Combination therapy

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

The Adequate Treatment of Osteoporosis (A-TOP) Research Group was authorized in the year 2000 by the Japan Society of Osteoporosis and assisted by the Public Health Research Foundation to obtain clinical evidence regarding osteoporosis treatment. It conducted a clinical trial comparing monotherapy with alendronate, a new bisphosphonate at the time, and combination therapy with alendronate and alfacalcidol, an active vitamin D_3 derivative developed in Japan (Japanese Osteoporosis Intervention Trial: JOINT-02). The incidence of vertebral fracture was significantly reduced in the combination therapy group during the first 6 months of treatment, and in both subgroups of patients with multiple vertebral fractures and grade 3 vertebral fractures by semiquantitative assessment during the 2-year treatment period (Fig. 14) [18]. The incidence of non-vertebral fracture (weight-bearing bones) was also significantly reduced in the combination therapy group. Based on these results, combination therapy with alendronate and an active vitamin D_3 derivative is recommended for the prevention of incident vertebral and non-vertebral fracture in patients at a high risk of fracture.

Secondary osteoporosis

Osteoporosis secondary to other diseases

Secondary osteoporosis is defined as decreased BMD and deteriorated bone quality (pathologic state specific to osteoporosis) having one or more causes in addition to genetic factors, lifestyle, menopause, and aging. Secondary osteoporosis that is caused by a disease, such as hyperparathyroidism, can be improved by treating the underlying disease.

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

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

Osteoporosis secondary to lifestyle-related diseases

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

Factors		*n*	HR	95% CI	*p* value
All randomized		2016	0.89	0.64–1.25	0.51
Age (years)	<75	805	0.87	0.47–1.63	0.67
	75≤ <80	662	1.19	0.67–2.13	0.54
	80≤	549	0.66	0.38–1.16	0.15
25(OH)vitamin D (ng/mL)	<20	435	1.02	0.47–2.24	0.96
	20≤	1426	0.84	0.57–1.23	0.36
Number of prevalent vertebral fracture	0	805	1.73	0.85–3.55	0.13
	1	626	1.28	0.66–2.47	0.46
	2≤	585	0.51	0.32–0.84	0.01
Maximum grade of prevalent vertebral fracture	0	805	1.74	0.85–3.55	0.13
	1	391	1.04	0.33–3.21	0.96
	2	395	0.89	0.46–1.71	0.72
	3	425	0.55	0.38–0.94	0.03

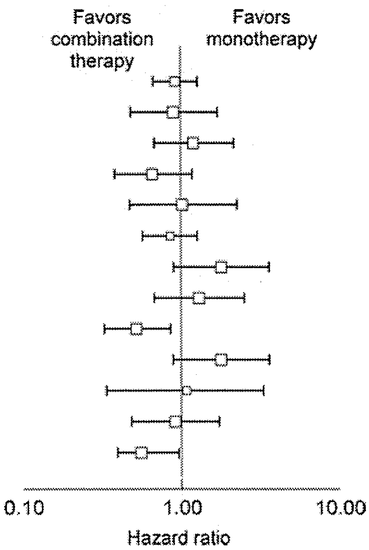

Fig. 14 Efficacy of combination therapy with alendronate and active vitamin D_3 on vertebral fracture. *HR* hazard ratio of incident vertebral fracture, *CI* confidence interval (Orimo [18] (Copyright© 2011 Informa Plc.))

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

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

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

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

Treatment-related osteoporosis

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

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

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

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

Conflicts of interest None.

References

1. Yoshimura N, Muraki S, Oka H et al (2009) Prevalence of knee osteoarthritis, lumbar spondylosis, and osteoporosis in Japanese men and women: the research on osteoarthritis/osteoporosis against disability study. J Bone Miner Metab 27:620–628
2. Orimo H, Yaegashi Y, Onoda T et al (2009) Hip fracture incidence in Japan: estimates of new patients in 2007 and 20-year trends. Arch Osteoporos 4:71–77
3. Yoshimura N, Kinoshita H, Oka H et al (2006) Cumulative incidence and changes in prevalence of vertebral fractures in a rural Japanese community: a 10-year follow-up of the Miyama cohort. Arch Osteoporos. doi:10.1007/s11657-006-0007-0
4. Orimo H, Hayashi Y, Fukunaga M et al (2001) Diagnostic criteria for primary osteoporosis: year 2000 revision. J Bone Miner Metab 19:331–337
5. You K (2011) Osteoporos Jpn 19:626, in Japanese
6. Nishizawa Y, Ohta h, Miura M, et al. Guidelines for the use of bone metabolic markers in the diagnosis and treatment of osteoporosis (2012 Edition). J Bone Miner Metab. doi:10.1007/s00774-012-0392-y
7. Orito S, Kuroda T, Onoe Y et al (2009) Age-related distribution of bone and skeletal parameters in 1322 Japanese young women. J Bone Miner Metab 27:698–704
8. Orimo H, Hosoi T, Fukunaga M (eds) (2009) Manual for osteoporosis screening and health guidance. Life Science Publishing, Tokyo, in Japanese
9. MacLean C, Newberry S, Maglione M et al (2008) Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. Ann Intern Med 148:197–213
10. Papadimitropoulos E, Wells G, Shea B et al (2002) Meta-analysis of the efficacy of vitamin D treatment in preventing osteoporosis in postmenopausal women. Endocr Rev 23:560–569
11. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC et al (2004) Effect of vitamin D on falls: a meta-analysis. JAMA 291:1999–2006
12. Matsumoto T, Ito M, Hayashi Y et al (2011) A new active vitamin D_3 analog, eldecalcitol, prevents the risk of osteoporotic fractures: a randomized, active comparator, double-blind study. Bone 49:605–612
13. Cockayne S, Adamson J, Lanham-New S et al (2009) Vitamin K and the prevention of fractures: systematic review and meta-analysis of randomized controlled trials. Arch Intern Med 166:1256–1261
14. Hagino H, Nishizawa Y, Sone T et al (2009) A double-blinded head-to-head trial of minodronate and alendronate in women with postmenopausal osteoporosis. Bone 44:1078–1084
15. Matsumoto T, Hagino H, Shiraki M et al (2009) Effect of daily oral minodronate on vertebral fractures in Japanese postmenopausal women with established osteoporosis: a randomized placebo-controlled double-blind study. Osteoporos Int 20:1429–1437
16. Orimo H, Morii H, Inoue T et al (1996) Effect of elcatonin on involutional osteoporosis. J Bone Miner Metab 14:73–78
17. Nakano T (2011) Clinical effect of calcitonin (elcatonin) on acute pain for osteoporotic vertebral fracture: semi blind randomized controlled trial. Osteoporos Jpn 19:279
18. Orimo H, Nakamura T, Fukunaga M et al (2011) Effects of alendronate plus alfacalcidol in osteoporosis patients with a high risk of fracture: the Japanese Osteoporosis Intervention Trial (JOINT)–02. Curr Med Res Opin 27:1273–1284

Effects of Exercise and Amino Acid Supplementation on Body Composition and Physical Function in Community-Dwelling Elderly Japanese Sarcopenic Women: A Randomized Controlled Trial

Hun Kyung Kim, PhD,[*] Takao Suzuki, MD, PhD,[†] Kyoko Saito, PhD,[*] Hideyo Yoshida, MD, PhD,[*] Hisamine Kobayashi, DVM,[‡] Hiroyuki Kato, MS,[‡] and Miwa Katayama, DVM[‡]

OBJECTIVES: To evaluate the effectiveness of exercise and amino acid supplementation in enhancing muscle mass and strength in community-dwelling elderly sarcopenic women.

DESIGN: Randomized controlled trial.

SETTING: Urban community in Tokyo, Japan.

PARTICIPANTS: One hundred fifty-five women aged 75 and older were defined as sarcopenic and randomly assigned to one of four groups: exercise and amino acid supplementation (exercise + AAS; n = 38), exercise (n = 39), amino acid supplementation (AAS; n = 39), or health education (HE; n = 39).

INTERVENTION: The exercise group attended a 60-minute comprehensive training program twice a week, and the AAS group ingested 3 g of a leucine-rich essential amino acid mixture twice a day for 3 months.

MEASUREMENTS: Body composition was determined using bioelectrical impedance analysis. Data from interviews and functional fitness parameters such as muscle strength and walking ability were collected at baseline and after the 3-month intervention.

RESULTS: A significant group × time interaction was seen in leg muscle mass (P = .007), usual walking speed (P = .007), and knee extension strength (P = .017). The within-group analysis showed that walking speed significantly increased in all three intervention groups, leg muscle mass in the exercise + AAS and exercise groups, and knee extension strength only in the exercise + AAS group (9.3% increase, P = .01). The odds ratio for leg muscle mass and knee extension strength improvement was more than four times as great in the exercise + AAS group (odds ratio = 4.89, 95% confidence interval = 1.89–11.27) as in the HE group.

CONCLUSION: The data suggest that exercise and AAS together may be effective in enhancing not only muscle strength, but also combined variables of muscle mass and walking speed and of muscle mass and strength in sarcopenic women. **J Am Geriatr Soc 60:16–23, 2012.**

Key words: sarcopenic women; exercise; amino acid supplementation; muscle mass; muscle strength

Sarcopenia, defined as age-related involuntary loss of skeletal muscle mass and strength,[1,2] has been associated with physical disability, functional decline, falls, impaired mobility, and mortality in elderly people.[3,4] Therefore, treating or reversing sarcopenia is important in the maintenance of health and life expectancy in the elderly population. Although many factors, such as chronic disease, physical inactivity, and decreased muscle protein synthesis, may contribute to loss of muscle mass,[5–7] it has been suggested that only skeletal muscle disuse and undernutrition are potentially preventable or reversible with targeted interventions.[8]

Many studies have shown a strong relationship between resistance exercise and strength improvement, through which the efficacy of resistance exercise for the prevention and treatment of sarcopenia has been confirmed.[9] The previous studies have also shown that ingestion of essential amino acids can induce muscle protein anabolism in elderly adults.[10,11] One study showed that the combination of resistance exercise and essential amino acid supplementation (AAS) augmented muscle protein

From the [*]Research Team for Promoting Independence of the Elderly, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan; [†]National Institute for Longevity Sciences, Aichi, Japan; and [‡]Ajinomoto Co. Inc., Kawasaki, Japan.

Address correspondence to Hun Kyung Kim, Research Team for Promoting Independence of the Elderly, Tokyo Metropolitan Institute of Gerontology, 35-2 Sakaecho, Itabashi-ku, Tokyo 173-0015, Japan. E-mail: kimhk@tmig.or.jp

DOI: 10.1111/j.1532-5415.2011.03776.x

JAGS 60:16–23, 2012

0002-8614/12/$15.00

synthesis, suggesting it as a strategy to reverse sarcopenia[12] but in a small sample size. There are few randomized controlled trials (RCTs) on the effects of exercise and AAS on body composition and functional capacity.

The purpose of this study was to investigate the effects of exercise and AAS on muscle mass, strength, and walking ability in sarcopenic women.

METHODS

Subjects

A letter outlining the comprehensive geriatric health examination survey, describing its objective and the way that the personal data would be used, was mailed to the women randomly selected from the Basic Resident Register of 5,932 people aged 75 and older residing in the Itabashi ward of metropolitan Tokyo inviting them to participate in the study. Two thousand eighteen people responded to the mailed letters of invitation to participate in the study, with 1,670 people agreeing and 348 people declining to participate. The baseline assessment was conducted at the Tokyo Metropolitan Institute of Gerontology (TMIG) from October 12 to November 3, 2008. One thousand three hundred eighty-three women aged 75 and older were screened; 287 who originally agreed to participation were absent. Written informed consent was obtained for baseline screening; six people did not sign the informed consent form and were not included in this study.

Three hundred four of 1,377 women (22.1%) were operationally defined as sarcopenic (Figure 1), with selection based on categorization into one or more of the following inclusion criteria groups: appendicular skeletal muscle mass/height^2 less than 6.42 kg/m^2 and knee extension strength less than 1.01 Nm/kg[13,14] (n = 68), appendicular skeletal muscle mass/height^2 less than 6.42 kg/m^2 and usual walking speed less than 1.22 m/s (n = 65),[14] body mass index (BMI) less than 22.0 kg/m^2[14] and knee

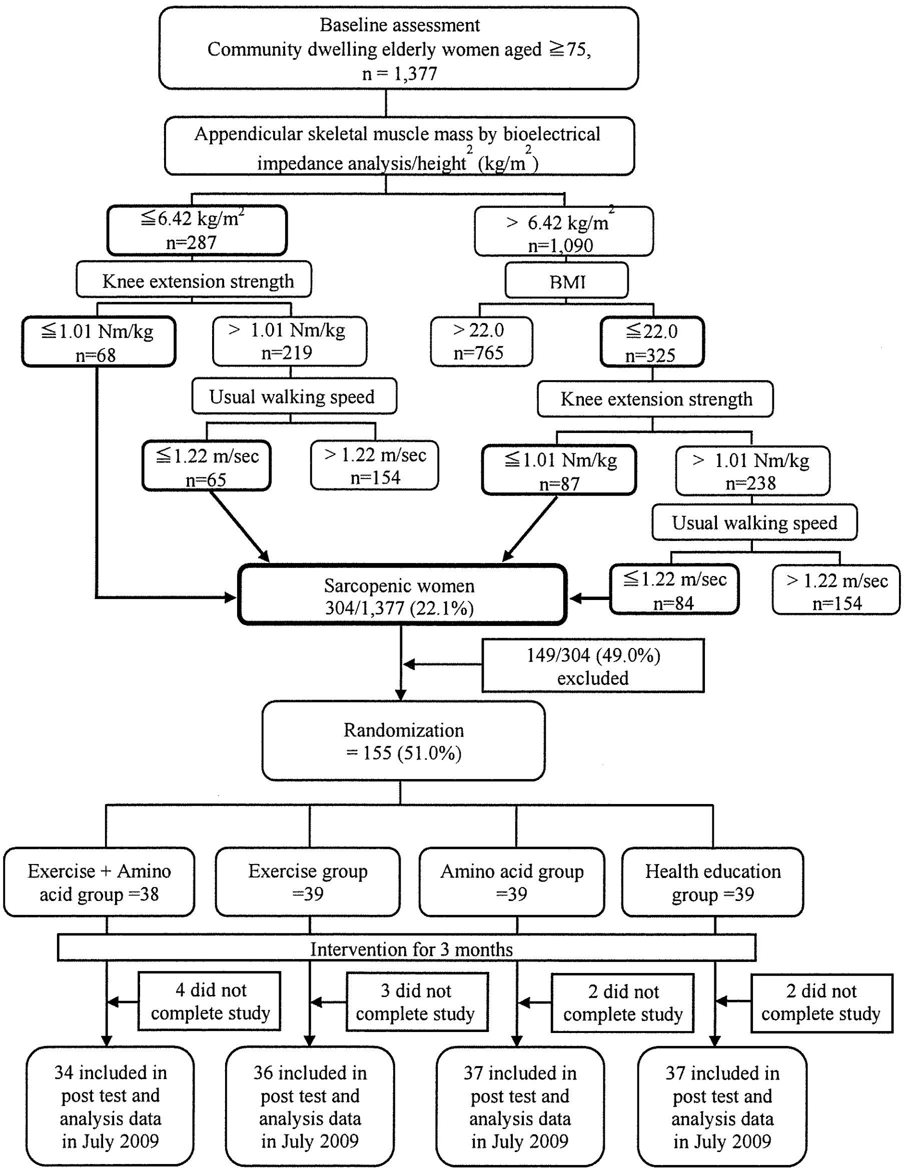

Figure 1. Algorithm for the selection of women who were operationally defined as sarcopenic and flowchart of participants in the randomized controlled trial of exercise and amino acid supplementation.

extension strength less than 1.01 Nm/kg (n = 87), and BMI less than 22.0 kg/m^2 and usual walking speed less than 1.22 m/s (n = 84). Exclusion criteria were severe knee or back pain; severely impaired mobility; impaired cognition (Mini-Mental State Examination (MMSE) score < 24);[16] missing baseline data; and unstable cardiac conditions such as ventricular dysrhythmias, pulmonary edema, or other musculoskeletal conditions. One hundred forty-nine (49.0%) of the potential sarcopenic participants were excluded because they were classified into one or more of the exclusion criteria or declined participation. The Clinical Research Ethics Committee of TMIG approved the study protocol. The intervention procedures were fully explained to all participants, and written informed consent was obtained (Figure 1).

Randomization

Randomization was performed after the baseline assessment; any variable that identified personal information was not included in the randomization process. Computer-generated random numbers were assigned to 155 participants who were then sorted and divided into four equal groups. The groups were randomly assigned to one of the four interventions groups: exercise + AAS (n = 38), exercise (n = 39), AAS (n = 39), or health education (HE; n = 39). All participants agreed to the group allocations that were mailed to them. There was no attempt to equalize the size of the groups based on their characteristics or to recruit subjects with specific characteristics. The co-investigators were blind to the randomization procedure and group allocations, separate physical therapy staff members who were also blind to the allocation of treatments collected data.

Outcome Measures

Outcome measures were evaluated according to data collected from interviews, body composition assessments using bioelectrical impedance analysis (BIA), and physical fitness tests at baseline and after the 3-month intervention.

Interview Survey

Face-to-face interviews were conducted to assess the individual's history of fractures and falls over the previous year, number of falls, cause of falls, urinary incontinence, exercise habits, smoking status, and MMSE score.

Body Composition Assessment

Measurements of height and weight were used to calculate BMI (kg/m^2). Body composition was measured using a segmental multifrequency BIA instrument that operated at frequencies of 5, 50, 250, and 550 kHz (Well-Scan 500, Elk Corp., Tokyo, Japan). Participants removed their socks, stood on two metallic electrodes on the floor scale barefoot, and held metallic grip electrodes placed in the palm of the hand with the fingers wrapped around the handrails. Using segmental body composition and muscle mass values of both legs, both arms, and the trunk, appendicular skeletal muscle mass and leg muscle mass values were obtained

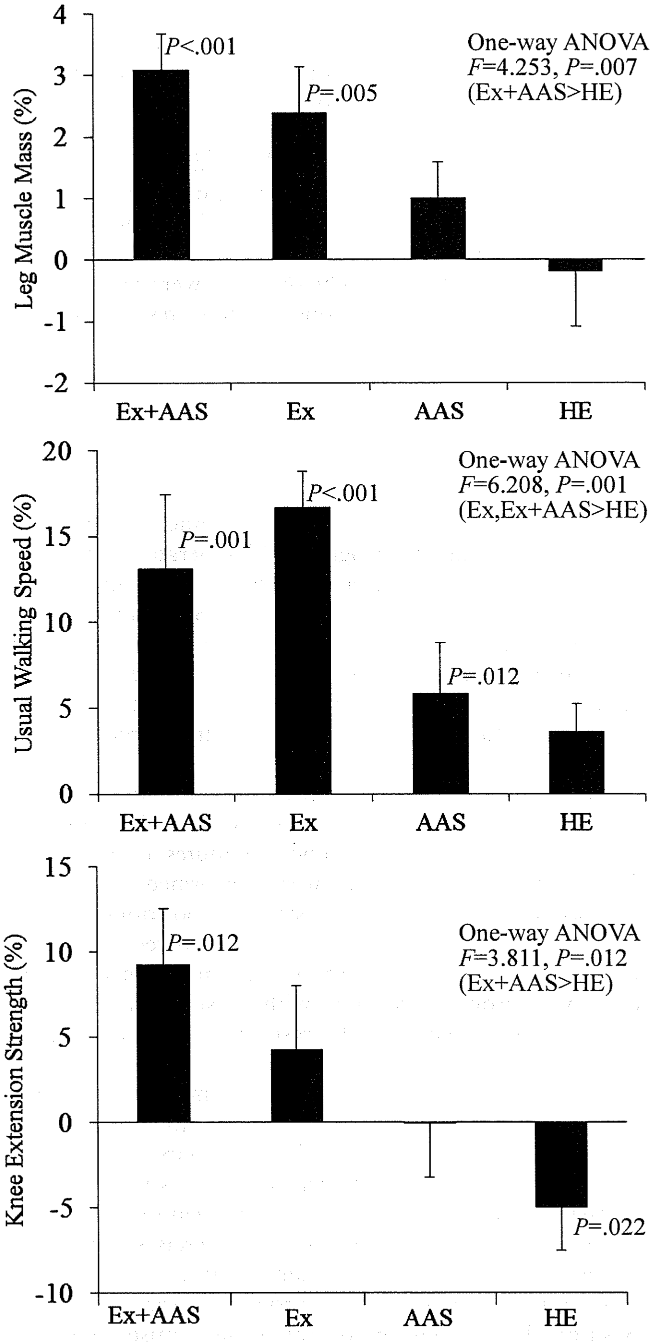

Figure 2. Mean percentage changes (standard errors) in leg muscle mass, usual walking speed, and knee extension strength after exercise (Ex), amino acid supplementation (AAS), both (Ex + AAS), or health education (HE). Bars indicate average changes from baseline to after the 3-month intervention. ANOVA = analysis of variance.

and used for analysis by summing the appropriate segmental muscle mass values.[13,17,18] Reliability of body composition measurements in all 155 participants in this study was not analyzed, although for the AAS group (n = 39), measurements were taken for a second time 1 week after baseline testing, and reliability was examined; the intraclass correlation coefficients (ICC) were: 0.98 for the right arm, 0.97 for the left arm, 0.97 for the right leg, 0.96 for the left leg, and 0.93 for the trunk.

Functional Fitness Test

Calf girth and functional fitness variables including usual and maximum walking speeds and knee extension strength were measured. In measures of walking speed, participants were allowed to use assistive walking devices only if they expressed strong concerns about walking without a device or if there was any danger of falling. The knee extension strength measurement was taken twice, and the higher value divided by body weight (Nm/kg) were analyzed. The procedures for the functional fitness tests have been described in detail in previous reports.[19,20]

Intervention

Exercise

A comprehensive physical fitness and muscle mass enhancement training program of moderate intensity was provided for the participants in the exercise groups. The exercise intervention consisted of 60-minute exercise sessions held at the TMIG twice per week for 3 months. Each exercise intervention group was divided into two subgroups, with participants exercising together within their assigned group in one of four exercise sessions offered per day.

Each exercise session consisted of a 5-minute warm-up, 30 minutes of strengthening exercise, 20 minutes of balance and gait training, and 5 minutes of cool down. The strengthening exercises were performed in a progressive sequence from seated to standing positions. For each type of exercise, participants were instructed to complete up to eight repetitions of the movements. When the exercises were properly executed without significant fatigue or loss of proper execution, the resistance was increased. The progressive resistance was provided through the use of resistance bands or ankle weights. Intensity was maintained at approximately 12 to 14 on the Borg Rate of Perceived Exertion scale.[21] The principal investigator, along with the exercise instructor and assistant trainers, assessed each individual's ability to increase intensity.

Chair exercise: The chair-seated exercises were used in the early stages of the program because the participants were frail older adults and it provided a secure and stable position. Repetitions of toe raises, heel raises, knee lifts, knee extensions, and others were performed while seated on a chair. Hip flexions, lateral leg raises, and repetitions of other exercises were performed standing upright behind the chair and holding the back of the chair for stability.

Ankle-weight exercise: To strengthen lower extremities, a fixed weight was placed on the ankle while participants performed strengthening exercises. Weights of 0.50, 0.75, 1.00, and 1.50 kg were prepared and used in accordance with each participant's strength level as the resistance progressively increased. The exercises performed using these ankle weights included seated knee flexion and extension and standing knee flexion and extensions.

Exercises using a resistance band: Resistance bands were used to strengthen the upper and lower body. Lower body exercises included leg extension and hip flexion. Upper body exercises included double-arm pull downs and biceps curls.

Balance and gait training: The balance training was focused on improvement of static, dynamic, and lateral balancing ability. Exercises included standing on one leg, multidirectional weight shifts, tandem stand, and tandem walk. Participants practiced proper gait mechanics that focused on the maintenance of stability during walking and increasing stride length, toe elevation of the forward limb, heel elevation of the rear limb, frequency of stepping, and heel–floor angle. Exercises included raising the toes (dorsiflexion) during the forward swing of the leg, kicking off the floor with the ball of the foot, walking with directional changes, and gait pattern variations.

Amino Acid Supplementation

Essential AAS was provided for the participants in the AAS groups every 2 weeks. Packets of powdered amino acid supplements (42.0% leucine, 14.0% lysine, 10.5% valine, 10.5% isoleucine, 10.5% threonine, 7.0% phenylalanine, and 5.5% other) were provided for the participants to be taken with water or milk, and they were instructed to take the 3-g supplement two times a day (6 g daily) every day for 3 months.[22] To monitor their amino acid intake accurately, participants were given record sheets that were collected every 2 weeks on which they recorded what time of day they took the supplement and the amount of amino acid taken every day.

Health Education

Participants in the HE group took a class once a month for 3 months, a total of three times. The classes focused on cognitive function, osteoporosis, and oral hygiene. Participants were asked to continue their regular lifestyle habits, and no specific instructions on diet or physical activity were given.

Data Analysis

Sample size calculations using univariate one-factor repeated-measures analysis of variance (ANOVA) to examine significant differences in means at baseline and after the 3-month intervention ($\alpha = 0.05$, power = 0.80) with an effect size of 0.15 required a sample size of 28 participants. Esimating a potential attrition rate of 25%, 38 subjects per group were required.[23] One-way ANOVA was used to test any differences in baseline measures and percentage changes between groups, and chi-square tests were performed on categorical variables. Percentage changes in muscle mass and functional fitness after the intervention were calculated using the following formula: % change = ((postintervention value–baseline value)/(baseline value) × 100). Two-way repeated-measures ANOVA was used to evaluate the differences in the effect of the intervention on the outcome measures between groups, and a post hoc test was done on variables showing significant differences to determine which groups were different. Multiple logistic regressions were performed to compare the effects of the four intervention groups on each outcome variable after 3 months of intervention. All analyses were performed using SPSS version 15.0 of Windows (SPSS, Inc., Tokyo, Japan).

RESULTS

The baseline demographic, fitness, and interview variables of the participants in the four groups are summarized in Table 1. All of the baseline characteristics were similar between the groups.

The mean attendance rates during the 3-month intervention were 70.3% in the exercise + AAS group, 80.5% in the exercise group, 72.2% in the AAS group, and 71.8% in the HE group. Eleven participants (exercise + AAS = 4, exercise = 3, AAS = 2, HE = 2) were unable to complete the study after randomization because of spouse care (n = 3), admission to nursing home (n = 2), lack of motivation (n = 2), severe knee or back pain (n = 1), death (n = 1), falls and hip fracture (n = 1), and hospitalization (n = 1; Figure 2).

In comparing the pre- and postintervention changes in body composition and functional fitness of the groups (Table 2), there was a significant group × time interaction for leg muscle mass ($F = 4.253$, $P < .007$; exercise + AAS > HE), usual and maximum walking speeds (exercise and exercise + AAS > HE), and knee extension strength ($F = 3.558$, $P = .02$; exercise + AAS > HE).

The within-group analysis showed significant changes in leg muscle mass in the exercise + AAS ($P < .001$) and exercise ($P = .005$) groups and changes in usual walking speed in the exercise + AAS ($P = .001$), exercise ($P < .001$), and AAS groups ($P = .01$). Knee extension strength improved significantly only in the exercise + AAS group ($P = .01$), no improvement was seen in exercise or AAS, and a statistically significant decrease was observed in the HE group ($P = .02$; Figure 1).

Table 3 shows the effects of the type of intervention on changes in combined variables of muscle mass and physical function. Significant increases in leg muscle mass and knee extension strength (odds ratio (OR) = 4.89, 95% confidence interval (CI) = 1.89–11.27) and leg muscle mass and usual walking speed (OR = 4.11, 95% CI = 1.33–13.68) were observed in only the exercise + AAS group.

DISCUSSION

Although many definitions of sarcopenia have been reported,[1–3,24] there has recently been a focus not only on the loss of appendicular skeletal muscle mass, but also on functional decline.[25] In this study, sarcopenic women were operationally defined based on declines in muscle strength or walking ability that accompany the loss of skeletal muscle mass or low BMI. Because defining sarcopenia was beyond the scope of this study, the focus of the discussion will be on the effects of the intervention. To evaluate the intervention effects, the changes observed in the single variables as well as the combined variables will be discussed.

Many studies have focused on exercise or nutrition as interventions to reverse sarcopenia, but the results of these studies have not always been consistent.[8,9,12,26]

This study demonstrated that appendicular muscle mass and walking speed increased with the combination of exercise and essential amino acid ingestion, as well as with the separate exercise and amino acid interventions, but muscle strength improved only with the combination of exercise and amino acid ingestion.

A recently published meta-analysis[9] and a Cochrane review article also confirmed that resistance training two to three times a week can improve physical function and functional limitations and can reduce disability and muscle weakness in older people.[27] Previous studies have demonstrated that resistance training in elderly people produces

Table 1. Selected Variable Characteristics of Participants at Baseline According to Study Group

Characteristic	Exercise + AAS (n = 38)	Exercise (n = 39)	AAS (n = 39)	Health Education (n = 39)	F-Value*	P-Value*
Age, mean ± SD	79.5 ± 2.9	79.0 ± 2.9	79.2 ± 2.8	78.7 ± 2.8	0.577	.63
Height, cm, mean ± SD	147.1 ± 6.7	147.7 ± 4.4	145.8 ± 4.5	146.5 ± 4.9	0.960	.41
Body weight, kg, mean ± SD	39.5 ± 5.5	41.1 ± 4.7	40.1 ± 3.2	40.4 ± 3.9	0.874	.46
Body mass index, kg/m², mean ± SD	18.3 ± 2.5	18.9 ± 2.0	18.9 ± 1.6	18.8 ± 1.7	0.745	.53
Calf girth, cm, mean ± SD	18.3 ± 2.5	18.9 ± 2.0	18.9 ± 1.6	18.8 ± 1.7	0.745	.53
Lean body mass, kg, mean ± SD	29.1 ± 3.4	30.0 ± 2.6	28.8 ± 2.0	29.3 ± 2.4	1.505	.22
Muscle mass, kg, mean ± SD	26.9 ± 3.1	27.7 ± 2.3	26.5 ± 1.8	27.0 ± 2.2	1.538	.21
Appendicular muscle mass, kg, mean ± SD	13.3 ± 1.6	13.7 ± 1.3	13.1 ± 1.0	13.3 ± 1.2	1.502	.22
Legs muscle mass, kg, mean ± SD	9.8 ± 1.2	10.1 ± 1.0	9.7 ± 0.7	9.9 ± 0.9	1.570	.20
Usual walking speed, m/s, mean ± SD	1.26 ± 0.27	1.29 ± 0.28	1.29 ± 0.20	1.18 ± 0.22	1.701	.17
Maximal walking speed, m/s, mean ± SD	1.62 ± 0.37	1.67 ± 0.31	1.67 ± 0.27	1.55 ± 0.32	1.150	.33
Knee extension strength, Nm, mean ± SD	45.9 ± 11.3	46.6 ± 11.1	46.7 ± 7.8	47.4 ± 10.5	0.139	.94
Falls, %	21.1	17.9	15.4	20.5	0.519	.91
Exercise habit, %	26.3	25.6	38.5	33.3	2.029	.57
Urinary incontinence, %	44.7	38.5	41.0	25.6	3.414	.33
Osteoporosis history, %	36.8	43.6	48.7	30.8	2.987	.39
Heart disease history, %	10.5	15.4	12.8	17.9	0.977	.81
Diabetes mellitus history, %	7.9	5.1	5.1	12.8	2.156	.54

* One-way analysis of variance for continuous variables and chi-square test for categorical variables.
AAS = amino acid supplementation; SD = standard deviation.

Table 2. Comparison of Muscle Mass and Functional Fitness Variables Between Groups After 3-Month Intervention

Variable	Group	Mean ± Standard Deviation: Baseline	Mean ± Standard Deviation: After 3-Month Intervention	Analysis of Variance (Group × Time), *P*-Value	Post Hoc Analysis*
Muscle mass, kg	Exercise + AAS	26.76 ± 2.77	27.26 ± 3.04	*F* = 1.076, .36	
	Exercise	28.09 ± 1.90	28.51 ± 2.39		
	AAS	26.25 ± 1.81	26.53 ± 2.10		
	HE	27.48 ± 2.04	27.66 ± 2.23		
Appendicular muscle mass, kg	Exercise + AAS	13.25 ± 1.35	13.59 ± 1.53	*F* = 1.354, .26	
	Exercise	13.90 ± 1.06	14.19 ± 1.33		
	AAS	12.86 ± 0.99	13.03 ± 1.10		
	HE	13.57 ± 1.16	13.67 ± 1.05		
Legs muscle mass, kg	Exercise + AAS	9.76 ± 1.01	10.07 ± 1.13	*F* = 4.253, .007	Exercise + AAS > HE
	Exercise	10.28 ± 0.81	10.53 ± 1.05		
	AAS	9.55 ± 0.73	9.65 ± 0.83		
	HE	10.14 ± 0.87	10.11 ± 0.81		
BMI, kg/m^2	Exercise + AAS	18.30 ± 2.64	18.14 ± 2.68	*F* = 0.606, .61	
	Exercise	18.80 ± 1.30	18.50 ± 1.41		
	AAS	18.84 ± 1.43	18.56 ± 1.62		
	HE	18.83 ± 1.75	18.77 ± 1.67		
Usual walking speed, m/s	Exercise + AAS	1.27 ± 0.25	1.43 ± 0.29	*F* = 4.213, .007	Exercise and Exercise + AAS > HE
	Exercise	1.31 ± 0.24	1.50 ± 0.23		
	AAS	1.30 ± 0.18	1.36 ± 0.18		
	HE	1.19 ± 0.21	1.22 ± 0.23		
Maximum walking speed, m/s	Exercise + AAS	1.64 ± 0.34	1.92 ± 0.37	*F* = 9.374, <.001	Exercise and Exercise + AAS > HE
	Exercise	1.72 ± 0.27	2.04 ± 0.27		
	AAS	1.71 ± 0.28	1.92 ± 0.27		
	HE	1.57 ± 0.31	1.64 ± 0.31		
Knee extension strength, Nm/kg	Exercise + AAS	1.15 ± 0.27	1.23 ± 0.29	*F* = 3.558, .02	Exercise + AAS > HE
	Exercise	1.12 ± 0.30	1.14 ± 0.26		
	AAS	1.15 ± 0.25	1.14 ± 0.25		
	HE	1.14 ± 0.26	1.00 ± 0.26		

* A post hoc analysis was performed using the Scheffe method.
AAS = amino acid supplementation; HE = health education; BMI = body mass index.

Table 3. Change in Leg Muscle Mass and Functional Fitness After Intervention According to Study Group

Dependent Variable*	Adjusted Odds Ratio (95% Confidence Interval): AAS	Exercise	Exercise + AAS
Change in leg muscle mass and knee extension strength	1.99 (0.72–5.65)	2.61 (0.88–8.05)	4.89 (1.89–11.27)
Change in leg muscle mass and usual walking speed	1.35 (0.45–4.08)	2.41 (0.79–7.58)	4.11 (1.33–13.68)

Reference: health education.
* 1 = improve, 0 = no change or decrease.
AAS = amino acid supplementation.

9% to 15% increases in strength and approximately 5% in thigh muscle volume.[28,29] Also, many studies have shown that resistance training in elderly people must be conducted at high intensities and volumes to see improvements.[9,27] In contrast, less-intense resistance exercise programs have produced little or no strength gains.

The data in this study show improvements of 2.4% in leg muscle mass, 2.0% in appendicular muscle mass, and 4.3% in leg strength in the exercise group. The moderate-intensity exercise provided in this trial produced strength gains that were smaller than those seen in previous studies, but the combination of moderate intensity exercise and AAS increased muscle mass 3.1% and muscle strength 9.3%, gains that are comparable with those observed in previous studies of high-intensity exercise.[28]

The results of the current study showed that total muscle mass, appendicular muscle mass, and walking speed significantly increased in the exercise group, suggesting that exercise is effective in the improvement of muscle mass and functional fitness, but increases in muscle strength were not observed. These results indicate that exercise alone is insufficient for recovery in sarcopenic elderly women.

Previous studies have indicated that declines in muscle mass are related to declines in muscle protein synthesis rates in older adults and that leucine-enriched essential amino acid mixtures are primarily responsible for the amino acid-induced muscle protein anabolism in elderly people.[11,22] These studies investigated the effects of different amino acid dosages (from 6.7 to 20.0 g/d) on protein synthesis, and the 6.0-g/d dosage provided in this study is lower than in previous studies, but the mean weights of the subjects in such studies were from 71.0 to 81.3 kg, making the dosage of amino acid between 0.090 and 0.246 g/kg of body weight. The amino acid dosage in the current study was 0.151 g/kg, which is comparable with the amounts found in the literature.[11,22,26] The results of the current study showed that muscle mass, appendicular muscle mass, and leg muscle mass significantly increased in the AAS group, which is consistent with previous findings.

Many studies have demonstrated an increase in muscle mass from nutritional supplementation, but an increase in muscle strength does not always accompany an increase in muscle mass. A recent study concluded that essential AAS alone was not sufficient to increase muscle strength.[26] Similarly, although the results of the current study showed that AAS alone increased muscle mass, improvement in muscle strength was not observed. The results of the present study showed that muscle mass increased significantly with exercise or essential AAS, although muscle strength, measured according to knee extension strength, improved significantly only in the exercise + AAS group.

Next, the discussion will focus on the changes in the combined variables. One study that investigated the effects of resistance exercise and nutritional supplementation on muscle mass and strength in older adults concluded that high-intensity resistance exercise was beneficial in increasing muscle mass and muscle strength, but the nutritional supplementation, which contained only a small percentage of a soy-based protein within a mixture of mainly carbohydrates, did not contribute to those gains.[8] As illustrated in Figure 2, exercise alone was effective in enhancing single variables such as leg muscle mass or usual walking speed. Similarly, the AAS group improved usual walking speed, but rationally, to treat sarcopenia, improvements in single variables are not sufficient. Improvements observed in the combined variables would presumably lead to the most-efficient reversal of sarcopenia. Significant improvements in the combinations of leg muscle mass, knee extension strength, and walking speed were seen only in the exercise + AAS group. Although whether exercise + AAS was better than either intervention alone remains inconclusive, these results suggest that exercise + AAS may be necessary for benefits in muscle mass and strength.

This study has several limitations. First is the measurement of body composition estimated using BIA. Although magnetic resonance imaging (MRI), computed tomography, and dual-energy X-ray absorptiometry are common, accurate clinical methods of measuring muscle mass,[30,31] they are cost ineffective and are not always appropriate for field studies. BIA is simple, noninvasive, and inexpensive and has been widely used in field studies. The comparison of MRI and BIA measurements has revealed a strong correlation between the two, confirming the validity of the BIA method for muscle mass measurement in older adults.[13,17,18] Therefore, the validity of the data collected using BIA has little influence on the interpretation of the results of this study. Second, it has been reported that AAS enhances muscle protein synthesis,[11,22,32] but the mechanism of the increase in muscle mass from AAS was not explored in the current investigation. Therefore, the results of this study were interpreted based on the assumption that muscle protein synthesis had been enhanced. Third, the effects of the exercise + AAS should have been determined with the use of placebos, but placebo treatments were not provided in this study, so future research should include placebos to observe the effects of exercise and AAS on physical function and muscle strength. Fourth, the total number of dropouts in this study was 11 people, and they were not included in the data analysis. Many studies have used intention-to-treat (ITT) analyses to determine the effects of RCTs, and the use of ITT analyses are increasing, although one previous study found that only approximately 35% of 274 RCTs used ITT analyses.[33] The current study was not an ITT analysis because it confirmed that there were no significant differences between the dropouts and the participants who completed the study, and the exclusion of the 11 dropouts from the analysis did not affect the integrity of the baseline randomization. Finally, previous research has shown that milk contains essential amino acids.[34,35] Because some of the participants took the AAS with milk, the exact essential amino acid dosage in this study could not be determined, and the effect of drinking milk on the results of this study was not confirmed. Future research should avoid the intake of milk with amino acids when investigating the effects of amino acids on muscle strength and mass and physical function.

This study demonstrated that exercise and nutrition may be necessary for the basic treatment of increasing muscle mass and strength to reverse the effects of sarcopenia in community-dwelling sarcopenic women. Exercise and AAS together have significant effects on enhancing not only muscle strength, but also the combined variables of muscle mass and walking speed and of muscle mass and strength in this study population, but further follow-up studies on larger populations are required to confirm these results.

ACKNOWLEDGMENTS

We thank E. Hosoi, who assisted in the revision of the manuscript.

Conflict of Interest: This study was supported by a Research Grant of the Ministry of Health and Welfare of Japan and a Grant-in-Aid for Scientific Research B of the Japan Society for the Promotion of Science (22300243). The authors have no conflict of interest to disclose.

Author Contributions: H. Kim developed the study concept and design, recruited subjects, developed the intervention program, analyzed and interpreted the data, and prepared the manuscript. S. Takao interpreted the data and reviewed the manuscript for accuracy. K. Saito assisted in AAS and supervised the interview survey. Y. Hideyo assisted in subject recruitment, supervised the

interviewers, and interpreted the data. M. Kobayashi assisted in AAS and subject recruitment and interpreted the data. H. Kato assisted in assisted AAS and body composition assessment. M. Katayama assisted in AAS and interview survey.

Sponsor's Role: The sponsors had no role in the design of this study, subject recruitment, baseline and post survey, development of the intervention program, data analysis, or preparation of the manuscript.

REFERENCES

1. Rosenberg IH. Summary comments. Am J Clin Nutr 1989;50:1231–1233.
2. Evans WJ. What is sarcopenia? J Gerontol A Bio Sci Med Sci 1995;50A:5–8.
3. Baumgartner RN. Body composition in healthy aging. Ann N Y Acad Sci 2000;904:437–448.
4. Janssen I, Baumgartner RN, Ross R et al. Skeletal muscle cutpoints associated with elevated physical disability risk in older men and women. Am J Epidemiol 2004;159:413–421.
5. Baumgartner RN, Waters DL, Gallagher D et al. Predictors of skeletal muscle mass in elderly men and women. Mech Ageing Dev 1999;107:123–136.
6. Iannuzzi-Sucich M, Prestwook KM, Kenny AM. Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women. J Gerontol A Biol Sci Med Sci 2002;57A:M772–M777.
7. Bortz WM II. Disuse and aging. JAMA 1982;248:1203–1208.
8. Fiatarone MA, O'Neill EF, Ryan ND et al. Exercise training and nutritional supplementation for physical frailty in very elderly people. N Engl J Med 1994;330:1769–1775.
9. Peterson MD, Rhea MR, Sen A et al. Resistance exercise for muscular strength in older adults: A meta-analysis. Ageing Res Rev 2010;9:226–237.
10. Paddon-Jones D, Sheffield-Moore M, Katsanos CS et al. Differential stimulation of muscle protein synthesis in elderly humans following isocaloric ingestion of amino acids or whey protein. Exp Gerontol 2006;41:215–219.
11. Katsanos CS, Kobayashi H, Sheffield-Moore M et al. Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids. Am J Clin Nutr 2005;82:1065–1073.
12. Drummond MJ, Dreyer HC, Pennings B et al. Skeletal muscle protein anabolic response to resistance exercise and essential amino acids is delayed with aging. J Appl Physiol 2008;104:1452–1461.
13. Chien MY, Huang TY, Wu YT. Prevalence of sarcopenia estimated using a bioelectrical impedance analysis prediction equation in community-dwelling elderly people in Taiwan. J Am Geriatr Soc 2008;56:1710–1715.
14. Manini TM, Visser M, Won-Park S et al. Knee extension strength cutpoints for maintaining mobility. J Am Geriatr Soc 2007;55:451–457.
15. Kulminski AM, Arbeev KG, Kulminskaya IV et al. Body mass index and nine-year mortality in disabled and nondisabled older U.S. individuals. J Am Geriatr Soc 2008;56:105–110.
16. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198.
17. Janssen I, Heymsfield SB, Baumgartner RN et al. Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol 2000;89:465–471.
18. Tengvall M, Ellegard L, Malmros V et al. Body composition in the elderly: Reference values and bioelectrical impedance spectroscopy to predict total body skeletal muscle mass. Clin Nutr 2009;28:52–58.
19. Kim H, Suzuki T, Yoshida Y et al. Effectiveness of multidimensional exercise for the treatment of stress urinary incontinence in elderly community-dwelling Japanese women: A randomized, controlled, crossover trial. J Am Geriatr Soc 2007;55:1932–1939.
20. Suzuki T, Kim H, Yoshida H et al. Randomized controlled trial of exercise intervention for the prevention of falls in community-dwelling elderly Japanese women. J Bone Miner Metab 2004;22:602–611.
21. Borg GA. Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377–381.
22. Katsanos CS, Kobayashi H, Sheffield-Moore M et al. A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. Am J Physiol Endocrinol Metab 2006;291:E381–E387.
23. Cohen J. A power primer. Psychol Bull 1992;112:155–159.
24. Baumgartner RM, Koehler KM, Gallagher D et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 1998;147:755–763.
25. Cruz-Jentoft AJ, Baeyens JP, Bauer JM et al. Sarcopenia: European consensus on definition and diagnosis. Age Ageing 2010;39:412–423.
26. Dillon EL, Moore MS, Jones DP et al. Amino acid supplementation increases lean body mass, basal muscle protein synthesis, and insulin-like growth factor-I expression in older women. J Clin Endocrinol Metab 2009;94:1630–1637.
27. Liu C, Latham NK. Progressive resistance strength training for improving physical function in older adults. Cochrane Database Syst Rev 2009;3: CD002759.
28. Borst SE. Interventions for sarcopenia and muscle weakness in older people. Age Ageing 2004;33:548–555.
29. Roth SM, Ivey FM, Martel GF et al. Muscle size responses to strength training in young and older men and women. J Am Geriatr Soc 2001;49:1428–1433.
30. Wang Z, Visser M, Ma R et al. Skeletal muscle mass: Evaluation of neutron activation and dual-energy X-ray absorptiometry methods. J Appl Physiol 1996;80:824–831.
31. Mitsiopoulos N, Baumgartner RN, Heymsfield SB et al. Cadaver validation of skeletal muscle measurement by magnetic resonance imaging and computerized tomography. J Appl Physiol 1998;85:115–122.
32. Volpi E, Kobayashi H, Sheffield-Moore M et al. Essential amino acids are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults. Am J Clin Nutr 2003;78:250–258.
33. Herman A, Botser IB, Tenenbaum S et al. Intention-to-treat analysis and accounting for missing data in orthopaedic randomized clinical trials. J Bone Joint Surg Am 2009;91:2137–2143.
34. Elliot TA, Cree MG, Sanford AP et al. Milk ingestion stimulates net muscle protein synthesis following resistance exercise. Med Sci Sports Exerc 2006;38:667–674.
35. Wilkinson SB, Tarnopolsky MA, MacDonald MJ et al. Consumption of fluid skim milk promotes greater muscle protein accretion after resistance exercise than does consumption of an isonitrogenous and isoenergetic soy-protein beverage. Am J Clin Nutr 2007;85:1031–1040.

Knee Surg Sports Traumatol Arthrosc
DOI 10.1007/s00167-012-2010-x

KNEE

Three-dimensional in vivo motion analysis of normal knees employing transepicondylar axis as an evaluation parameter

Osamu Tanifuji · Takashi Sato · Koichi Kobayashi · Tomoharu Mochizuki · Yoshio Koga · Hiroshi Yamagiwa · Go Omori · Naoto Endo

Received: 22 October 2011 / Accepted: 12 April 2012

Abstract

Purpose The transepicondylar axis (TEA) has been used as a flexion axis of the knee and a reference of the rotational alignment of the femoral component. However, no study has showed dynamic normal knee kinematics employing TEA as the evaluation parameter throughout the full range of motion in vivo. The purpose of this study was to analyze dynamic kinematics of the normal knee through the full range of motion via the 3-dimensional to 2-dimensional registration technique employing TEA as the evaluation parameter.

Methods Dynamic motion of the right knee was analyzed in 20 healthy volunteers (10 female, 10 male; mean age 37.2 years). Knee motion was observed as subjects squatted from standing with knee fully extended to maximum flexion. The following parameters were determined: (1) Anteroposterior translations of the medial and lateral ends of the TEA; and (2) changes in the angle of the TEA on the tibial axial plane (rotation angle).

Results The medial end of the TEA demonstrated anterior translation (3.6 ± 3.0 mm) from full extension to 30° flexion and demonstrated posterior translation (18.1 ± 3.7 mm) after 30°, while the lateral end of the TEA demonstrated consistent posterior translation (31.1 ± 7.3 mm) throughout knee flexion. All subjects exhibited femoral external rotation (16.9 ± 6.2°) relative to the tibia throughout knee flexion.

Conclusion Compared to previously used parameters, the TEA showed bicondylar posterior translation from early flexion phase. These results provide control data for dynamic kinematic analyses of pathologic knees in the future and will be useful in the design of total knee prostheses.

Keywords Normal knee · Transepicondylar axis · Knee kinematics · Fluoroscopy · In vivo kinematics · 3-dimensional to 2-dimensional registration technique

O. Tanifuji (✉) · T. Mochizuki · H. Yamagiwa · N. Endo
Division of Orthopaedic Surgery, Department of Regenerative and Transplant Medicine, Niigata University Graduate School of Medicine and Dental Science, 757 Asahimachi-dori 1, Niigata, Niigata 951-8510, Japan
e-mail: tanifuji06242000@yahoo.co.jp

O. Tanifuji · T. Sato · Y. Koga
Department of Orthopaedic Surgery, Niigata Medical Center, Niigata, Japan

K. Kobayashi
Department of Health Sciences, Niigata University School of Medicine, Niigata, Japan

G. Omori
Center for Transdisciplinary Research, Institute for Research Promotion, Niigata University, Niigata, Japan

Published online: 28 April 2012

Introduction

Motion analyses of normal knees provide references for analyzing pathologic knees as in cases of osteoarthritis or ligament injury. Additionally, these analyses could prove useful in the design of total knee prostheses. To describe normal knee motion, methods employing anatomically defined axes at the femur have been utilized in many previous studies.

The transepicondylar axis (TEA) is a line connecting medial and lateral femoral epicondyles and has been used as a flexion axis of the knee [3, 5, 6, 8] and reference of the rotational alignment of the femoral component [1, 4, 16, 17, 19, 21, 27] of total knee arthroplasty (TKA). The goal of TKA is now not only to treat pain, but also to restore function that is more similar to the normal knee. In this situation, it is important to evaluate the normal knee kinematics using TEA to understand that movement throughout the full range of motion. This will be useful data for designing a TKA to restore function, especially for regaining deep flexion by TKA.

Some studies have shown normal knee kinematics using cadavers and employing TEA as an evaluation parameter [5, 7, 15]. Then, Kozanek et al. [12] reported in vivo dynamic normal knee gait analysis employing TEA. However, no study to date has studied in vivo dynamic normal knee kinematics employing TEA as an evaluation parameter throughout the full range of motion.

Other studies have shown in vivo dynamic kinematics of the normal knee through the wide range of motion [11, 14, 23]. These studies employed the contact-point or Geometric center axis (GCA) as an evaluation parameter. However, there is a possibility that similar movement is not seen if TEA is employed as an evaluation parameter in vivo dynamic knee kinematics as cadaver studies have shown a different movement between the TEA and the GCA [15].

The purpose of this study was to analyze in vivo dynamic kinematics of the normal knee through the full range of motion via the 3D-to-2D registration technique [2, 3, 10–12, 14, 15, 23, 26] employing TEA as an evaluation parameter, and to compare the results with previous reports employing GCA as an evaluation parameter.

It is hypothesized that if a different axis is used to evaluate in vivo dynamic kinematics of normal knees, different motion may be observed, even if these result from the same knee motions.

Materials and methods

20 healthy volunteers (10 male, 10 female) with no knee-related symptoms (pain, instability, click, locking, or limited range of motion), history of major trauma, or obvious deformity in the lower extremities participated in this study. The mean age was 37.2 years (range 24–61 years).

This study was performed according to the protocol approved by the Investigational Review Board of our institutions. All subjects provided informed consent to participate in this study.

Motion of the right knee was analyzed in all subjects. Computed tomography (CT) (SOMATOM® Sensation 16; Siemens, Munich, Germany) of the femur and tibia was obtained for each subject, with a 1-mm interval. A 3D digital model of the femur and tibia was constructed from CT data using 3D visualization and modeling software (ZedView®; LEXI, Tokyo, Japan) and the anatomic coordinate systems were established referencing several bony landmarks [20]. The tibial Z-axis was defined by a line connecting the midpoint of the tibial eminence and the midpoint of the medial and lateral tops of the talar dome.

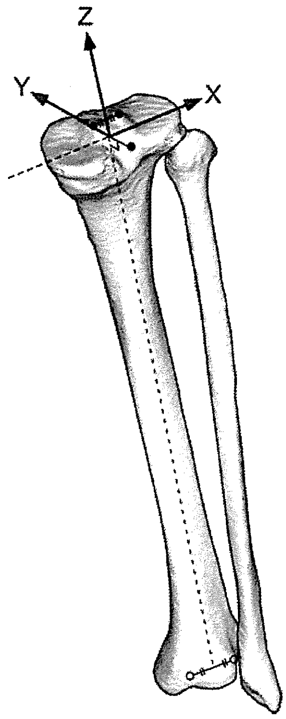

Fig. 1 The tibial coordinate system was established referencing several bony landmarks

The tibial *Y*-axis (positive anteriorly) was defined as a line drawn perpendicularly from the medio-lateral center of the insertion of the posterior cruciate ligament to the *Z*-axis. The tibial *X*-axis was defined as the cross product of the *Z*-axis and *Y*-axis. The *XY* plane in this coordinate system was defined as the tibial axial plane (Fig. 1).

Knee motion was observed as subjects squatted from a standing position (knee fully extended to maximum flexion) and was recorded via a flat panel detector (AXIOM Artis® dTA; Siemens). All subjects stood with their feet in a comfortable rotation position (neutral rotation). The sampling frequency was 15 Hz, with an image area of 380 × 300 mm and resolution of 1,240 × 960 pixels. The mean duration of one flexion of the knee was 8.4 s. The mean angular velocity and sampling rate were 17.2 degrees/second and 1.2 images/degree of knee flexion, respectively. The series of static lateral images were stored digitally. After the contours of the femur and tibia were manually detected in these images, a 3D-to-2D technique using an automated shape-matching algorithm was employed to determine the relative 3D positions of the femur and tibia in each fluoroscopic image (KneeMotion®; LEXI, Tokyo, Japan) (Fig. 2). By performing this procedure for all images, relative motion between the femur and tibia could be obtained. The root mean square error (RMSE) was 0.3–0.8 mm for in-plane translation, 2.2 mm for out-of-plane translation, and 0.2°–0.6° for rotation [10, 23].

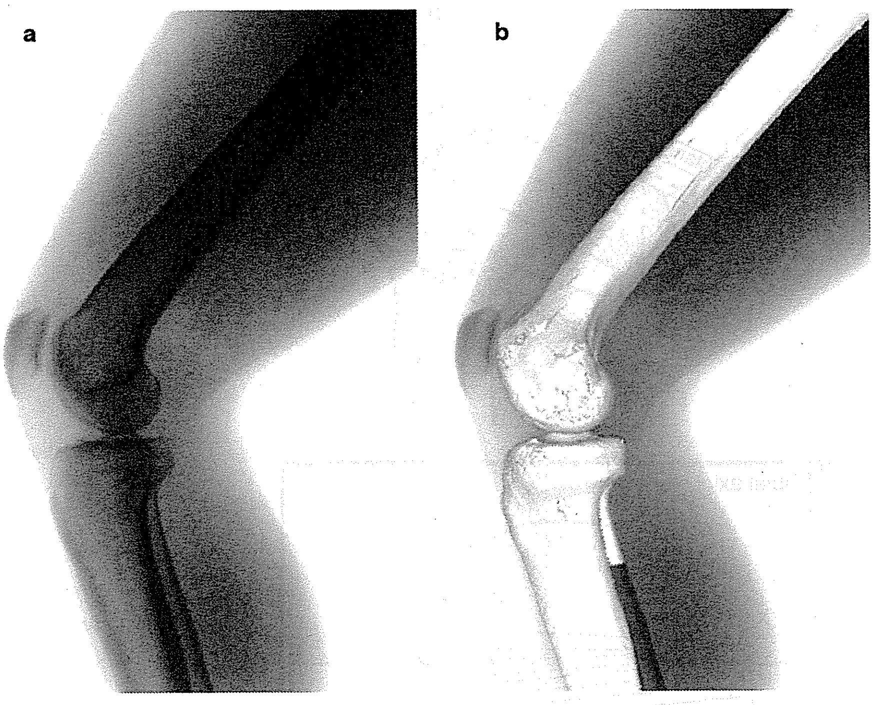

Fig. 2 Example of the 3D to 2D registration techniques are shown. **a** 2D fluoroscopic images of the knee were downloaded and **b** 3D bone models were matched onto a 2D fluoroscopic images

Relative motion between the femur and tibia was quantified as the movement of TEA projected onto the axial (*XY*) plane of the tibial coordinate system. Since the medial sulcus is not always detected [22, 24, 27], we used clinical (or anatomical) TEA, which connects the prominent points of medial and lateral femoral epicondyles, as the evaluation parameter (Fig. 3). We also set the medial and lateral prominence in separate slices because the bony landmarks are not always present in one slice [22].

We determined the following parameters: (1) Anteroposterior (AP) translations of the medial and lateral ends of the TEA; and (2) changes in the angle of the TEA on the tibial axial plane (rotation angle). AP locations of the medial and lateral ends of all projected TEAs were evaluated as *Y* values of the tibial coordinate system (Fig. 4).

To examine the reproducibility of knee motion patterns, changes to the angle of the TEA (rotation angle) and AP translations of the medial and lateral ends of the TEA, three subjects in this series were chosen for examination on two different days. At the time of the second examination, all subjects were asked to repeat the activities of the first examination while being recorded and examined using the same techniques. The intra-observer reproducibility of our parameters was then examined via intra-class correlation coefficient (ICC). The mean and maximum differences in rotation angle of TEA between the two examinations were 1.7° and 3.0°, respectively. The mean and maximum differences in total AP translation of the medial and lateral ends of the TEA were 3.5 and 6.6 mm (medial) and 2.2 and 2.9 mm (lateral), respectively. The ICC of the TEA rotation angle, AP translation of the medial end of the TEA,

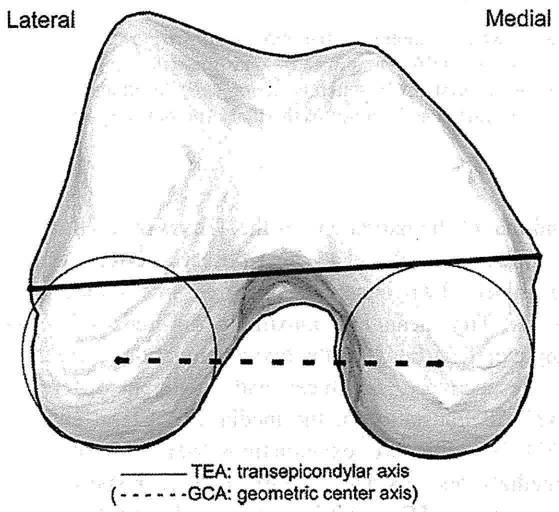

Fig. 3 The clinical transepicondylar axis (*TEA*) is a *line* connecting the prominent points of medial and lateral femoral epicondyles. The geometric center axis (*GCA*) is the *line* connecting the centers of spheres that represent the medial and lateral femoral posterior condyles

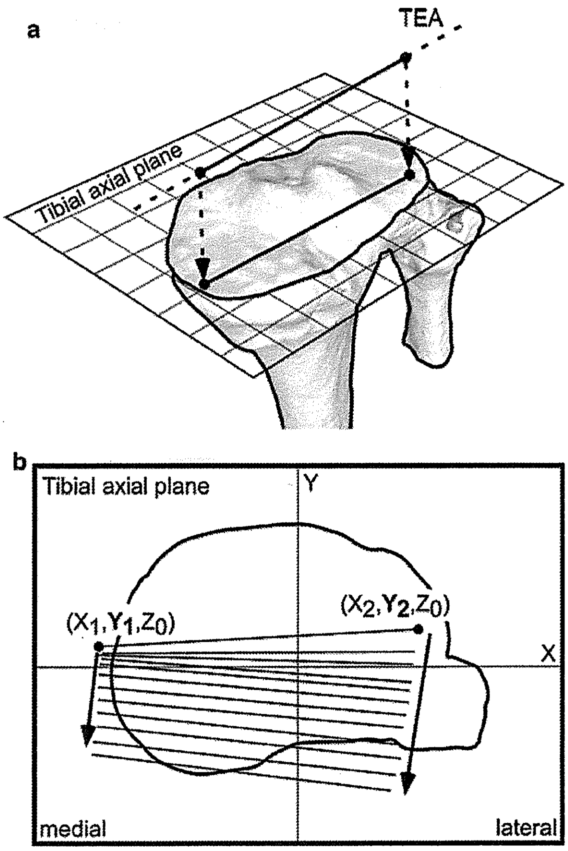

Fig. 4 Relative motion of the femur compared to the tibia. **a** Movement of the TEA was projected onto the axial plane of the tibial coordinate system. **b** Anteroposterior (*AP*) locations of the TEAs were evaluated as *Y* values of the tibial coordinate system

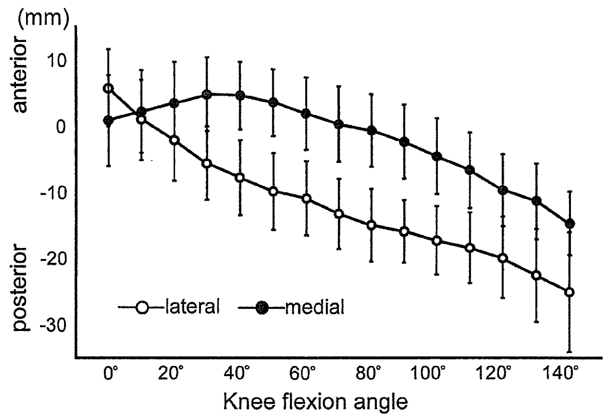

Fig. 5 AP translation of the medial and lateral ends of the TEA (mean ± SD)

and that of the lateral end of the TEA were 0.98, 0.91, and 0.85, respectively. The inter-observer errors were also examined. Two observers analyzed five subjects in this series. The mean and maximum differences in rotation angle of TEA between the two examinations were 2.6° and 3°, respectively. The mean and maximum differences in total AP translation of the medial and lateral ends of the TEA between two examinations were 1.5 and 4.6 mm (medial), and 0.8 and 2.2 mm (lateral), respectively. The ICC of the TEA rotation angle, AP translation of the medial end of the TEA, and AP translation of the lateral end of the TEA were 0.92, 0.86, and 0.99, respectively.

Statistical analysis

All data is expressed as mean ± SD. The difference between changes in the angle of the TEA on the tibial axial plane (rotation angle) and those of the GCA were obtained by a previous study using Student's *t* test with a significance level of $P < 0.05$.

Results

AP translations of the medial and lateral ends of the TEA

With regard to these parameters, the values in the range of knee flexion angle (0°–140°) that could be obtained by all subjects were employed for calculations. Figure 4 show the AP translations of the medial and lateral ends of the TEA in that range. The medial end of the TEA demonstrated anterior translation from 0° to nearly 30° flexion (mean translation 3.6 ± 3.0 mm, range 0.9 mm posterior to 8.9 mm anterior) and demonstrated posterior translation after nearly 30°–140° (mean translation, 18.1 ± 3.7 mm, range, 13.4 mm posterior to 26.8 mm posterior), while the lateral end demonstrated consistent posterior translation throughout knee flexion (mean translation 31.1 ± 7.3 mm, range 19.8–45.4 mm posterior) (Fig. 5). Compared to the movement of the GCA [23], both lateral ends showed similar movement that were consistent with posterior translation throughout knee flexion. Regarding the medial ends, the peak of anterior translation of the TEA was earlier (30°) than that of the GCA (100°) (Fig. 6).

Changes in the angle of the TEA on the tibial axial plane (rotation angle)

In all subjects, the TEA exhibited external rotation on the axial plane of the tibial coordinate system throughout knee flexion. This indicates that all subjects demonstrated internal rotation of the tibia relative to the femur throughout knee flexion. The mean ± SD rotation angle was 16.9 ± 6.2° (range 5.0°–26.0°; female 18.3° ± 6.2°; male 15.5° ± 6.2°). Compared to the GCA, the GCA also exhibited external rotation on the axial plane of the tibial coordinate system throughout knee flexion. Mean rotation angle was

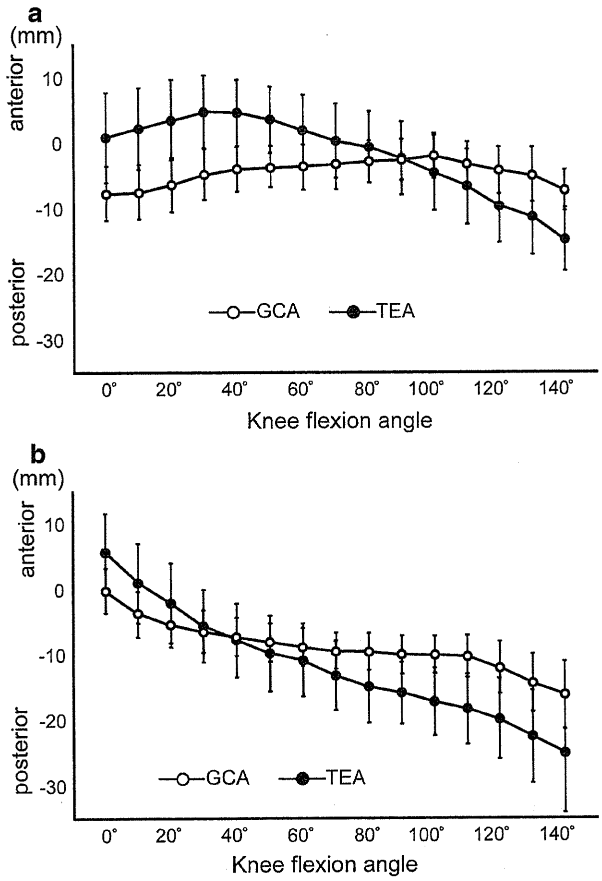

Fig. 6 **a** AP translation of the medial end of the TEA and GCA (mean ± SD). **b** AP translation of the lateral end of the TEA and GCA (mean ± SD)

26.1 ± 6.3° (range 11.8°–40.3°; female 28.3° ± 6.1°; male 23.9° ± 6°) [23]. The angle of the TEA was significantly smaller than the angle of the GCA ($P < 0.001$).

Discussion

The most important finding of the present study was that the medial end of the TEA showed posterior translation from 30° knee flexion and this medial side's early posterior translation made bicondylar posterior translation after mid-flexion. In our study, in vivo 3D dynamic kinematics of normal knees was evaluated through the full range of motion using the TEA as an evaluating parameter. The results were then compared with those of previous studies using the GCA as an evaluating parameter.

Regarding the AP translations of the medial and lateral ends of the TEA in our study, the medial end demonstrated an anterior translation of 3.6 mm from full extension to nearly 30° flexion followed by a posterior translation of 18.1 mm after nearly 30° to full flexion, while the lateral end demonstrated consistent posterior translation (31.1 mm) throughout knee flexion. The notable difference with GCA is the peak of anterior translation and the amount of posterior translation of the medial end. The medial end of the GCA does not reach the peak of anterior translation until nearly 100°. On the other hand, the medial end of the TEA reaches earlier (at nearly 30°). Regarding the amount of posterior translation, the medial end of the TEA moved 18.1 mm posteriorly after reaching the peak of the anterior translation (30°), while the GCA moved only 3.9 mm posteriorly. This result supported our hypothesis. Additionally, this result confirmed the results of past cadaveric studies. Most et al. [15] evaluated the passive motion kinematics of cadaveric knees from full extension to 150° flexion by the 3D-to-2D registration technique utilizing the GCA and TEA as evaluation parameters. In their study, the medial end of the TEA demonstrated a posterior translation from nearly 30° flexion to 150°, while the medial end of the GCA maintained anterior translation from full extension to 120°.

In the sagittal view, the lateral end of the TEA and GCA showed similar posterior movement throughout knee flexion because of roll-back of the lateral femoral condyle. The medial end of the TEA is located more anterior than the medial end of the GCA at full extension. Then, the medial end of the TEA moved posteriorly over the medial end of the GCA that itself showed less movement throughout knee flexion (Fig. 7). This is because the medial end of the TEA is anatomically located more anterior than the medial end of the GCA. If the surgical TEA was used as an evaluating parameter, this might show similar movement to the GCA because the medial end of the surgical TEA that is connecting the sulcus of the medial condyle and the prominent point of the lateral femoral condyle is located more posterior than that of the clinical TEA and closer to the medial end of the GCA. Victor et al. [25] evaluated geometrical references of the distal femur. In this study, the surgical TEA was almost parallel to the GCA (They expressed it femoral transverse axis) with a mean relative external rotation of 0.21° while the clinical TEA had a mean external rotation relative to GCA of 3.40°. From this result, it is expected that the surgical TEA shows similar movement to the GCA.

Regarding the rotation angle, Most et al. reported the mean total rotation angles of the GCA and TEA were 19.9° and 7.2°, respectively [15]. In our study, the mean rotation angle of the TEA was 16.9°. This was also significantly smaller than the angle of the GCA (26.1°) and supported our hypothesis. So the results obtained in vivo dynamic active knee motion showed a similar tendency to the results obtained by cadaveric passive knee motion. The medial end of the GCA did not move significantly until nearly 120° knee flexion. On the other hand, the medial end of the

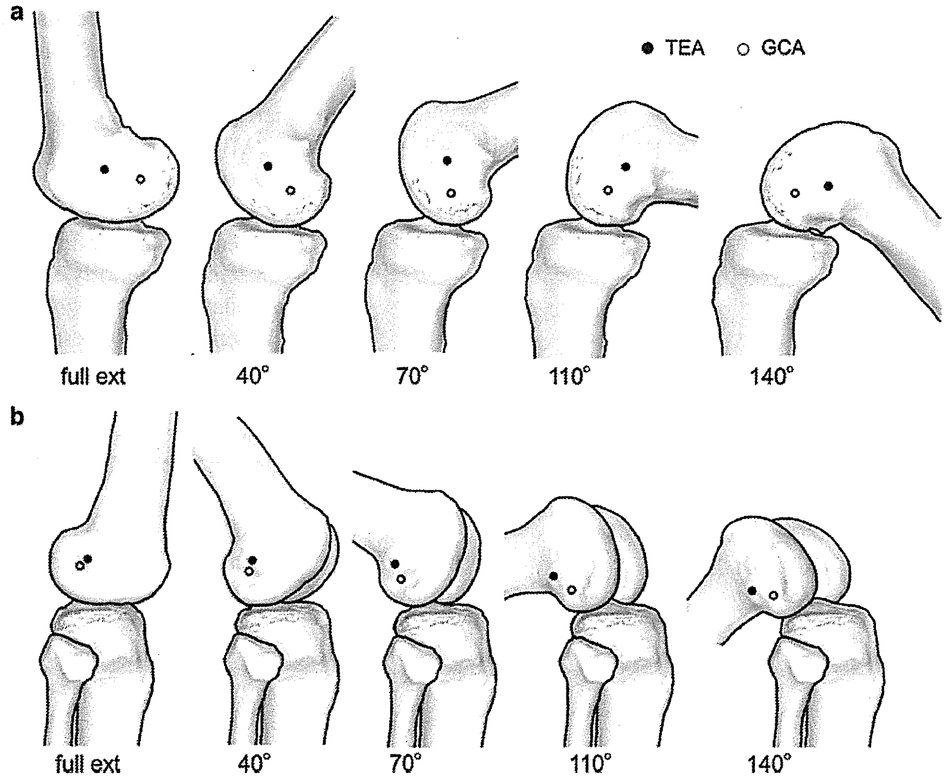

Fig. 7 **a** The relationship between the medial end of the TEA and GCA are shown. The medial end of the TEA is located more anterior than the GCA at full extension. Then, the medial end of the TEA moved posteriorly over the GCA throughout knee flexion. Therefore, the medial end of the TEA is located more posterior than the GCA at 140°. **b** The relationship between the lateral end of the TEA and GCA are shown

TEA moved posteriorly, similar to the lateral end, beginning at nearly 30° knee flexion (Fig. 8). This made the rotation angle of the TEA smaller compared to the GCA.

There have been many studies regarding normal knee kinematics using various evaluating parameters [2, 3, 7, 9, 11–15, 23]. Kurosawa et al. [13] reported normal knee kinematics using the GCA as an evaluating parameter. In their study, from 0 to 120° the medial femoral condyle showed insignificant movement, the lateral moved posteriorly by 17 mm, and there was an axial rotation of 20°. Asano et al. [2] also evaluated in vivo normal knee kinematics using the GCA. In their study, the maximum length of the translation from hyperextension to

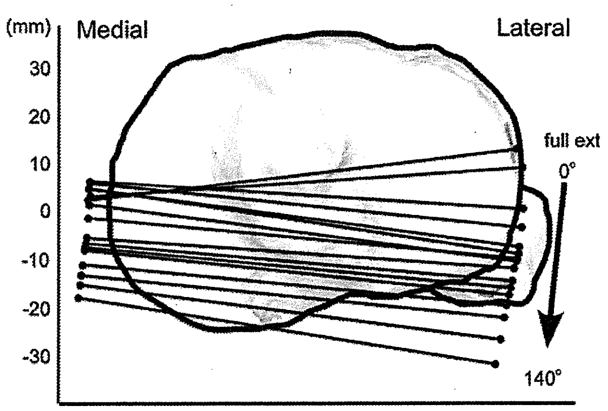

Fig. 8 The typical appearance in this series of projected TEAs on the tibial axial plane every 10° in one knee

flexion at an angle of 120° was 5.8 mm medially and 21.2 mm laterally. The maximum recorded axial rotation angle was 29.1°. Iwaki et al. [9] evaluated the stop-motion kinematics of cadaveric knees from full extension to 120° flexion by magnetic resonance imaging utilizing the FFC as an evaluation parameter. In their study, during flexion the combination of no anteroposterior movement medially and backward rolling laterally made a 20° internal rotation of the tibia around a medial axis with flexion. Komistek et al. [11] and Moro-oka et al. [14] analyzed the in vivo normal dynamic knee kinematics using the contact point as an evaluating parameter. They both showed the lateral condyle experienced more anteroposterior translation than the medial condyle during squatting motion.

Thus, in cases FFC, GCA and contact point were used as evaluating parameters, normal knee kinematics showed less medial motion, more anteroposterior translation laterally from full extension to nearly 120° knee flexion. Additionally, several studies showed bicondylar posterior translation. However, this phenomenon was observed after 120° knee flexion [18, 23]. On the contrary, our study found that the medial end of the TEA showed posterior translation from 30° knee flexion. It is important to understand that different motion patterns can be observed by using different evaluating parameters, even if the same knee movements are being measured.

The TEA has been used as a reference of the rotational alignment of the femoral component [1, 4, 16, 17, 19, 21, 27].

If the ultimate goal of TKA is to closely resemble the normal knee, the fact that TEA shows bicondylar posterior translation during midflexion may be an important aspect of normal knee kinematics, especially regarding gaining full flexion of the total knee. Then, the femoral component, the tibial insert, and the operation technique that represent the kinematics in this manner may be needed to achieve the goal.

This study has several limitations. First, the image registration technique using single-plane fluoroscopy is limited in out-of-plane accuracy. This reduced accuracy might influence the results when determining relative position between the femur and tibia. Second, we did not evaluate the knee motion using the surgical TEA as an evaluating parameter. This data might provide additional useful information.

The data of normal knees in this study provide references for analyzing pathologic knees as in cases of osteoarthritis or ligament injury. Additionally, these analyses could prove useful in the design of total knee prostheses. Especially, bicondylar posterior translation during midflexion of the TEA is a notable features.

Conclusions

When observing in vivo dynamic kinematics of the normal knee, the medial end of the TEA demonstrated anterior translation from 0° to nearly 30° flexion and demonstrated posterior translation after nearly 30°–140°, while the lateral end demonstrated consistent posterior translation throughout knee flexion. This medial side's early posterior translation made bicondylar posterior translation after mid-flexion. As a result, the rotation angle of TEA was not very large (16.9°). Compared to the motion of the GCA, a different rotation angle and time that the medial side begins to translate posteriorly were observed.

Acknowledgments The authors would like to thank the entire staff of the Department of Radiology of the Niigata University Medical and Dental Hospital for their technical support and cooperation and Steve Lenio for his cooperation.

References

1. Aglietti P, Sensi L, Cuomo P, Ciardullo A (2008) Rotational position of femoral and tibial components in TKA using the femoral transepicondylar axis. Clin Orthop Relat Res 466:2751–2755
2. Asano T, Akagi M, Tanaka K, Tamura J, Nakamura T (2001) In vivo three-dimensional knee kinematics using a biplanar image-matching technique. Clin Orthop Relat Res 388:157–166
3. Asano T, Akagi M, Nakamura T (2005) The functional flexion-extension axis of the knee corresponds to the surgical epicondylar axis: in vivo analysis using a biplanar image matching technique. J Arthroplasty 20:1060–1067
4. Berger RA, Rubash HE, Seel MJ, Thompson WH, Crossett LS (1993) Determining the rotational alignment of the femoral component in total knee arthroplasty using the epicondylar axis. Clin Orthop Relat Res 286:40–47
5. Churchill DL, Incavo SJ, Johnson CC, Beynnon BD (1998) The transepicondylar axis approximates the optimal flexion axis of the knee. Clin Orthop Relat Res 356:111–118
6. Colle F, Bignozzi S, Lopomo N, Zaffagnini S, Sun L, Marcacci M (2012) Knee functional flexion axis in osteoarthritic patients: comparison in vivo with transepicondylar axis using a navigation system. Knee Surg Sports Traumatol Arthrosc 20:552–558
7. Eckhoff DG, Dwyer TF, Bach JM, Spitzer VM, Reining KD (2001) Three-dimensional morphology of the distal part of the femur viewed in virtual reality. J Bone Joint Surg Am 83(Suppl 2):43–50
8. Eckhoff D, Hogan C, DiMatteo L, Robinson M, Bach J (2007) Difference between the epicondylar and cylindrical axis of the knee. Clin Orthop Relat Res 461:238–244
9. Iwaki H, Pinskerova V, Freeman MA (2000) Tibiofemoral movement 1: the shapes and relative movements of the femur and tibia in the unloaded cadaver knee. J Bone Joint Surg Br 82:1189–1195
10. Kobayashi K, Tanaka N, Odagawa K, Sakamoto M, Tanabe Y (2009) Image-based matching for natural knee kinematics measurement using single-plane fluoroscopy. J Jpn Soc Exp Mech 9:162–166
11. Komistek RD, Dennis DA, Mahfouz M (2003) In vivo fluoroscopic analysis of the normal human knee. Clin Orthop Relat Res 410:69–81
12. Kozanek M, Hosseini A, Liu F, Van de Velde SK, Gill TJ, Rubash HE, Li G (2009) Tibiofemoral kinematics and condylar motion during the stance phase of gait. J Biomech 42:1877–1884
13. Kurosawa H, Walker PS, Abe S, Garg A, Hunter T (1985) Geometry and motion of the knee for implant and orthotic design. J Biomech 18:487–499
14. Moro-oka T, Hamai S, Miura H, Shimoto T, Higaki H, Fregly BJ, Iwamoto Y, Banks SA (2008) Dynamic activity dependence of in vivo normal knee kinematics. J Orthop Res 26:428–434
15. Most E, Axe J, Rubash H, Li G (2004) Sensitivity of the knee joint kinematics calculation to selection of flexion axes. J Biomech 37:1743–1748
16. Olcott CW, Scott RD (1999) The Ranawat Award. Femoral component rotation during total knee arthroplasty. Clin Orthop Relat Res 367:39–42
17. Olcott CW, Scott RD (2000) A comparison of 4 intraoperative methods to determine femoral component rotation during total knee arthroplasty. J Arthroplasty 15:22–26
18. Pinskerova V, Samuelson KM, Stammers J, Maruthainar K, Sosna A, Freeman MA (2009) The knee in full flexion. J Bone Joint Surg Br 91:830–834
19. Poilvache PL, Insall JN, Scuderi GR, Font-Rodriguez DE (1996) Rotational landmarks and sizing of the distal femur in total knee arthroplasty. Clin Orthop Relat Res 331:35–46
20. Sato T, Koga Y, Omori G (2004) Three-dimensional lower extremity alignment assessment system. J Arthroplasty 19:620–628
21. Stiehl JB, Abbott BD (1995) Morphology of the transepicondylar axis and its application in primary and revision total knee arthroplasty. J Arthroplasty 10:785–789
22. Tan SP, Liau JJ, Chen WT, Cheng CK (2007) The accuracy of posterior condylar angles mesured by one MR images. Clin Orthop Relat Res 456:159–163
23. Tanifuji O, Sato T, Kobayashi K, Mochizuki T, Koga Y, Yamagiwa H, Omori G, Endo N (2011) Three-dimensional in vivo motion analysis of normal knees using single-plane fluoroscopy. J Orthop Sci 16:710–718

24. Uehara K, Kadoya Y, Kobayashi A, Ohashi H, Yamano Y (2002) Bone anatomy and rotational alignment in total knee arthroplasty. Clin Orthop Relat Res 402:196–201
25. Victor J, Van Doninck D, Labey L, Van Glabbeek F, Parizel P, Bellemans J (2009) A common reference frame for describing rotation of the distal femur: a ct-based kinematic study using cadavers. J Bone Joint Surg Br 91:683–690
26. Yamazaki T, Watanabe T, Nakajima Y, Sugamoto K, Tomita T, Yoshikawa H, Tamura S (2004) Improvement of depth position in 2-D/3-D registration of knee implants using single-plane fluoroscopy. IEEE Trans Med Imaging 23:602–612
27. Yoshino N, Takai S, Ohtsuki Y, Hirasawa Y (2001) Computed tomography measurement of the surgical and clinical transepicondylar axis of the distal femur in osteoarthritic knees. J Arthroplasty 16:493–497

J Orthop Sci
DOI 10.1007/s00776-013-0383-4

ORIGINAL ARTICLE

Quadriceps muscle strength and its relationship to radiographic knee osteoarthritis in Japanese elderly

Go Omori · Yoshio Koga · Masaei Tanaka · Atsushi Nawata · Hiroshi Watanabe · Kentaro Narumi · Kazuo Endoh

Received: 5 November 2012 / Accepted: 15 March 2013

Abstract

Background Knee osteoarthritis (OA) is a multifactorial disease and strongly affected by mechanical factors. The aims of the present study were to assess validity and reliability of a new muscle strength measuring device, the Quadriceps Training Machine (QTM) and evaluate the relationship between quadriceps strength measured by QTM and radiographic knee OA by epidemiological survey.

Methods The isometric knee extension muscle strength of QTM was compared with BIODEX in 24 healthy adults. Then, the relationship between radiographic knee OA and quadriceps strength using QTM was investigated with 2,032 knees in 1,016 subjects by an epidemiological survey (Matsudai Knee Osteoarthritis Survey).

Results Significant correlation was observed between QTM and BIODEX ($r = 0.69, 0.82$). In the Matsudai Knee Osteoarthritis Survey, the prevalence of radiographic OA (grade II or higher upon Kellgren–Lawrence classification) was: 13, 36.9, 67.8, and 86.5 %, regarding women in their fifties, sixties, seventies, and eighties, respectively, and was 1.7, 13.4, 33.5, and 66.2 % regarding men, respectively. Quadriceps muscle strength declined following 50 years of age, and significant decline was observed in the their sixties and seventies. Quadriceps muscle strength of the OA group (grades II, III and IV) was significantly declined compared with that of the Non-OA group (grade-0 and I). Furthermore, the tendency of the muscle strength level to decline with the progression of knee OA grade was particularly observed between grade 0 and grade I in both men and women and between grade I and grade II in men.

Conclusion The relationship between radiographic knee OA and quadriceps strength was quantitatively evaluated by an epidemiological survey, and we found a correlation between knee OA and the decline in quadriceps strength. Furthermore, it was suggested that the decline in quadriceps muscle strength may be more strongly related to the incidence of knee OA than to its progression.

This study was performed in Niigata University, 2-8050, Igarashi, Nishi-ku, Niigata City 950-2181, Niigata, Japan.

G. Omori (✉)
Center of Transdisciplinary Research,
Institute for Research Promotion, Niigata University,
2-8050, Igarashi, Nishi-ku, Niigata City 950-2181,
Niigata, Japan
e-mail: gosuke@med.niigata-u.ac.jp

Y. Koga · H. Watanabe
Department of Orthopaedic Surgery, Niigata Medical Center,
3-27-11, Kobari, Nishi-ku,
Niigata City 950-2022, Niigata, Japan

M. Tanaka
Niigata Institute for Health and Sports Medicine,
67-12, Seigoro, Chuo-ku, Niigata City 950-0933, Niigata, Japan

A. Nawata · K. Narumi
Medical Engineering Laboratory, Alcare Co., Ltd,
1-21-10, Kyojima, Sumida-ku, Tokyo 131-0046, Japan

K. Endoh
Niigata University of Health and Welfare, 1398, Shimami-cho,
Kita-ku, Niigata City 950-3198, Niigata, Japan

Introduction

Knee osteoarthritis (OA) is a chronic degenerative disease of the knee joint accompanying aging, causing a decline in the knee joint function while standing and walking when it has advanced and greatly affecting daily life. Regarding the prevalence of knee OA, it is reported that radiographic

Published online: 05 April 2013

knee OA is observed in 37 % of adults aged 60 years old or older and, furthermore, symptomatic knee OA is observed in 12 % in the United States [1]. Meanwhile, in Japan, Yoshimura et al. [2] reported that radiographic OA was observed in 42 % of men and 62 % of women aged 40 years or older in the ROAD (Research on Osteoarthritis/ Osteoporosis Against Disability) study. Knee OA is a multifactorial disease and several previous studies have described various risk factors associated with its incidence and progression. They included age, gender, ethnicity, obesity, smoking, occupation, presence of knee injuries, metabolic diseases, quadriceps muscle strength, knee alignment, osteoporosis, hormones, genes, etc. However, there are still many factors that remain unclear [3–22].

Among these, it is believed that mechanical factors such as body weight, knee alignment, joint stability, bone mineral density, muscle strength of the lower extremity, thrust while walking, and adduction moment may have a large effect on the incidence and progression of knee OA. Among them, we focused on quadriceps strength, which is believed to be effective for prevention and suppression of the disease.

In order to clarify the relationship between knee OA and quadriceps strength, a detailed and quantitative analysis and evaluation with a large number of subjects needs to be conducted in the field of epidemiologic study. However, currently, in terms of devices that may quantitatively evaluate muscle strength of the lower limbs in detail, only large devices installed in major institutes exist such as Cybex, Biodex, etc. Therefore, we developed a new muscle strength measuring device (QTM) allowing for detailed quantitative measurement of the quadriceps strength, which is also lightweight and portable.

The first purpose of the present study was to assess validity and reliability of a new muscle strength measuring device. The second purpose was to investigate the relationship between radiographic knee OA and quadriceps strength by an epidemiological survey with a large number of subjects using this device.

Subjects and method

Investigation of validity and reliability of QTM

The Quadriceps Training Machine (QTM) (QTM-05F, Alcare Co., Ltd. Tokyo, Japan) was developed based on the method for quadriceps setting training in a knee extension position, which is one exercise of quadriceps muscle training. The present device is 300 mm in height, 350 mm in width, and 100 mm in height with a total weight of 3.4 kg, thus making it small, lightweight and portable. This device has a knee holding part at its center corresponding to the knee joint with approximately 20° of flexion (Fig. 1).

The QTM has 3 functions including a load measuring mode, body composition mode, and training mode. Among these, the load measuring mode allows for chronological measurement of the knee extension muscle strength by a strain gauge measurement. The sampling rate of the muscular strength measurement data was 250 ms, the smallest measurement unit was 0.1 kg, and the maximum measured value was 135 kg.

The subjects carried out knee extension exercises by putting their knee joint on the knee holding part of the QTM, with the load pressure applied to the QTM in the popliteal region at this time measured and displayed as the isometric knee extension muscle strength (quadriceps strength) (Fig. 2). In order to investigate the accuracy of the measuring value of QTM, the isometric knee extension muscle strength using QTM and the Biodex system 3 (BDX-3, Biodex Medical System Inc., Shirley, New York, USA) were compared with 24 healthy adults (13 men, 11

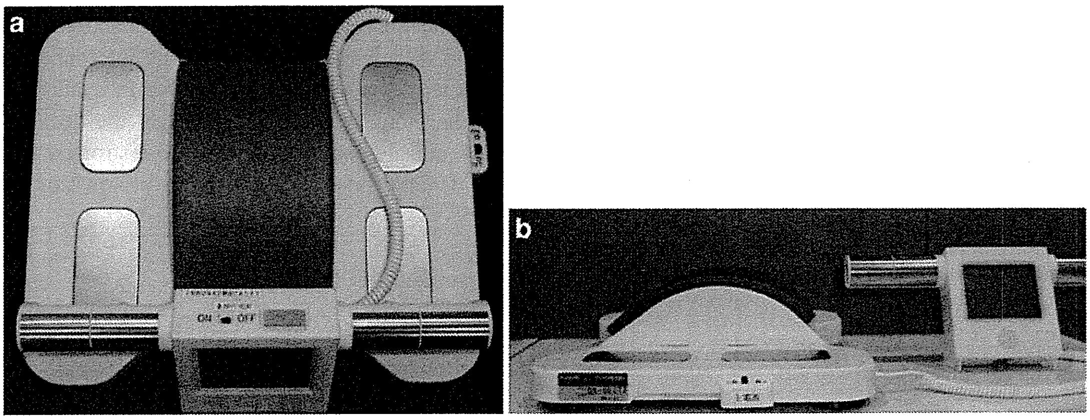

Fig. 1 Quadriceps muscle training machine (QTM). **a** Top view, **b** side view. QTM is 300 mm in height, 350 mm in width, and 100 mm in height with a total weight of 3.4 kg