board and ethics committee of the Tokyo Metropolitan Institute of Gerontology approved the study under the condition that the participants should not be disadvantaged, the crossover design was adopted.

Outcome Measures

Outcome measures were evaluated according to interview and a functional fitness test at baseline, after the 3-month intervention, and at 1-year follow-up.

Interview Survey

A face-to-face interview was performed to assess UI. The first question was, "Have you experienced urine leakage during the previous year?" If the person responded yes, the frequency of the leakage was asked about and scores of urine leakage were calculated based on response by interview as follows: 0 for no urine leakage, 1 for less than once a month, 2 for one to three times per month, 3 for one to two times per week, 4 for once every 2 days, and 5 for every day. The scale was based on the International Consultation on Incontinence Questionnaire (ICIQ),[14] modified to capture the status of urine leakage in elderly community-dwelling Japanese. A person whose response ranged from 2 to 5 was defined as having UI.[15]

UI type was classified based on inquires about urine leakage in relation to 12 possible antecedents. Stress UI was recorded when interviewees reported urine leakage associated with increased abdominal pressure such as coughing, sneezing, laughing, lifting something heavy, standing up, running, climbing up or down stairs, standing for a long time, 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 characteristics of stress and urge UI types were present, it was determined to be mixed UI.[15]

Subjects were asked about the onset and duration of UI, volume of urine leaked, frequency of daytime and nighttime voiding, and the psychological and functional effect of UI.

A 3-day diary has been reported to have high validity and reliability.[16,17] In the present study, data were collected in a 3-day diary to cross-check the validity of the results of the frequency of urine leakage episodes retrieved during the interview.

The primary outcome variable of this study was the frequency of urine leakage episodes (not volume) assessed using the 6-point scale used for the data retrieved during interview. The effect of the intervention on urine leakage episodes was assessed based on shifts of the data from the 6-point scale from the interview, which was conducted at baseline, completion of the intervention, and 1-year follow-up; it was assessed as cured when urine leakage episodes disappeared, improved when the frequency of urine leakage episodes decreased, unchanged when there was no change in frequency was present, and worsened when the frequency increased.

Functional Fitness Test

Measurements of height and body weight were converted into body mass index (BMI, kg/m^2). Grip strength was assessed using a handheld Smedley-type dynamometer in the dominant hand. To test walking speed, subjects were asked to walk on a flat, straight, 11-m-long walkway one time at their usual speed and two times at their maximum speed. Walking speed was measured over a 5-m distance between the marks indicating the 3- and 8-m distance, starting from the beginning of the walkway. For maximum walking speed, the faster time recorded was used. Hip adductor muscle strength was measured twice in each of two positions using a handheld dynamometer (μTasMF-01, ANIMA, Japan): first, with the subject seated and the height of the chair adjusted such that the knees were at a 90° angle and, second, with the subject lying down, the knees were extended. In both positions, the knees were placed hip-width apart, the sensor of the measuring device was placed on the medial side of the knee, the subject was instructed to squeeze the knees together, the maximum contraction strength was measured, and the higher value was used.

Intervention

The intervention consisted of 60-minute exercise sessions held at the Tokyo Metropolitan Institute of Gerontology Health Promotion Classes two times per week for 12 weeks. During the intervention period, the exercises were performed as a group. During the follow-up period, the home-based exercise was performed individually. Control subjects were instructed to lead a normal life and to refrain from special exercises aiming to increase muscle strength (not only PFM) or walking speed, to decrease BMI, or to improve their dietary habits. The exercises are described here.

Warm-Up and Stretching Exercise

Before the PFM exercise and muscle strengthen training, participants performed 10 to 15 minutes of warm-up and stretching exercises, including shoulder rotation, waist rotation, and others.

PFM Exercises

At the beginning of the PFM training, the subjects were taught the structure of the PFMs and asked to pay attention to become conscious of these muscles. They were taught that straining the abdomen would increase abdominal pressure and exert pressure on the PFMs. Subjects were trained to exert force only on the PFMs without excessively straining the abdomen. The exercise regimen was designed to strengthen the fast- and slow-twitch muscle fibers located at the pelvic floor. Participants were initially instructed to perform 10 fast contractions (3 seconds) and 10 sustained contractions (6–8 seconds) with 10-second relaxation periods between the contractions. The PFM exercise was performed in sitting, lying, and standing positions with the legs apart, emphasizing contraction of the PFMs and relaxation of the other muscles.

Fitness Exercises

Body awareness, breathing, relaxation, and strength training of the thigh, abdominal, and back muscles were performed between PFM exercise positions, with additional training including bending the knees, tilting the pelvis backward and forward, lifting the buttocks on the back with the knees bent, raising one leg while lying on the back, and others. Other exercises included the use of two kinds of training balls: a small one (21 cm in diameter) and a large one (45–55-cm diameter). The exercises included sitting on

the ball, rolling the ball and the pelvis forward and backward, moving from side to side while squeezing the thighs, and others.

Second-Stage Intervention

After the intervention group completed the first stage of the exercise training, the control group was also given the same 3-month exercise.

Follow-Up

During the 1-year follow-up period, subjects attended group exercise classes once per month in addition to receiving a home-based exercise program. The home-based program consisted of two to three sets of the 13 exercises and the PFM exercise that they had learned during the group exercise session. They were advised to perform the home-based exercises at least two times per week for approximately 30 minutes per day. To accurately monitor the exercise times and the number of sets during the follow-up period, a pamphlet illustrating the PFM and strengthening exercises and a recording sheet were distributed to the subjects, who were instructed to record the time and sets of exercises performed at home every day, along with the presence or absence of urine leakage. 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. An experienced physical therapist prescribed and managed the home-based exercise program.

Data Analysis

The mean differences between the intervention and the control groups were analyzed using the *t*-test for continuous variables and the chi-square test for categorical variables. For continuous variables, the paired *t*-test was used to compare pre- and postintervention data within the group. To evaluate the differences between the groups in the effect of the intervention on functional fitness, repeated-measures two-way analysis of variance (ANOVA) was performed on selected outcome variables. Significant interactions were analyzed to determine whether the effects were greater in the intervention or control group. The Mann–Whitney *U*-test was used to compare the effect between the groups of the 3-month exercise on cure rate of urine leakage. To evaluate the differences between the groups in frequency score of urine leakage at baseline, after the exercise program, and at the 1-year follow-up, repeated-measures two-way ANOVA was performed. Repeated-measures one-way ANOVA was performed to evaluate the within-group effect of the intervention on frequency score of urine leakage at a baseline, after the 3-month exercise program, and at 1-year follow-up. Effectiveness of the intervention was assessed by comparing the frequency of the urine leakage episodes obtained from the 6-point scale based on interview. The Cochran Q-test was used to evaluate the within-group differences in the effect of the exercise program on urine leakage episodes for preintervention, postintervention, and follow-up data. For variables showing significant differences, a post hoc analysis was performed using the McNemar method. The percentage improvement in functional fitness when the intervention ended was calculated using the following formula: % improvement = ((postintervention value–baseline value)/baseline value × 100). Percentage improvement was divided into tertiles. The power of this study was calculated at 80% to demonstrate the difference in the outcome variable of at least 20% at a significance level of $\alpha = 0.05$. All analyses were performed using SPSS software, Windows version 13.0 (SPSS, Inc., Tokyo, Japan).

RESULTS

Participant Characteristics at Baseline

As a result of randomization, the intervention (n = 35) and control (n = 35) groups were similar in mean age, BMI, walking speed, chronic medical conditions, duration of urine leakage, and frequency of urine leakage episodes (Table 1).

Table 1. Selected Variables Characteristic of Participants at Baseline by Study Group

Variable*	Intervention Group (n = 35)	Control Group (n = 35)	*P*-Value*
Age, mean ± SD	76.6 ± 5.0	76.6 ± 3.8	.96
Height, cm, mean ± SD	146.3 ± 5.4	147.7 ± 5.3	.30
Body weight, kg, mean ± SD	51.7 ± 9.4	54.1 ± 9.7	.30
Body mass index, kg/m^2, mean ± SD	24.1 ± 4.3	24.7 ± 3.7	.55
Grip strength, kg, mean ± SD	17.7 ± 4.1	18.2 ± 4.5	.65
Adductor muscle strength, Nm, mean ± SD			
Seated	48.8 ± 14.5	49.9 ± 11.8	.67
Supine	42.0 ± 14.3	40.1 ± 10.2	.47
Usual walking speed, m/s, mean ± SD	1.1 ± 0.3	1.1 ± 0.2	.86
Maximum walking speed, m/s, mean ± SD	1.6 ± 0.4	1.7 ± 0.4	.97
Chronic medical conditions, %			
Hypertension	56.3	50.0	.62
Stroke	6.3	12.5	.67
Diabetes mellitus	6.3	12.5	.67
Osteoporosis	21.9	18.8	.76
Hyperlipemia	34.4	43.8	.44
Onset age of urine leakage, mean ± SEM	71.2 ± 1.8	68.1 ± 2.4	.30
Duration of urine leakage, year, mean ± SEM	7.0 ± 1.4	9.2 ± 2.1	.41
Frequency of toilet in the daytime, times, mean ± SD	8.6 ± 2.9	8.3 ± 4.3	.81
Frequency of toilet in the nighttime, times, mean ± SD	2.2 ± 1.5	1.8 ± 1.3	.42
Frequency score of urine leakage, point, mean ± SD	3.4 ± 1.3	3.0 ± 1.3	.14
Frequency of urine leakage episodes, %			
Daily	31.4	20.0	.40
1 every 2 days	5.8	11.4	
1–2 per week	25.7	17.2	
1–3 per month	37.1	51.4	
Avoid going out because of worry about urine leakage, %	40.6	33.3	.56
Restricted sports activity because of urine leakage, %	31.3	22.2	.44
Restricted social contact because of urine leakage, %	31.3	18.5	.26

SD = standard deviation; SEM = standard error of the mean.

* Two group *t*-test for continuous variables and chi-square test for categorical variables.

Participant Attendance

Attendance rate during the intervention period ranged from 71.9% to 93.8%, with a mean of 82.4%. Intervention group participants who participated in 15 or more of the 24 exercise sessions were considered to have completed the intervention. Ten subjects (28.6%) attended all 24 sessions. Of the 33 subjects who completed the intervention, 23 (69.7%) participated in more than 20 exercise sessions. Five participants (intervention group = 2, control group = 3) were not able to complete the study after randomization because of hospitalization (n = 1), asthma (n = 1), knee pain (n = 1), or a fracture (n = 2). Exercise frequency during the follow-up period was reported to be every day in 30.3% of the subjects, two to three times per week in 45.5%, and once or less per week in 24.2%. Mean exercise duration was 24.5 minutes, and the mean number of contractions of the PFMs was 48 times per day during the follow-up period.

Functional Fitness and Urinary Incontinence According to Group

Significant ($P<.05$) increases in adductor muscle strength and maximum walking speed after the 3-month intervention were observed in the intervention group. Body weight, BMI, and frequency score of urine leakage episodes decreased significantly in the intervention group, with no significant changes in the control group. Moreover, 54.5% of the intervention group and 9.4% of the control group reported being cured ($P<.001$) in terms of urine leakage episodes based on an interview after the 3-month exercise program (Table 2).

Frequency Score and Cure Rate of Urine Leakage in Full Group

The data from this study suggest that the 3-day diary underestimated the frequency of mild urine leakage and hence tended to overestimate the effect of intervention. For this reason, the 3-day diary data were not used; instead, whether the immediate intervention group and the crossover intervention group responded similarly, the changes in the frequency score of urine leakage based on the 6-point scale according to the interview was used. As shown in Figure 2, both groups showed similar patterns of changes, with no significant differences between the two groups ($P=.31$). Within-group scores were compared, and significant changes were observed in the immediate intervention group ($F=10.805$, $P<.001$) and the crossover intervention group ($F=4.565$, $P=.01$), with the frequency score of urine leakage decreasing significantly after the intervention.

The cure rates of urine leakage based on the 6-point scale of the interview of the immediate intervention group, the crossover intervention group, and the full group are shown in Table 3. The cure rate in the full group was 50.8% after the 3-month exercise program and 30.8% at the 1-year follow-up survey, showing significant improvement.

Correlation Between UI and Functional Fitness

Table 4 shows the distribution of the cured subjects according to tertiles of changes from baseline values of BMI, maximum walking speed, and adductor muscle strength. Within the group that was cured of UI, a significantly higher proportion had a decreased BMI at 3 months ($P=.03$) and increased walking speed at 3 and 12 months ($P=.04$ and

Table 2. Comparison of Functional Fitness and Incontinence Variables Between the Intervention (n = 33) and Control (n = 32) Groups After the 3-Month Exercise Program

Variable	Group	Baseline	3-Month Exercise	Analysis of Variance (Group × Time)	*P*-Value
Body weight, kg, mean ± SD	I	52.2 ± 9.2	50.8 ± 9.2*	$F(1, 63) = 9.1$	.004
	C	53.1 ± 9.4	52.9 ± 9.1		
Body mass index, kg/m², mean ± SD	I	24.5 ± 4.2	23.8 ± 4.0*	$F(1, 63) = 5.9$	.02
	C	24.2 ± 3.8	24.1 ± 3.6		
Usual walking speed, m/s, mean ± SD	I	1.1 ± 0.3	1.1 ± 0.2*	$F(1, 63) = 1.0$	.31
	C	1.1 ± 0.2	1.1 ± 0.3		
Maximum walking speed, m/s, mean ± SD	I	1.6 ± 0.4	1.7 ± 0.4	$F(1, 63) = 4.7$	.04
	C	1.7 ± 0.3	1.6 ± 0.3		
Grip strength, kg, mean ± SD	I	17.5 ± 4.3	18.2 ± 4.0	$F(1, 63) = 0.1$	.73
	C	18.5 ± 4.8	18.9 ± 4.8		
Adductor muscle strength, Nm, mean ± SD					
Seated	I	48.6 ± 14.4	59.4 ± 14.7*	$F(1, 63) = 13.4$	.001
	C	50.2 ± 12.0	51.5 ± 13.1		
Supine	I	42.3 ± 14.6	49.2 ± 17.3*	$F(1, 63) = 10.8$	.002
	C	39.8 ± 10.1	40.7 ± 11.2		
Frequency score of urine leakage, point, mean ± SD	I	3.4 ± 1.3	1.5 ± 1.8*	$F(1,63) = 6.0$	.02
	C	3.0 ± 1.4	2.4 ± 1.4	$Z = 3.863$†	<.001
Cured of urine leakage, %	I	0.0	54.5		
	C	0.0	9.4		

SD = standard deviation; I = intervention group; C = control group.

*Paired *t*-test of the baseline and 3-month exercise within-group difference, $P<.05$.

†Mann–Whitney *U*-test.

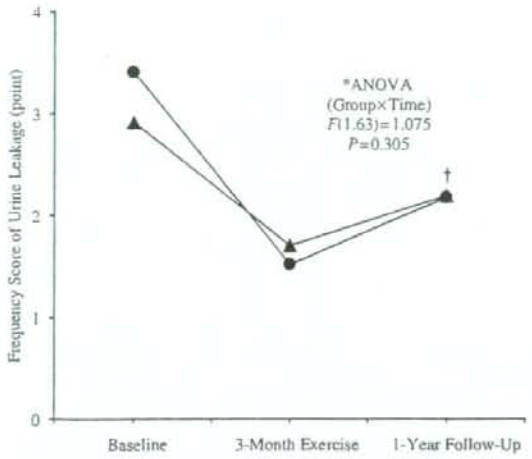

Figure 2. Changes in mean score of urine leakage from a 6-point scale based on interview at baseline, after the 3-month exercise program, and at 1-year follow-up. •: immediate intervention group; ▲: crossover intervention group. *Comparison of urine leakage scores between immediate and crossover intervention groups. †Comparison of within-group urine leakage scores at baseline (B), after the 3-month exercise program (P), and at 1-year follow-up (F): immediate intervention group ($F = 10.805$, $P < .001$; Scheffe post hoc = B > P, F); crossover intervention group ($F = 4.565$, $P = .01$; Scheffe post hoc = B > P). ANOVA = analysis of variance.

$P = .047$) than those with increased or unchanged BMI and decreased or unchanged walking speed. There was no difference at either time point in proportion of cured subjects with improved adductor muscle strength.

DISCUSSION

This randomized, controlled trial demonstrated the efficacy of a multidimensional exercise in reducing urine leakage episodes and in improving functional fitness. To confirm the effects of the exercise in elderly people more accurately, the crossover subjects were provided with the same exercise for 3 months after the first-stage intervention was completed. The reduction in urine leakage episodes in the crossover intervention group was similar to that of the immediate intervention group. These results confirmed the effectiveness of the exercises in emphasizing the PFMs and fitness exercises to improve UI.

The effectiveness of the behavioral treatment of UI in older women has been reported to be a 61% reduction in older rural women[13] and a 73.9% reduction in homebound older adults.[18] These previous reports had an intervention that targeted only the PFM, without including any additional functional exercises. The current study offered not only PFM training, but also functional exercises to improve stress UI. The relationship between changes in muscle strength, walking speed, and BMI and reduction in urine leakage episodes based on a 6-point scale by interview was analyzed in detail.

The theoretical rational of the strength training and PFM exercise has been described in detail elsewhere.[19,20] In this study, we included the PFM exercise along with exercise items that can strengthen the adductor muscles. Although it was not possible to measure PFM strength, we anticipated that strengthening the adductor muscles (presumed to reflect the PFMs) would contribute to reducing leakage episodes. Although adductor muscle strength increased significantly (Table 2), the data do not support a positive correlation between strengthening of the adductor muscles and improvement in UI, as shown in Table 4. Moreover, grip strength, which assesses muscle strength of the upper extremities, was not significantly different between the two groups, and no improvement was observed. No relationship was found between grip strength and improvement in UI.

The relationship between walking speed and urine leakage episodes was analyzed. As shown in Table 4, there was a significant cure rate in subjects with increased walking speed. These results indicate that increase in walking speed contributes to the cure of urine leakage episodes. The data suggest the possibility that an increase of 10.0% or more in walking speed may lead to improvement in UI, although this study does not provide an explanation of the mechanism of how increased walking speed improves the UI.

Many studies have indicated that BMI is a risk factor for UI.[21,22] As shown in Table 4, the cure rate for urine leakage episodes was significantly higher in those whose BMI decreased. The data suggest the possibility that a decrease in BMI of 5.0% or more may lead to treatment of UI.

Several studies have made a long-term observation of the effect of PFM exercises.[8–12,23] As the previous studies indicated, although the follow-up period ranged from 1 to 15 years in various studies,[8,9] all previous studies except one[9] concluded that the postintervention effect was maintained during the follow-up period, thus confirming the long-term efficacy of PFM exercises. In the present study, the 1-year follow-up survey showed that 30.8% of the full

Table 3. Cured of Urine Leakage After 3-Month Exercise Program and at 1-Year Follow-Up in Immediate, Crossover Intervention, and Full Groups

Group	Baseline	3-Month Exercise	1-Year Follow-Up	Cochran Q-Value	P-value	McNemar Post Hoc Analysis
	n (%)					
Immediate intervention	0 (0.0)	18 (54.5)	11(33.3)	20.316	<.001	P,F>B
Crossover intervention	0 (0.0)	15 (46.9)	9 (28.1)	10.167	.006	P>B
Full group	0 (0.0)	33 (50.8)	20 (30.8)	50.242	<.001	P>F>B

B = baseline; P = after 3-month exercise program; F = after 1-year follow-up.

Table 4. Cured of Urine Leakage According to Body Mass Index (BMI), Maximum Walking Speed, and Adductor Muscle Strength Tertiles

Variable Changes Compared with Baseline	Cured of Urine Leakage, n (%)	Cochran Q-Value	P-Value	McNemar Post Hoc Analysis
3-month exercise (n = 33)*				
BMI				
Decreased	16 (48.5)	7.091	.03	De, No > In
No change	13 (39.4)			
Increased	4 (12.1)			
Maximum walking speed				
Increased	17 (51.5)	6.545	.04	In > De
No change	11 (33.3)			
Decreased	5 (15.2)			
Adductor muscle strength				
Increased	11 (33.3)	4.545	.10	
No change	6 (18.2)			
Decreased	16 (48.5)			
1-Year Follow-up (n = 20)				
BMI				
Decreased	10 (50.0)	3.700	.16	
No change	3 (15.0)			
Increased	7 (35.0)			
Maximum walking speed				
Increased	10 (50.0)	6.100	.047	In > De
No change	8 (40.0)			
Decreased	2 (10.0)			
Adductor muscle strength				
Increased	9 (45.0)	3.100	.21	
No change	8 (40.0)			
Decreased	3 (15.0)			

* Decreased (De) means lower range (0.0–33.3%), no change (No) means medium range (33.4–66.6%), and increased (In) means upper range (66.7–100%) of tertile.

group was cured, maintenance of the improvement effect similar to that of the previous studies.

Several studies have suggested various factors influencing the effect of exercises during the follow-up period. One study[23] emphasized that compliance with PFM exercises is critical to maintaining a long-term effect. In this study, 75.8% of the participants performed PFM and fitness exercises regularly, twice per week or more, during the 1-year follow-up period. The high adherence during the follow-up period may partially explain the high cure rate.

The relationship between the changes in BMI, walking speed, and adductor muscle strength and cure of the urine leakage episodes after the 1-year follow-up was analyzed (Table 4). These data suggest that lower BMI and greater adductor muscle strength contribute to improvement in UI. Although the latter was not statistically significant, more research is required. However, 50.0% of the cure rate was observed in the group that increased its maximum walking speed, and the data demonstrate that the increase in walking speed during the 1-year follow-up contributed significantly to maintaining the cured urine leakage episodes.

This study has several limitations. First, information on urine leakage was self-reported based on interview. Several studies support the validity and reliability of information on UI reported by elderly people.[24] To be more exact and to confirm the information obtained by interview, that information was compared with information obtained from the 3-day diaries.[15,25] The 3-day diary accurately assessed the frequency of people with severe urine leakage episodes at a frequency of at least once a day or every 2 days (agreement of 91.7% between the diary and interview), but for people with mild urine leakage at a frequency of once or twice per week or once or twice per month (who were included in the study population), urine leakage episodes may not be successfully recorded in the 3-day diary (agreement of 67.4% between the diary and interview). For this reason, the results of the 3-day diary were not reported. Therefore, whenever a study population includes people with mild urine leakage, a 3-day diary alone may not be sufficient, and an additional diary reflecting the duration of urine leakage frequency of all subjects may be needed. Second, 1-year follow-up information was not available for the control group, because the crossover design was used to avoid disadvantaging the control group; the control group was provided with the same 3-month exercises immediately after the first-stage intervention was completed. Third, PFM strength, which is likely to have improved through the PFM exercises, was not measured. Therefore, whether incontinence improvement was correlated with improvement in PFM strength could not be explored.

These results indicate that a multidimensional exercise targeting PFMs, walking speed, muscle strength, and BMI was effective in improving functional fitness and treatment of stress UI in elderly community-dwelling Japanese women. The effects of improvement in urine leakage and functional ability were maintained 1 year after the intervention.

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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. Y. Yuko assisted in subject recruitment, supervised the functional fitness test, assisted in the follow-up survey, and interpreted the data. Y. Hideyo assisted in subject recruitment, supervised the interviewers, and interpreted the data.

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介護保険で要支援と認定された者の転倒予防を目指す介入プログラムの成果と課題について

金　憲経，吉田英世，鈴木隆雄

Effects of a 3-month Fall Risk Reduction Exercise Program for Determined Care Level of Assistance Required Under the Japanese Long-Term Care Insurance System

Hunkyung KIM, Hideyo YOSHIDA and Takao SUZUKI

Abstract

We evaluated the effects of a 3-month exercise program in reducing risk factors of falls in determined care level of assistance required under the long-term care insurance program. A pamphlet containing information on "Fall Prevention Exercise Classes" was mailed to 185 potential participants with assistance required. Thirty five agreed to join the exercise classes. For a 12-week intervention period, participants received exercise program twice a week focused on improving muscle strength, balance, and walking ability. Outcome measures included physical fitness, Tokyo Metropolitan Institute of Gerontology (TMIG) index score, and fear of falling. The research protocol was approved by the institutional review board of TMIG, and informed consent was obtained from each participant. Of participants, 65% perceived that they were able to walk stably, and 60.0% were confident that they were able to prevent falling by themselves. The maximum walking speed increased significantly from 1.14±0.46 m/s at baseline to 1.39±0.47 m/s after intervention (improved 21.4%, $P<0.001$), and knee extension power increased from 17.67±6.01 kg at baseline to 23.57±8.49 kg after 3-month exercise program (increased 33.4%, $P<0.001$). The percentage of fear of falling was significantly decreased from 90.5% before intervention to 61.9% after 3-month exercise ($P=0.031$). These results suggest that exercise program targeting modifiable muscle strength, balance, and walking ability is a safe and effective intervention to reduce the risk factors of falls, and fear of falling in frail elderly.

Keywords　: assistance required, falls, fear of falling, intervention
キーワード：要支援，転倒，転倒恐怖感，介入

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Ⅰ．緒　言

2000年４月から実施されてきた介護保険制度は，2006年４月から予防重視型システムへと制度改革を行い，サービスの充実を図っている．予防重視型システムにおいて，合理的な介護予防策を立てるためには，要介護状態になる原因を明らかにし，関連要因の改善を目指す支援が必要であろう．平成16年度に厚生労働省が発表した国民生活基礎調査によれば[14]，介護が必要となった主な原因は，脳卒中などの脳血管疾患が25.7％，高齢による衰弱16.3％，転倒・骨折10.8％，認知症10.7％などと疾病よりも廃用症候群による影響が大きいことが明らかになっている．

自分の意志からではなく，地面またはより低い場所に，膝や手などが接触することと定義される[8]転倒は，高齢者の寝たきり原因の１つである大腿骨頚部骨折の主因であり[10]，転倒を経験することによって移動に対する自信感を失う転倒後症候群(post fall syndrome)[18]が生じ，それが活動制限につながるとの大きな問題を抱えている．これまで報告されてきた先行研究によれば，地域高齢者の１年間の転倒率は約10～30％であるが[4,29]，要支援者の転倒率は健常者より高いことが指摘されている[12]．

高齢者の健康や自立に様々な悪影響を及ぼす転倒を減らすためには，転倒の理由や原因を詳細に把握したうえで，改善可能性が高い危険因子を選び出し，危険因子の改善に焦点を当てた取り組みが有効であることが多くの研究で指摘されている[25]．

高齢者の転倒率の減少を目的とした取り組みには，運動，教育，環境改善など多岐にわたっているが，運動を中心とした介入の成果が数多く報告されている．これらの成果によれば，介入プログラムに参加することによって，転倒の危険因子として指摘されている筋力，バランス，歩行機能が顕著に向上される[16,17,23]とともに転倒率の低下[3]や転倒恐怖感の解消効果[24]が指摘されている．介護保険制度の定着とともに要支援や要介護１など軽いサービス利用者が急増し，要支援者の転倒率や転倒恐怖感を持っている者の割合は健常者より高いことが指摘されているにも関らず[12]，要支援者に対する取り組みの成果は見当たらないのが現状である．とくに，要支援者に運動を適用する時には，健常者とは異なる様々な限界が内在することから，参加者の年齢や体力水準，健康状態，有病状態などに応じた無理の無い範囲で気軽に実践できる運動を取り入れることがポイントであろう．

これらの背景を踏まえて，本研究では，介護保険で要支援と認定された者を対象に３ヶ月間，転倒の危険因子として知られている筋力，歩行機能，バランス能力の改善を目指す介入プログラムを提供したときに得られる成果と課題を詳細に分析することを目的とした．

Ⅱ．方　法

１．対象者

2000年度に全国共通の調査票とかかりつけ医意見書のデータに基づき，東京都Ｋ市の介護認定審査会で要支援と決定された185名全員に，転倒予防教室の必要性，日程，指導期間，指導内容など詳細を記述した案内文を郵送し，参加者を募集した．教室参加希望者40名を対象に事前調査を行ったが，教室参加者は66～93歳（平均年齢=78.6±6.3歳）の高齢男女35名（男性９名，女性26名），不参加者５名（男性１名，女性４名）であった．不参加の理由は，家族の反対（２名），腰痛（１名），入院（１名），参加意志喪失（１名）であった．参加希望者の中に，遠距離歩行困難者が多く含まれていることから，参加者の自宅と会場を結ぶ巡回バスで送迎を行った．

対象者の中に認知機能の低下者が含まれている場合，質問紙調査が正確に把握できない可能性がある．このことから，本研究では，市役所で行った要介護認定規準に基づいて認知機能低下者の有無を確認したところ，認知機能低下者は含まれていないことから，本研究結果の解釈に影響はないと判断された．

2．調査・測定項目

1）調査項目

個別面接調査により次の項目を調査した．既往歴，痛み，過去1年間の転倒・骨折歴，転倒恐怖感[7,9,12]，転倒恐怖感による外出控え（有，無），健康度自己評価[21]，基本的生活機能（移動，食事，入浴，着替え，トイレ）[11]は3つのカテゴリーに分類（①普通にできる，②一部の介助が必要，③全面介助）し，①に答えた場合自立，②と③に答えた場合非自立と判定した．老研式活動能力指標の13項目[15]は，各項目に「できる」の答えに1点，「できない」の答えに0点を与えて総合13点とし，下位尺度の点数が「手段的自立」5点，「知的能動性」4点，「社会的役割」4点の場合は，それぞれ自立と判定した．教室終了後，参加者の主観的体力と転倒予防に対する自信の変化は，4カテゴリーに分けて評価した．

2）測定項目

(1) 形態一般

身長，体重，血圧，心拍数，体脂肪率を測定した．体脂肪率はインピーダンス法（body fat analyzer：TBF-305, TANITA）により求めた．

(2) 身体機能

① 握力：スメドレー式握力計（hand dynamometer）を用いて，右，左のそれぞれに2回ずつ測定し（0.5kg単位），高い値を採用した．

② 開眼片足立ち：対象者は一辺40cmの四角の範囲内で，視線の高さで前方1mに設定された指標点を注視しながら腰に手を当て任意の足を挙上し，片足立ちを保持するように指示し，挙上した足が床面に接した時，あるいは立脚した足が移動した時を片足立ちの終了とした．最大30秒までの時間を2回測定し，良い記録を採用した．

③ 歩行速度：11mの平坦な歩行路に3mと8mの地点にラインテープを貼り，歩行開示後3mのラインテープを体幹の一部が超える時点から，8mのテープを超える時点までの5mの歩行時間を計測した．通常速度歩行は「いつも歩いている速さで歩いて下さい」，最大速度歩行は「出来る限り速く歩いて下さい，しかし走らないで下さい」と対象者に指示した．初めに通常速度歩行を1回，次に最大速度歩行を2度測定した．最大速度歩行は速い方を採用した．

④ タンデム歩行：平坦な床面に2.5mのテープを貼り，その線上に沿って「つぎ足歩行（片足の足先に他方の片足の踵を付けながら歩く）」を行い，完全にできた歩数のみを記録した．測定は2度行い良い記録を採用した．

⑤ 重心動揺：対象者は，重心動揺計（アニマ社製：グラブコーダ GS-10型）の上に両脚を揃えたロンベルグ足位で起立した．約1m離れた壁に貼られた目印を注視しながら，両腕を体側にそって自然におろし，姿勢を正し，開眼と閉眼条件それぞれ1回ずつ20秒間計測し，重心動揺軌跡長と動揺面積を求めた．

⑥ 膝伸展力：対象者は椅子に座り利き足の長さにセンサー部を合わせた上で，最大の力を発揮するように指示し，最大の力が発揮できる角度である90°においてマスキュレーター（GT-30：OG GIKEN）を用いて2回測定し，良い記録を採用した．

⑦ Functional reach：壁に横向きに自然立位に立って，伸展した両手を肩の高さまで挙げて両手の指先の先端を0cmに設定した後に片手を下ろし，次いで身体を可能な限り前傾して片手を床面と水平に伸展し続け，前傾した最大距離を計測した．3回測定し，平均値を採用した．

⑧ ペグ移動：対象者をPurdue Pegboard（Model 32020）前に座らせ，30秒間に差し込んだ数を2回計測し，良い記録を採用した．

3．介入の概要

1）運動指導の概要：対象者の事前調査の歩行速度と膝伸展力のデータの四分位を求め，第1四分位は体力レベルが高い群，第2四分位はやや高い群，第3四分位はやや低い群，第4四分位は低い群に分けた（1～3群：各9名，4群：8名）．担当スタッフ7名が対象者の安全性を確保した上で，各レベルに適した指導を行った．担当スタッフは，危機管理および疾病相談（医師1名），血圧測定お

よび健康管理（保健師１名），運動指導（健康運動指導士１名），指導補助（ヘルパー３名），教室管理およびプログラムの構成（専門家１名）の役割を担って，東京都内K市の公民館で週２回，１回当たり60分，12週間の運動指導を行った．要支援者が持つ身体機能や疾病状況に個人差が大きいことから，運動強度は，参加者が少しきつく感じるレベルに設定した．

２）運動プログラムの内容：運動指導は，準備運動，主運動，整理運動と構成し，次の内容を指導した[13]．

(1) 準備運動：指先の屈曲・伸展，腕の回内・回外，肘の上げ・下げ，腕上げ・横倒し（脇腹伸ばし），腰の前後曲げなど

(2) 主運動

①筋力アップ

a. 椅子に腰掛け：爪先上げ下げ・踵上げ下げ，片足上げ・膝伸ばし，片膝上げ・胸寄せ，膝合わせなど

b. 立位：踵上げ・下げ，踵上げ・膝曲げ，片足体重掛け，片足横上げなど

c. 座位：足首の伸展・屈曲，片足上げ・膝伸ばし，両足上げ・前後移動，足の裏合わせ・上げ下げなど

d. セラバンド体操：腕の水平開き閉じ，片腕後方斜め下げ，腕交差開閉，腰の前倒し・伸ばし，肘の曲げ伸ばし，膝の開閉，片足膝上げ胸寄せなど

②バランス訓練：パラレルスタンス（開眼・閉眼），セミタンデムスタンス（開眼・閉眼），タンデムスタンス（開眼・閉眼），片足立ち（開眼・閉眼），前後左右重心移動（開眼・閉眼）など

③歩行訓練：歩行中つま先上げ，片足体重掛け歩行，方向転換，歩幅調整横歩き，ステップ台昇り降りなど

(3) 整理運動：足踏み，肩回し，上体の前後倒し，深呼吸など

４．資料分析

項目別の平均値と標準偏差を求め，事前・事後の目的変数の変化を比較するために，連続変数については対応のあるｔ検定を，カテゴリー変数についてはχ^2検定を（McNemar法）行った．一部のアンケート調査項目については，項目毎に頻度分布を算出し，転倒予防教室参加後の変化を検討した．統計学的な危険率は５％とした．

Ⅲ．結　果

表１　参加回数別の人数

回　数	人　数	定　義
24回	2	
23回	3	
22回	4	
21回	3	
20回	4	完
19回	2	了
18回	1	
17回	0	
16回	2	
15回	1	
14回	0	
13回	0	
12回	0	
11回	0	
10回	1	
9回	0	
8回	0	脱
7回	0	
6回	0	落
5回	0	
4回	0	
3回	1	
2回	1	
1回	0	
0回	10	

出席率の範囲は45.7％～65.7％として平均出席率は55.9％であった．本研究では24回中，15回以上参加者（60.0％以上）を教室完了者（22名）と定義し，14回以下参加者（13名）を脱落者と定義した．24回参加者は２名（5.8％），20回以上参加者は16名（45.7％）であった（表１）．

介入前の対象者の健康度自己評価で健康だと答えた者の割合は51.4％であり，基本的生活機能は90％以上が自立，老研式活動能力指標による手段的自立や知的能動性の自立度は６割以上であったが，社会的役割の自立度は低かった．過去１年間の転倒率は42.9％（15/35）と高く，転倒者の73.3％が２回以上の複

表2　介入前における対象者（n=35）の諸特性

領域	変数	カテゴリー	n（%）
健康状態	健康度自己評価	健康	18（51.4）
基本的生活機能[1]	歩行	自立	33（94.3）
	食事	自立	33（94.3）
	トイレ	自立	34（97.1）
	入浴	自立	33（94.3）
	着替え	自立	34（97.1）
高次生活機能[2]			
手段的自立	バスや電車を使って1人で外出	できる	25（71.4）
	日用品の買物	できる	29（82.9）
	自分で食事の用意	できる	30（85.7）
	請求書の支払い	できる	29（82.9）
	預金・貯金の出し入れ	できる	28（80.0）
知的能動性	年金などの書類を書く	できる	22（62.9）
	新聞を読んでいる	できる	30（85.7）
	本や雑誌を読んでいる	できる	25（71.4）
	健康記事や番組に関心がある	できる	31（88.6）
社会的役割	友達の家を訪ねることがある	できる	17（48.6）
	家族や友達の相談にのる	できる	19（54.3）
	病人を見舞う	できる	19（54.3）
	若い人に自分から話しをかける	できる	24（68.6）
転倒関連	過去1年間の転倒経験	有	15（42.9）
	転倒恐怖感	有	31（88.6）

1）Katz ADL index
2）老研式活動能力指標

数回転倒（11/15）であった．転倒恐怖感を持っている者の割合は88.6%と高かった（表2）．

教室終了後の主観的体力の変化について調べたところ（表3），体が柔らかくなったと答えた者の割合が高く（80.0 %），バランス能力は60.0%が良くなったと答えた．足（55.0%）と腰（50.0 %）の筋力がアップしたと答えた者の割合は高かったが，腹部の筋力がアップしたと答えた者の割合（30.0%）は低かった．歩行は安定した20.0 %，やや安定した45.0 %であった．教室終了後に転倒予防の自信が付いてきた20.0 %，やや自信が付いてきた40.0 %と約6割は自信が付いてきたと答えた．

介入前後における身体機能の変化をみると（表4），最大速度歩行は事前1.14±0.46m/sから事後1.39±0.47m/s（21.4%改善，$P<0.001$），膝伸展力は事前17.67±6.01kgから事後23.57±8.49kg（33.4 %改善，$P<0.001$），ペグ移動は事前10.33±1.85個から事後11.48±1.89個（11.1 %改善，$P=0.013$）では介入後の値が有意に高かった．しかし，静的バランス能力を評価する動揺奇跡長と動揺面積には有意な変化が見られなかった．

表3　転倒予防教室修了後の主観的体力および転倒予防に対する自信の変化（n=20）

項目	カテゴリー	割合（%）*
柔軟性	体が柔らかくなった	30.0
	やや柔らかくなった	50.0
	変わらない	20.0
	やや硬くなった	0.0
バランス	良くなった	10.0
	やや良くなった	50.0
	変わらない	40.0
	やや悪くなった	0.0
足の筋力	アップした	25.0
	ややアップした	30.0
	変わらない	45.0
	やや低下した	0.0
腰の筋力	アップした	15.0
	ややアップした	35.0
	変わらない	50.0
	やや低下した	0.0
腹部の筋力	アップした	5.0
	ややアップした	25.0
	変わらない	70.0
	やや低下した	0.0
歩行	安定した	20.0
	やや安定した	45.0
	変わらない	35.0
	やや不安定になった	0.0
転倒予防に対する自信	自信が付いてきた	20.0
	やや自信が付いてきた	40.0
	変わらない	40.0
	やや自信がなくなった	0.0
	自信がなくなった	0.0

*事後調査参加者は22名であったが，2名の記入漏れのため20名のデータ分析

表4　転倒予防教室参加前後の身体機能の変化

変数	N	介入前 M±SD	介入後 M±SD	P値	改善率(%)
握力（kg）	22	18.77 ± 6.29	20.05 ± 6.86	0.134	6.8
開眼片足立ち（秒）	22	8.73 ± 8.54	8.18 ± 9.45	0.818	− 6.3
通常速度歩行（m/s）	22	0.72 ± 0.29	0.81 ± 0.34	0.114	12.2
最大速度歩行（m/s）	22	1.14 ± 0.46	1.39 ± 0.47	<0.001	21.4
膝伸展力（kg）	21	17.67 ± 6.01	23.57 ± 8.49	<0.001	33.4
Functional reach（cm）	21	29.15 ± 6.41	28.37 ± 6.82	0.617	− 2.7
ペグ移動（n/30s）	21	10.33 ± 1.85	11.48 ± 1.89	0.013	11.1
開眼動揺軌跡長（cm）	21	44.85 ± 18.16	47.84 ± 17.51	0.210	6.7
開眼動揺面積（cm²）	21	11.35 ± 9.28	8.87 ± 5.14	0.100	−21.9
閉眼動揺軌跡長（cm）	20	70.36 ± 22.47	71.28 ± 26.98	0.834	1.3
閉眼動揺面積（cm²）	20	15.78 ± 10.09	17.14 ± 13.81	0.656	8.6

表5　3ヶ月間の介入が転倒恐怖感と社会的役割に及ぼす影響

1）転倒恐怖感

		事後 無	有	合計
事前	無	2	0	2（9.5%）
	有	6	13	19（90.5%）
	合計	8（31.8%）	13（61.9%）	21（100.0%）

McNemar　検定　$P = 0.031$

2）転倒恐怖感による外出控え

		事後 無	有	合計
事前	無	9	3	12（60.0%）
	有	5	3	8（40.0%）
	合計	14（70.0%）	6（30.0%）	20（100.0%）

McNemar　検定　$P = 0.625$

3）社会的役割*

		事後 障害	自立	合計
事前	障害	11	5	16（80.0%）
	自立	0	4	4（20.0%）
	合計	11（55.0%）	9（45.0%）	20（100.0%）

McNemar　検定　$P = 0.063$
*老研式活動能力指標の下位尺度

3ヶ月の介入が転倒恐怖感と社会的役割に及ぼす影響について検討したところ（表5），転倒恐怖感は事前90.5％から事後61.9％と統計学的に有意（$P=0.031$）な減少が確認された．社会的役割の自立は事前20.0％から事後45.0％と統計学的に有意（$P=0.063$）ではないが，増加傾向が観察された．しかし，転倒恐怖感による外出制限には有意な変化が見られなかった．

Ⅳ．考　察

本研究では，要支援者35名を対象に約3ヶ月間の運動指導を行ったところ，運動プログラムによる脱落よりも家族の反対（3名），入院（2名），入所（3名），腰痛（2名），膝の痛み（1名），喘息（2名）などによって脱落者が多く，事後テストに参加した者は

22名（62.9％）であったが，幾つかの新たな知見を得ることができた．まず，主観的体力の変化として，からだが柔らかくなり，バランス能力がよくなり，足の筋力がアップされ，歩行が安定したとの肯定的な回答が得られたことである．次に，60.0％が転倒予防に対する自信がついてきたとの意識の変化とともに転倒恐怖感が有意に解消されたことの意義は大きいといえる．３番目に，歩行速度と足の筋力が有意に向上されたことを確認したことである．しかし，本研究のデータからは，３ヶ月間の運動指導によって，体力が有意に改善された者や改善が見られなかった者の特性を明らかにすることは不可能であった．これらの結果は，本研究で行った取り組みは要支援者の身体機能の改善のみではなくて，転倒恐怖感や転倒予防に対する自信など転倒関連意識の改善にも有効であったことを示唆するものである．

高齢者の転倒を効率的に予防するためには，対象者が持っている危険因子の中で，可変的な要因を選び出し，その危険因子の解消に焦点を当てた介入プログラムの構成がポイントであろう．転倒の原因を明らかにしようとする研究が数多く報告され，Whippleら[26]は，下肢筋力は転倒と強く関連することを，Woolleyら[28]は，バランスと移動機能は転倒の最も有効な予知因子であることを，Chuら[5]は，下肢の虚弱とタンデム歩行が転倒発生の最も有効な予知因子であることを，転倒の相対的な危険度は，筋力の低下（RR=4.4），転倒歴（RR=3.0），歩行障害（RR=2.9），バランス障害（RR=2.9）であるとの報告は[1]，今後の転倒予防の方向性を示唆する結果である．

転倒の危険因子の改善を目指す介入の成果について，Mulrowら[17]は，移動能力が15.5％の有意な改善効果がみられたことを，Lordら[16]は，筋力，反応時間，重心動揺などが有意に改善され，運動プログラムへの出席率が高い群で転倒発生率が有意に低かったと指摘し，介入プログラムの有効性を強調している．Buchnerら[3]は，介入によって初回転倒までの時間の有意な延長，転倒率の顕著な減少，入院期間の短縮，医療費の低減効果が得られたことを，Suzukiら[23]は，介入プログラムに参加することによって，筋力や動的バランス能力が有意に向上するとともに転倒率が有意に低下することを検証している．しかし，Rubensteinら[20]は，長期ケア施設入所者の中で転倒経験者を対象に行った介入の成果によれば，介入群は対照群より入院や入院期間は有意に改善されるが，転倒率は改善されないことを指摘し，施設入所者である虚弱高齢者の転倒予防を目指す取り組みの成果を上げるのは非常に困難であると結論付けている．Reinschら[19]は，高齢者を対象に行った介入によって転倒率，初回転倒までの時間，複数回転倒率，転倒によるケガだけではなくてバランス能力や筋力，転倒恐怖感，健康度自己評価においても効果が見られなかったことを指摘し，介入の効果がみられなかった理由としては，運動強度が弱いことや介入頻度が少なかったことが考えられると推察している．これらの先行研究の結果を踏まえて，本研究では要支援者の筋力やバランス能力，歩行機能の改善に焦点を当て３ヶ月間運動中心の指導を行った．その結果，多くの先行研究で転倒の危険因子として指摘されている下肢の筋力が30％以上向上する効果が得られ，本研究で行った介入は要支援者の転倒の危険因子の解消に大きく寄与したと考えられる．もう一つは，歩行機能の改善である．転倒の多くは歩行中に発生し，転倒の50％以上は「つまずく」ことが原因であることが指摘されている[2]．さらに，鈴木ら[22]は，通常歩行速度が遅い群の転倒率（26.3％）が速い群の転倒率（11.4％）より高いことを指摘し，転倒予防には歩行機能の改善が必要であることを強調している．本研究では，歩行機能を評価する最大歩行速度が介入後に20％以上向上する傾向が観察され，Mulrowら[17]の結果より優れる成果が得られた．本研究で得た，筋力の向上や歩行機能の改善は，要支援者の転倒率を抑制する方向へと働くと推測できる．

要支援者が直面しているもう一つの問題は，転倒恐怖感である．Howlandら[9]は地域

高齢者の55％が転倒恐怖感を持ち，転倒恐怖感を持っている者の56％が活動を制限することを，金ら[12]は75歳以上の要支援者は90％以上が転倒恐怖感を有し，男性66.7％，女性60.4％は転倒恐怖感のために外出を控える傾向にあると報告し，転倒恐怖感の解消を目的とした介入の必要性を強調している．転倒恐怖感のために外出など日常生活動作が制限される[7]と身体機能の低下が加速されるとともに社会的交流が減ることによって，閉じこもりや寝たきりになる危険性が増すことも否定できないことから，転倒恐怖感の解消策を早い段階に提供することは，虚弱高齢者の生活機能の自立支援策として不可欠な要因であろう．本研究では，転倒恐怖感が事前90.5％から事後61.9％と有意（$P=0.031$）に低下する傾向が観察されたことの意義は大きいといえる．本研究で提供した介入プログラムに参加することによって，筋力や歩行能力が有意に向上されるとともに転倒予防に自信が付いてきたとの意識の変化が，転倒恐怖感の解消に寄与したと推測できる．

さらに、本研究では指先の屈曲・伸展，指の押し合わせ，腕の回内・回外などの体操を行うことによって手の器用さを評価するペグ移動の値が改善されたと推測できる．要支援者が日常生活において，家事や洗濯，食事の後片付けなど手や腕を使用する動作は多く，手の器用さが改善されることによって要支援者の基本的生活機能の改善に寄与すると考えられる．

もう一つは，要支援者のバランス能力である．運動プログラムの中に，静的バランス能力と動的バランス能力の改善を目指す項目を取り入れ，補助を付け慎重に指導したが，バランス能力の改善効果は見られなかった．とくに，要支援者の動的バランス能力を向上させるためには集中的な指導が必要であるとの知見が得られた．事前調査でタンデム歩行が１～４歩出来た対象者は２人，33名が１歩もできなかったことであり，事後調査で１～４歩出来た者は４名であったことから，表４からタンデム歩行記録を除外した．今後，要支援者のバランス能力を高める介入の成果に期待を寄せる．

本研究には幾つかの限界点がある．まず，対象者が会場まで自力で来られない虚弱高齢者として地域に散在している状況から無作為割付け試験による対照群の設定が出来なかったことであり，介入群に３ヶ月間の介入を行い介入前後間の群内変化を検討した点である．二つ目は，介入後の転倒率を調査するための追跡調査が出来なかったことである．転倒率を調査するためには，少なくとも１年間の追跡調査が必要であるが，本研究では３ヶ月間の介入後に転倒の危険因子として指摘されている体力要素の変化に焦点を当てた分析に過ぎない点である．故に，本研究の意義は，転倒の危険因子として指摘されている体力要素の改善と転倒恐怖感の解消に及ぼす成果として認められるといえる．

本研究の終了に当たって見えてきた問題点は，入院・入所などの原因による脱落者が多かったことである．しかし，本研究では脱落者を減らすための具体的な対策を講じなかった．Dayら[6]は，運動だけの介入よりも運動指導に家庭内障害の解消や視力改善を取り入れる複合的な介入プログラムが転倒率の低下に有効であったことを，Wolf-Klein[27]らは，対象者の聴覚，眼，足の疾患に関する情報を共有しながら老年医，神経医，心臓医，理学療法士のチームアプローチによって転倒率が急減することを確認し，転倒予防に最も重要な要因は患者やサービス提供者の教育と血圧の定期的な管理，視力障害の改善，移動や歩行訓練など多面的な介入が必要であると指摘している．しかし，本研究では運動中心の介入プログラムだけ提供し，その効果を検証したものであり，複合的な介入プログラムの効果検証が今後の課題といえる．

V．まとめ

介護保険で要支援と認定された虚弱高齢者を対象に転倒予防を目指す３ヶ月間の介入プログラムを行ったところ，主観的体力が改善

されるとともに60.0 %が転倒予防に自信がついてきたとの回答を得た．さらに，膝伸展力と最大歩行速度を始めとする身体機能の有意な改善効果が観察され，要支援者に対する介入の意義は大であると判断された．しかし，介入後の転倒率の変化に関する追跡調査が今後の課題である．

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DIFFERENTIAL MINI-MENTAL STATE EXAMINATION PROFILES OF OLDER PEOPLE WITH DIABETES MELLITUS WITH EARLY ALZHEIMER'S DISEASE

To the Editor: The link between diabetes mellitus (DM) and dementia has recently attracted considerable attention.[1] In routine care, mild cognitive decline remains undetected and untreated in a considerable proportion of patients, resulting in several difficulties when treating diabetic elderly. Because diabetes mellitus may increase the risk for Alzheimer's disease (AD), screening and early diagnosis of AD is of great importance.[2,3]

Type 2 diabetes mellitus in elderly subjects can cause cognitive impairment, and memory and mental processing speed are the cognitive domains most often compromised.[4] When AD occurs silently in patients with DM, cognitive impairment from diabetes mellitus may conceal the early symptoms of AD. Thus, a brief cognitive measurement is needed to identify the transitional state between aging and early AD in elderly people with DM. The Mini-Mental State Examination (MMSE), comprising a series of items to measure orientation, memory, attention, and language, is a convenient and reliable tool to evaluate cognitive ability.[5] In this study, a preliminary cross-sectional analysis was conducted to characterize the profiles of MMSE items in patients with DM with early AD.

One hundred forty-six subjects aged 65 and older being treated at Kobe University Hospital and consisting of four groups (41 subjects without DM or AD (control), 52 subjects with DM but not AD (DMs), 23 subjects with DM and AD (DM-ADs), and 30 subjects with AD but not DM (ADs) were recruited. The four groups of subjects had means and standard deviations that were similar for age (75.4 ± 6.8, 74.4 ± 6.9, 75.4 ± 6.8, 73.4 ± 5.5, respectively) and education (11.5 ± 3.0, 10.2 ± 2.7, 10.5 ± 2.9, and 11.2 ± 2.4 years, respectively). Subjects suffering from alcohol abuse and with neurological deficits due to a previous stroke were excluded. DM was diagnosed based on information on clinical charts.[6] The control group members did not have DM and were assessed as having normal cognition based on a neurological evaluation. All participants were evaluated using a standardized, reliable assessment of dementia.[7] AD was clinically diagnosed as probable AD according to the clinical criteria of National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association.[8] Early AD was defined as a MMSE score of 24 or greater. The diagnosis of every patient was reassessed at a 1-year follow-up. The data were analyzed using Stat-View version 5.0 (SAS Institute, Inc., Cary, NC). Analysis of variance was used for all between-group comparisons, and significance was set at .05.

Total MMSE score was significantly higher for the control group than the other three groups, and DMs had higher MMSE scores than DM-ADs and ADs (Table 1). Temporal orientation was significantly more impaired in DM-ADs and ADs than in controls and DMs. Scores on Serial 7s, which examines attention and calculation, were lower for DMs and DM-ADs than for controls and were lower for DM-ADs than for ADs. Although registration

Table 1. Comparison of Mini-Mental State Examination (MMSE) Standard Scores and Individual Item Scores

Characteristic	Control	Subjects without AD with DM	Subjects with DM with AD	Subjects without DM with AD
	Mean ± Standard Deviation			
MMSE	27.3 ± 1.8	26.4 ± 1.9[a]	24.7 ± 0.8[b,c]	25.5 ± 1.5[b,d]
Temporal orientation	4.8 ± 0.5	4.8 ± 0.5	4.2 ± 1.0[e,f]	4.2 ± 1.0[e,g]
Spatial orientation	4.9 ± 0.3	4.8 ± 0.5	4.7 ± 0.6	4.7 ± 0.5
Registration	3.0 ± 0.2	3.0 ± 0.1	3.0 ± 0.0	3.0 ± 0.0
Attention/calculation	4.2 ± 1.2	3.3 ± 1.7[h]	2.8 ± 1.3[b,i]	3.7 ± 1.4
Recall	1.8 ± 0.9	1.8 ± 0.9	1.1 ± 0.9[j,k]	1.0 ± 0.8[b,c]
Naming	2.0 ± 0.0	2.0 ± 0.1	2.0 ± 0.0	2.0 ± 0.0
Repetition	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	1.0 ± 0.2
Three-stage command	3.0 ± 0.2	3.0 ± 0.2	3.0 ± 0.0	3.0 ± 0.2
Read and obey	1.0 ± 0.1	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0
Writing	1.0 ± 0.2	0.9 ± 0.3	1.0 ± 0.2	1.0 ± 0.2
Copy drawing	1.0 ± 0.2	0.9 ± 0.2	1.0 ± 0.2	1.0 ± 0.2
AD index	28.3 ± 3.4	28.6 ± 3.3	24.4 ± 4.0[b,c]	23.7 ± 4.5[b,c]

Note: The Alzheimer's disease (AD) index was calculated with the formula (temporal orientation+recall)/(total MMSE - Serial 7's) × 100 (%).
P-value vs [a]control = .02, [b]control < .001, [c]subjects without AD with diabetes mellitus type 2 (DM) < .001, [d]subjects without AD with DM = .002, [e]control = .003, [f]subjects without AD with DM = .02, [g]control = .001, [h]control = .006, [i]patients without DM with AD = .03, [j]control = .007, [k]subjects without AD with DM = .002.

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was comparable in all groups, recall was significantly more impaired in DM-ADs and ADs than in controls and DMs. There were no differences in the results for naming, repetition, three-stage command, reading, writing, and copy drawing. For psychometric screening of early AD, an AD index was constructed that represents the ratio of temporal orientation and recall to total MMSE score not including Serial 7 s. As expected, this index was much lower for DM-ADs and ADs than for controls and DMs, with a significant difference between DMs and DM-ADs. When a cutoff value of 26.3 was adopted for the AD index, screening for DM-ADs showed a sensitivity of 82.6% and a specificity of 71.2% for all subjects with DM.

These results imply that DMs overall had more cognitive impairment than controls. The MMSE subset analysis identified impaired attention and calculation as a specific characteristic of DMs, whereas patients with AD had lower scores in temporal orientation and recall.[9] To the authors' knowledge, no studies have shown an explicitly lower Serial 7 s scores for subjects with DM. A combination of features of cognitive decline due to DM and early AD seemed to characterize DM-ADs.

The MMSE was originally designed as a bedside screening instrument for dementia, with information for individual items apparently useful for differentiation between dementing conditions.[9] However, for a comparison of cognitive dysfunction in DMs and DM-ADs, a narrower range of the MMSE standard score is necessary to differentiate mental status between the two. In spite of this complication, this AD index could be used to assess potential early AD with reasonable sensitivity and specificity. Future prospective studies should be conducted to clarify whether this AD index can serve to identify patients with DM who are at risk of AD.

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ASSOCIATION BETWEEN VITAMIN B_6 AND WHITE MATTER HYPERINTENSITIES IN PATIENTS WITH ALZHEIMER'S DISEASE NOT MEDIATED BY HOMOCYSTEINE METABOLISM

To the Editor: In an earlier study,[1] we described in patients with Alzheimer's disease (AD) an inverse relationship between plasma vitamin B_6 levels and number of white matter hyperintensities (WMHs), as seen using magnetic resonance imaging (MRI). We suggested the involvement of homocysteine (Hcy) metabolism, because high levels of Hcy are considered to be a risk factor for WMH.[2] Hcy is partially metabolized through the transsulfuration pathway, in which Hcy condenses with serine to cystathionine, in a vitamin B_6–dependent reaction. Thus, Hcy could form the link between B_6 levels and degree of WMH. Hcy is also converted into methionine by the transmethylation pathway, which requires folate and vitamin B_{12}.

In the present study, plasma samples of patients with AD visiting the memory clinic during 2003 to 2006 were collected to investigate whether Hcy metabolism (Hcy, vitamin B_{12}, folate, and vitamin B_6) is associated with the occurrence of WMH in AD.

Seventy-six patients with probable AD from the VU University Medical Center memory clinic with complete

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Different effects of monocarboxylates on neuronal survival and β-amyloid toxicity

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Abstract

Glucose is a principal metabolic fuel in the central nervous system, but, when glucose is unavailable, the brain can utilize alternative metabolic substrates such as monocarboxylates to sustain brain functions. This study examined whether the replacement of glucose with monocarboxylates (particularly pyruvate and lactate) had an equivalent effect of glucose on neuronal survival in rat hippocampal organotypic slice cultures, or ameliorate the neurotoxicity induced by amyloid β-peptide (Aβ). The possible mechanism was also explored. We found that pyruvate and lactate alone increased cell death in the hippocampal slice cultures at 24 and 48 h. Supplementation of glucose-containing culture media and Aβ-treated culture media with pyruvate, but not lactate, attenuated cell death as strong as with trolox, known as a reactive oxygen species scavenger, and niacinamide, an NAD^+ precursor, and this protective effect was reversed by α-cyano-4-hydroxycinnamic acid. Pyruvate significantly increased the aconitase activity and the NAD^+ levels in the hippocampal slices in the presence of Aβ, but did not maintain the ATP levels. Our results indicate that pyruvate and lactate alone cannot replace glucose as an alternative energy source to preserve the neuronal viability in the hippocampal slice cultures. Pyruvate, in the presence of glucose, improves neuronal survival in the hippocampal slice cultures and also protects neurons against Aβ-induced cell death in which mitochondrial NAD(P) redox status may play a central role.

Introduction

Alzheimer's disease (AD) is a progressive senile dementia characterized by accumulation of neurofibrilly tangles and senile plaques in the brain. The deposition of β-amyloid protein (Aβ), the primary protein constituent of senile plaques, has been proposed to play a crucial role in the development of AD. Aβ is a 4-kDa peptide of 39–42 residues that has multi-neurotoxic effects leading to the dysfunction and death of neurons (Yanagisawa, 2000). The molecular mechanisms of Aβ inducing neuronal death are still controversial. Some reports suggest that the mechanism of Aβ-induced neurotoxicity results from Aβ-induced oxidative stress in culture (Mark *et al.*, 1996) or indirectly through intracellular production of reactive oxygen species (ROS) (Behl *et al.*, 1994; Schubert *et al.*, 1995) and the Aβ-induced neurotoxicity can be protected by antioxidants (Pereira *et al.*, 1999).

MCTs have gained interest as a neuroprotective agent. Lactate can be utilized as an energy substrate instead of glucose in the immature brain (Wada *et al.*, 1997), or as a sole energy substrate that can support synaptic function in the hippocampal slice (Schurr *et al.*, 1988), although its role in the synaptic activity in the adult brain is still debatable (Roberts, 1993; Takata *et al.*, 2001, 2004). Pyruvate has been reported to have a protective effect on neurons against the neurotoxicity of hydrogen peroxide *in vitro* (Desagher *et al.*, 1997), and also prevents oxidant-induced apoptosis in endothelial cells (Lee *et al.*, 2003), inhibits zinc toxicity in retinal cells (Yoo *et al.*, 2004) and protects neurons against Aβ-induced neuronal death in primary neuronal cultures (Alvarez *et al.*, 2003). By contrast, the role of pyruvate as an alterative to glucose in the maintenance of synaptic activity is still controversial (Kanatani *et al.*, 1995). Therefore, even the current numerous findings do not fully elucidate the role of MCTs on brain function.

In the present study, we have investigated whether MCTs can support neuronal viability instead of glucose and whether MCTs have a protective effect against Aβ-induced neuronal cell death in hippocampal slice cultures. Slice cultures may provide an ideal *in vitro* system to study the relationship between neuronal survival and substrate availability as they can offer the good conditions where glial and neuronal coupling is minimally disrupted during the experimental procedure. We also examined the different effects of two MCTs, lactate and pyruvate, on neuronal survival, and the potential protective effects of these MCTs against Aβ toxicity. In addition, we measured the effect of MCTs on aconitase activity, which has been shown to be a sensitive target of ROS (Liang *et al.*, 2000; Tretter & Adam-Vizi, 2000). These two MCTs are known to be the ATP source for hippocampal slices instead of glucose (Kanatani *et al.*, 1995; Takata & Okada, 1995). Another important cascade by which pyruvate can demonstrate a protective effect against cell injury is the preservation of NAD^+ levels (Sheline *et al.*, 2000). To investigate the possible role of pyruvate for an NAD^+ provider, we determined both the ATP and the NAD^+ levels of culture slices.

Materials and methods

Preparation of organotypic hippocampal slices

Organotypic hippocamal slices were prepared from the septal half of the hippocampus as described (Stoppini *et al.*, 1991). Nine- to

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11-day-old Wistar rats (Hartey, SLC, Japan) were killed by decapitation according to the guidelines for animal experimentation at Kobe University School of Medicine. The hippocampus was rapidly dissected at 4–6 °C and cut into 400-μm slices using a Mcillwain Tissue Chopper (Mickle Laboratory Engineering Co. Ltd, UK). The slices were immediately placed onto a 30-μm-diameter pored membrane (Millicell-CM, Millipore, Bedford MA, USA), transferred into a six-well microplate (Costar Corning Inc., NY, USA, four slices per well) with 1 mL slice culture medium per well and finally maintained at 37 °C in a 95% humidified atmosphere with 5% CO_2 incubator (Sanyo, Tokyo, Japan). The slice culture medium consisted of 50% minimum essential medium (MEM; Gibco, CA, USA), 25% Hanks' balanced salt solution (HBSS; Gibco), 25% heat inactivated horse serum (Gibco) supplemented 6.5 mg/mL glucose, 1% penicillin/streptomycin, and 1% Glutamax-†T (Gibco). The medium was changed every 3 days and cultures were used for the experiments after 14 days *in vitro*.

Treatment of hippocampal slices

After 14 days *in vitro*, the slices were washed, and then exposed for 24 or 48 h to glucose (10 mM), pyruvate (10 mM), lactate (10 mM), sucrose (10 mM) medium, or to the combinations of glucose (10 mM) with pyruvate (5 mM), pyruvate (10 mM), lactate (5 mM), trolox (1 mM), niacinamide (10 mM) or α-cyano-4-hydroxycinnamic acid (4-CIN; 0.2 mM). All the reagents listed above were supplemented in a serum-free and glucose-free medium containing 90 mM NaCl, 4 mM KCl, 0.1 mM $KHPO_4$, 0.1 mM $MgCl_2$, 0.5 mM $MgSO_4$, 0.1 mM Na_2HPO_4, 0.5 mM NaH_2PO_4, 14 mM $NaHCO_3$, 1.2 mM $CaCl_2$, 2 mM essential and non-essential amino acids, 0.02 mM vitamins, 1% Glutamax-‡T, and 2% B-27 supplement without antioxidants (Gibco), without or with 40 μM $A\beta_{25-35}$.

To establish the Aβ-induced neurotoxicity, slices were treated with two kinds of Aβ peptides ($A\beta_{25-35}$ and $A\beta_{1-42}$; Peptide Institute Inc., Osaka, Japan) in various concentrations. To obtain the oligomer of Aβ, Aβ was pretreated before applying it to each medium according to Roselli's method (Roselli *et al.*, 2005). Aβ was dissolved in DMSO at 2 mM, and thereafter it was diluted ten-fold in sterile PBS, vortexed for 30 min (at room temperature), and centrifuged at 15 000*g* at 4 °C for 1 h. The supernatant (180 μM) was aliquoted (100 μL) and frozen at −20 °C. Aliquots were diluted in culture medium to a final concentration immediately before use.

Assessment of cell death in hippocampal slices

The propidium iodide (PI) method was applied for the assessment of neuron death in hippocampal slices at 6, 24 and 48 h after each treatment in the CA1 region of the hippocampus. To label the nuclei of dead neurons, 4.6 μg/mL PI (Sigma, Louis St, MO, USA) was added to the wells of the culture microplates for 20 min. PI is a polar compound which only enters cells with damaged cell membranes. Inside the cells it binds to nucleic acids and becomes brightly red fluorescent. The dye is basically non-toxic to neurons and has been used as an indicator of neuronal integrity and cell viability (Macklis & Madison, 1990). Thus, the intensity of fluorescence is parallel to the cell death. After 20 min, digital imagines of PI fluorescence were obtained with an inverted fluorescence microscope (4× objective) equipped with a digital camera (Olympus IX70, Tokyo, Japan). After 14 days of *in vitro* culture, prior to conditioning the slices, the PI fluorescence intensity was adjusted to zero equivalent to the negative control (0% cell death). After the final image, all the living neurons were killed by adding 10 μM *N*-methyl-D-aspartic acid (NMDA; Sigma) and the final PI fluorescence intensity was adjusted to 100% equivalent to total neuronal cell death. The mean intensity (green values) of the PI fluorescence was measured using an image program Lumina Vision (v.24.3; Mitani Inc., Osaka, Japan).

Determination of aconitase activity

Aconitase activity was measured at 24 h after each treatment. Four slices were immediately homogenized in homogenization buffer, which consists of 50 mM Tris-HCl_2, pH 7.6, containing 1 mM cysteine, 1 mM citrate and 0.5 mM $MnCl_2$, and aconitase activity was then measured immediately to avoid any inactivation by O_2 after the extract had been centrifuged. Aconitase activity was measured in an assay medium containing the following: 50 mM Tris-HCl_2, 0.6 mM $MnCl_2$, 6 mM sodium citrate, 0.2% Triton X-100, 2 U/mL isocitrate dehydrogenase ($NADP^+$-dependent), and 1 U/mL catalase at 37 °C, pH 7.4. The reaction was initiated by the addition of 0.2 mM $NADP^+$. The fluorescence intensity was determined with a Wallac 1420 ARVOsx (Perkin Elmer Life Science, Tokyo, Japan) at 340 nm (Tretter *et al.*, 2005).

Measurement of ATP levels

At 6 or 24 h after each treatment, four slices were immediately homogenized in 0.5 mM perchloric acid with 1 mM thylene-diaminetetra acetic acid and centrifudged for 15 min at 300 *g*. The supernatant was neutralized with 2 M K_2HCO_4, recentrifuged and stored at −30 °C until assay of ATP. ATP was quantified by a luciferin-luciferase luminescence assay (Sigma). The protein content of the slices was determined by the method of Lowry and Passonneau (Okada, 1974).

Determination of NAD^+ levels

The NAD^+ levels of hippocampal slices were measured at 6 or 24 h after each treatment. Four slices were immediately homogenized by addition of 75% ethanol–0.05 M K_2HPO_4. Protein was precipitated by the addition of 0.02 M ZnCl and centrifuged at 13 000*g* at 4 °C for 15 min; the supernatant was stored at −80 °C until assay of NAD^+ levels (Tilton *et al.*, 1991). NAD^+ was measured after its enzymatic conversion to NADH by alcohol dehydrogenase, thus resulting in an increase in the fluorescence spectrum between 400 and 600 nm after an excitation at 340 nm using a Wallac 1420 ARVOsx (Perkin Elmer life science, Tokyo, Japan) (Sander *et al.*, 1976).

Materials

Trolox was purchased from Calbiochem (Darmstadt, Germany). Sodium pyruvate, sodium lactate, and 4-CIN were obtained from Sigma, and all other chemicals were from Wako (Tokyo, Japan) or Nacalai (Kyoto, Japan).

Statistical analysis

The data were expressed as the mean ± standard error of the mean (SEM) from three independent experiments. Statistical significance was established by ANOVA followed by Fisher's PLSD *post-hoc* test using Statview (v.5.0.1.0; SAS Institute Inc., Cary, NC, USA)