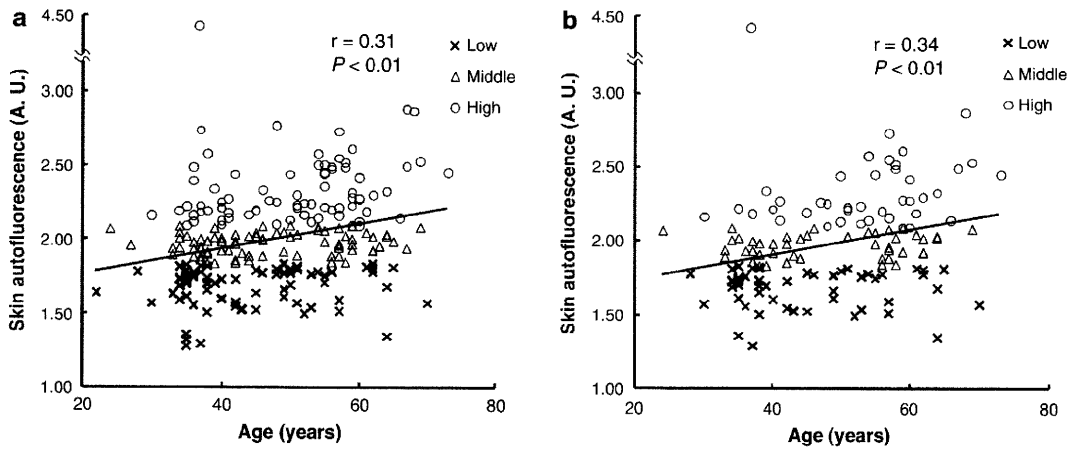

Fig. 2 Correlation between skin autofluorescence and age in analysis I (**a**) and analysis II (**b**). Spearman rank correlation test was performed. *Cross*, *triangle*, and *circle symbols* are represented as the *lower*, *middle*, and *higher* tertile of skin autofluorescence, respectively

Table 2 Relationship of the tertile of skin autofluorescence with grip strength ($n = 232$)

Range (unit, AU)	Tertiles of skin autofluorescence			P for trend[a]
	Low (1.28–1.84)	Middle (1.84–2.09)	High (2.09–4.44)	
No. of participants	78	77	77	–
Grip strength (kg)				
Crude	44.7 (43.3, 46.1)	41.7 (40.3, 43.1)[f]	41.8 (40.4, 43.2)[f]	<0.01
Model 1[b]	44.3 (43.0, 45.7)	41.8 (40.4, 43.1)[f]	42.1 (40.8, 43.5)	0.03
Model 2[c]	44.5 (43.2, 45.9)	42.0 (40.7, 43.4)[f]	41.6 (40.2, 43.0)[f]	<0.01
Model 3[d]	44.5 (43.2, 45.9)	42.0 (40.7, 43.3)[f]	41.7 (40.3, 43.0)[f]	<0.01
Model 4[e]	44.5 (43.2, 45.9)	42.0 (40.6, 43.3)[f]	41.7 (40.3, 43.1)[f]	<0.01

Data are means (95% confidence interval). Unit of grip strength is kg

AU arbitrary units

[a] Analysis of variance or analysis of covariance

[b] Adjusted for age (continuous variables, log-transformed), body mass index (continuous variables, log-transformed)

[c] Additionally adjusted for physical activity (tertiles), smoking status (never, former, or current), drinking status (never, ≥1 drinks/week, or 7 drinks/week), depressive symptoms (self-rating depression scale ≥45), educational level (≥college), occupation (desk work or non-desk work), and total energy consumption (continuous variables, log-transformed)

[d] Additionally adjusted for metabolic syndrome (Japanese Society for the Study of Obesity) (no or yes), diabetes (no or yes), and kidney disease (no or yes)

[e] Additionally adjusted for dietary intake of vitamin C (continuous variables, log-transformed)

[f] Significantly different from lowest skin autofluorescence tertile (Bonferroni correction), $P < 0.05$

(16.6, 19.1) W/kg for the lowest tertile, 17.5 (16.4, 18.7) W/kg for the middle tertile, and 16.0 (14.9, 17.1) W/kg for the highest tertile (P for trend = 0.04).

Discussion

The present study examined the relationship between skin AF representing AGE accumulation and muscle strength and power and power among Japanese adult men. Consistent with previous studies (Dalal et al. 2009; Semba et al. 2010), our results showed that the level of skin AF was independently associated with muscle strength and power. These results suggest that greater AGE accumulation is associated with reduced muscle strength and power not only in older people but also in younger adults, and that AGE accumulation may be a predisposing factor for muscle force reduction along the course of aging finally leading to sarcopenia.

There is an increasing evidence supporting the hypothesis that AGEs may play a role in the decline of muscle

Table 3 Characteristics of the participants according to the tertiles of skin autofluorescence in analysis II ($n = 138$)

Range (unit, AU)	Tertiles of skin autofluorescence			P for trend[a]
	Low ($n = 46$) (1.28–1.84)	Middle ($n = 46$) (1.84–2.09)	High ($n = 46$) (2.09–4.44)	
Age (years)	42.5 (35.0, 53.3)	43.5 (37.0, 57.0)	55.5 (46.8, 60.0)	<0.01
BMI (kg/m)	23.7 (21.7, 25.6)	23.8 (21.9, 25.8)	23.4 (21.5, 25.9)	0.92
Waist circumference (cm)	84.0 (77.0, 92.0)	87.0 (78.8, 92.0)	86.0 (80.8, 91.3)	0.38
SBP (mmHg)	128.0 (119.5, 137.8)	130.0 (115.5, 140.3)	132.0 (117.5, 140.0)	0.59
DBP (mmHg)	80.0 (73.5, 88.3)	80.0 (73.5, 90.3)	81.5 (75.5, 86.3)	0.61
Fasting blood glucose (mg/dl)	93.0 (88.8, 100.3)	90.5 (88.0, 96.0)	96.0 (88.5, 105.3)	0.02
TG (mg/dl)	111.5 (69.5, 154.3)	140.0 (75.8, 187.8)	131.5 (84.0, 186.0)	0.41
LDL (mg/dl)	117.5 (91.0, 137.5)	123.0 (105.3, 133.0)	121.0 (109.0, 152.8)	0.27
HDL (mg/dl)	53.0 (45.5, 61.8)	52.0 (43.8, 59.0)	53.5 (44.0, 60.0)	0.73
Total energy intake (kcal/d)	1887.1 (1509.9, 2378.0)	1783.3 (1580.2, 2244.2)	1655.2 (1354.0, 2314.1)	0.47
Vitamin C intake ([mg/d]/2000 kcal)	82.4 (61.4, 127.7)	97.1 (65.9, 124.5)	103.7 (76.2, 132.5)	0.36
High PA (%, median values: 48.0 METs·h/week)	39.1	28.3	32.6	0.54
Middle PA (%, median values: 12.1 METs·h/week)	32.6	34.8	32.6	0.97
Smoking status				
Current (%)	28.3	34.8	41.3	0.43
Former (%)	10.9	19.6	15.2	0.52
Drinking status				
7 drinks/week (%)	28.3	34.8	17.4	0.17
≥1 drinks/week (%)	60.9	52.2	56.5	0.73
Depressive symptoms (SDS ≥ 45, %)	28.3	34.8	32.6	0.56
Education (≥college, %)	39.1	37.0	39.1	0.97
Desk work (%)	89.1	69.6	84.8	0.05
Diabetes (%)	6.5	6.5	19.6	0.09
Kidney disease (%)	2.2	2.2	2.2	1.00
MS (JASSO, %)	19.6	26.1	21.7	0.75

Data are medians (interquartile range) or proportions

AU arbitrary units, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *LDL* low-density lipoprotein cholesterol, *HDL* high-density lipoprotein-cholesterol, *PA* physical activity, *SDS* self-rating depression scale, *MS* metabolic syndrome, *JASSO* Japanese Society for the Study of Obesity

[a] Analysis of variance or logistic regression

function, which may eventually lead to sarcopenia in the older age. First, AGE accumulation in skeletal muscle is greater in fast muscle fiber types, which are well known to possess a faster shortening velocity and larger force production (Snow and Thompson 2009). Second, AGE-modified proteins in skeletal muscle include several critical enzymes involved in energy production, such as creatine kinase (Snow et al. 2007). Third, glycation of skeletal muscle myosin changed the structural property of the protein and reduced simultaneously the in vitro motility speed (Ramamurthy et al. 2001). Moreover, because the binding of AGEs to RAGE results in depletion of cellular antioxidant defense mechanisms and the generation of oxygen-free radicals (Schmidt et al. 1994), oxidant damage to myofibrillar proteins may play a role in the age-related reduction of contractile capacity (Thompson 2009). AGE–RAGE interaction also induces microcirculatory dysfunction by endothelial dysfunction or inflammation (Brownlee 2001; Payne 2006). Thus, AGE accumulation may contribute to decreased muscle function with aging through a variety of mechanisms.

It is well known that vitamin C is one of the primary antioxidants. Because greater intake of vitamin C was independently associated with muscle strength (Cesari et al. 2004), dietary intake of vitamin C may potentially influence the relationship between skin AF and muscle strength and power. In this study, because the relationship between higher skin AF and lower muscle strength and power remained even after adjusting the intake of vitamin C, higher skin AF could be associated with lower muscle strength and power independent of dietary intake of vitamin C in healthy adult men.

Table 4 Relationship of the tertile of skin autofluorescence with log-transformed leg extension power ($n = 138$)

Range (unit, AU)	Tertiles of skin autofluorescence			P for trend[a]
	Low (1.29–1.81)	Middle (1.81–2.07)	High (2.07–4.44)	
No. of participants	46	46	46	–
Leg extension power (W/kg)				
Crude	18.6 (17.0, 20.0)	17.4 (16.2, 19.1)	15.5 (14.5, 16.2)[f]	<0.01
Model 1[b]	18.2 (17.0, 19.5)	17.4 (16.2, 18.6)	15.8 (14.8, 17.0)[f]	0.01
Model 2[c]	17.8 (16.6, 19.1)	17.4 (16.2, 18.6)	15.8 (14.8, 17.4)	<0.05
Model 3[d]	17.8 (16.6, 19.1)	17.4 (16.2, 18.6)	16.2 (14.8, 17.4)	0.05
Model 4[e]	17.8 (16.6, 19.1)	17.5 (16.4, 18.7)	16.0 (14.9, 17.1)	0.04

Data are geometric means (95% confidence interval). Unit of leg extension power is W/kg

AU arbitrary units

[a] Analysis of variance or analysis of covariance

[b] Ajusted for age (continuous variables, log-transformed), body mass index (continuous variables, log-transformed)

[c] Additionally adjusted for physical activity (tertiles), smoking status (never, former, or current), drinking status (never, ≥1 drinks/week, or 7 drinks/week), depressive symptoms (self-rating depression scale ≥45), educational level (≥college), occupation (desk work, or non-desk work), and total energy consumption (continuous variables, log-transformed)

[d] Additionally adjusted for metabolic syndrome (Japanese Society for the Study of Obesity) (no or yes), diabetes (no or yes), and kidney disease (no or yes)

[e] Additionally adjusted for dietary intake of vitamin C (continuous variables, log-transformed)

[f] Significantly different from lowest skin autofluorescence tertile (Bonferroni correction), $P < 0.05$

In this study, skin AF was used as a measure for skin AGE accumulation. Previous studies reported that skin AF is correlated with blood AGEs (Tanaka et al. 2009), or not (Hartog et al. 2008). In this study, our findings conform to previous studies which measured circulating CML (Dalal et al. 2009; Semba et al. 2010). Thus, it is speculated that skin AF is potentially correlated with blood AGEs in our participants.

This study has other limitations. First, this study focused only on men. Whether the relationship is present in younger women is unknown. Moreover, although we adjusted for confounders such as lifestyle factors or disease, we cannot exclude the possibility that muscle strength and power was affected by other factors associated with lifestyle, disease, or protein damage in skeletal tissue that correlate with AGE accumulation. Finally, because this study was a cross-sectional study, we could not conclude whether AGE accumulation in tissue decreased muscle strength and power. A prospective study or trial should be undertaken to further confirm the causal relationship between AGE accumulation and muscle strength and power.

Conclusion

The participants—apparently healthy adult men—with higher skin AF associated with AGE accumulation had lower muscle strength and power. Further studies are needed to confirm whether increased AGE accumulation in tissue predict a decline in muscle strength and power with advancing age in younger adults.

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Conflict of interest None of the authors have any conflicts of interest to disclose.

References

Brownlee M (2001) Biochemistry and molecular cell biology of diabetic complications. Nature 414:813–820

Cesari M, Pahor M, Bartali B, Cherubini A, Penninx BW, Williams GR, Atkinson H, Martin A, Guralnik JM, Ferrucci L (2004) Antioxidants and physical performance in elderly persons: the Invecchiare in Chianti (InCHIANTI) study. Am J Clin Nutr 79:289–294

Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P (2003) International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35:1381–1395

Dalal M, Ferrucci L, Sun K, Beck J, Fried LP, Semba RD (2009) Elevated serum advanced glycation end products and poor grip strength in older community-dwelling women. J Gerontol A Biol Sci Med Sci 64:132–137

Fountoulakis KN, Iacovides A, Samolis S, Kleanthous S, Kaprinis SG, St. Kaprinis G, Bech P (2001) Reliability, validity and psychometric properties of the Greek translation of the Zung Depression Rating Scale. BMC Psychiatry 1:6

Fukuda K, Kobayashi S (1973) A study on a self-rating depression scale (author's transl). Seishin Shinkeigaku Zasshi 75:673–679 (in Japanese)

Guo H, Niu K, Monma H, Kobayashi Y, Guan L, Sato M, Minamishima D, Nagatomi R (2010) Association of Japanese dietary pattern with serum adiponectin concentration in Japanese adult men. Nutr Metab Cardiovasc Dis. doi:101016/jnumecd201006006

Hartog JW, Hummel YM, Voors AA, Schalkwijk CG, Miyata T, Huisman RM, Smit AJ, Van Veldhuisen DJ (2008) Skin-autofluorescence, a measure of tissue advanced glycation end-products (AGEs), is related to diastolic function in dialysis patients. J Card Fail 14:596–602

Haus JM, Carrithers JA, Trappe SW, Trappe TA (2007) Collagen, cross-linking, and advanced glycation end products in aging human skeletal muscle. J Appl Physiol 103:2068–2076

Makita Z, Radoff S, Rayfield EJ, Yang Z, Skolnik E, Delaney V, Friedman EA, Cerami A, Vlassara H (1991) Advanced glycosylation end products in patients with diabetic nephropathy. N Engl J Med 325:836–842

Matsuzawa Y (2005) Metabolic syndrome—definition and diagnostic criteria in Japan. J Atheroscler Thromb 12:301

Meerwaldt R, Graaff R, Oomen PH, Links TP, Jager JJ, Alderson NL, Thorpe SR, Baynes JW, Gans RO, Smit AJ (2004) Simple non-invasive assessment of advanced glycation endproduct accumulation. Diabetologia 47:1324–1330

Meerwaldt R, Hartog JW, Graaff R, Huisman RJ, Links TP, den Hollander NC, Thorpe SR, Baynes JW, Navis G, Gans RO, Smit AJ (2005) Skin autofluorescence, a measure of cumulative metabolic stress and advanced glycation end products, predicts mortality in hemodialysis patients. J Am Soc Nephrol 16:3687–3693

Na R, Stender IM, Henriksen M, Wulf HC (2001) Autofluorescence of human skin is age-related after correction for skin pigmentation and redness. J Invest Dermatol 116:536–540

Payne GW (2006) Effect of inflammation on the aging microcirculation: impact on skeletal muscle blood flow control. Microcirculation 13:343–352

Ramamurthy B, Hook P, Jones AD, Larsson L (2001) Changes in myosin structure and function in response to glycation. FASEB J 15:2415–2422

Sasaki S (2005) Serum biomarker-based validation of a brief-type self-administered diet history questionnaire for Japanese subjects. The Study Group of Ministry of Health, Labor and Welfare of Japan, Tanaka H, chairman, "A research for assessment of nutrition and dietary habit in "Kenko Nippon 21", 10–42 (in Japanese)

Schleicher ED, Wagner E, Nerlich AG (1997) Increased accumulation of the glycoxidation product *N*(epsilon)-(carboxymethyl)lysine in human tissues in diabetes and aging. J Clin Invest 99:457–468

Schmidt AM, Hori O, Brett J, Yan SD, Wautier JL, Stern D (1994) Cellular receptors for advanced glycation end products. Implications for induction of oxidant stress and cellular dysfunction in the pathogenesis of vascular lesions. Arterioscler Thromb 14:1521–1528

Semba RD, Bandinelli S, Sun K, Guralnik JM, Ferrucci L (2010) Relationship of an advanced glycation end product, plasma carboxymethyl-lysine, with slow walking speed in older adults: the InCHIANTI study. Eur J Appl Physiol 108:191–195

Singh R, Barden A, Mori T, Beilin L (2001) Advanced glycation end-products: a review. Diabetologia 44:129–146

Snow LM, Thompson LV (2009) Influence of insulin and muscle fiber type in nepsilon-(carboxymethyl)-lysine accumulation in soleus muscle of rats with streptozotocin-induced diabetes mellitus. Pathobiology 76:227–234

Snow LM, Lynner CB, Nielsen EM, Neu HS, Thompson LV (2006) Advanced glycation end product in diabetic rat skeletal muscle in vivo. Pathobiology 73:244–251

Snow LM, Fugere NA, Thompson LV (2007) Advanced glycation end-product accumulation and associated protein modification in type II skeletal muscle with aging. J Gerontol A Biol Sci Med Sci 62:1204–1210

Tanaka T, Katoh T, Asai J, Nemoto F, Suzuki H, Asahi K, Sato K, Sakaue M, Miyata T, Watanabe T (2009) Relationship of skin autofluorescence to cardiovascular disease in japanese hemodialysis patients. Ther Apher Dial 14:334–340

Thompson LV (2009) Age-related muscle dysfunction. Exp Gerontol 44:106–111

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ORIGINAL ARTICLE

Effect of office-based brief high-impact exercise on bone mineral density in healthy premenopausal women: the Sendai Bone Health Concept Study

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Abstract Although there is ample evidence supporting the effectiveness of physical activity in the prevention and treatment of osteoporosis, there are no previous studies to examine the effect of office-based brief high-impact exercise (HIE) on bone mineral density (BMD) in healthy premenopausal women. This study evaluated the effects of office-based HIE on BMD in healthy premenopausal Japanese women. Ninety-one healthy premenopausal women were randomized to receive stretching exercise (SE) or HIE (stretching, along with up to 5 × 10 vertical and versatile jumps) for 12 months. The BMD of the lumbar spine and proximal femur was measured using dual-energy X-ray absorptiometry. Several cardiovascular risk factors and leg strength also were assessed. An accelerometer-based recorder was used to measure daily impact loading in four 1-week samples. The progression of the HIE program was ensured by the accelerometer. Thirty-three women (71.7%) in the SE group and 34 (75.6%) in the HIE group completed the study. There was a significant difference in the change in the femoral neck BMD between the groups in favor of the HIE group [0.6% (95% CI: −0.4, 1.7) vs. −1.0% (95% CI: −2.2, 0.2)]. Adiponectin, LDL, HDL, and the leg strength of participants in both the groups improved during the intervention. These finding suggested that office-based brief HIE can be recommended for premenopausal women for preventing bone mineral loss.

Keywords Osteoporosis · Impact exercise · Bone mineral density · Accelerometer

Trial Registration: http://www.umin.ac.jp/ctr/index.htm
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Introduction

Osteoporosis is a major risk factor for fractures in the elderly [1]. It has been estimated that there are more than 10 million osteoporotic patients in Japan, 70% of whom are female [2]. Incidence of fractures of the femoral neck, which severely impair the quality of life (QOL), has

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doubled between 1987 and 1997, and the increment has continued until recently [3, 4].

Preventing osteoporosis after menopause involves either raising the peak BMD or attenuating the decline in BMD [5–7]. Exercise, nutrition, and medication are currently recommended for the prevention and treatment of osteoporosis [8]. There is evidence supporting the effectiveness of physical activity, especially impact exercise, in the prevention and treatment of osteoporosis [9–14]. Moreover, Bassey et al. [15] have reported that a short high-impact exercise (HIE) program including 50 vertical jumps increases the BMD of the femoral neck in Caucasian premenopausal women.

Despite the widespread dissemination of information concerning the negative health consequences associated with sedentary living, adult physical activity in many industrialized nations fails to follow such regimes because of lack of time, motivation, and adherence [16, 17]. Thus, to improve exercise adherence, a simple new office-based HIE program was chosen and tested in this study.

The aim of this randomized controlled study was to examine the effects of office-based HIE on lumbar spine and femoral neck BMD among premenopausal women.

Materials and methods

Study design and participants

The Sendai Bone Health Concept Study (S-BHCS) was a 12-month randomized controlled trial conducted between November 2006 and October 2007 at the Tohoku branch of the NTT Solco Corporation (a telecom company), Japan. In this company, most of workers were premenopausal women, who were predominantly sitting at a desk all day (desk jobs). Participants were recruited for the study by the personnel department of the company between May 2006 and July 2006. One hundred eight individuals out of 373 female employees aged 25–50 years were screened for eligibility (Fig. 1). After filling out a questionnaire on their health condition, diet, medical history, lifestyle, and menstrual status, 91 women were enrolled in the study under the following inclusion criteria: (1) no intake of steroid hormones (e.g., corticosteroids or estrogen); (2) no metabolic diseases related to calcium turnover (hyper- or hypothyroidism, hyper- or hypoparathyroidism, renal or liver disease, etc.), (3) no history of rheumatoid arthritis, (4) no history of ovariectomy, (5) no current or planned pregnancy, and (6) the ability to participate in intervention and examination programs for 12 months. Bone density, physical activity level, calcium intake, leg strength, anthropometrics, blood pressure, and QOL were assessed at baseline and after 12 months. The study protocol was approved by the Local Ethical Committee. All participants provided their written informed consent for inclusion in the study.

Questionnaires

Information on the subjects' age, smoking status, drinking status, menstrual cycle, use of medication, and disease history was obtained through a questionnaire. Levels of daily physical activity were estimated using the International Physical Activity Questionnaire (IPAQ, Japanese version) [18]. Before and after the trial, we assessed the QOL on the basis of the physical and mental composite scores obtained using the Medical Outcomes 36-Item Short-Form Health Survey (MOS, SF-36, Japanese version) (both scores have a population norm of 50 points, with lower scores representing a lower QOL) [19].

Daily dietary total energy, protein, fat, carbohydrate, and calcium intake were assessed before and after the intervention using a brief self-administered diet history questionnaire (BDHQ) that included questions on 75 food items and specified their serving sizes. The reproducibility and validity of the BDHQ have been described in detail previously [20].

Bone mineral density

The BMD of the lumbar spine (L1–L4) and proximal femur (at the neck, Ward's triangle, trochanter, and intertrochanteric region) was measured at baseline and after 12 months by using a dual-energy X-ray absorptiometer (DXA, Hologic QDR 4500A, Bedford, MA). The values were expressed in terms of grams per square centimeter.

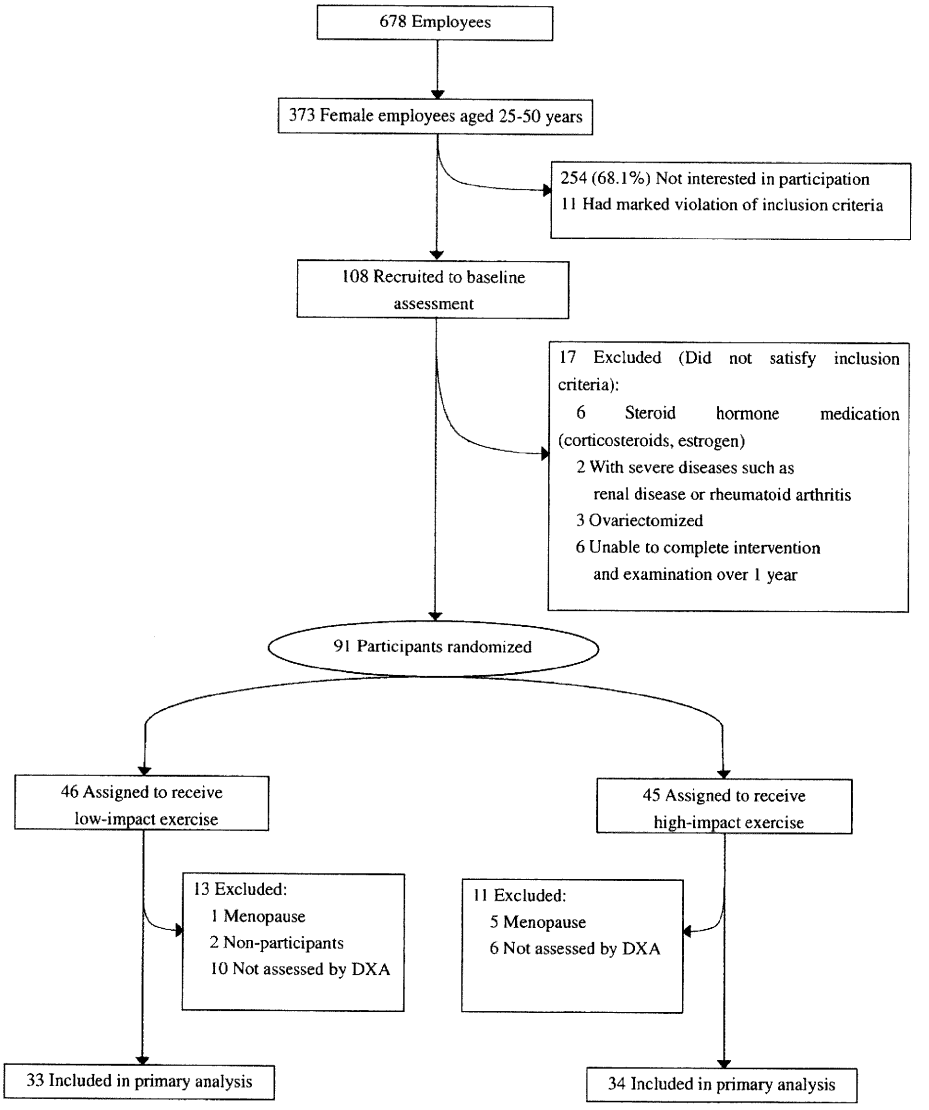
Maximal leg strength

Leg extension power in watts was measured by a well-trained physiotherapist while the subjects were sitting with the knees bent to an angle of 90° (Aneropress 3500, Combi Wellness, Tokyo) [21]. The isometric contractions of the leg muscles lasted for 5 s each and were separated by 15-s rest intervals. The average of the 2 highest measurements obtained in 5 trials was determined. To adjust for differences in the subjects' body mass, the leg extension power was expressed as the average peak value relative to the body weight (W/kg).

Anthropometrics, blood pressure and blood samples

Body height and weight were measured and body mass index (BMI) was calculated using the following formula: weight (kg)/height^2 (m^2). Systolic (SBP) and diastolic blood pressure (DBP) in the left upper arm was measured twice using an automatic device (HEM747IC; Omron Life

Fig. 1 Flow of participants



Science Co. Ltd., Tokyo, Japan) following a 5-min rest in the sitting position.

The blood samples were collected at the same time of the day for all participants. The total cholesterol (T-C), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) concentrations were measured by enzymatic methods using appropriate kits (T-C: Denka Seiken, Tokyo, Japan; LDL-C: Sekisui Medical Co. Ltd., Tokyo, Japan; HDL-C: Daiichi Pure Chemicals, Tokyo, Japan). The serum albumin level was also determined using standard laboratory procedures. High-sensitivity C-reactive protein (hsCRP) concentrations were determined by an immunoassay performed using a Behring BN II analyzer (Dade Behring, Tokyo, Japan. detection limit: 0.02 mg/l [22]. The serum adiponectin concentration was measured using a specific enzyme-linked immunosorbent assay (R&D Systems Inc., Minneapolis, MN; mean sensitivity: 246 pg/ml; intra- and inter-assay coefficients of variation: 3.5% and 6.5%).

Physical activity measurements

An accelerometer-based physical activity recorder (Newtest Ltd., Oulu, Finland) was used to measure the daily impact loading of the subjects. All the subjects were requested to continuously carry the recorder during all waking hours for 1 week every 3 months (November, February, June, and September). The recorder was worn on a belt close to the iliac crest. The data were downloaded onto a computer after each 1-week measurement period.

The physical activity recorder has previously been described in detail [23, 24]. The device recorded the number of vertical acceleration peaks, i.e., impacts exceeding $0.3g$, where g is the acceleration due to gravity (9.81 m/s^2). The acceleration of gravity $1g$ was subtracted, i.e., $0g$ corresponded to the standing position. The average number of impacts recorded daily was calculated at 32 acceleration levels, and a 32-level histogram was obtained for each individual using these data. To assess compliance, the subjects were requested to maintain a diary noting their use of the recorder, and compliance was also checked from accelerometer data.

Exercise program

At the end of the baseline assessment, the participants were age matched and randomly allocated to the stretching exercise (SE) group ($n = 45$) or the HIE group ($n = 46$). The subjects were advised to attend video-guided exercise sessions at least 3 times a week. The sessions were scheduled when the subjects had breaks from work. The participants remained in their work clothes and were requested to wear sport shoes or light gymnastic shoes. Each exercise session included a 3-min warm-up (stretching), 10 min of stretching or HIE (SE, stretching exercise; HIE, stretching, along with up to 5×10 vertical and versatile jumps, with two legs together, using an arm swing in counter movement style, and landing with flexion of the ankles, knees, and hips), and a 3-min cool-down (stretching). The SE group continued to perform stretching and balance exercises throughout the intervention period.

The intention of the jumps in HIE program was to create nonhabitual strains in order to enhance the mechanical competence of bone. Initially, however, the primary objective of the routine was to accustom the subjects to jumping. The programs were modified monthly by increasing the number of jumps up to 50 jumps during the first 3 months. After 6 months, we ensured that the HIE program progressed in intensity by including a 10-cm step bench (Stepwell, Combi, Tokyo, Japan). The training sessions were done with the accompaniment of music and supervised at least 4 times a month by an experienced health fitness instructor.

The compliance with supervised exercise was assessed with personal diaries. Adherence to the protocol was calculated on the basis of the number of sessions attended.

Power calculation

The mean femoral neck BMD of premenopausal Japanese women was 0.763 [25]. Based on the preliminary study [26], we estimated $\geq$3% (SD 0.027 [15]) difference between the HIE and SE groups at the post-intervention femoral neck BMD measurement. To establish statistical significance (alpha) at 5%, with a statistical power of 0.8 and assuming a dropout rate of 20%, a minimum of 28 participants per group was required.

Statistical analysis

All statistical analyses were performed by using the Statistical Analysis System for Windows, version 9.1 (SAS Institute Inc., Cary, NC). For normally distributed continuous variables, the arithmetic means and standard deviations (SDs) were calculated, and for logarithmically transformed continuous variables the geometric means, and SDs were computed. For a baseline comparison between the SE and HIE groups, the Pearson method was used to analyze the categorical data, the statistical result being distributed by the χ^2 test or Fisher's exact test. For comparing the continuous variables related to the basic characteristics of the two groups, unpaired t tests were performed. Paired t tests were performed to compare the change in the outcome variables within groups, while repeated-measure ANOVA was performed to compare these changes between groups. We also applied repeated-measures analysis of covariance (ANCOVA) analyses to evaluate the BMD changes for the 2 groups after adjustment for changes in the BMI and energy-adjusted calcium intake (mg/day) during the trial. The effect size was calculated as the difference (HIE minus SE) between changes (initial minus final) in these mean values. The corresponding standardized difference was calculated by subtracting the difference (HIE minus SE) between changes (initial minus final) in these mean values divided by the pooled SD [square root of the $((N_{\mathrm{HIE}} - 1)\mathrm{SD}^2_{\mathrm{HIE}} + (N_{\mathrm{SE}} - 1)\mathrm{SD}^2_{\mathrm{SE}})/(N_{\mathrm{HIE}} + N_{\mathrm{SE}} - 2)$] of HIE and SE group SDs. The relationships between variables were assessed using Pearson's product moment correlations (or Spearman's if the data are skewed). All the tests for statistical significance were 2 sided, and $P = 0.05$ was considered statistically significant.

Results

Figure 1 shows the flow of participants from the time they were screened to the end of the study, i.e., after 12 months. Ninety-one women met the inclusion criteria and consented to participate in the trial. Their baseline characteristics are presented in Table 1. There were no significant differences between the SE and HIE groups at baseline.

Both the SE and the HIE intervention programs were tolerated well by the study participants, and no treatment-related adverse events occurred. Twenty-four subjects were excluded from the primary analysis (16 were not assessed

Table 1 Baseline characteristics of trial participants

Variables	Stretching exercise ($n = 46$)	High-impact exercise ($n = 45$)	P values[a]
Age (years)	38.1 (1.2)	39.7 (1.2)	0.35
BMI (kg/m^2)	22.3 (1.2)	21.9 (1.2)	0.69
Weight (kg)	56.5 (9.9)	55.6 (12.7)	0.71
Height (cm)	158.3 (5.3)	157.6 (5.8)	0.53
SBP (mmHg)	113.8 (13.4)	116.4 (17.9)	0.44
DBP (mmHg)	74.6 (10.9)	77.4 (13.1)	0.26
Total serum protein (g/dl)	7.5 (1.1)	7.4 (1.1)	0.32
Albumin (g/dl)	4.7 (1.1)	4.6 (1.0)	0.46
Total cholesterol (mg/dl)	185.8 (26.9)	190.7 (27.4)	0.39
TG (mg/dl)	78.7 (1.6)	85.2 (1.9)	0.51
LDL (mg/dl)	96.7 (30.6)	102.8 (29.9)	0.34
HDL (mg/dl)	65.9 (14.6)	64.5 (17.0)	0.69
CRP (ng/ml)	212.4 (3.1)	282.5 (4.4)	0.30
Adiponectin (μg/ml)	8.6 (1.8)	7.7 (2.0)	0.43
Smoker			
Current smoker	32.6	28.9	0.70[b]
Ex-smoker	8.7	13.3	0.52[c]
Physical activity (METs h/week)	11.7 (3.3)	11.5 (2.9)	0.94
SF-36 (total scores)	86.2 (1.2)	80.4 (1.3)	0.15
Leg-power (W/kg)	8.6 (3.5)	8.2 (3.4)	0.61
Energy-adjusted Ca intake (mg/d × 2,000 kcal)	463.3 (164.6)	454.3 (169.0)	0.80
BMD by DXA (g/cm^2)			
Spine (L1–L4)	0.980 (0.128)	0.976 (0.132)	0.88
Proximal femur			
Femoral neck	0.767 (0.092)	0.749 (0.128)	0.45
Trochanter	0.627 (0.077)	0.622 (0.101)	0.79
Intertrochanteric	0.997 (0.108)	0.983 (0.141)	0.59
Femoral total	0.852 (0.087)	0.842 (0.126)	0.65
Ward's triangle	0.651 (0.122)	0.626 (0.168)	0.42

Convert from milligram per deciliter (mg/dl) to millimole per liter (mmol/l), divide by 38.67 (for total cholesterol, LDL, and HDL), or 88.57 (for TG)

Values are mean (standard deviation) or %

BMD bone mineral density, *BMI* body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *LDL* low density lipoprotein cholesterol, *HDL* high-density lipoprotein-cholesterol, *CRP* C-reactive protein, *SF-36* MOS short-form 36-item health survey, *DXA* dual energy X-ray absorptiometry

[a] *t* test

[b] Chi-squared test

[c] Fisher's exact test

during the final measurement because of job-based reasons, such as job transfer or resignation, 2 dropped out of the study, and 6 naturally attained menopause); of the remaining 67 women, 33 (71.7%) were classified into the SE group and 34 (75.6%) into the HIE group. The dropout rate was 26.4%. There were no significant differences in any of the baseline variables of the dropout subjects and the subjects who completed the study. For the women who completed the study, compliance, defined as the number of exercise sessions attended, had a median (interquartile range) value of 2.4 (0.8–3.2) times per week. There were no significant differences in compliance between the SE and HIE groups.

The accelerometer-based method enabled differentiation between the exercise intensities used. The average numbers of impacts recorded daily during the different measurement periods are shown in Fig. 2. During the first 6 months (measurement periods I and II), there was no difference between the 2 groups. During the last 6 months (measurement periods III and IV), the number of impacts at high

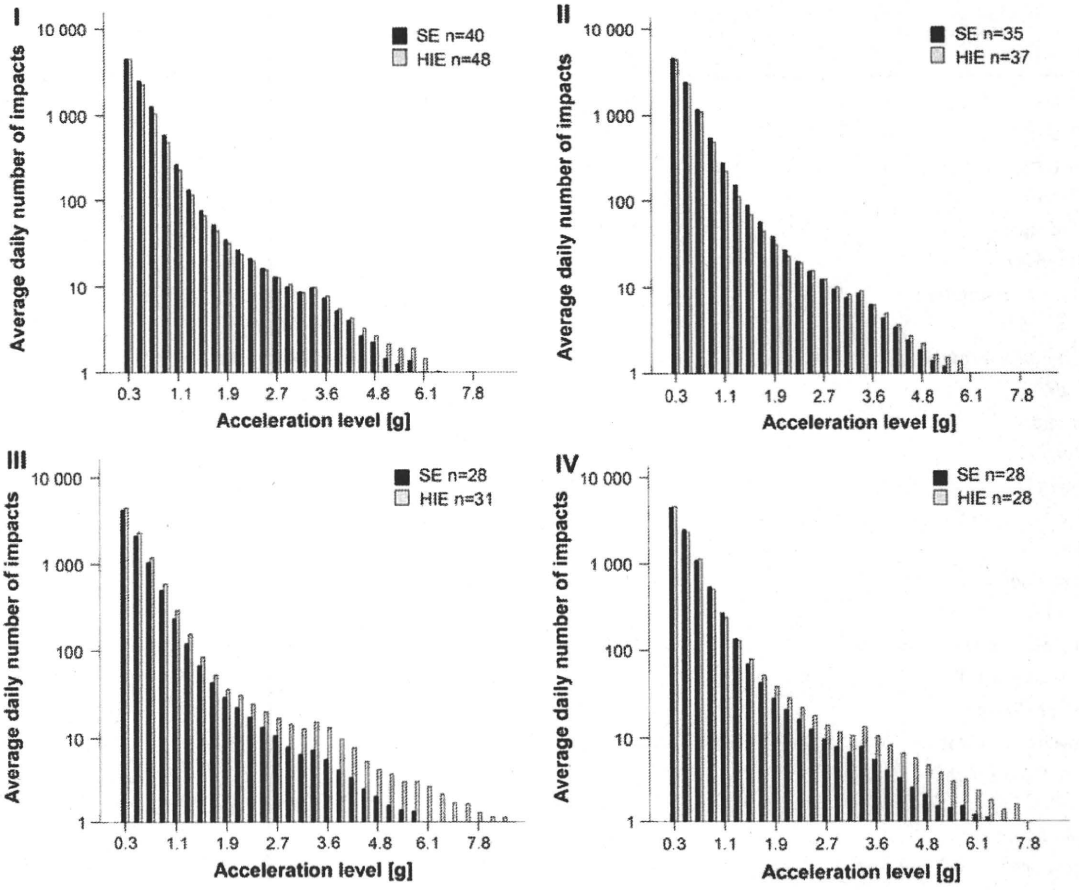


Fig. 2 Average number of impacts recorded daily at different acceleration levels during the four 1-week measurement periods (I–IV) in the 12-month study. Stretching exercise (*SE*) and high-impact exercise (*HIE*) groups

Table 2 Comparison of BMD and its changes between the groups at baseline and after 12-month follow-up

Variables	Stretching exercise ($n = 33$)		High-impact exercise ($n = 34$)		Effect size	P values[a] (time × group)	P values[b] (time × group)
	Baseline	At 12 months	Baseline	At 12 months			
DXA BMD (g/cm^2)							
Spine (L1–L4)	0.983 (0.131)	0.985 (0.129)	0.999 (0.133)	1.007 (0.131)[c]	0.316	0.20	0.10
Proximal femur							
Femoral neck	0.766 (0.090)	0.758 (0.090)	0.763 (0.136)	0.767 (0.135)	0.514	0.04	0.02
Trochanter	0.631 (0.082)	0.629 (0.080)	0.637 (0.105)	0.636 (0.107)	0.086	0.73	0.64
Intertrochanteric	1.002 (0.111)	0.999 (0.114)	0.998 (0.150)	0.997 (0.143)	0.039	0.87	0.43
Femoral total	0.856 (0.091)	0.852 (0.094)	0.858 (0.134)	0.857 (0.128)	0.150	0.54	0.26
Ward's triangle	0.658 (0.130)	0.654 (0.125)	0.642 (0.176)	0.643 (0.163)	0.127	0.61	0.26

Values are mean (standard deviation)

BMD bone mineral density, *DXA* dual-energy X-ray absorptiometry

[a] P values for differences between the low-impact exercise group and the high-impact exercise group over the 12-month study period (repeated-measure ANOVA)

[b] P values for differences between the low-impact exercise group and the high-impact exercise group over the 12-month study period (repeated-measure ANCOVA: adjusted for changes in the BMI and energy-adjusted Ca intake during the trial)

[c] $P < 0.05$, annual change within the group (paired samples t test)

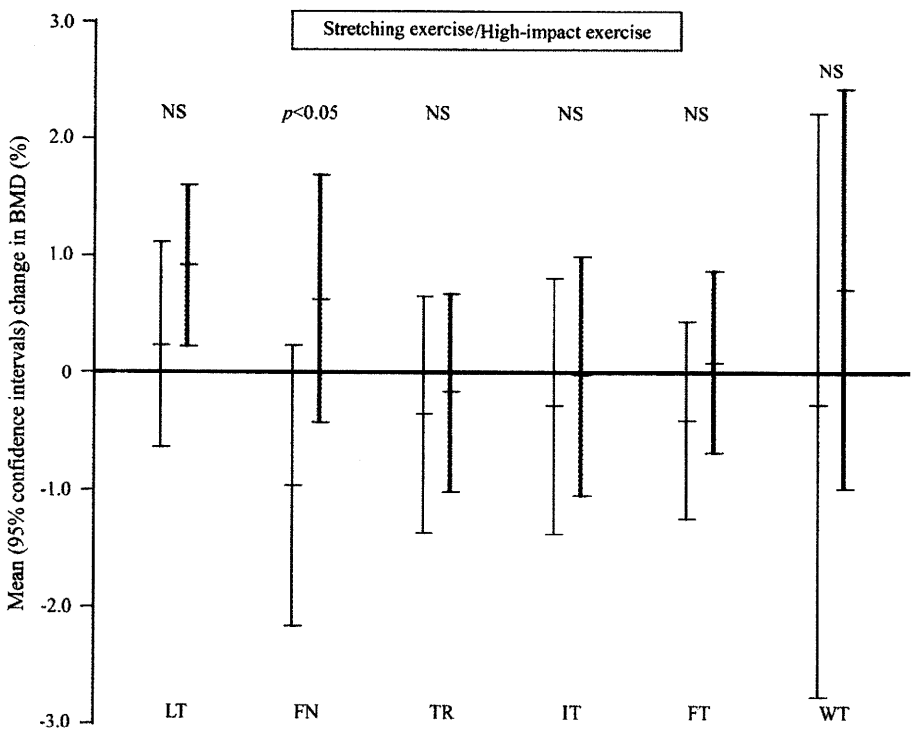


Fig. 3 Mean percent changes (95% confidence intervals) in the BMD of the whole lumbar spine and femur over the 12-month study period. *LT* total lumbar spine, *FN* femoral neck, *TR* greater trochanter, *IT* intertrochanteric region, *FT* total femur, and *WT* Ward's triangle. *P* values indicate the difference between the stretching and high-impact exercise groups over the 12-month study period (unpaired *t* test)

acceleration levels (>3.3 g) in the HIE group was more than twofold that in the SE group.

Table 2 shows the groupwise changes in BMD over 12 months. The HIE group maintained their femoral neck BMD, and there was a significant difference in change in BMD compared to the SE group (0.6% (95% CI: −0.4, 1.7) vs. −1.0% (95% CI: −2.2, 0.2) Fig. 3). The statistically significant difference remained after adjustment for changes in BMI and energy-adjusted Ca intake during the trial. The effect size also suggested that a HIE-intervention led to one-half of a SD increase in femoral neck BMD (Table 2). The BMD of the whole lumbar spine (L1–L4) increased within the HIE group ($P = 0.02$). There were no significant inter-group changes in other bone regions (L1–L4, trochanter, intertrochanteric region, total femur, and Ward's triangle). Because BMI is strongly associated with femoral neck BMD [27] and hip fracture risk [28], we also analyzed the relationship between BMI change and femoral neck BMD change over 12 months. There was no significant relationship between BMI change and femoral neck BMD change (correlation coefficient 0.12; *P* value = 0.50). Furthermore, no significant relationship was found between BMI change and average number of impacts, even when analyzed at different acceleration levels.

Complete cardiovascular risk factors, QOL, and leg strength data were obtained from 63 women (31 in the SE group and 32 in the HIE group) (Table 3). Although no significant intergroup differences were observed, SBP and LDL-C significantly decreased in both groups, while HDL-C, adiponectin concentration, and leg extension power significantly increased in both groups. Furthermore, the DBP and T-C significantly increased in the SE group, while BMI increased significantly in the HIE group. There were no significant inter-group differences in the changes of energy-adjusted Ca, protein, fat, and carbohydrate intake and total physical activity during the trial ($P > 0.10$).

Discussion

The present trial demonstrated that a brief office-based high impact exercise program prevents femoral neck bone loss in healthy premenopausal women. Moreover, both office-based stretching and impact exercise have a positive influence on cardiovascular risk factors and leg strength.

In a previous intervention with Finnish women aged between 35 and 40 [24], the threshold for improving femoral BMD appeared to be less than 100 impacts per day exceeding 3.9 g. The present results support the previous findings for effective bone exercise. However, there is some concern whether the improved femoral neck BMD in the HIE group is maintained after withdrawal. There is some controversy in the previous studies. A study of Winters et al. indicated that the positive benefits of impact plus strength training on the BMD in premenopausal women reverse when training was withdrawn [29], whereas

Table 3 The change in cardiovascular risk factors and leg strength over time and the difference between the groups at baseline and after 12-month follow-up

Variables	Stretching exercise ($n = 31$)		High-impact exercise ($n = 32$)		P values[a] (time × group)
	Baseline	At 12 months	Baseline	At 12 months	
BMI (kg/m^2)	22.6 ± 1.2	22.8 ± 1.2	22.0 ± 1.2	22.5 ± 1.2[b]	0.13
SBP (mmHg)	114.0 ± 11.9	105.8 ± 22.0[b]	116.3 ± 18.8	108.4 ± 25.3[b]	0.96
DBP (mmHg)	75.5 ± 11.4	86.3 ± 21.5[b]	75.8 ± 12.2	79.9 ± 15.7	0.16
Total cholesterol (mg/dl)	187.3 ± 25.5	193.0 ± 29.1[b]	189.2 ± 27.3	190.3 ± 27.5	0.30
TG (mg/dl)	76.8 ± 1.6	75.0 ± 1.8	88.7 ± 2.1	87.9 ± 1.9	0.31
LDL (mg/dl)	106.0 ± 28.8	79.3 ± 22.9[b]	105.3 ± 30.5	81.4 ± 23.8[b]	0.65
HDL (mg/dl)	65.8 ± 16.2	71.3 ± 17.5[b]	63.3 ± 17.6	68.8 ± 20.1[b]	1.00
CRP (ng/ml)	210.7 ± 2.5	225.0 ± 3.0	290.3 ± 4.3	274.8 ± 4.0	0.22
Adiponectin (μg/ml)	9.2 ± 1.9	11.7 ± 1.6[b]	6.8 ± 2.1	10.2 ± 2.0[b]	0.35
SF-36 (total scores)	85.6 ± 1.3[c]	82.7 ± 1.3[c]	83.4 ± 1.2	79.2 ± 1.4	0.97
Energy-adjusted Ca intake (mg/d × 2,000 kcal)	462.4 ± 150.0[c]	545.7 ± 177.3[b,c]	445.5 ± 172.1	559.0 ± 262.5[b]	0.47
Leg extension power (W/kg)	9.2 ± 3.6[d]	10.9 ± 3.5[b,d]	8.2 ± 3.0[d]	10.2 ± 3.5[b,d]	0.60

Convert from milligram per deciliter (mg/dl) to millimole per liter (mmol/l), divide by 38.67 (for total cholesterol, LDL, and HDL) or 88.57 (for TG)

BMI body mass index, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *TG* triglyceride, *LDL* low density lipoprotein cholesterol, *HDL* high-density lipoprotein-cholesterol, *CRP* C-reactive protein, *SF-36* MOS short-form 36-item health survey

Values are mean ± standard deviation

[a] P values for differences between the low-impact exercise group and the high-impact exercise group over the 12-month study period (repeated-measure ANOVA)

[b] $P < 0.05$, annual change within the group (paired samples t test)

[c] $n = 29$

[d] $n = 30$

another study by Kontulainen et al. [30] showed that the training-induced BMD difference between the trainees and controls was maintained even 3.5 years after the intervention. Due to the lack of longitudinal data on the effect of premenopausal exercise on osteoporotic fractures in older age, continuation of osteogenic exercise can be recommended throughout life.

After 12 months of exercise, a significant increase was observed in the BMD of the femoral neck among the women in the HIE group relative to the SE group. Furthermore, a significant change was observed in the total lumbar (L1–L4) BMD within the HIE group but not within the SE group. These results are in agreement with a previous randomized controlled HIE intervention conducted on British premenopausal women [15]. A systematic review also indicated that both high-impact and nonimpact exercises had a positive effect on the BMD of the lumbar spine, while only HIE had a positive effect on that of the femoral neck [14]. This might be due to the fact that the femoral neck is subjected to compressive and bending forces during take-off and landing. The present study suggests that even a simple, office-based program may result in bone effects in the femoral neck similar to those in more demanding programs. A previous study conducted over 18 months by Heinonen et al. [31] showed that HIE significantly increased also the BMD of the total lumbar spine. This controversy may be due to the differences in the proportion of non-impact components of the exercise programs that exerts certain force to the lumbar spine. Further long-term trials are required to clarify this issue by appropriately measuring or estimating the strain and impact on lumbar spine.

Several studies have indicated that HIE has beneficial effects in the cortical bone of the femoral neck [32, 33]. In this study we used only standard DXA, with which cortical and trabecular bone cannot be discriminated, and details of the changes in cortical bone geometry remain unclear. The mechanism by which HIE improves BMD is most probably through the dynamic strains it engenders in bone tissue. A review of studies of humans suggested that physical activities involving both gravitation and muscular loading are capable of generating impact forces and are therefore likely to have beneficial effects on bone metabolism [34]. However, recent study has indicated that HIE did not induce dose-related alterations in bone metabolism markers, but had a dose-dependent effect on serum basal

parathyroid hormone (PTH) concentration, suggesting that the osteogenic effects of loading may partly be mediated by PTH [35].

Because bone adapts to habitual loading, one important feature of an exercise program is progression [36]. Here, we were able to ensure the progression of the HIE program using the acceleration-based measurement of impact loading. The daily acceleration distribution was very similar during the first 2 measurement periods; we used this information to modify the exercise protocol. The accelerometer-based measurements indicated the changes in exercise intensity for the latter half of the study.

In addition to bone health, regular exercise has a beneficial effect also on patients with cardiovascular disease and type 2 diabetes [37]. In this study, we assessed the effects of SE and HIE on several cardiovascular risk factors, including the serum lipid profile, hsCRP, and adiponectin concentration. Adiponectin is a peptide hormone secreted exclusively by adipose tissue. The adiponectin protein is abundantly expressed in plasma (range 5–30 μg/ml); however, adiponectin levels decrease in patients with obesity-linked diseases, including coronary artery diseases and type 2 diabetes [38]. In accordance with a previous study [39], we found that HIE also improved serum lipid profiles and significantly increased adiponectin concentration within groups. This improvement was found in both exercise groups, suggesting that it was mainly a result of the low-impact component of the exercise program. Thus, both HIE and SE had beneficial effects not only on bone health, but also on cardiovascular risk factors in healthy premenopausal women.

Although we assumed that the office-based setting in this study would minimize the dropout rate, the dropout rate of 26.4% over the 12-month study duration was not as low as expected. Among the dropout cases, 6 participants were excluded from the final analysis because of naturally attained menopause. The dropout of 16 study participants was due to unexpected resignation of the participants from the company or to the job transfer within the company. There were only 2 dropout cases due to non-compliance. Considering that the dropout rates reported in previous randomized controlled HIE interventions conducted in Western premenopausal women were 14–33% [10, 15, 31], the dropout rate of this study is within an acceptable range. Therefore, we suggest that the office-based brief HIE program may be an eligible option for the prevention of bone mineral loss.

Based on the previous and current studies, we can offer a bone health concept that is suitable for quite sedentary Japanese women. In this subject group, progression of the exercise program should be gradual. With the selected short office-based exercise program, significant changes in bone mineral density and fitness may be obtained.

In conclusion, the results of this 12-month trial indicate that simple office-based high impact exercise is a safe and effective method for preventing bone loss in the femoral neck. This type of exercise can be recommended for healthy premenopausal Japanese women in order to prevent bone mineral loss.

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Conflict of interest Doctors Korpelainen, Vainionpää, and Jämsä have a patent application with Newtest Ltd. Doctor Jämsä is also a minor shareholder of Newtest Ltd.

References

1. Gass M, Dawson-Hughes B (2006) Preventing osteoporosis-related fractures: an overview. Am J Med 119:S3–S11
2. Fujiwara S (2003) Osteoporosis epidemiology and fracture risk (in Japanese). Hormone Front Gynecol 10:335–340
3. Orimo H, Hashimoto T, Sakata K, Yoshimura N, Suzuki T, Hosoi T (2000) Trends in the incidence of hip fracture in Japan, 1987–1997: the third nationwide survey. J Bone Miner Metab 18:126–131
4. Hagino H, Furukawa K, Fujiwara S, Okano T, Katagiri H, Yamamoto K, Teshima R (2009) Recent trends in the incidence and lifetime risk of hip fracture in Tottori, Japan. Osteoporos Int 20:543–548
5. Nordin BE, Need AG, Chatterton BE, Horowitz M, Morris HA (1990) The relative contributions of age and years since menopause to postmenopausal bone loss. J Clin Endocrinol Metab 70:83–88
6. Riggs BL, Wahner HW, Seeman E, Offord KP, Dunn WL, Mazess RB, Johnson KA, Melton LJ 3rd (1982) Changes in bone mineral density of the proximal femur and spine with aging. Differences between the postmenopausal and senile osteoporosis syndromes. J Clin Invest 70:716–723
7. Lindquist O, Bengtsson C, Hansson T, Roos B (1981) Bone mineral content in relation to age and menopause in middle-aged women. A study of bone density in lumbar vertebrae by dual photon absorptiometry in a population sample of women. Scand J Clin Lab Invest 41:215–223
8. Winzenberg TM, Oldenburg B, Frendin S, De Wit L, Jones G (2005) Effects of bone density feedback and group education on osteoporosis knowledge and osteoporosis self-efficacy in premenopausal women: a randomized controlled trial. J Clin Densitom 8:95–103
9. Warburton DE, Nicol CW, Bredin SS (2006) Health benefits of physical activity: the evidence. CMAJ 174:801–809
10. Vainionpää A, Korpelainen R, Leppäluoto J, Jämsä T (2005) Effects of high-impact exercise on bone mineral density: a randomized controlled trial in premenopausal women. Osteoporos Int 16:191–197

11. Cussler EC, Going SB, Houtkooper LB, Stanford VA, Blew RM, Flint-Wagner HG, Metcalfe LL, Choi JE, Lohman TG (2005) Exercise frequency and calcium intake predict 4-year bone changes in postmenopausal women. Osteoporos Int 16:2129–2141
12. Judge JO, Kleppinger A, Kenny A, Smith JA, Biskup B, Marcella G (2005) Home-based resistance training improves femoral bone mineral density in women on hormone therapy. Osteoporos Int 16:1096–1108
13. Stengel SV, Kemmler W, Pintag R, Beeskow C, Weineck J, Lauber D, Kalender WA, Engelke K (2005) Power training is more effective than strength training for maintaining bone mineral density in postmenopausal women. J Appl Physiol 99:181–188
14. Wallace BA, Cumming RG (2000) Systematic review of randomized trials of the effect of exercise on bone mass in pre- and postmenopausal women. Calcif Tissue Int 67:10–18
15. Bassey EJ, Rothwell MC, Littlewood JJ, Pye DW (1998) Pre- and postmenopausal women have different bone mineral density responses to the same high-impact exercise. J Bone Miner Res 13:1805–1813
16. Robison JI, Rogers MA (1994) Adherence to exercise programmes. Recommendations. Sports Med 17:39–52
17. Takao S, Kawakami N, Ohtsu T (2003) Occupational class and physical activity among Japanese employees. Soc Sci Med 57:2281–2289
18. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund U, Yngve A, Sallis JF, Oja P (2003) International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35:1381–1395
19. Fukuhara S, Bito S, Green J, Hsiao A, Kurokawa K (1998) Translation, adaptation, and validation of the SF-36 Health Survey for use in Japan. J Clin Epidemiol 51:1037–1044
20. Sasaki S (2005) Serum Biomarker-based Validation of a Brief-type Self-administered Diet History Questionnaire for Japanese Subjects (in Japanese), The Study Group of Ministry of Health, Labor and Welfare of Japan, Tanaka H, chairman, "A research for assessment of nutrition and dietary habit in "Kenko Nippon 21", Tokyo, pp 10–42
21. Bassey EJ, Short AH (1990) A new method for measuring power output in a single leg extension: feasibility, reliability and validity. Eur J Appl Physiol Occup Physiol 60:385–390
22. Ledue TB, Weiner DL, Sipe JD, Poulin SE, Collins MF, Rifai N (1998) Analytical evaluation of particle-enhanced immunonephelometric assays for C-reactive protein, serum amyloid A and mannose-binding protein in human serum. Ann Clin Biochem 35(Pt 6):745–753
23. Jämsä T, Vainionpää A, Korpelainen R, Vihriälä E, Leppäluoto J (2006) Effect of daily physical activity on proximal femur. Clin Biomech (Bristol, Avon) 21:1–7
24. Vainionpää A, Korpelainen R, Vihriälä E, Rinta-Paavola A, Leppäluoto J, Jämsä T (2006) Intensity of exercise is associated with bone density change in premenopausal women. Osteoporos Int 17:455–463
25. Orimo H, Sugioka Y, Fukunaga M et al (1997) Diagnostic criteria for primary osteoporosis: year 1996 revision (in Japanese). J Bone Miner Metab 14:219–233
26. Sakon S, Komatsu S (2004) Effect of a simple-jumping exercise on bone mineral density in pre-menopausal women (in Japanese). In: Proceeding of the Sendai University Graduate School of Science in Sports 5, pp 161–168
27. Morin S, Tsang JF, Leslie WD (2009) Weight and body mass index predict bone mineral density and fractures in women aged 40 to 59 years. Osteoporos Int 20:363–370
28. De Laet C, Kanis JA, Oden A, Johanson H, Johnell O, Delmas P, Eisman JA, Kroger H, Fujiwara S, Garnero P, McCloskey EV, Mellstrom D, Melton LJ 3rd, Meunier PJ, Pols HA, Reeve J, Silman A, Tenenhouse A (2005) Body mass index as a predictor of fracture risk: a meta-analysis. Osteoporos Int 16:1330–1338
29. Winters KM, Snow CM (2000) Detraining reverses positive effects of exercise on the musculoskeletal system in premenopausal women. J Bone Miner Res 15:2495–2503
30. Kontulainen S, Heinonen A, Kannus P, Pasanen M, Sievänen H, Vuori I (2004) Former exercisers of an 18-month intervention display residual aBMD benefits compared with control women 3.5 years post-intervention: a follow-up of a randomized controlled high-impact trial. Osteoporos Int 15:248–251
31. Heinonen A, Kannus P, Sievanen H, Oja P, Pasanen M, Rinne M, Uusi-Rasi K, Vuori I (1996) Randomised controlled trial of effect of high-impact exercise on selected risk factors for osteoporotic fractures. Lancet 348:1343–1347
32. Nikander R, Kannus P, Dastidar P, Hannula M, Harrison L, Cervinka T, Narra NG, Aktour R, Arola T, Eskola H, Soimakallio S, Heinonen A, Hyttinen J, Sievanen H (2009) Targeted exercises against hip fragility. Osteoporos Int 20:1321–1328
33. Nikander R, Sievänen H, Heinonen A, Karstila T, Kannus P (2008) Load-specific differences in the structure of femoral neck and tibia between world-class moguls skiers and slalom skiers. Scand J Med Sci Sports 18:145–153
34. Kohrt WM, Barry DW, Schwartz RS (2009) Muscle forces or gravity: what predominates mechanical loading on bone? Med Sci Sports Exerc 41:2050–2055
35. Vainionpää A, Korpelainen R, Väänänen HK, Haapalahti J, Jämsä T, Leppäluoto J (2009) Effect of impact exercise on bone metabolism. Osteoporos Int 20:1725–1733
36. Turner CH (1998) Three rules for bone adaptation to mechanical stimuli. Bone 23:399–407
37. Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, Bauman A (2007) Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Circulation 116:1081–1093
38. Guerre-Millo M (2008) Adiponectin: an update. Diabetes Metab 34:12–18
39. Vainionpää A, Korpelainen R, Kaikkonen H, Knip M, Leppäluoto J, Jämsä T (2007) Effect of impact exercise on physical performance and cardiovascular risk factors. Med Sci Sports Exerc 39:756–763

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Association of Japanese dietary pattern with serum adiponectin concentration in Japanese adult men

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Abstract *Background and aims:* Although previous studies suggest that the traditional Japanese dietary pattern is independently associated with a low cardiovascular disease mortality risk, the mechanisms mediating or linking this association are not well understood. Adiponectin has emerged as a valuable biomarker for cardiovascular diseases. The aim of present study was to evaluate whether dietary patterns are associated with serum adiponectin concentration in Japanese adult men.

Methods and results: We designed a cross-sectional study of 702 men (median [interquartile range] age, 44.5 [37.8–54.2] years) living in Japan. Dietary consumption was assessed via a 75-item food frequency questionnaire. We used principal-components analysis to derive 3 major dietary patterns-"Japanese", "sweets-fruits" and, "Izakaya (Japanese Pub)"- from 39 food groups. Serum adiponectin concentration was measured by using a specific sandwich enzyme-linked immunosorbent assay. After adjustment for potential confounders, the geometric mean (95% confidence interval) for log-transformed adiponectin concentration associated with "Japanese" dietary pattern factor score tertiles were 5.24 (4.84–5.69) for the lowest tertile, 5.82 (5.39–6.29) for the middle tertile, and 5.95 (5.47–6.46) for the highest tertile (P for trend <0.01). In contrast, a significant inverse association was found between the "Izakaya" pattern factor score tertiles and adiponectin concentration (P for trend $= 0.03$).

Conclusions: Greater adherence to the "Japanese" dietary pattern was independently associated to a higher serum adiponectin concentration in Japanese adult men. This finding supports the hypothesis that the traditional Japanese diet may have a potentially beneficial effect on adiponectin concentrations. A long-term prospective study or randomized trials are required to clarify this causality.

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Introduction

Lifestyle-related illness remains a major cause of mortality and morbidity worldwide [1]. Considerable evidence has accumulated that dietary factors are the cornerstone for the prevention and treatment of lifestyle-related illness [2]. Moreover, because diets are composed of a wide variety of foods containing complex combinations of nutrients, surveys that analyze a single nutrient component in foods may not adequately account for the complicated interactions and cumulative effects on human health.

The traditional Japanese diet is characterized by a high consumption of soybean products, fish, seaweeds, vegetables, fruits, and green tea [3]. Many epidemiological studies have shown that the consumption of these food items or adherence to the Japanese dietary pattern in itself is inversely associated with lifestyle-related illness such as cardiovascular disease (CVD), cancer, blood pressure (BP), serum lipids, diabetes, etc [3–6]. However, the mediating factors underlying these associations have not been fully identified.

Adiponectin is a peptide hormone secreted exclusively by the adipose tissue [7]. Plasma adiponectin levels are known to be associated with cases of CVD and type 2 diabetes [8,9]. Several epidemiological and experimental studies have also shown that low adiponectin levels are associated with an increased risk of cancer [10]. Studies with experimental animal models have shown that adiponectin inhibits tumorigenesis [11]. Moreover, clinical studies have shown that low adiponectin levels was associated with hypertension [12], and hypercholesterolemia [13].

Because several components of the "Japanese" dietary pattern, such as fish [14], soybean [15], vegetable [16], and green tea [17] were associated with increased insulin sensitivity, reduced risk of CVD, hypertension, and cancer, we hypothesized that the "Japanese" dietary pattern might be associated with adiponectin. However, to the best of our knowledge, no previous study has assessed the association between the Japanese dietary pattern and adiponectin.

In the present study, we designed a cross-sectional study to investigate whether dietary pattern is associated with adiponectin in Japanese adult men.

Methods

Subjects

The current analysis used data from a prospective cohort study to investigate the risk factors of chronic diseases among adult employees. The study was based on annual health examinations [18] at the Sendai Oroshisho Center. In order to stratify for potential confounders, we have added several assessment parameters to the health examination: 1) questionnaires (please see details), 2) physical performance measurement (leg extension power and grip strength), 3) blood examination (adiponectin, etc.), and 4) daily physical activity (PA) assessment using a three-dimensional accelerometer, etc.

We used baseline data in this study. The sample selection process is described in Fig. 1. There were 1833 individuals had received health examinations (lifestyle-related illnesses and health examinations A, which include blood examinations; or health examinations B, which do not include blood examinations) [18]. We invited all subjects who received lifestyle-related illnesses and health examination A (n = 1253) to participate in the study. Of those invited, 1154 agreed to participate and provided informed consent for their data to be analyzed (response rate = 92.1%). The protocol of our study was approved by the Institutional Review Board of the Tohoku University Graduate School of Medicine. Because we found that gender differences in adiponectin levels (median value and [interquartile range] of males vs. females: 5.73 [4.14–7.68] vs. 10.65 [7.71–13.20]; P value <0.0001), and the number of female subjects (n = 273) was too small to perform factor analysis [19], females were excluded from final analysis. We also excluded subjects, who did not have any dietary information (n = 48), who had a history of CVD (n = 5), and who used anti-hypertensive (n = 91), lipid-lowering (n = 14), or anti-diabetic agents (n = 16). Owing to these exclusions, the final study population comprised 702 subjects (median [interquartile range] age: 44.5 [37.8, 54.2] years).

Assessment of dietary intake

The participants were instructed to complete a brief, self-administered diet history questionnaire (BDHQ) that included questions on 75 food items along with their specified serving sizes [20]. The participants indicated their mean frequency of consumption of the food over the past month by checking 1 of the 7 frequency categories, ranging from "almost never" to "2 or more times/day". The mean daily consumption of nutrients was calculated using an *ad hoc* computer program developed to analyze the questionnaire. The Japanese food composition tables, 5th edition were used as the nutrient database. Foods from the BDHQ were categorized into 39 food subgroups, which were used to derive dietary patterns via principal-components analysis.

Measurement of serum adiponectin concentration

Adiponectin was measured using a specific sandwich enzyme-linked immunosorbent assay (Otsuka Pharmaceutical, Tokyo, Japan). The detection limit of the assay was 23.4 pg/ml, the measurement range was 0.375–12.0 ng/ml, and the intra- and inter-assay coefficients of variation were less than 10%.

Assessment of other variables

Depressive symptoms were assessed according to the Japanese version of the Self-Rating Depression Scale (SDS) [21]. An SDS score ≥40 was taken as the cutoff point indicating relatively mild or severe depressive symptoms [22]. BP was measured twice from the upper left arm by using an automatic device (YAMASU605P; Kenzmedico, Saitama, Japan) after 5 min of rest in the sitting position. The mean of the 2 measurements was taken as the BP value.

Blood samples were collected in siliconized vacuum glass tubes containing sodium fluoride, for analyzing fasting

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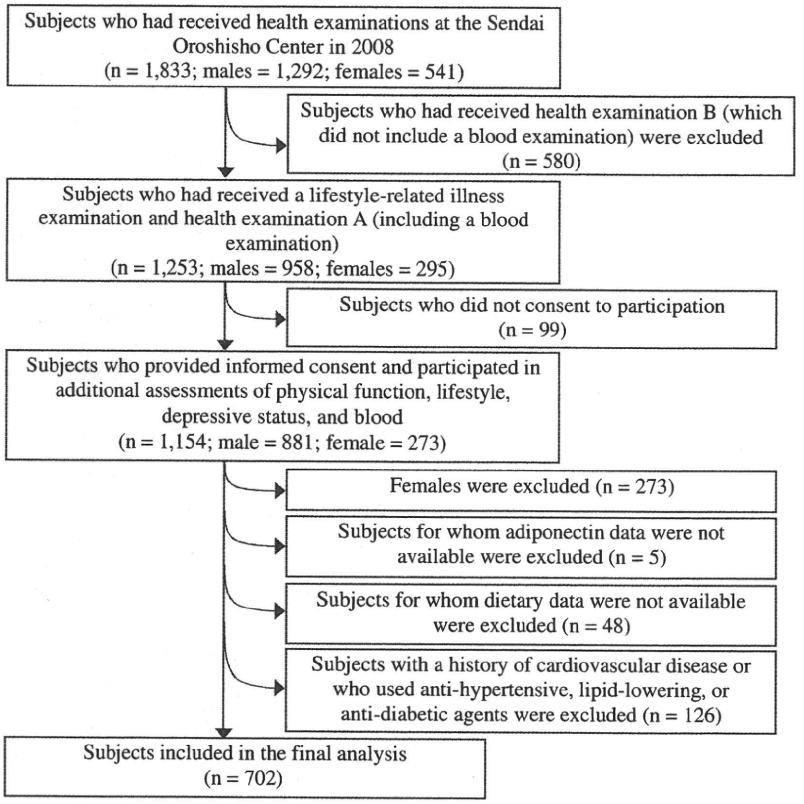

Figure 1 Flow chart of the sample selection process.

blood glucose and no additives, for analyzing lipids and adiponectin. Fasting blood glucose (FBG) was measured by using enzymatic methods (Eerotec, Tokyo, Japan). The concentrations of triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were measured by enzymatic methods using appropriate kits (Sekisui Medical, Tokyo, Japan).

Body mass index (BMI) was calculated as weight/height^2 (kg/m^2). The educational level was assessed by determining the last grade level and was divided into 2 categories: <college or ≥ college. History of physical illness and current medication were noted from "yes" or "no". Information on age, sex, smoking status, sleep duration, occupation, marital status (yes/no), and living status (alone or with others) were obtained by conducting a questionnaire survey. Levels of PA were estimated using the International Physical Activity Questionnaire [23]. Total daily PA (METs × hours/week) were calculated [23]. PA was categorized into tertiles with a similar number of individuals.

Statistical analysis

All statistical analyses were performed using the Statistical Analysis System 9.1 edition (SAS Institute Inc., Cary, NC, USA). Factor analysis (principal-components analysis) was used to derive dietary patterns and to determine factor loadings. Factors were rotated with varimax rotation to maintain uncorrelated factors and enhance interpretability [24]. A combined evaluation of the eigenvalues, scree plot test, and factor interpretability was used in determining the number of retained factors. The distinctive dietary patterns were well described by the 3 factors. For each dietary pattern and each subject, we calculated a factor score by summing the consumption from each food item weighted by its factor loading as follows [24]:

$$\sum[(\text{food group}_i \text{ servings/d}) \times (\text{food group}_i \text{ factor loading})]$$

where i = food groups 1–39. For further analyses, factor scores were categorized into 3 equal groups by using tertiles cutoffs.

In this study, because the distribution of all continuous variables was non-normal, the natural logarithm was applied to normalize the data before analysis of variance (ANOVA) or analysis of covariance (ANCOVA). Descriptive data are presented as the geometric mean (95% confidence interval, CI) for continuous variables and percentages for categorical variables. Log-transformed adiponectin were used as dependent variables, and dietary pattern factor scores tertiles as independent variables. Differences among dietary pattern factor score tertiles were examined using ANOVA for continuous variables and logistic regression analysis for proportional variables. ANCOVA was used to examine relationships between dietary pattern factor score tertiles and log-transformed adiponectin. These analyses were adjusted for various variables in 3 models. In model 1, the variables adjusted for were age, BMI, PA, smoking status

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(nonsmoker, ex-smoker, or current smoker), depressive symptoms, sleep duration (6–7 h, 7–8 h, or other), educational level, occupation (desk work, or non-desk work), and energy intake. In model 2, the variables adjusted for were those of model 1 plus systolic BP, FBG, TG, LDL-C, and HDL-C. In model 3, the variables adjusted for were those of model 2 plus the score categories of the other 2 dietary patterns. Bonferroni-corrected *P* values were used for comparisons between dietary pattern factor score tertiles. All *P* values for linear trends were calculated using the median score of dietary pattern factor scores tertiles. Interactions between dietary pattern factor score tertiles and confounders of log-transformed adiponectin were tested by the addition of cross-product terms to the regression model. All tests were two-tailed and $P < 0.05$ was defined as statistically significant.

Results

Food items and factor loading scores are presented in Appendix Table 1. Factor 1, identified as a traditional "Japanese" dietary pattern was characterized by a high consumption of vegetables, seaweeds, soybean products, fish, miso soup, and green tea. This factor was positively associated with total fish, seaweeds, total vegetables, soybean products, total fruits, dairy products, green tea, total energy intake, animal protein, vegetable protein, animal fat, vegetable fat, total fiber, calcium, and eicosapentaenoic acid (EPA)+docosahexaenoic acid (DHA), and negatively associated with cola and carbohydrate (*P* for trend <0.01) (Appendix Table 2). Factor 2 was typified by a greater consumption of ice cream, cake, fruits, dairy products, cola, and lower consumption of alcohol (named the "sweets-fruits" pattern). This factor was positively associated with total fruit, dairy products, coffee, cola, total energy intake, vegetable protein, animal fat, vegetable fat, carbohydrate, total fiber, and calcium, and negatively associated with total fish, EPA + DHA, and alcohol (*P* for trend <0.05). Incidentally, although dairy product consumption is lower in the "Japanese" dietary pattern than in the "sweets-fruits" pattern, the "Japanese" dietary pattern is associated with high calcium consumption. Factor 3 was typified by a greater consumption of fish, meat, and alcohol (named the "Izakaya (Japanese Pub)" pattern). This factor was positively associated with total meat, total fish, seaweed, total fruit, green tea, black or oolong tea, total energy intake, animal protein, animal fat, EPA + DHA, alcohol, and calcium, and negatively associated with dairy products, vegetable protein, and carbohydrate (*P* for trend < 0.05). These 3 patterns explained 31.5% of the variance in dietary consumption (17.8% for factor 1, 7.3% for factor 2, and 6.4% for factor 3). These dietary patterns were similar to those reported in a previous study [3].

The participant characteristics in relation to the tertiles of each dietary pattern and factor score are presented in Table 1. Compared to subjects in the lowest "Japanese" dietary pattern tertile, the highest tertile group tended to be older (*P* for trend <0.0001) with a higher proportion of subjects having low PA ($P < 0.01$), and a lower proportion of current smokers ($P = 0.03$) and individuals with depressive symptoms ($P < 0.0001$; data not shown). Compared to subjects in the lowest "sweets-fruits" pattern tertile, the highest tertile group tended to be younger; had higher BMI and LDL; lower SBP, DBP, and HDL; and lower proportions of individuals with a sleep duration of 7–8 h (data not shown) and current smokers (*P* for all trends <0.05). Compared to subjects in the lowest "Izakaya" pattern tertile, the highest tertile group had higher SBP, TG, and lower LDL, and a higher proportion of individuals with low PA (*P* for all trends <0.05). Other than these results, no significant differences were observed between the tertiles of each dietary pattern factor score. Furthermore, we also analyzed the relationships between the "sweets-fruits" and "Izakaya" patterns and marital and living statuses (data not shown). No relationship was found between these dietary patterns and these statuses (*P* for trend, >0.08).

Table 2 shows the adjusted relationships between tertiles of dietary pattern and the adiponectin. In the final models, the adjusted geometric mean (95% CI) of log-transformed adiponectin associated with the "Japanese" dietary pattern were 5.24(4.87–5.69) for the lowest tertile, 5.82(5.39–6.29) for the middle tertile, and 5.95 (5.47–6.46) for the highest tertile (*P* for trend <0.01). The geometric mean of log-transformed adiponectin associated with the highest "Japanese" dietary pattern tertile was 13.5% higher than that associated with the lowest tertile (Bonferroni-corrected P value $= 0.03$). In contrast, a significant inverse association was found between "Izakaya" pattern tertiles and adiponectin (*P* for trend = 0.03). No relationship was found between tertiles of "sweets-fruits" pattern score and adiponectin. We also analyzed the relationships between 8 other dietary patterns (factor loading score: >1; range: 1.01–1.62) and adiponectin, but found no relationship between them. The tests for interactions between the tertiles of "Japanese" dietary pattern factor scores and other potential confounders in the final models were also not statistically significant (interaction *P* values >0.09).

Furthermore, we analyzed how food items that contributed substantially (factor loading scores >0.40) to the "Japanese" and "Izakaya" dietary patterns (as shown in Appendix Table 1) and main nutrients were associated to adiponectin (Appendix Table 3). In the final models, significant association with adiponectin were observed between other root vegetables, carrot/pumpkin, and mushrooms (*P* for trend = 0.03, 0.049, and 0.03, respectively). Although not statistically significant, higher consumption of fish and fermented soybeans coincided with higher levels of adiponectin (trend P value $= 0.30$, and 0.08, respectively). Because the "Izakaya" dietary pattern was associated with lower LDL, we analyzed how food items that contribute to this pattern were associated with LDL. In the final models (model 3), we found that only alcohol consumption was significantly and strongly associated with lower LDL (*P* for trend <0.01).

Furthermore, we also analyzed the relationships between "Japanese" dietary pattern and several other CVD risk factors including SBP, DBP, FBG, TG, LDL, and HDL adjusted to all confounding factors. The adjusted geometric mean (95% CI) of SBP, DBP, and TG across the

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