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Height Loss Starting in Middle Age Predicts Increased Mortality in the Elderly

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ABSTRACT

The purpose of this study was to determine the mortality risk among Japanese men and women with height loss starting in middle age, taking into account lifestyle and physical factors. A total of 2498 subjects (755 men and 1743 women) aged 47 to 91 years old underwent physical examinations during the period 1994 to 1995. Those individuals were followed for mortality status through 2003. Mortality risk was estimated using an age-stratified Cox proportional hazards model. In addition to sex, adjustment factors such as radiation dose, lifestyle, and physical factors measured at the baseline—including smoking status, alcohol intake, total cholesterol, blood pressure, and diagnosed diseases—were used for analysis of total mortality and mortality from each cause of death. There were a total of 302 all-cause deaths, 46 coronary heart disease and stroke deaths, 58 respiratory deaths including 45 pneumonia deaths, and 132 cancer deaths during the follow-up period. Participants were followed for 20,787 person-years after baseline. Prior history of vertebral deformity and hip fracture were not associated with mortality risk. However, more than 2 cm of height loss starting in middle age showed a significant association with all-cause mortality among the study participants (HR = 1.76, 95% CI 1.31 to 2.38, $p = 0.0002$), after adjustment was made for sex, attained age, atomic-bomb radiation exposure, and lifestyle and physical factors. Such height loss also was significantly associated with death due to coronary heart disease or stroke (HR = 3.35, 95% CI 1.63 to 6.86, $p = 0.0010$), as well as respiratory-disease death (HR = 2.52, 95% CI 1.25 to 5.22, $p = 0.0130$), but not cancer death. Continuous HL also was associated with all-cause mortality and CHD- or stroke-caused mortality. Association between height loss and mortality was still significant, even after excluding persons with vertebral deformity. Height loss of more than 2 cm starting in middle age was an independent risk factor for cardiovascular and respiratory-disease mortality among the elderly, even after adjusting for potential risk factors. © 2012 American Society for Bone and Mineral Research.

KEY WORDS: HEIGHT LOSS; MORTALITY; VERTEBRAL DEFORMITY; CORONARY HEART DISEASE; RESPIRATORY DISEASE

Introduction

Many studies have shown increased fracture risk(1–3) and mortality(4–8) after clinical vertebral fracture. Even subjects with no clinical fracture and little pain but with vertebral deformity detected by X-ray showed slightly increased mortality.(9) Other studies, however, showed no evidence of increased mortality among elderly with vertebral fracture.(10) Increased mortality after hip fracture was observed in several studies.(7,11,12)

Kyphosis and height loss are thought to result mainly from underlying vertebral fractures, but have not yet gained much clinical interest other than as markers for osteoporosis.(13–18) Height loss, however, not only could be caused by vertebral fracture, but also to some extent by intervertebral disk degeneration that decreases disk height; osteoarthritic conditions of the spine, hip, or knee, various inflammatory and structural/congenital spinal deformities; and weakness of the back muscles.(19,20) Our previous report showed that height loss and vertebral deformity significantly and independently affected quality of life (QOL) in the elderly, and height loss aggravated QOL more significantly than did vertebral deformity in all domains, even with different effect patterns between height loss and vertebral deformity.(21) The mechanism behind such decreased height loss–associated QOL remains uncertain. Recent reports have suggested that hyperkyphotic posture or marked height loss might predict future fracture risk(22) and mortality.(23–25)

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In the present study, we assessed whether height loss starting in middle age affects all-cause and specific-cause mortality, after taking into account vertebral deformity and hip fracture in Japanese men and women.

Materials and Methods

Data source

Study participants comprised cohort members of the Adult Health Study (AHS), which was established to investigate late health effects of radiation exposure among atomic-bomb survivors in Hiroshima and Nagasaki. The original AHS cohort was comprised of about 20,000 atomic-bomb survivors and their controls selected from residents of Hiroshima and Nagasaki, based on the 1950 national census. Since 1958, the AHS cohort members have been followed through biennial health examinations, including physical examinations; measurements of height, body weight, and blood pressure; and chest X-rays. The health study participants were interviewed by nurses to obtain disease histories and lifestyle information, such as smoking status and alcohol intake. Participation rates in the study were around 70% to 80% throughout the follow-up period. Further information about the cohort and details of the health examinations are available elsewhere.(26–28)

Subjects of this study numbered a total of 2498 individuals (755 men and 1743 women) aged 47 to 91 years old, undergoing physical examinations in Hiroshima during the health study's 1994 to 1995 examination cycle (Fig. 1). Measurements of height, using a stadiometer, were available for all subjects at each examination since 1962. Participants were measured without shoes, with their heels, buttocks, and back against an upright board. The participants with hyperkyphosis were instructed to stand straight and stretch the muscles in their backs as much as possible. We defined height loss starting in middle age (HL) as the difference between a participant's average height in their 40s and height measured in 1994 to 1995. We calculated average height based on from two to five measurements at ages in the 40s for each participant. If a participant did not have data on average height in the 40s, we then defined HL as the difference between his or her average height in the 50s and height measured in 1994 to 1995 (those for whom height in their 50s was used: 12.5%). We also defined marked HL as a difference of more than 2 cm based on results from receiver operating characteristic (ROC) analysis for mortality.

The subjects underwent bone mineral density (BMD) measurements at the spine (L1-4, anteroposterior direction) and the total hip using dual X-ray absorptiometry (DXA, QDR-2000 [Hologic Inc, Waltham, MA, USA]) at the time of the examinations in 1994 1995. Morphometric vertebral deformity was diagnosed by lateral and posterior-anterior chest and spinal X-ray examinations. An experienced radiologist diagnosed vertebral deformity using semi-quantitative procedures.(29,30) We defined "prevalent vertebral deformity" as vertebral deformity at thoracic and lumbar vertebrae diagnosed during the 1994 to 1995 examination cycle, that is, prevalent cases in 1994 to 1995. Diagnosis of hip fracture was based on history-taking by a physician. Pathologic fractures or fractures due to traffic accidents or falls from heights were excluded.

The study follow-up of all participants began in the 1994 to 1995 examination cycle. The accumulation of each participant's person-years of risk ended at the date of death, or the date of the last examination before December 2003. Mortality follow-up was conducted through checks of the vital status of cohort members using the Japanese family registration system. We were thus able to completely follow the mortality status of the cohort members.

Statistical Methods

The rates of many diseases increase as some power of age, so a simple linear adjustment factor would undercontrol for age effects. To avoid this bias, we used an age-stratified Cox proportional hazard analysis, whereby people are assigned to an age stratum reflecting their age at baseline according to five-year age intervals. After confirming the assumption that hazard ratios were proportional, we used an age-stratified Cox proportional

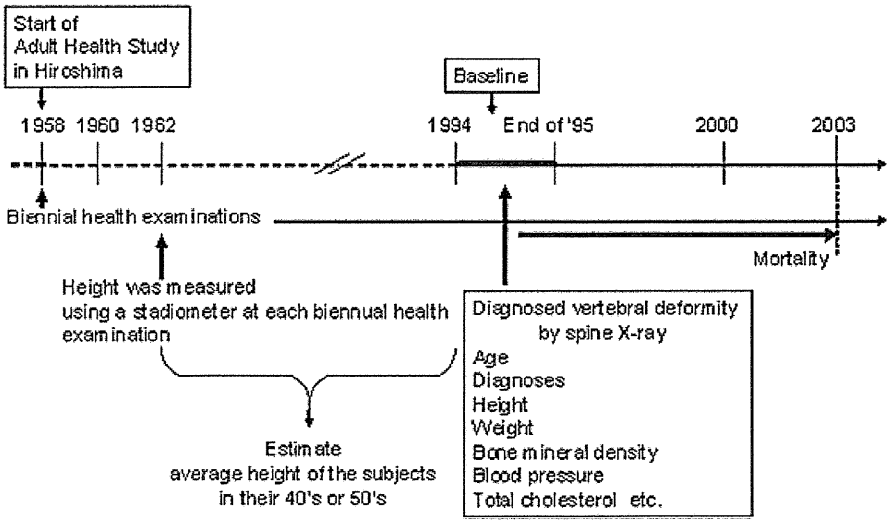

Fig. 1. Timeline of the study.

hazards model to assess the multivariate-adjusted hazard ratio (HR) for mortality. Fitted as categorical variables in the adjustment were assessments obtained at the 1994 to 1995 baseline: prevalent vertebral deformity (yes/no), prevalent hip fracture (yes/no), smoking status (never, current, former smoker, and unknown), alcohol intake (never, current occasional, current often, former drinker, and unknown), preexisting hypertension (yes/no), preexisting hyperlipidemia (yes/no), preexisting diabetes (yes/no), preexisting cardiovascular disease (yes/no), preexisting cancer (yes/no), marked HL ($HL \geq 2$ cm/$HL < 2$ cm). Weight, height, body mass index (BMI: calculated as weight in kilograms divided by height in meters squared), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol, BMD at baseline, radiation dose, and HL were fitted as continuous variables. For each risk factor, we first evaluated all-cause mortality using an univariate model. We then conducted evaluation with multivariate model, including variables found to be significantly associated with all-cause mortality. We obtained a final model after removing nonsignificant terms. As a result, we included such variables as sex, preexisting cancer, preexisting cardiovascular disease (CVD), preexisting diabetes, radiation dose, marked HL, smoking status, and alcohol intake in the model. We also evaluated mortalities caused by coronary heart disease (CHD) or stroke, respiratory disease, pneumonia, and cancer. In the same procedure, we analyzed participants excluding 191 participants with prevalent vertebral deformities. We used individual radiation dose estimates on the Radiation Effects Research Foundation's Dosimetry System 2002 (DS02).(31)

For the mortality analysis, we used the PHREG procedure in SAS program (SAS version 9.1, SAS Institute Inc, Cary, NC, USA), with stratification by 5-year intervals of baseline age, for estimation of the parameters and testing. With consideration for parameter distributions, we tested differences between the alive group and the death group using Student's *t*-tests for continuous variables and χ^2 tests for categorical variables. A value of $p < 0.05$ was used for determination of statistical significance.

Ethical considerations

The present study was carried out in accordance with such national regulations as the *Ethical Guidelines Concerning Epidemiological Studies* (Ministry of Education, Culture, Sports, Science and Technology [MEXT], and Ministry of Health, Labour and Welfare [MHLW]). The study was approved by the Research Protocol Committee and the Human Investigation Committee at the Radiation Effects Research Foundation. At the time of the health examinations, informed consent was obtained from the participants. All participants provided written consent for all aspects of the examinations.

Results

Characteristics of the participants taken at baseline are shown in Table 1. In men, mean ages ± 1 standard deviation (SD) in the 1994 to 1995 examination period for the alive group were 61.2 ± 8.9 years, and 70.3 ± 9.1 years for the death group, ranging from 47 to 91 years. In women, mean ages were 64.7 ± 9.1 years and 73.5 ± 8.9 years, respectively, ranging from 47 to 91 years. Mean age of the "death" group was significantly higher than that of the "alive" group. Mean height loss starting in middle age was 0.83 cm for men and 1.85 cm for women. Figure 2 shows HL distribution by sex. We used ≥ 2 cm as the cut-off value through the sensitivity analysis, and compared the death group with the alive group. Twenty-one men and 170 women had prevalent vertebral fracture, and 12 men and 44 women had prior history of hip fracture in the 1994 to 1995 examination period. Prevalence of diseases at baseline is presented in Table 1. The proportion of individuals with cancer and CVD appeared to be higher in the death group than in the alive group in both men and women. The proportion of individuals with hypertension appeared to be higher in the death group than in the alive group in women. Approximately 90% of women were postmenopausal with an average age at menopause of 47.7 years.

Through December 2003, there were 302 all-cause deaths, 46 CHD and stroke deaths, 58 respiratory-disease deaths including 45 pneumonia deaths, and 132 cancer deaths. Mean follow-up was 8.3 years (Table 2). Participants were followed for 20,787 person-years after baseline. The death rate was 14.5 per 1000 person-years.

Multivariate adjustments were made for variables including physical and lifestyle factors, as described in "Methods," which were further adjusted for estimation of mortality risk (Table 3). After these adjustments, mortality hazard ratio for the marked HL was 1.76 (95% CI, 1.31to 2.38), $p = 0.0002$.

Mortality risk also was analyzed for specific causes of death. Adjusted mortality risk results are presented in Table 4. When causes of death were classified, increased mortality risk for marked HL was observed in CHD- or stroke-caused death ($HR = 3.35$, 95% CI 1.63 to 6.86, $p = 0.0010$) and respiratory disease-caused death ($HR = 2.52$, 95% CI 1.25 to 5.22, $p = 0.0130$), but not cancer-caused death ($p = 0.3143$). No significant increase in mortality from cancer was observed. With significance, continuous HL also was associated with all-cause mortality ($HR = 1.08$ per 1 cm HL increase, 95% CI 1.03 to 1.14, $p = 0.0034$) and CHD- or stroke-caused death ($HR = 1.11$, per 1 cm HL increase, 95% CI 1.00 to 1.23, $p = 0.0465$). Previous history of vertebral deformity and hip fracture were not associated with all-cause mortality risk (Table 4).

The hazard ratios for marked HL were reduced only slightly when the 191 prevalent cases of vertebral deformity were excluded (eg, HR of 1.65, rather than 1.76 for all-cause mortality) (analyses not shown).

Discussion

HL and mortality

This is the first study to show that HL of more than 2 cm increased the risk of all-cause death, CHD- or stroke- and respiratory disease-caused death, but not cancer death, with vertebral fracture assessed simultaneously. Furthermore, the present study showed that HL treated as a continuous variable was

Table 1. Baseline (1994–1995) Characteristics of Study Population by Sex and Vital Status

	Men		Women	
Variable	Alive	Dead	Alive	Dead
Number of subjects	627	128	1569	174
Age (years)	61.2 (8.9)	70.3 (9.1)**	64.7 (9.1)	73.5 (8.9)**
Height (cm)	163.9 (6.0)	161.5 (6.3)**	150.7 (5.7)	147.6 (6.4)**
Weight (kg)	61.4 (8.8)	58.2 (9.2)**	52.8 (8.7)	48.6 (9.3)**
BMI (kg/m^2)	22.8 (2.9)	22.3 (3.0)	23.2 (3.6)	22.3 (3.9)**
height at 40s or 50s (cm)[a]	164.5 (5.8)	162.9 (5.8)**	152.3 (5.2)	150.9 (5.4)**
HL (cm)	0.69 (1.01)	1.50 (1.46)**	1.69 (1.94)	3.34(2.76)**
marked HL (%)	67 (10.7)	42 (32.8)**	556 (35.4)	127 (73.0)**
BMD (g/cm2)				
Spine (L1-4)	0.960 (0.155)	0.972 (0.164)	0.796 (0.154)	0.739 (0.148)**
Total hip	0.739 (0.115)	0.709 (0.109)**	0.626 (0.107)	0.571 (0.093)**
Prevalent hip fracture	7 (1.1%)	5 (3.9%)*	34 (2.2%)	10 (5.8%)**
Prevalent vertebral deformity	15 (2.4%)	6 (4.7%)	138 (8.8%)	32 (18.4%)**
SBP	131.8 (20.3)	136.3 (22.1)*	130.7 (21.1)	136.4 (21.4)**
DBP	80.8 (11.4)	77.3 (15.2)**	77.3 (11.4)	76.4 (12.5)
Total cholesterol	203.2 (34.0)	202.0 (36.7)	221.3 (34.6)	211.1 (42.6)**
Diagnosed disease				
Hypertension	185 (32.9%)	37 (39.0%)	390 (27.7%)	50 (40.7%)**
Hyperlipidemia	44 (7.8%)	6 (6.3%)	194 (13.8%)	15 (12.2%)
Diabetes	96 (15.3%)	28 (21.9%)	162 (10.3%)	23 (13.2%)
CVD	288 (45.9%)	78 (60.9%)**	660 (42.1%)	113 (64.9%)**
Cancer	40 (6.4%)	18 (14.1%)*	153 (9.8%)	33 (19.0%)**
Alcohol intake				
Never	105 (16.7%)	27 (21.1%)	769 (49.0%)	102 (58.6%)*
Current occasional	107 (17.1%)	29 (22.7%)	256(16.3%)	31 (17.8%)
Current often	262 (41.8%)	31 (24.2%)**	113 (7.2%)	9 (5.2%)
Former	14 (2.2%)	8 (6.2%)*	13 (0.8%)	5 (2.9%)*
Unknown	139 (22.2%)	33 (25.8%)	418 (26.7%)	27 (15.5%)**
Smoking status				
Never	88 (15.6%)	9 (11.7%)	920 (64.5%)	67 (58.6%)
Current	210 (33.5%)	42 (32.8%)	104 (6.6%)	11 (6.3%)
Former	167 (26.6%)	35 (27.4%)	47 (3.0%)	6 (3.5%)
Unknown	152 (24.3%)	36 (28.1%)	406 (25.9%)	55 (31.6%)*
Radiation dose (Gy)	0.382 (0.634)	0.432 (0.608)	0.297 (0.514)	0.407 (0.568)

HL, historical height loss starting in middle age; BMI, body mass index; BMD, bone mineral density; SBP, systolic blood pressure; DBP, diastolic blood pressure; CVD, cardiovascular disease.

Mean (SD).

With consideration for parameter distributions, we tested difference between death or alive using *t*-test for height, weight, BMI, height at 40s or 50s, marked HL, BMD, SBP, DBP, total cholesterol, radiation dose, using a Wilcoxon test for age, and using χ^2-test for prevalence of hip fracture, prevalence of vertebral deformity, alcohol intake, smoking status, and diagnosed diseases.

[a] Longitudinal data of height are available for all study participants of the cohort since 1962. We defined height loss starting in middle age (HL) as the difference between a participant's average height in his or her 40s and height measured in 1994 to 1995.

*$p < 0.05$.

**$p < 0.01$.

associated with significantly increased risk of all-cause mortality and CHD- or stroke-caused mortality.

Our previous report(21) showed that height loss and vertebral deformity affected QOL significantly and independently in the elderly. Even after excluding individuals with vertebral deformity, height loss was associated with decreased QOL. Furthermore, it is observed that factors other than vertebral deformity, such as intervertebral disk degeneration and osteoarthritic conditions, also caused height loss. In the present study, we observed association between mortality and height loss starting in middle age, but not prevalent vertebral deformity. The presence of certain adverse health conditions, for example poor muscle strength, possibly causing height loss may be implicated.

Wannamethee et al. followed 4213 men measured for height at ages 40 to 59 and again 20 years later, observing 760 deaths occurring after six more years. In the aforementioned study, Wannamethee et al. described how osteoporotic disease complicated by vertebral fractures was not likely to explain

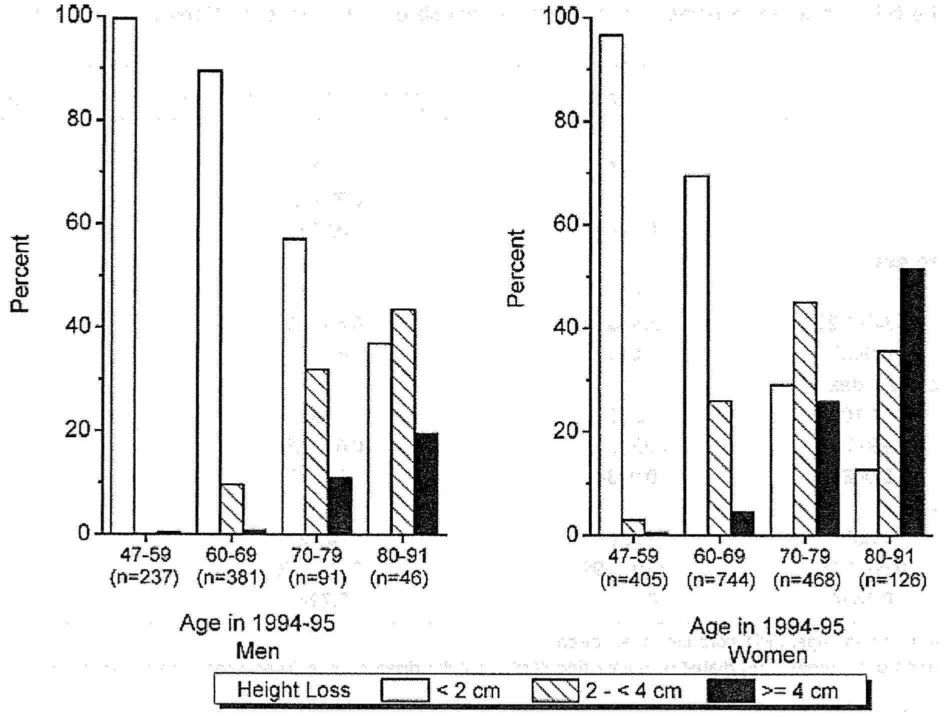

Fig. 2. Percentage of those with height loss starting in middle age, for men and women.

increased mortality risk associated with height loss. Poor muscular strength and low skeletal muscle mass have been linked to bone loss and poor bone structure in men, which could result in height loss.(32) The increased risk of CHD and all-cause mortality associated with height loss may thus reflect poor muscular strength and skeletal muscle mass loss from aging (sarcopenia), both of which have been shown to be predictors of mortality.(33–35) Wannamethee et al. also discussed the idea that height loss might serve as a marker for sarcopenia and frailty.(24) Hyperkyphosis, commonly used as a marker of aging, is frequently observed in the elderly. It is known that hyperkyphosis is associated with restrictive pulmonary disease(36) and poor physical function.(37–39) These findings suggest that hyperkyphosis also might be associated with occurrence of other states of poor health. Some studies have suggested association between kyphosis and mortality.(22,23,25) Recently, Kado et al.(25) conducted a prospective cohort study of 610 older white women who were diagnosed with kyphosis, and assessed mortality rates over an average follow-up of 13.5 years. They concluded that hyperkyphosis predicted increased risk of death independent of prevalent vertebral fractures. In addition, Kado et al.(23) followed 1353 men and women over a period of 4.2 years, with mortality and cause of death confirmed by review of death certificates. They observed that older men and women with hyperkyphotic posture had higher mortality rates.

Table 2. Deaths Observed Between Baseline Examinations in 1994 to 1995 and December 2003

	Men	Women	Total
Number of individuals	755	1743	2498
Number of all-cause deaths	128	174	302
Person-years	6188	14,599	20,787
Mean follow-up period (years)	8.2	8.4	8.3
Death rate (per 1000 person-years)	20.7	11.9	14.5
Number of deaths by cause			
Coronary heart disease and stroke	21	25	46
Respiratory disease	27	31	58
Pneumonia	19	26	45
Cancer	66	66	132

Table 3. Hazard Ratios (HRs) Using Age-Stratified Cox Regression Analysis for All-Cause Mortality[a]

Baseline factor in 1994–1995		Hazard ratio	95% CI
Sex	Women/Men	0.39	0.28–0.53**
Marked HL	Yes/No	1.76	1.31–2.38**
Preexisting cancer	Yes/No	1.55	1.12–2.15**
Preexisting CVD	Yes/No	1.32	1.03–1.71*
Preexisting DM	Yes/No	1.48	1.07–2.05*
Radiation dose	1 Gy increment	1.22	1.01–1.48*
Alcohol habit	Current occasional/ Never	1.14	0.82–1.57
	Current often/Never	0.55	0.36–0.84**
	Former/Never	1.86	1.02–3.39*
	Unknown/Never	0.71	0.51–0.99*

CI, confidence interval; HL, height loss starting in middle age; CVD, cardio vascular disease.

[a] The analysis included all variables in the table simultaneously.

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

Table 4. Hazard Ratios (HRs) Using Age-Stratified Cox Regression Analysis by Continuous HL, Marked HL, Vertebral Fracture, and Hip Fracture for Mortality

Death	Continuous HL	Marked HL	Prevalent Vertebral Deformity	Prevalent Hip Fracture
All-cause death				
HR	1.08	1.76	1.13	1.26
95% CI	1.03–1.14	1.31–2.38	0.78–1.64	0.72–2.18
p value	0.0034	0.0002	0.5267	0.4183
CHD- or Stroke-caused death				
HR	1.11	3.35	1.89	1.97
95% CI	1.00–1.23	1.63–6.86	0.86–4.16	0.67–5.82
p value	0.0465	0.0010	0.1123	0.2186
Respiratory disease–caused death				
HR	1.10	2.52	1.35	0.71
95% CI	0.99–1.23	1.25–5.22	0.63–2.89	0.17–2.95
p value	0.0684	0.0130	0.4378	0.6316
Cancer-caused death				
HR	1.05	1.26	0.92	1.17
95% CI	0.96–1.15	0.80–1.99	0.48–1.76	0.47–2.92
p value	0.2634	0.3143	0.7944	0.7367

HL, height loss starting in middle age; CHD, coronary heart disease.
Adjusted for sex, radiation dose, preexisting diabetes, preexisting cardiovascular disease, preexisting cancer, smoking status, and alcohol intake.

For CHD mortality, our results are consistent in principle with the results of the two previous studies. Additionally, we observed association between respiratory disease mortality and height loss starting in middle age in both men and women. Furthermore, height loss was associated with mortality even after individuals with vertebral deformity were excluded. The mechanism regarding how height loss might be associated with subsequent mortality is not currently well understood. Resulting height loss could affect normal functioning of the respiratory and gastrointestinal systems,(13) which in turn might lead to early satiety, poor nutritional status, and weight loss.(13) Height loss also appears to be related to sarcopenia,(32) which is defined as the loss of skeletal muscle mass and strength with aging and is associated with weight loss(40–43) and increased mortality.(33–35)

We found increased mortality associated with marked HL due to CHD or stroke and respiratory diseases, but no increased cancer mortality. Kado et al. reported that hyperkyphotic posture was specifically associated with increased rate of death due to atherosclerosis.(23) Browner et al. reported that low bone mass was significantly associated with death from CVD and specifically stroke.(44) Some evidence indicated similar pathophysiological mechanisms underlying both osteoporosis and cardiovascular disease.(45,46) Risk factors such as age, diabetes, hypertension, inflammation, dislipidemia, homocystienemia, and estrogen deficiency are prevalent in both disorders.(44,47)

Osteoporotic fracture and mortality

Bliuc et al.(48) reported that excess mortality was highest immediately after almost all fragility fracture events and then declined. The researchers observed that 30% of all post–hip-fracture deaths occurred in the first six months and 21% in the next 18 months. Other studies reported that increased mortality after hip and vertebral fractures was consistent over the initial five-year period.(4,6,8,11)

In the present study, prevalent morphometric vertebral deformity and prevalence of hip fracture were not associated with increased mortality. Inconsistency between our report and many previous studies can be explained by differences between incidence and prevalence of fracture, because prevalent vertebral deformity and hip fracture in our study included those cases that had developed many years in the past. In addition, in the follow-up period, such differences as whether or not to include morphometric vertebral fracture and adjustment of potential confounders might have resulted in the inconsistency.

Strengths and limitations

One strength of this study is that the investigation was based on measured height using consistent methods throughout biennial health examinations conducted since 1962, thus reducing measurement errors. Since mean height in most age groups has increased recently in many regions around the world, including Japan, height loss would be overestimated in cross-sectional studies, and bias would be significant if recalled height were used.(49) Our study was carried out using measured height at ages 40 to 49 and again some years later in a population-based study of men and women. Second, mortality follow-up has been carried out through checks of the vital status of cohort members using the Japanese family registration system. We were thus able to completely follow mortality of the cohort members.

There are some limitations to our findings. First, baseline data for physical activity and lung function were not available. Second, diagnosis of hip fracture was based on history taking by a physician, not X-ray examination. Furthermore, participants were atomic bomb survivors and thus not representative of the general Japanese population, although we adjusted for radiation, and there are no indications from earlier studies of this cohort that radiation affected BMD and fracture frequency.(38,48,50)

Conclusion

In conclusion, height loss starting in middle age is considered to be a factor associated with CVD and respiratory-disease mortality, independent of vertebral deformity, in Japanese elderly men and women. Further studies will be needed to elucidate the mechanisms behind such findings. Although the mechanisms are unknown, height loss, regardless of its causes, is a clinically important finding.

Disclosures

All the authors state that they have no conflicts of interest.

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Authors' roles: N Masuna and S Fujiwara made substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data. F Kasagi, I Takahashi, and M Yamada contributed to acquisition of data. T Nakamura made contributions to interpretation of data.

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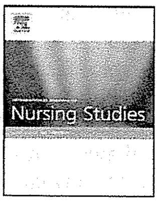

The effects of multidimensional exercise treatment on community-dwelling elderly Japanese women with stress, urge, and mixed urinary incontinence: A randomized controlled trial

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ABSTRACT

Background: Urinary incontinence is one of the most prevalent health problems and a significant cause of disability and dependence in the elderly. Pelvic floor exercise is effective in reducing stress urinary incontinence, but few studies have investigated the effect of behavioral management on urge and mixed incontinence.

Objectives: To determine the effects of multidimensional exercise treatment on reducing urine leakage in elderly Japanese women with stress, urge, and mixed urinary incontinence.

Design: Randomized controlled, follow-up trial.

Settings: Urban community-based study.

Participants: 127 community-dwelling women aged 70 and older with stress, urge, and mixed urinary incontinence were randomly assigned to the intervention ($n = 63$) or the control group ($n = 64$).

Methods: Urine leakage and fitness data were collected at baseline, and after the intervention and follow-up. The intervention group received a multidimensional exercise treatment twice a week for 3-month. After treatment, the participants were followed for 7-month.

Results: There were significant differences in changes of functional fitness and incontinence variables between the intervention and control groups. The intervention group showed urine leakage cure rates of 44.1% after treatment and 39.3% after follow-up ($\chi^2 = 21.96$, $p < 0.001$); whereas, the control group showed no significant improvement. The multidimensional exercise treatment was significantly effective in decreasing all three types of urinary incontinence. However, the effects of the exercise treatment were greater on stress urinary incontinence than on urge or mixed urinary incontinence. At the 7-month follow-up, while cure rates of all three types of urinary incontinence were significantly maintained, a slight reversal was seen only in the urge and mixed urinary incontinence ($\chi^2 = 10.28$, $p = 0.008$). According to the logistic regression model, urine leakage volume (adjusted odds ratio OR = 0.69, 95% confidence interval CI = 0.39–0.98), compliance (OR = 1.03, 95%CI = 1.01–1.16), and BMI reduction (OR = 0.67, 95%CI = 0.48–0.89) were significantly associated with the cure of urine leakage after intervention. The cure rate of urine leakage after the follow-up was significantly associated with compliance (OR = 1.13, 95%CI = 1.02–1.29) and BMI reduction (OR = 0.78, 95%CI = 0.60–0.96).

Conclusions: The intervention group showed higher urine leakage cure rates than control group. This result suggests that multidimensional exercise strategies may be effective for all three types of urinary incontinence. BMI reduction and compliance to the intervention was the consistent predictor for the effectiveness of the exercise treatment.

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What is already known about the topic?

- Several factors such as overweightness, high body mass index, and increased abdominal fat have been associated with higher risk of urinary incontinence.
- Behavioral management is effective in the treatment of stress urinary incontinence and is therefore recommended as a first-line therapy.
- Compliance has a positive influence on the effects of the exercise treatment.

What this paper adds

- Multidimensional exercise treatment targeting pelvic floor muscles and abdominal fat and/or BMI reduction are equally effective in reducing stress, urge, and mixed urinary incontinence after the intervention and follow-up.
- BMI reduction as well as compliance to the prescribed exercise regimen was the most consistently significant predictors of the short- and long-term effectiveness to the behavioral therapy.
- Multidimensional exercise treatment should be considered for the elderly as a strategy for reducing incontinence and improving functional capacity.

1. Introduction

Urinary incontinence (UI) in elderly people is a common condition that contributes greatly to the loss of independence, decrease in quality of life, restriction of social activities, and increase in risk for hospitalization or long-term care. The estimated prevalence of UI ranged from 17 to 55% depending on the definition of UI, the population characteristics, and the methodological approach (Thom, 1998). A number of methods are used to treat or deal with UI. Pelvic floor muscle (PFM) exercise, devised by Kegel (1948), is recommended as a first line of treatment in the management of stress UI and many investigators have validated the short- and long-term effects on stress UI (Cammu and Van Nylen, 1995; Goode et al., 2003; Kim et al., 2007). PFM exercise is hypothesized to enhance urethral resistance by increasing the strength and endurance of the periurethral and perivaginal muscles and by improving the anatomic support given to the bladder neck and proximal urethra (Kegel, 1951; Bo et al., 1999). One previous study found that PFM exercise reduces urine leakage in urge and mixed UI because of inhibition of the bladder reflex associated with PFM contraction; however, this study had no control group (Nygaard et al., 1996).

Several studies have reported that obesity and high BMI are associated with UI (Bump et al., 1992; Brown et al., 1999). One study reported objective and subjective resolution of stress and urge UI after surgically inducing weight loss in morbidly obese women (Bump et al., 1992). These results suggest that weight reduction is desirable for UI treatment (Subak et al., 2005; Auwad et al., 2008; Wing et al., 2010). We hypothesized that fitness exercises focused on strengthening the abdominal muscles would reduce abdominal fat and/or BMI, and thereby reduce abdominal wall pressure, intravesicular pressure, and the risk of UI in elderly women.

We conducted a randomized controlled trial to measure the effects of a multidimensional exercise treatment (FPM and fitness exercises) on urine leakage episodes in community-dwelling elderly Japanese women with stress, urge, and mixed UI, and to identify the factors that influence the effectiveness of the trial.

2. Methods

2.1. Subjects

The subjects in this study were randomly selected from the Basic Resident Register of 5935 women aged 70 and older that resided in the Itabashi ward (district) of Tokyo as of April 1, 2006. Information about the study was mailed to potential subjects. The baseline survey was conducted in November 2006, and 957 (16.1%) women participated. Out of the participants, 416 (43.5%) were experiencing some urinary incontinence, and 194 (46.6%) were classified as experiencing urine leakage more than once a week.

The inclusion criteria were: (1) suffering from urge, stress, or mixed UI; (2) being $\geq$70 years old; (3) having urine leakage episodes more than once a week; and (4) completing a 1-week urinary diary. The exclusion criteria included (1) an unclear UI type; (2) having urine leakage episodes less than once a week; (3) not completing the 1-week urinary diary; (4) impaired cognition (a Mini-Mental State Examination score of <24) (Folstein et al., 1975; McDowell et al., 1999) and (5) unstable cardiac conditions such as ventricular dysrhythmias, pulmonary edema, or other musculoskeletal conditions. Sixty seven (34.5%) of the potential participants were excluded because they were classified into one or more of the exclusion criteria. The study protocol was approved by the Clinical Research Ethics Committee of Tokyo Metropolitan Institute of Gerontology (TMIG). The procedures were fully explained to all participants, and written informed consent was obtained (Fig. 1).

2.2. Randomization

Randomization was performed after the baseline assessment and completion of the 1-week urinary diary, and any variable that identified personal information was not included in the randomization process. The assigned identification numbers of 127 participants (stress = 37, urge = 47, and mixed = 43) were divided into two groups based on the computer-generated random numbers. One group was randomly assigned to the intervention group ($n = 63$), and the other to the control group ($n = 64$). There was no attempt to equalize the size of the groups based on their characteristics or to recruit subjects with specific characteristics. The randomization procedure was blinded, and the investigators that evaluated the effects of the exercise treatment were blind to the allocation of interventions.

2.3. Outcome measures

The primary outcome of this trial was the cure rate of urine leakage episodes, which was assessed by the self-

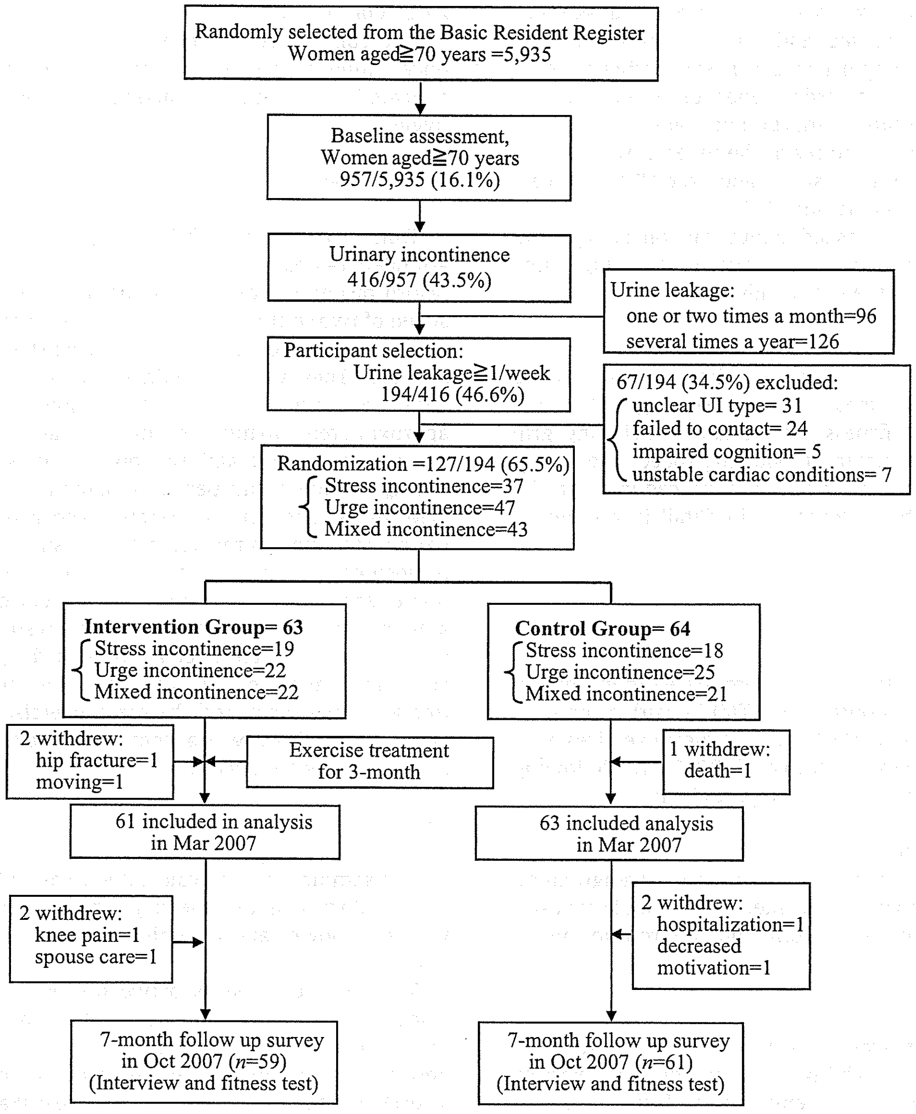

Fig. 1. Flow of the participants through the randomized controlled trial of exercise treatment and analyses.

reported urinary diary data (Wyman et al., 1988; Locher et al., 2001). The effects of the exercise treatment on urine leakage episodes were assessed based on the changes in the 5-point scale (1 = no urine leakage, 2 = less than once a week, 3 = once a week, 4 = two or three times a week, and 5 = everyday) recorded in the 1-week urinary diary, which was obtained pretreatment, after the 3-month exercise and 7-month follow-up. Complete cessation of urine leakage episodes was defined as cured.

2.3.1. Interview survey and urinary diary

A face-to face interview was conducted to assess temporary UI conditions based on the modified International Consultation on Incontinence Questionnaire (ICIQ) (Avery et al., 2004). The ICIQ was easily completed with low levels of missing data (mean 1.6%), good construct validity, and acceptable convergent validity. Reliability was good with moderate to very good stability in test-retest analysis and a Cronbach's alpha of 0.95 (Avery et al., 2004; Gotoh et al., 2009). The first question was "Have you experienced urine leakage during the previous year?" If the person responded that urine leakage episodes occurred more than once a week, to confirm the pretreatment frequency of urine leakage episodes, potential subjects were provided with a 1-week urinary diary. The subjects documented the time of every void and urine leakage episode, as well as the amount and circumstance of each episode. To confirm the changes of frequency, the urine leakage scores were calculated based on the self-reported 1-week urinary diary as follows: 0 = no urine leakage, 1 = less than once a week, 2 = once a week, 3 = two or three times a week, and 4 = every day.

UI type was classified based on inquiries about urine leakage in relation to 8 possible antecedents (Avery et al., 2004). Stress UI was recorded when urine leakage was associated with increased abdominal pressure such as coughing, sneezing, or participating in some other physical activity. Urge UI was recorded when urine leakage was reported to be associated with running water or an urge to void and not being able to reach the toilet in time. When the characteristics of both stress and urge UI types were present, it was defined as mixed UI.

The subjects were asked about the onset age and duration of UI, frequency of daytime and nighttime voiding, and chronic medical conditions.

2.3.2. Functional fitness test

Measurements of height and body weight were converted to body mass index (BMI, kg/m^2), waist circumference, and fitness test variables including grip strength, usual and maximum walking speed, and seated hip adductor muscle strength. The procedures for the fitness tests have been described in detail in a previous report (Kim et al., 2007).

2.4. Intervention

2.4.1. Intervention group

The participants attended an exercise treatment session 2 times a week for 3-months at the TMIG health promotion classes. The protocols of the PFM and fitness exercises have been published previously (Kim et al., 2007). The following exercises were performed by the participants.

2.4.2. Stretching exercise

Before the PFM exercise and muscle strengthening training, the participants performed 5–10 min of warm-up and stretching exercises, including shoulder rotation, waist rotation, and others.

2.4.3. PFM exercises

The subjects were trained to exert force only on the PFM without excessively straining the abdomen. The exercise regimen was designed to strengthen the fast- and slow-twitch muscle fibers located on the pelvic floor. The participants were initially instructed to perform 10 fast contractions (3 s) with a 5-s relaxation and 10 sustained contractions (8–10 s) with a 10-s relaxation between the contractions. The PFM exercise was performed in the sitting, lying, and standing positions with the legs apart, while emphasizing contraction of the PFM and relaxation of the other muscles.

2.4.4. Fitness exercises

Strength training of the thigh and abdominal muscles was performed between the PFM exercises. The fitness exercise included: lifting the foot (or both feet) and pointing toes then slowly pulling toes back toward the shin, slowly lifting one knee (or both knees), tilting the pelvis backward and forward, lifting the buttocks while on the back with the knees bent, raising one leg while lying on the back, and others. The ball exercises included actions like sitting on the ball, rolling the ball and the pelvis forward and backward, and moving from side to side, squeezing the thighs, lifting the ball with the legs, and others.

2.4.5. Control group

The control group received general education classes once a month for three months, where participants were educated on cognitive function, osteoporosis, and oral hygiene.

2.5. Follow-up

During the 7-month follow-up period, the participants attended 1-h exercise classes once a month at the TMIG health promotion center. The home-based program consisted of two to three sets of the 13 exercises and the PFM exercises that they had learned during the group exercise sessions. They were encouraged to perform the home-based exercises at least three times per week for approximately 30 min per day. To accurately monitor the exercise times and the number of sets performed during the follow-up period, a pamphlet illustrating the PFM and strengthening exercises and a recording sheet were distributed to the subjects. The subjects were asked to document the time and sets of exercises performed at home each day, the urine leakage episodes, and the amount and circumstances of each episode. The record sheets were collected once a month at the group exercise class and analyzed to calculate the mean exercise frequency per week and the mean exercise time per day. When a participant was absent from an exercise class, we mailed the record sheet to the individual.

2.6. Data analysis

The sample size was calculated to allow detection of a 20.0% reduction in urine leakage episodes between groups with 80% power and a significance level of 0.05 (Burgio et al., 2002).

The mean differences between groups were analyzed using the *t*-test for continuous variables and the chi-square test for categorical variables. To evaluate the differences between the groups in the effects of the intervention on selected continuous variables and urine leakage score at the baseline, after the 3-month exercise, and at the 7-month follow-up, a repeated-measures two-way analysis of variance (ANOVA) was performed. Significant interactions were analyzed to determine whether the effects were greater in the intervention or control group. A repeated-measures one-way ANOVA was also performed to evaluate the within group. A *post hoc* analysis was performed using the Scheffe method. The generalized estimating equation was used to compare the effects between the groups after 3-month exercise and at the 7-month follow-up on the cure rate of UI. The Kruskal–Wallis test was used to evaluate the differences of UI type in the effect of the exercise treatment on urine leakage episodes. The Cochran Q-test was used to evaluate the within-group differences in the effect of the exercise program on urine leakage episodes for baseline, 3-month exercise, and follow-up data.

Multiple logistic regressions were performed to identify variables that were associated with cured urine leakage after 3-month of exercise and at the 7-month follow-up after intervention. All analyses were performed using SPSS software, Windows version 15.0 (SPSS, Inc., Tokyo, Japan).

Table 1
Selected variables characteristics of participants at baseline by study group.

Variables[a]	Intervention group ($n = 63$)	Control group ($n = 64$)	p Value[b]
Age (yr)	76.1 ± 4.3	75.7 ± 4.4	0.625
Height (cm)	148.4 ± 5.8	148.9 ± 6.2	0.639
Body weight (kg)	51.8 ± 8.7	54.0 ± 7.9	0.202
BMI (kg/m^2)	23.4 ± 3.3	24.3 ± 3.0	0.195
Waist circumference (cm)	78.9 ± 10.2	78.5 ± 9.9	0.853
Grip strength (kg)	19.2 ± 4.6	18.6 ± 4.7	0.561
Adductor muscle strength (kg)	20.6 ± 6.9	21.5 ± 4.8	0.502
Usual walking speed (m/s)	1.2 ± 0.3	1.1 ± 0.3	0.282
Maximal walking speed (m/s)	1.7 ± 0.4	1.7 ± 0.4	0.423
Onset age of incontinence (yr)	71.3 ± 7.6	71.0 ± 7.1	0.865
Period of incontinence (year)	4.8 ± 6.4	4.6 ± 6.0	0.890
Frequency of toilet in daytime (times)	7.7 ± 3.1	7.4 ± 2.3	0.525
Frequency of toilet in night (times)	1.9 ± 1.2	1.8 ± 1.3	0.581
Frequence of urine leakage (%)			
Everyday	46.0	50.0	0.714
1 every two days	11.1	7.8	
More than once a week	42.9	42.2	
Amount of urine leakage, large (%)	23.8	32.8	0.210
Chronic medical conditions, yes (%)			
Hypertension	57.1	57.8	0.918
Hyperlipemia	36.5	40.6	0.712
Diabetes	17.5	15.6	0.780

[a] Data are presented as M (mean) and SD (standard deviation) for continuous variables, and percentage for categorical variables. BMI = body mass index.
[b] Two group t-tests for continuous variables and chi-square test for categorical variables.

3. Results

3.1. Subjects characteristics and compliance

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

The attendance rate during the 3-month exercise treatment ranged from 63.5% to 81.1%, with a mean of 70.3%. Seven participants (intervention group = 4, control group = 3) were unable to complete the study after

Table 2
Comparison of functional fitness and incontinence variables between intervention ($n = 59$) and control ($n = 61$) after 3-months of exercises and the 7-month follow-up.

Variables[a]	G[b]	Baseline	3-month exercise	7-month follow-up	ANOVA[c] G × T	p Value
Body Weight (kg)	I	52.0 ± 8.9	51.9 ± 8.8	50.9 ± 8.9	$F = 5.78$	0.018
	C	53.9 ± 8.2	53.9 ± 8.2	53.9 ± 8.1		
BMI (kg/m^2)	I	23.7 ± 3.4	23.5 ± 3.0	23.2 ± 3.1	$F = 11.49$	0.001
	C	24.1 ± 2.9	24.0 ± 2.7	24.4 ± 3.4		
WC (cm)	I	78.8 ± 10.3	77.8 ± 9.7	77.7 ± 9.9	$F = 4.06$	0.041
	C	79.3 ± 10.4	79.2 ± 10.5	78.9 ± 9.6		
UWS (m/s)	I	1.2 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	$F = 2.79$	0.099
	C	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.2		
MWS(m/s)	I	1.7 ± 0.4	1.8 ± 0.4	1.8 ± 0.4	$F = 5.10$	0.027
	C	1.7 ± 0.4	1.6 ± 0.3	1.6 ± 0.4		
GS (kg)	I	19.0 ± 4.7	20.7 ± 5.0	19.8 ± 5.7	$F = 0.37$	0.547
	C	19.0 ± 4.2	20.2 ± 3.5	19.5 ± 3.8		
AMS (kg)	I	20.5 ± 7.1	24.1 ± 7.7	24.3 ± 7.9	$F = 11.00$	0.001
	C	21.2 ± 4.8	22.1 ± 4.8	21.8 ± 4.9		
ULS (point)	I	5.0 ± 1.0	3.0 ± 2.0	3.6 ± 2.2	$F = 7.64$	0.007
	C	5.1 ± 1.0	4.4 ± 1.6	4.8 ± 1.6		
Cure of urine leakage	I	0.0	44.1	39.3	21.96	<0.001
	C	0.0	1.6	1.6		
Cure of urine leakage in intervention group	Stress	0.0	63.2[d]	66.7[e]	15.77	<0.001
	Urge	0.0	35.0[d]	26.1[e]	7.49	0.032
	Mixed	0.0	40.1[d]	30.0[e]	9.56	0.016

[a] Data are presented as mean and standard deviation.. WC = waist circumference; UWS = usual walking speed; MWS = maximum walking speed; GS = Grip strength; AMS = adductor muscle strength; ULS = urine leakage score.
[b] G = group, I = intervention group, C = control group.
[c] ANOVA = analysis of variance, T = time. Chi-square and p values are from generalized estimating equation. Conhran's Q-value.
[d] Kruskal–Wallis test: chi-square = 1.99, $p = 0.391$.
[e] Kruskal–Wallis test: chi-square = 10.28, $p = 0.008$. (Scheffe's *post hoc* = stress > urge, mixed urinary incontinence).

randomization due to hip fracture ($n = 1$), moving ($n = 1$), knee pain ($n = 1$), spouse care ($n = 1$), death ($n = 1$), hospitalization ($n = 1$), and decreased motivation ($n = 1$) (Fig. 1). The exercise frequency during the 7-month follow-up period was reported to be every day in 35.7% of the subjects, two to three times a week in 42.9%, and once or less per week in 21.4%. The mean exercise time was 29.3 min, and the mean number of contractions of the PFM was 52 times a day during the 7-month follow-up period.

3.2. Functional fitness and urinary incontinence

The comparison of the effects of the treatment on selected variables between the intervention and control group are summarized in Table 2. A repeated measures ANOVA and generalized estimating equation revealed significant increases in adductor muscle strength ($F = 11.00$, $p = 0.001$) and maximum walking speed ($F = 5.10$, $p = 0.027$) after the 3-month exercise and at the 7-month follow-up in the intervention group compared with the control group. Body weight ($F = 5.80$, $p = 0.018$), BMI ($F = 11.49$, $p = 0.001$), waist circumference ($F = 4.06$, $p = 0.041$), and the urine leakage score ($F = 7.64$, $p = 0.007$) decreased significantly in the intervention group, whereas no significant changes were seen in the control group. The women who reported no urine leakage episodes in their 1-week urinary diaries accounted for 44.1% of the intervention group and 1.6% of the control group after the 3-month exercise treatment, and 39.3% of the intervention group and 1.6% of the control group at the 7-month follow-up ($\chi^2 = 21.96, p < 0.001$). After the 3-month exercise, the cure rates of urine leakage increased significantly across the three subgroups of UI. At the 7-month follow-up, although slight decreases were observed in the cure rates of urine leakage related to urge and mixed UI, the cure rates of all three subtypes; stress (Q-value = 15.77, $p < 0.001$), urge (Q-value = 7.49, $p = 0.032$), and mixed (Q-value = 9.56, $p = 0.016$) UI were significantly maintained. However, the efficacy of the exercise treatment on stress UI was greater than the effects on urge or mixed UI after 7-month follow-up ($\chi^2 = 10.28$, $p = 0.008$; *post hoc* = stress > urge, mixed UI).

Before treatment, the urine leakage score was similar between the groups (Fig. 2). However, the urine leakage score significantly decreased after the 3-month exercise treatment and at the 7-month follow-up in the intervention group compared with the control group ($F = 7.22$, $p = 0.009$) (A). The effect of the treatment across the intervention period was assessed for each subgroup of UI (B). At baseline, the urine leakage scores were similar across the three subgroups, although the mixed UI subgroup had a slightly higher score. A repeated measures ANOVA also showed significant subgroup by time interaction ($F = 5.13$, $p = 0.008$). The stress subgroup showed a significant decline in urine leakage score after the 3-month exercise treatment and the 7-month follow-up ($F = 8.23$, $p < 0.001$). The urge ($F = 3.46$, $p = 0.034$) and mixed ($F = 4.10$, $p = 0.019$) subgroups each also showed significant declines in urine leakage scores after the 3-month exercise, although slight reverse patterns of increase were observed at the 7-month follow-up, these changes were not significant.

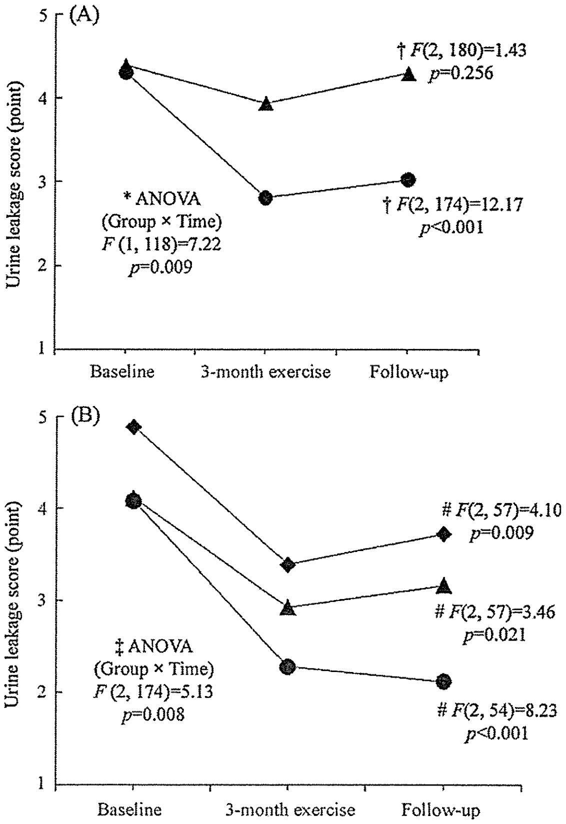

Fig. 2. Changes in the mean urine leakage score on a 5-point scale based on self-reported urinary diaries at the baseline, after 3-months exercise, and at the 7-month follow-up. (A) (●) intervention group; (▲) control group. (*) A comparison of urine leakage scores between the intervention and control groups ($F = 7.22$, $p = 0.009$. (†) A comparison of urine leakage scores at the baseline (b), after 3-months exercise (p), and at the 7-month follow-up (f) within group: intervention group ($F = 12.17$, $p < 0.001$; Scheffe's *post hoc* = b >p, f); control group ($F = 1.43$, $p = 0.256$). (B) (●) Stress incontinence; (▲) urge incontinence; (◆) mixed incontinence. (‡) A comparison of urine leakage scores among stress, urge, and mixed urinary incontinence in the intervention group. # A comparison of urine leakage scores at the baseline (b), after 3-months exercise (p), and at the 7-month follow-up (f) within group: stress incontinence ($F = 8.23$, $p < 0.001$; Scheffe's *post hoc* = b > p, f); urge incontinence ($F = 3.46$, $p = 0.021$; Scheffe's *post hoc* = b > p, f); mixed incontinence ($F = 4.10$, $p = 0.009$; Scheffe's *post-hoc* = b > p, f).

3.3. Predictor variables

As shown in Table 3, the amount of urine leakage (OR = 0.69, 95%CI = 0.39–0.98), compliance to the exercise treatment (OR = 1.03, 95%CI = 1.01–1.16), and BMI reduction (OR = 0.67, 95%CI = 0.48–0.89) were significantly associated with being cured of urine leakage after the 3-month exercise. The cure of urine leakage at the 7-month follow-up was significantly associated with compliance (OR = 1.13, 95%CI = 1.02–1.29) and BMI reduction (OR = 0.78, 95%CI = 0.60–0.96).

4. Discussion

While the ratio of participation by the random population was very low, a baseline of 957 people is an

Table 3
Adjusted OR for cure of urine leakage after intervention and the 7-month follow-up.

	After 3-month exercise			After 7-month follow-up		
Variable	Adjusted OR[a]	95%CI	*p* Value	Adjusted OR[a]	95%CI	*p* Value
Amount of urine leakage	0.69	0.39–0.98	0.049	0.78	0.26–1.88	0.600
Frequency of urine leakage	1.16	0.24–5.79	0.856	1.63	0.73–4.01	0.248
Compliance to exercise	1.03	1.01–1.16	0.048	1.13	1.02–1.29	0.031
Decreased of BMI	0.67	0.48–0.89	0.011	0.78	0.60–0.96	0.028
Increased of walking speed	0.97	0.91–1.04	0.414	0.99	0.94–1.06	0.913
Period of urine leakage	1.01	0.91–1.13	0.919	1.01	0.91–1.14	0.913

[a] Dependent variable; cure of urinary incontinence: 1 = cured, 0 = urine leakage. Independent variables: (a) Amount of urine leakage: large amount, 1 = requiring change of undergarments or soaked outerwear, small amount, 0 = wet undergarments. (b) Frequency of urine leakage: high frequency 1 = every day, low frequency, 0 = less than once every two days. (c) Compliance to exercise: full compliance, 1 = more than 60.0% attendance, partial compliance, 0 = less than 59.9% attendance. OR = odds ratio; CI = confidence interval.

acceptable sample size for analysis of UI in the community-dwelling elderly. Analysis of the efficacy of a 3-month exercise treatment for UI, demonstrated that exercise treatment was equally effective in reducing stress, urge, and mixed UI; although the cure rates of urine leakage were maintained until the 7-month follow-up for all the three types of UI, the efficacy of the treatment was greater for stress UI than urge or mixed UI in the intervention group. However, the changes of UI cure rate were not significant in the control group. These results suggest that improvements in primary outcomes may be observed in an intervention group but such improvements may not be expected in a control group.

PFM exercise is known to be an effective treatment for stress UI (Bo et al., 1990; McDowell et al., 1999; Kim et al., 2007). However, a previous study reported that the mean number of incontinent episodes per day decreased not only stress but also urge and mixed UI, so PFM exercises are equally effective against all three urodynamic conditions, and no urodynamic test is necessary before behavioral treatment (Nygaard et al., 1996). Another study showed that behavioral training achieved comparable improvements in urge UI (Burgio et al., 2002). These previous studies had no control or follow-up data. Recently, one study suggested that decrease in BMI and increase in walking speed may contribute to the decline in stress UI episodes, but they did not examine urge or mixed UI (Kim et al., 2007). In this study no significant relationship between hand grip strength and cure of urinary incontinence was shown. A significant relationship was seen between adductor muscle strength, maximum walking speed and cure of urinary incontinence.

After the 3-month intervention and 7-month follow-up, UI was defined as cured if no urine loss episodes were present in the 1-week urinary diary. Our trial confirmed that exercise treatment involving PFM training and fitness exercises can achieve a 63.2% cure rate in stress UI, a 35.0% in urge UI, and a 40.0% in mixed UI within the intervention group after 3-months of exercise. This exercise treatment had immediate effects in women with UI regardless of their urodynamic diagnosis, and the effects are comparable to those of the previous study. The efficacy of the exercise treatment was greater for stress UI than urge or mixed UI, and although the cure rates of urge and mixed UI showed slight decreasing trends after the 7-month follow up, the decreases were statistically not significant. Our data suggests that exercise treatment is more effective for stress UI than urge or mixed UI, and also raises the possibility that for both urge and mixed UI, a combined behavioral and drug therapy (Burgio et al., 2000) may be more effective than exercise treatment alone. However, this study does not provide an explanation for the slight reversal in the effectiveness of the treatment on urge and mixed UI after the follow up.

Many studies have indicated that BMI (Bump et al., 1992; Brown et al., 1999; Richter et al., 2010) and waist circumference (Krause et al., 2010) are a risk factor for UI, and decrease in BMI may contribute to the decline in stress UI episodes (Kim et al., 2007). Presumably, a decrease in BMI causes a decrease in abdominal-wall weight, decreasing intra-abdominal pressure and intra-vesicular pressure, which may have led to the improvement of stress UI. In this analysis, BMI reduction was significantly associated with the total cure rates of urge, mixed as well as stress UI, but the data does not explore the mechanism of how decreases in BMI improves urge and mixed UI. Also, previous studies have emphasized that compliance to exercise is the key factor to long-term success (Lagro-Janssen, 1998; McDowell et al., 1999). In this study, compliance to the multidimensional exercise treatment was the most significant and consistent predictor of efficacy post-intervention and follow-up. Our findings also support the idea that high compliance and BMI reduction have positive influences on urge, mixed and stress UI treatment. However, the current results were obtained based on a small sample size. The relationships need to be further researched in a population study which would contain a larger number of subjects and for a longer follow-up period.

This study has several limitations. First, the assessments of UI type and urine leakage episodes were self-reported. This could have led to a reporting bias, as subjects with UI may have underreported their symptoms, but a urinary diary is a reliable method for assessing episodes of urine leakage (Wyman et al., 1988; Locher et al., 2001). Thus, this study provided data that was reliable for objective assessment of the behavioral treatment on urinary incontinence. Second, PFM strength, which is likely to have increased through the PFM exercises, was not measured. Therefore, whether the cure rate of urine leakage is correlated with the increase in PFM strength or functional fitness, or the decrease in BMI or abdominal fat could not be explored.

The results suggest that a multidimensional exercise intervention may be equally effective for treatment of stress, urge, and mixed UI. BMI reduction as well as compliance to the prescribed exercise regimen was a significant and consistent predictor of the effectiveness of the behavioral therapy. Thus, multidimensional exercise treatments should be considered for elderly women as part of a strategy for improving functional capacity and UI. Health care for UI patients should undertake a team approach where physical therapists, doctors and nurses work together. Nurses should not only objectively assess the urinary diaries collected, they will play a very important role for the prevention of UI and maintenance of cured UI cases by instructing changes in daily lifestyle among the elderly.

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Ethical approval: The study protocol was approved by the Clinical Research Ethics Committee of Tokyo Metropolitan Institute of Gerontology. The procedures were fully explained to all participants, and written informed consent was obtained.

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ORIGINAL ARTICLE

Three-dimensional in vivo motion analysis of normal knees using single-plane fluoroscopy

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Abstract

Background Analysis of the movement of anatomically defined reference axes at the femoral condyles relative to the tibia is appropriate for evaluating knee kinematics. However, such parameters have been previously employed only in studies utilizing stop-motion techniques. The purpose of this study was to evaluate in vivo dynamic kinematics for full range of motion in normal knees using the three-dimensional to two-dimensional registration technique and to compare them with previously reported normal knee kinematics obtained via stop-motion techniques.
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 when subjects squatted from standing with the knee fully extended to maximum flexion. We determined the following parameters: (1) changes to angles of the geometric center axis (GCA) on the tibial axial plane (rotation angle); (2) anteroposterior translations of the medial and lateral ends of the GCA; and (3) motion patterns in each phase during knee flexion.
Results All subjects exhibited femoral external rotation (26.1°) relative to the tibia throughout knee flexion. The medial femoral condyle demonstrated anterior translation (5.5 mm) from full extension to 100° flexion, and demonstrated posterior translation (3.9 mm) after 100°, while the lateral femoral condyle demonstrated consistent posterior translation (15.6 mm) throughout knee flexion. All subjects showed medial pivot motion from full extension to nearly 120° flexion. From 120° flexion, bicondylar rollback motion was observed.
Discussion Although the behavior of the medial femoral condyle in our analysis differed somewhat from that seen in previous cadaver studies, the results obtained using dynamic analysis were generally equivalent to those obtained in previous studies employing stop-motion techniques. These results provide control data for future dynamic kinematic analyses of pathological knees.

Introduction

Motion analyses of normal knees provide references for the analysis of pathologic knees, as in cases of osteoarthritis or ligament injury, or in the design of total knee prostheses. To describe normal knee motion, methods employing anatomically defined axes at the femoral condyles have been utilized in many studies [1–11]. Asano et al. [1] reported on the motion of the medial and lateral femoral condyles relative to the tibia using the geometric center axis (GCA), defined as the segment connecting the centers of spheres representing the femoral posterior condyles,

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while Iwaki et al. [2] and Pinskerova et al. [3] also reported tibiofemoral movement using the medial and lateral flexion facet centers (FFC), represented by centers of circles conforming to the medial and lateral femoral posterior articular surfaces in the sagittal plane. In those studies, knee motion was analyzed via a series of images of various knee flexion angles taken under static conditions. (Hereafter, we will refer to this as the "stop-motion technique.")

Alternatively, in vivo three-dimensional (3D) knee motion studies have been performed since the 1990s using two-dimensional (2D) fluoroscopic images and several image registration techniques (e.g., image matching using a 2D image library, or 3D to 2D image registration), mainly for total knee arthroplasties [12–17]. In recent years, this technique has also been applied in studies of normal knee motion, utilizing contact points of the femur and tibia as evaluating parameters [18, 19]. Techniques employing these contact points are considered appropriate for examining contact conditions between femur and tibia and the movements of contact locations during knee motion [18, 19], which makes it possible to study the causes and the mechanisms of cartilage degeneration and injury in pathological knees [20], as well as the wear patterns of polyethylene inserts in total knee arthroplasty [15]. In such techniques, however, the positions of evaluation parameters (contact points) relative to femoral coordinates change with knee motion. In contrast, during techniques that employ anatomically defined axes or points, such as GCA or FFC, the positions of evaluation parameters relative to femoral coordinates do not change with knee motion. Therefore, such techniques are considered appropriate for assessing the relative motion between the femur and tibia, and especially when documenting the changes in relative position between the femoral and tibial condyles with knee motion in the medial and lateral compartments, respectively. However, no study to date has studied in vivo dynamic normal knee kinematics employing GCA or FFC as an evaluation parameter throughout the full range of motion. It is possible that the knee kinematics obtained under dynamic conditions may differ from those observed using stop-motion techniques due to the effects of acceleration and kinetic energy.

We hypothesized that normal knee kinematics obtained via in vivo dynamic motion analysis would yield different results from those previously reported using stop-motion techniques when knee kinematics are described by anatomically defined reference axes at the femoral condyles.

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, employing GCA as an evaluation parameter, and to compare the results with previous reports obtained using stop-motion techniques to evaluate this hypothesis.

Materials and methods

We asked 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 to participate in this study. 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.

The 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 at 1 mm intervals. A 3D digital model of the femur and tibia was reconstructed from CT data using 3D visualization and modeling software (ZedView®; LEXI, Tokyo, Japan), and the anatomic coordinate systems were established by referencing several bony landmarks [21]. The tibial z-axis was defined as a line connecting the midpoint of the tibial eminence and the midpoint of the medial and lateral top of the talar dome. The tibial y-axis (positive anteriorly) was defined as a line drawn perpendicularly from the mediolateral 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. Using previously applied methods [1, 4, 5, 9], the medial and lateral posterior femoral condyles were approximated as spheres that best matched the geometries of the condyles. The GCA was defined as the segment connecting the centers of the spheres (Fig. 1). Knee motion was observed when 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) [7].

The sampling frequency was 15 Hz, with an image area of 380 × 300 mm and resolution of 1240 × 960 pixels. The mean duration of one flexion of the knee was 8.4 s.

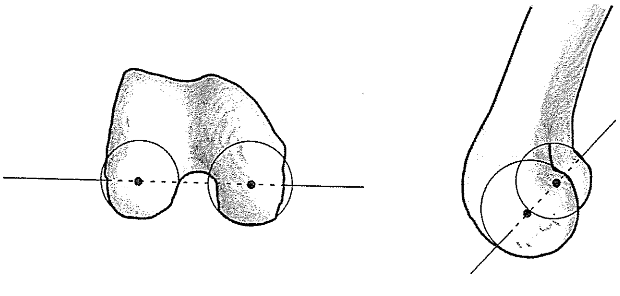

Fig. 1 The geometric center axis is the line connecting the centers of spheres that represent the medial and lateral femoral posterior condyles

The mean angular velocity and sampling rate were 17.8°/s and 0.8 images/degree of knee flexion, respectively. The series of static lateral images were stored digitally. After the contours of the femur and tibia had been detected manually in these images, a 3D-to-2D technique using an automated shape-matching algorithm [21] was employed to determine the relative 3D positions of the femur and tibia in each fluoroscopic image (KneeMotion®; LEXI) (Fig. 2). By performing this procedure for all images, the 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 [22].

Relative motion between the femur and tibia was quantified as the movement of GCA projected onto the axial (xy) plane of the tibial coordinate system. The anteroposterior (AP) locations of the medial and lateral ends of all projected GCAs were evaluated as y values of the tibial coordinate system (Fig. 3). We determined the following parameters: (1) changes in the angle of the GCA on the tibial axial plane (rotation angle); (2) AP translations of the medial and lateral ends of the GCA; and (3) motion patterns in respective phases during knee flexion. Changes in the angle of the GCA on the tibial axial plane were calculated as the rotation angle around the z-axis (longitudinal axis) of the tibia, which is the relative axial rotation between the femoral and the tibial coordinate system based on the concept developed by Grood et al. [23]. The AP translations of the medial and lateral ends of the GCA were described using both absolute and normalized values. The absolute values were used for comparisons to previous reports, while the normalized values are reference data for evaluating motions of pathologic knees in other groups in the future. The absolute values of AP translations were normalized using the AP diameter of the proximal tibia (the distance from the most anterior point to the most posterior point of the Y-axis on the axial plane, which includes the tip of the fibula head). The midpoint of the AP diameter was defined as the 0% point, while the most anterior and posterior points were defined as the "anterior 100%" and "posterior 100%" points, respectively (Fig. 4). The AP translations of the medial and lateral ends of the GCA were described using "percent distances" by calculating the change in their "percent locations." The motion pattern was determined by observing AP translations of the medial and lateral ends of the GCA and also by capturing the locations of intersecting points of GCAs in respective phases according to the concepts of Asano et al. [1]. If both ends of the GCA showed posterior translations in the same phase, "bicondylar rollback motion" was considered to be present. Likewise, if only one end of the GCA showed AP translation and intersections of GCAs were observed in the contralateral compartment in the same phase, "lateral" or "medial pivot motion" was considered to be present. However, as a footnote, the term "rollback" is not a truly correct expression for explaining the trajectories of the GCA, because the GCA itself does not demonstrate rollback motion. Moreover, femoral condyles do not necessarily exhibit merely "rolling;" they can exhibit "sliding" as well. The condition of rolling requires that the zero velocity point is at the contact point between two surfaces, in this case the femur and tibia [24]. In addition, the term "pivot motion" may not be appropriate, as a specific motionless fulcrum does not exist. However, in this study, we used the terms "pivot motion" and "rollback" for the simple reason that they have been frequently used and are conceptually understood by clinicians.

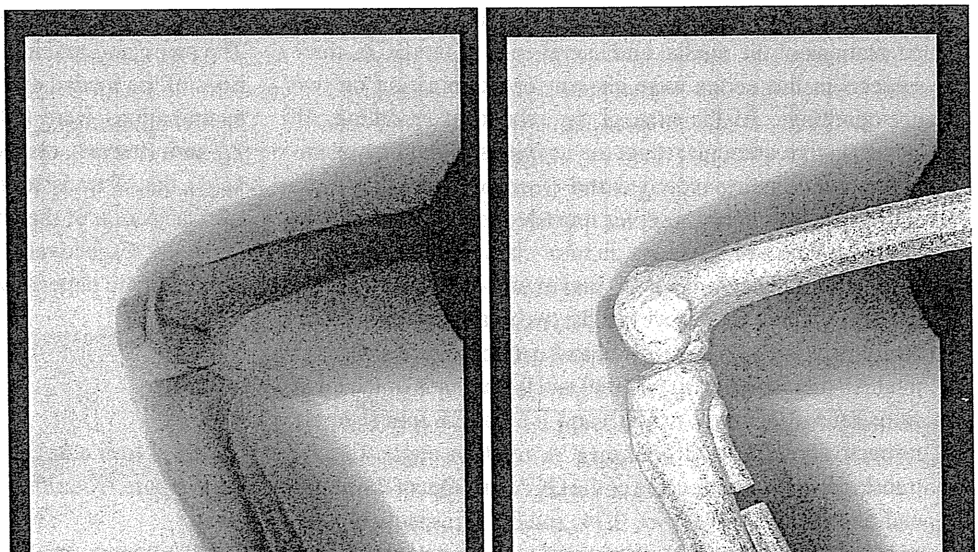

Fig. 2 Example of the three-dimensional (3D) to two-dimensional (2D) registration technique. A 2D fluoroscopic image of the knee was downloaded and a 3D bone model was matched onto a 2D fluoroscopic image

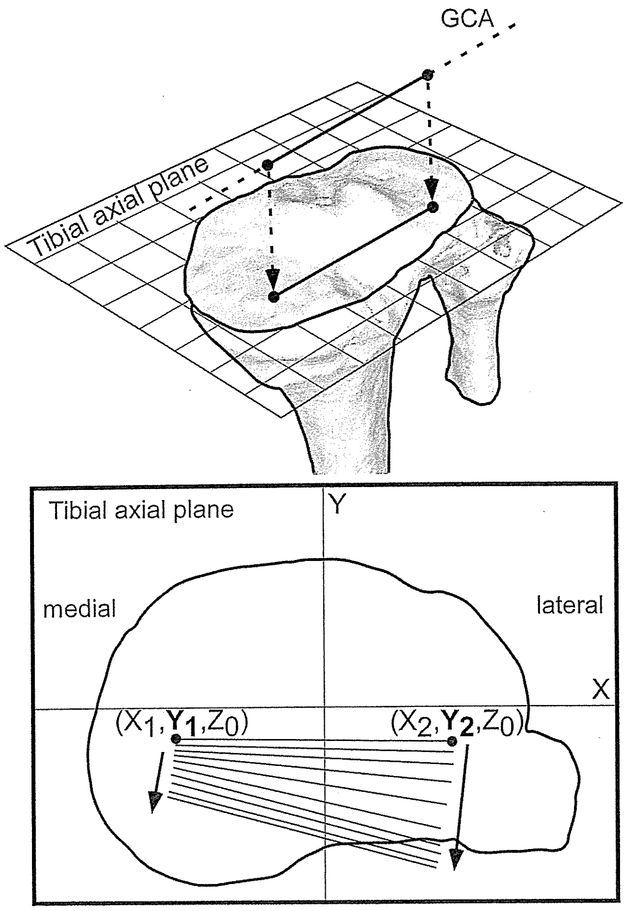

Fig. 3 Relative motion of the femur compared to the tibia. Movement of the GCA was projected onto the axial plane of the tibial coordinate system. Anteroposterior (AP) locations of the GCAs were evaluated as *y* values of the tibial coordinate system

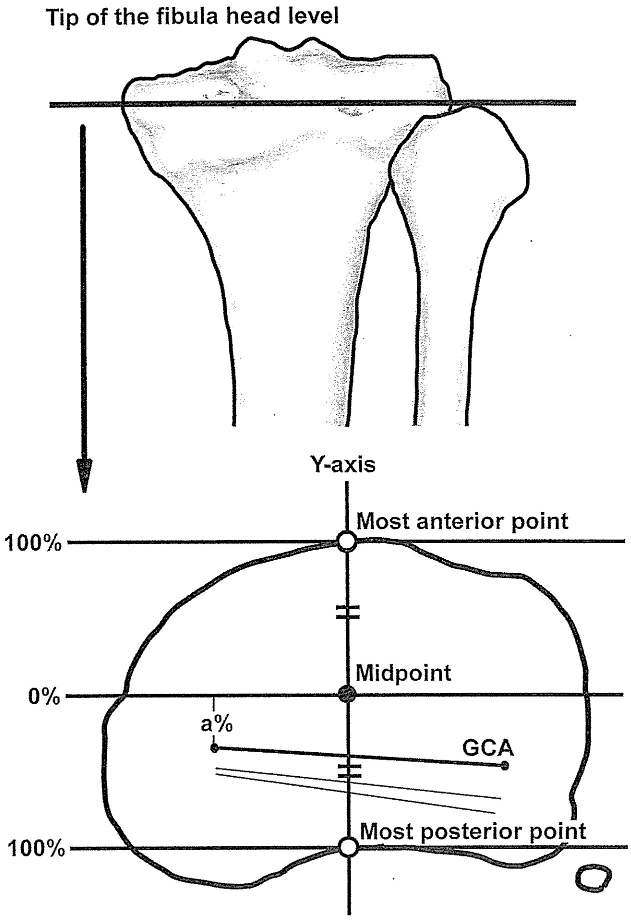

Fig. 4 The absolute values of AP translations were normalized. The AP translations of the medial and lateral ends of the GCA were described by percent distances obtained by calculating the change in the percent locations of them

To examine the reproducibility of knee motion patterns, changes to the angle of the GCA (rotation angle) and AP translations of the medial and lateral ends of the GCA, 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 an intra-class correlation coefficient (ICC). The mean and maximum differences in the rotation angle of GCA between the two examinations were 2° and 3°, respectively. The mean and maximum differences in total AP translation of the medial and lateral ends of the GCA were 1.6 and 2.7 mm (medial) and 1.7 and 2.8 mm (lateral), respectively. The ICC of the GCA rotation angle, the AP translation of the medial end of the GCA, and that of the lateral end of the GCA were 0.97, 0.74, and 0.87, respectively. All three knees displayed the same kinematics pattern in both examinations. The inter-observer errors were also examined. Two observers analyzed five subjects in this series. The mean and maximum differences in the rotation angle of GCA between the two examinations were 2.6° and 4°, respectively. The mean and maximum differences in the total AP translations of the medial and lateral ends of the GCA between two examinations were 0.8 and 2.7 mm (medial), and 1.1 and 2.7 mm (lateral), respectively. The ICC of the GCA rotation angle, the AP translation of the medial end of the GCA, and the AP translation of the lateral end of the GCA were 0.86, 0.81, and 0.98, respectively. In both examinations, relatively similar kinematic patterns were observed.

Results

Changes to the angle of the GCA on the tibial axial plane (rotation angle)

In all subjects, the GCA exhibited external rotation on the axial plane of the tibial coordinate system throughout knee flexion. This indicates that all subjects demonstrated