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Effects of Multicomponent Exercise on Cognitive Function in Elderly Korean Individuals

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Background and Purpose The aim of this study was to investigate the effects of multicomponent exercise on cognitive function, depression, and quality of life in elderly individuals.

Methods This study prospectively recruited 605 participants, and constructed an exercise pyramid comprising even distributions of daily physical activities, aerobic exercise, muscle-strengthening exercise, flexibility exercise, balance exercise, and activities that subjects could perform while sitting down. The exercise program was divided into six stages according to the participant's level of frailty. The 12-week exercise program intervention was conducted once yearly.

Results The exercise regimen was followed by 402 of the 605 enrolled participants, giving a dropout rate of 33.6%. The 27-month exercise program was completed by 60 participants. The scores for the Mini Mental State Examination for dementia screening (MMSE-DS), short form of the Geriatric Depression Scale, World Health Organization Quality of Life Assessment (WHOQOL-BREF), International Physical Activity Questionnaire (IPAQ), fear of falling, handgrip strength, and walking speed were improved after the exercise intervention. The analysis of frailty revealed that participants in the frail group showed greater improvements for the MMSE-DS, WHOQOL-BREF, IPAQ, fear of falling, handgrip strength, and walking speed.

Conclusions Individually customized, multicomponent exercise programs lead to improved levels of cognitive function, depression, and quality of life, especially among those who are more frail.

Key Words exercise, cognition, quality of life.

INTRODUCTION

Healthy aging is the process of developing and maintaining the functional abilities to facilitate the well-being of older individuals, which is of great social interest in the aging population. Maintaining cognitive functional abilities is an important part of healthy aging, and strategies are needed to slow the age-related decline of cognitive function and reduce disease-related cognitive impairment in older adults. Exercise is one such strategy because it improves not only physical health, by reducing the risk of health issues such as cardiovascular disease, stroke, diabetes, and functional disability,[1] but also mental health[2,3] and cognitive function in cognitively healthy older adults[4-6] as well as in older adults with cognitive impairment or dementia.[7,8] Despite the benefits of exercise, many older people lead less-active and more-sedentary lives. An exercise program that can be easily implemented by that population in the community is needed.

There are various types of exercise, including aerobic, muscle-strengthening, balance, and flexibility exercise. Among these types of exercise, cognitive function is most commonly as-

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sociated with aerobic exercise. Muscle-strengthening exercise is considered to have a positive effect on cognitive function, but this type of exercise was not as well-studied. There is a lack of evidence showing that exercise focused on flexibility and balance prevents cognitive decline. However, it is important to combine various types of exercise when attempting to promote healthy aging. Although aerobic exercise is occupies the largest portion, the American College of Sports Medicine (ACSM) and the American Heart Association (AHA)[9] encourage all kinds of exercise. Muscle strengthening exercise prevents age-related loss of muscle mass and balance exercise is important for elderly people who are at a high risk of falling. Several previous studies suggested that multicomponent exercise may have a larger effect on cognition in older adults than aerobic exercise alone.[5,10,11] However, the application of different exercise regimens in each study restricts the ability to identify the effects of multicomponent exercise.

An important aspect of aging that varies among individuals is frailty. Frailty is a geriatric syndrome characterized by increased vulnerability to possible stressors, and it is strongly predictive of mortality and disability.[12,13] The presence of three or more of the following five dimensions indicates frailty: weight loss, weakness, poor endurance, low energy level, and a low level of physical activity.[12] The severity of frailty can be divided into three levels: not frail, prefrail, and frail. Frailty has cognitive components as well as physical components, and these components exert adverse affects on each other.[14,15] Although exercise is an important method of managing frailty,[16] few studies have analyzed the effects of balanced multicomponent exercise on frailty in elderly people.

Based on the above-described situation, we developed individually customized multicomponent exercise programs that could be performed by elderly individuals in their homes. The present study analyzed the effectiveness of multicomponent exercise on the cognitive function, depression, and quality of life of elderly individuals. Our hypothesis was that a multicomponent exercise program would be effective at improving health-related problems in community-dwelling older individuals.

METHODS

Study participants

Participants who were older than 60 years and were followed by welfare centers for the elderly, Seongnam Center for Senior Health, and Seongnam Visiting Health Care Center were arbitrarily recruited from local communities. We visited these centers and advertised multicomponent exercise as a part of the public health care and welfare program. The participants were not compensated financially, and participated voluntarily. The exclusion criteria included subjects who had 1) participated in other clinical trials within the previous 4 weeks or had received a clinical trial drug treatment; 2) physical disabilities and could not walk independently; 3) signs of a severe or unstable physical illness, such as acute and severe asthma, severe and unstable cardiovascular disease, an active peptic ulcer, or renal disease to the extent of severe liver disease or requiring renal dialysis; 4) severe hearing or visual difficulties that inhibited the ability to evaluate the effectiveness of exercise; or 5) not agreed to participate in this study.

Applying the above criteria resulted in the recruitment of 605 subjects who were willing to participate voluntarily. Among them, 203 subjects were excluded from the analysis because they stopped performing the exercise before the first postexercise evaluation. Ethical approval was obtained from the Institutional Review Board of the Korea National Institute for Bioethics Policy (P01-201702-11-001). All participants provided written informed consent before enrollment.

The multicomponent exercise pyramid

To develop dementia prevention exercise regimens that are individually customized according to the physical strength of the individuals, we assembled a specialist team composed of two neurologists, a professor of medicine, a professor of biotechnology, social workers, physiotherapists, occupational therapists, and nurses. These specialists constructed an exercise pyramid model by referring to the ACSM/AHA recommendations for physical activity and public health in older adults.[9] The exercise pyramid was designed to encourage the participants to perform an even distribution of daily physical activities, aerobic exercise, muscle-strengthening exercise, flexibility exercise, balance exercise, and activities while sitting down. The sedentary activity included simple cognitive activities (e.g., reciting the names of 15 cities). The exercise pyramid is in the form of a triangular diagram that includes the optimal amount of each type of exercise on each stage so as to create a balanced regimen. The pyramid consists of six stages that differ in intensity and frequency: the frail, prefrail, and not-frail groups were assigned to stages 1 and 2, 3 and 4, and 5 and 6, respectively (Supplementary Material 1 in the online-only Data Supplement). The pyramid is designed so that a participant can perform a customized exercise regimen according to their degree of frailty. The frail group was excluded from the balance exercises in order to prevent accidents such as falls.

Assessment of frailty

To assign individually customized exercise programs, the participants were categorized into frail, prefrail, and not-frail groups according to the Fried frailty criteria.[12] These criteria assess the five dimensions of frailty using self-reported and performance-based measures. This study modified some of those dimensions for the context-specific situations in Korea. The five dimensions are as follows: 1) unintentional weight loss of 4.5 kg during the previous year; 2) muscle weakness as assessed by handgrip strength measurements, while accounting for sex and body mass index; 3) exhaustion, which was considered to be indicated by a score of 8 or higher on the short form of the Geriatric Depression Scale (GDS-SF)[17-19]; 4) walking speed, which was evaluated by a 3-m walk based on the typical characteristics of actual living spaces in Korea; and 5) low physical activity, as evaluated using the International Physical Activity Questionnaire (IPAQ). The weekly rate of energy expenditure was calculated and compared with reference values according to sex. After evaluating the five dimensions, frail, prefrail, and not-frail individuals were defined as those who met at least three criteria, one or two criteria, and none of the criteria, respectively (Supplementary Material 2 in the online-only Data Supplement).

Components and methods of the exercise program

A 12-week exercise program intervention was conducted yearly from April 2015 to July 2017. Participants were interviewed about their current lifestyle before the exercise training, including their habitual physical activity and current medication. During the exercise training, 15-minute educational sessions were conducted to improve awareness of the benefits of exercise on dementia and to motivate the participants. This was followed by the instructor demonstrating the exercises to the participants in a step-by-step manner for 30 minutes. Exercise training was conducted once monthly for a total of three times during the 12-week period in groups or individually. The participants performed daily exercise individually and voluntarily at home. During the 12-week period, we kept track of the participants on a weekly basis by phone, ensuring that they were exercising according to their assigned level and that they completed a self-assessment form daily (Fig. 1 and Supplementary Material 3 in the online-only Data Supplement).

Clinical assessment and outcomes

The following assessments were performed before and after each yearly implementation of the 12-week exercise program: cognitive status, using the Mini Mental State Examination for dementia screening (MMSE-DS); depression status, using the GDS-SF; quality of life, using the World Health Organization Quality of Life Assessment (WHOQOL-BREF); handgrip strength; 3-m walking speed; fear of falling, using a Visual Analog Scale for fear of falling (VAS-FOF); and level of physical activity, using the IPAQ. Depending on the participant's exercise duration, a maximum of six evaluations were conducted over the 27-month study period (Fig. 1).

The MMSE-DS is a screening test developed by Folstei et al. that is used for simple and rapid assessments of cognitive impairment.[20] Higher scores indicate better cognitive function, and the maximum score is 30 points. Cognitive impairment was defined as any score lower than the cutoff score of the MMSE-DS based on the education level, age, and sex. The GDS-SF is designed to detect depression in elderly people.[21,22] The original scale was developed as a 30-item test, but its 15-item short form was used in this study. Depression is characterized by a score of ≥8 on this test, with higher scores indicating more-severe depressive symptoms. The WHOQOL-BREF is a questionnaire developed by the World Health Organization for assessing the quality of life of individuals.[23,24] This questionnaire consists of 26 items that measure 4 domains: physical health, psychological health, social relationships, and environment. Each WHOQOL-BREF item is rated on a 5-point Likert Scale from 1 to 5, with higher scores indicating a higher quality of life. Fear of falling was measured using a Visual Analog Scale[25,26] ranging from 0 (no fear of falling) to 100 (extreme fear of falling). Finally, the IPAQ was used to measure health-related physical activity.[27-29] This measure assesses the intensity of the physical activities that people engage in over 7 days, and then quantifies the total physical activity as the metabolic equivalent task minutes per week and also based on the total sitting time. The intensity of physical activity is classified into vigorous, moderate, walking, and sitting. The recorded physical activity time was converted into the calories used for physical activity per week based on the IPAQ value conversion guidelines.

Statistical analysis

Descriptive data are presented as frequencies and percentages for categorical variables and mean±standard-deviation values for continuous variables. The chi-square test, *t*-test, and ANOVA were used for group comparisons. Two-way repeated-measures ANOVA for the continuous variables and generalized estimating equations for the categorical variables were used to identify annual changes in variables before and after the exercise intervention. One factor (before and after the intervention) shows the short-term effect of multicomponent exercise, and the other factor (annual change) shows the long-term effect of multicomponent exercise. Probability values of $p<0.05$ were considered statistically significant. All statistical analyses were performed with SAS® software (version 9.4, SAS Institute, Cary, NC, USA).

RESULTS

The exercise regimen was followed by 402 of the 605 enrolled participants. The duration of exercise varied with the voluntary will of individual participants. The 27-month exercise program (3 consecutive years) was completed by 60 subjects,

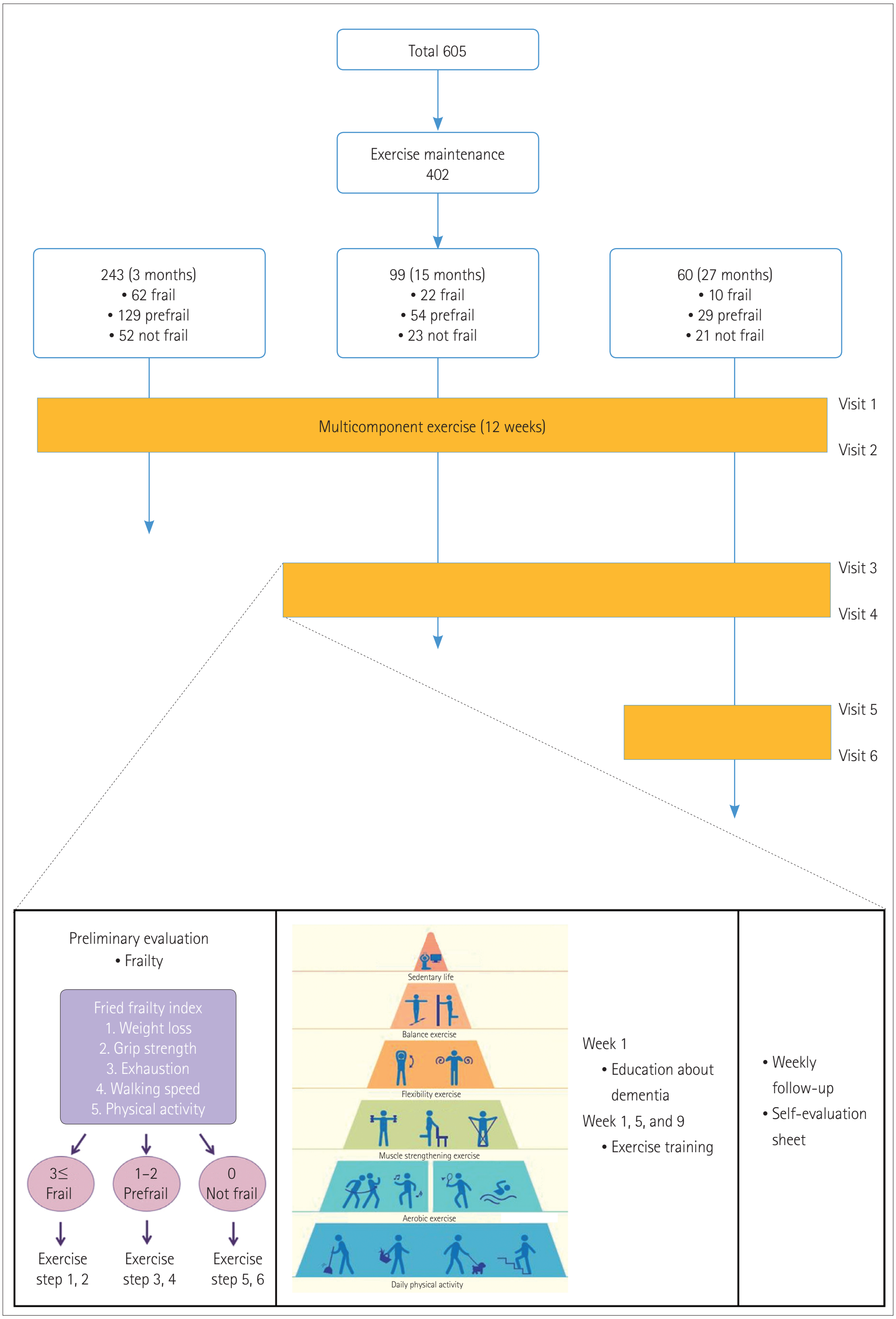

Fig. 1. Flow diagram of the study population and intervention.

while 243 subjects followed the regimen for 3 months and 99 subjects followed it for 15 months. Differences between the subjects who did and did not finish the program are listed in Table 1. The participants who maintained their exercise were aged 76.2±5.4 years, and 81.7% of them were female. The duration of education was 5.2±4.6 years. The MMSE-DS score was 24.2±4.9, and 16.7% of them had cognitive impairment. The scores on the GDS-SF, WHOQOL-BREF, and VAS-FOF were 3.5±3.4, 88.4±11.8, and 46.5±28.9, respectively. The values for the IPAQ and handgrip strength test were 1,372.4±1,396.6 kcal and 19.6±8.2 kg, respectively; these values were within the normal range for 95.0% and 56.7% of the participants, respectively. The walking speed was 0.9±0.3 m/s, and 81.7% of the participants had a walking speed within the normal range (Table 1).

The 60 subjects who completed the exercise program comprised 10, 29, and 21 who were defined as frail, prefrail, and not frail according to the Fried frailty index. The subjects were older in the frail group (78.7±4.8 years in the frail group vs. 76.6 ± 4.8 years and 74.4 ± 6.1 years in the prefrail and not-frail groups, respectively, p<0.001), and the frail group included subjects with significant illiteracy (p<0.001). There was no significant intergroup difference in the disease status except for heart disease. Compared to the other groups, the frail group had significantly lower MMSE-DS scores (p=0.003) and handgrip strength (p=0.028), and significantly higher rates of cognitive impairment (p=0.002), depression (p<0.001), and subjects with abnormal walking speeds (p<0.001) (Table 2).

Table 1. Baseline characteristics of subjects who were included in the 1-year follow-up and who completed the 27-month exercise program

	Total	Completed the study	One-year follow-up	*p*
Number of subjects	402 (100.0)	60 (14.9)	342 (85.1)	
Sex, female	344 (85.6)	49 (81.7)	295 (86.3)	0.351
Age, years	77.5±6.4	76.2±5.4	77.7±6.5	0.089
Education, years	5.2±4.6	5.2±4.6	5.3±4.6	0.974
Literate	321 (76.9)	45 (75.0)	276 (80.7)	0.310
Living alone	161 (40.0)	22 (36.7)	139 (40.6)	0.562
Medical insurance	306 (76.1)	60 (100.0)	246 (71.9)	<0.001
Diseases				
Hypertension	255 (64.4)	40 (66.7)	215 (62.9)	0.573
Diabetes	102 (25.4)	15 (25.0)	87 (25.4)	0.943
Hyperlipidemia	100 (24.9)	17 (28.3)	83 (24.3)	0.502
Heart disease	59 (14.7)	6 (10.0)	53 (15.5)	0.267
Stroke	24 (6.0)	3 (5.0)	21 (6.1)	0.731
Physical activity				
Vigorous	8 (1.2)	1 (1.7)	7 (2.2)	0.785
Moderate	152 (37.8)	11 (18.3)	141 (44.8)	<0.001
Walking	331 (82.3)	59 (98.3)	272 (86.4)	0.008
Sitting	218 (54.2)			
MMSE-DS score	24.5±4.2	24.2±4.9	24.6±4.0	0.554
Cognitive impairment	38 (9.5)	10 (16.7)	28 (8.2)	0.038
GDS-SF score	4.6±4.2	3.5±3.4	4.8±4.3	0.008
Depression	98 (24.4)	9 (15.0)	89 (26.0)	0.067
WHOQOL-BREF score	82.9±15.6	88.4±11.8	81.9±16.0	<0.001
VAS-FOF score	47.2±31.8	46.5±28.9	47.4±32.4	0.848
	298 (74.1)	46 (76.7)	252 (73.7)	0.627
IPAQ value, kcal	1,258.3±1,339.1	1,372.4±1,396.6	1,238.3±1,329.8	0.475
Normal	337 (83.8)	57 (95.0)	280 (81.9)	0.011
Handgrip strength, kg	18.5±7.2	19.6±8.2	18.3±7.0	0.208
Normal	174 (43.3)	34 (56.7)	140 (40.9)	0.023
Walking speed, m/s	0.9±0.3	0.9±0.3	0.9±0.3	0.058
Normal	270 (67.2)	49 (81.7)	221 (64.6)	0.010

The chi-square test and ANOVA were used for group comparisons. Data are *n* (%) or mean±standard-deviation values.
GDS-SF: short form of the Geriatric Depression Scale, IPAQ: International Physical Activity Questionnaire, MMSE-DS: Mini Mental State Examination for dementia screening, VAS-FOF: Visual Analogue Scale for fear of falling, WHOQOL-BREF: World Health Organization Quality of Life Assessment.

Table 2. Baseline characteristics of subjects in the three frailty groups who completed the 27-month study

	Total	Frail	Prefrail	Not frail	*p*
Number of subjects	60 (100.0)	10 (16.7)	29 (48.3)	21 (35.0)	
Sex, female	49 (81.7)	10 (100.0)	22 (75.9)	17 (81.0)	0.234
Age, years	76.2±5.4	78.7±4.8	76.6±4.8	74.4±6.1	<0.001
Education, years	5.2±4.6	1.2±2.8	4.8±4.6	7.8±3.8	0.236
Literate	45 (75.0)	3 (30.0)	21 (72.4)	21 (100.0)	<0.001
Living alone	22 (36.7)	4 (40.0)	13 (44.8)	5 (23.8)	0.458
Medical insurance	60 (100.0)	10 (100.0)	29 (100.0)	21 (100.0)	
Diseases					
Hypertension	40 (66.7)	7 (70.0)	18 (62.1)	15 (71.4)	0.763
Diabetes	15 (25.0)	3 (30.0)	8 (27.6)	4 (19.1)	0.729
Hyperlipidemia	17 (28.3)	1 (10.0)	9 (31.0)	7 (33.3)	0.365
Heart disease	6 (10.0)	0 (0.0)	1 (3.5)	5 (23.8)	0.031
Stroke	3 (5.0)	0 (0.0)	2 (6.9)	1 (4.8)	0.113
Dementia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.790
Physical activity					
Vigorous	1 (1.7)	0 (0.0)	0 (0.0)	1 (6.0)	
Moderate	11 (18.3)	0 (0.0)	5 (17.2)	6 (28.6)	
Walking	59 (98.3)	10 (100.0)	29 (100.0)	20 (95.2)	
MMSE-DS score	24.2±5.0	17.5±5.3	24.1±4.0	27.4±2.0	0.003
Cognitive impairment	10 (16.7)	5 (6.6)	5 (3.9)	0 (3.2)	0.002
GDS-SF score	3.5±3.4	6.6±3.9	3.2±3.6	2.4±1.8	0.004
Depression	9 (15.0)	6 (60.0)	3 (10.3)	0 (0.0)	<0.001
WHOQOL-BREF score	88.4±11.8	84.4±16.2	90.5±11.1	87.3±10.4	0.169
VAS-FOF score	46.5±28.9	65.0±30.3	44.1±31.1	41.0±22.1	0.105
IPAQ value, kcal	1,372.4±1,396.6	595.8±293.3	1,197.3±1,032.8	1,983.9±1,866.4	0.089
Normal	57 (95.0)	9 (90.0)	27 (93.1)	21 (100.0)	0.396
Handgrip strength, kg	19.6±8.2	11.8±4.1	19.6±9.1	23.3±5.6	0.028
Normal	34 (56.7)	0 (0.0)	13 (44.8)	21 (100.0)	<0.001
Walking speed, m/s	0.9±0.2	0.7±0.2	1.0±0.2	1.1±0.1	0.223
Normal	49 (81.7)	4 (40.0)	24 (82.8)	21 (100.0)	<0.001

The chi-square test and ANOVA were used for group comparisons. Data are *n* (%) or mean±standard-deviation values.
GDS-SF: short form of the Geriatric Depression Scale, IPAQ: International Physical Activity Questionnaire, MMSE-DS: Mini Mental State Examination for dementia screening, VAS-FOF: Visual Analogue Scale for fear of falling, WHOQOL-BREF: World Health Organization Quality of Life Assessment.

The scores for the MMSE-DS (p<0.001 for time), GDS-SF (p=0.017 for time and p=0.023 for intervention), and WHO-QOL-BREF (p<0.001 for intervention) improved significantly after the multicomponent exercise. The VAS-FOF score (p=0.001 for intervention), handgrip strength (p=0.010 for time and p=0.037 for intervention), and walking speed (p=0.027 for intervention) also improved significantly. There were statistically significant improvements in the WHOQOL-BREF score (p=0.003 for time) and IPAQ value (p=0.002 for time and p=0.001 for intervention), but a significant interaction was observed across time and exercise intervention for WHO-QOL-BREF (p=0.003) and IPAQ (p<0.001).

Analyzing the effects of multicomponent exercise according to the degree of frailty revealed that the frail group showed significant improvements in the MMSE-DS score (p=0.001 for time), WHOQOL-BREF score (p=0.049 for time and p=0.004 for intervention), VAS-FOF score (p=0.040 for time), IPAQ value (p=0.035 for intervention), handgrip strength (p=0.023 for time and p=0.009 for intervention), and walking speed (p=0.026 for intervention). However, the GDS-SF score did not change significantly, and there was no significant interaction across time and exercise for any of the variables. The prefrail group showed significant improvements in the MMSE-DS score (p<0.001 for time), WHOQOL-BREF score (p<0.001 for intervention), and handgrip strength (p=0.003 for time time), whereas the GDS-SF score, VAS-FOF score, IPAQ value, and walking speed did not change significantly. The not-frail group showed significant improvements in the MMSE-DS score (p=0.006 for time), WHOQOL-BREF score (p<0.001 for intervention), VAS-FOF score (p=0.009 for in-

Table 3. Effects of multicomponent exercise according to the degree of frailty

	Year 1		Year 2		Year 3		*p*		
	Before	After	Before	After	Before	After	year	Intervention	Year×intervention
MMSE-DS score									
Total (*n*=60)	24.2±4.9	24.4±4.6	25.4±3.8	25.8±4.0	25.9±3.5	26.3±3.6	<0.001	0.057	0.946
Frail (*n*=10)	17.5±5.3	19.4±4.4	20.1±2.9	20.8±3.7	22.3±4.1	22.1±4.6	0.001	0.072	0.309
Prefrail (*n*=29)	24.1±4.0	24.0±4.3	25.2±3.1	25.6±3.8	25.6±3.1	25.9±3.1	<0.001	0.576	0.594
Not frail (*n*=21)	27.4±2.0	27.5±1.9	28.2±1.9	28.5±1.3	28.0±1.8	28.7±1.2	0.006	0.154	0.362
Cognitive impairment									
Total	10 (16.7)	7 (11.7)	3 (5.0)	2 (3.3)	5 (8.3)	2 (3.3)	0.153	0.010	
Frail	5 (50.0)	4 (40.0)	2 (20.0)	1 (10.0)	2 (20.0)	1 (10.0)	0.131	<0.001	
Prefrail	5 (17.2)	3 (10.3)	1 (3.4)	1 (3.4)	2 (6.9)	1 (3.4)	0.276	0.249	
Not frail	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.8)	0 (0.0)			
GDS-SF score									
Total	3.5±3.4	3.3±3.5	3.3±3.7	2.2±3.0	2.7±3.1	2.6±3.3	0.017	0.023	0.082
Frail	6.6±3.9	4.9±4.0	5.2±4.2	3.9±3.8	4.9±4.0	4.5±3.5	0.309	0.074	0.622
Prefrail	3.2±3.6	3.3±3.9	3.5±3.9	2.0±2.8	2.8±3.1	2.7±3.5	0.288	0.140	0.061
Not frail	2.4±1.8	2.3±2.3	2.2±2.7	1.8±2.8	1.5±2.1	1.6±2.6	0.099	0.592	0.769
Depression									
Total	9 (15.0)	8 (13.3)	10 (16.7)	6 (10.0)	6 (10.0)	7 (11.7)	0.421	0.424	
Frail	6 (60.0)	3 (30.0)	3 (30.0)	2 (20.0)	3 (30.0)	2 (20.0)	0.357	0.162	
Prefrail	3 (10.3)	5 (17.2)	5 (17.2)	2 (6.9)	3 (10.3)	4 (13.8)	1.000	0.111	
Not frail	0 (0.0)	0 (0.0)	2 (9.5)	2 (9.5)	0 (0.0)	1 (4.8)	1.000	0.161	
WHOQOL-BREF score									
Total	88.4±11.8	93.8±13.7	87.5±13.8	98.2±15.5	93.9±16.1	97.6±14.7	0.003	<0.001	0.003
Frail	84.4±16.2	87.8±12.9	82.4±17.4	94.4±17.9	92.0±18.6	96.2±12.4	0.049	0.004	0.081
Prefrail	90.5±11.1	95.1±13.4	88.9±13.9	99.3±16.3	94.5±17.9	98.4±16.4	0.270	<0.001	0.111
Not frail	87.3±1.4	94.7±14.4	87.8±11.9	98.4±13.7	93.8±12.6	97.0±13.9	0.055	<0.001	0.090
VAS-FOF score									
Total	46.5±28.9	39.6±33.9	39.1±33.7	34.9±34.5	41.2±32.6	28.3±30.3	0.128	0.001	0.193
Frail	65.0±30.3	56.5±30.4	54.0±31.0	40.0±35.9	41.0±31.5	27.0±31.3	0.040	0.114	0.821
Prefrail	44.1±31.1	37.8±32.5	36.0±36.6	35.9±36.7	40.3±34.4	27.3±29.5	0.530	0.088	0.229
Not frail	41.0±22.1	34.1±36.2	36.2±30.1	31.2±31.9	42.4±32.2	30.2±32.3	0.839	0.009	0.682
IPAQ value, kcal									
Total	1,372.4±1,396.6	1,132.5±1,302.1	1,258.0±1,030.0	1,796.8±1,302.4	1,310.9±1,194.5	2,433.3±2,190.7	0.002	0.001	<0.001

Table 3. Effects of multicomponent exercise according to the degree of frailty (continued)

	Year 1		Year 2		Year 3		p		
	Before	After	Before	After	Before	After	year	Intervention	Year×intervention
Frail	595.8±293.3	526.9±700.1	660.0±385.0	1,479.4±1,258.4	739.5±563.1	1,365.3±1,007.4	0.118	0.035	0.225
Prefrail	1,198.3±1,032.8	1,025.5±1,408.3	1,461.0±1,041.4	1,925.2±1,479.4	1,315.8±1,043.6	2,798.4±2,366.7	0.001	0.016	<0.001
Not frail	1,983.9±1,866.4	1,568.6±1,266.9	1,262.3±1,142.7	1,770.5±1,073.2	1,576.3±1,518.0	2,437.8±2,257.3	0.346	0.097	0.055
Normal									
Total	57 (95.0)	49 (81.7)	55 (91.7)	58 (96.7)	53 (88.3)	57 (95.0)	1.000	0.008	
Frail	9 (90.0)	6 (60.0)	9 (90.0)	10 (100.0)	7 (70.0)	9 (90.0)	0.714	0.025	
Prefrail	27 (93.1)	23 (79.3)	28 (96.6)	27 (93.1)	26 (89.7)	28 (96.6)	0.350	0.385	
Not frail	21 (100.0)	20 (95.2)	18 (85.7)	21 (100.0)	20 (95.2)	20 (95.2)	0.301	0.072	
Handgrip strength, kg									
Total	19.6±8.2	19.9±9.1	20.9±8.4	21.6±8.2	20.3±7.5	21.0±7.8	0.010	0.037	0.807
Frail	11.8±4.1	13.8±3.0	14.1±3.3	16.0±3.9	13.8±2.8	15.0±2.8	0.023	0.009	0.798
Prefrail	19.6±9.1	18.9±9.8	20.8±9.3	21.7±9.2	20.2±7.9	21.1±8.9	0.003	0.337	0.124
Not frail	23.3±5.6	24.2±8.1	24.2±6.9	24.1±6.9	23.5±6.5	23.5±6.1	0.830	0.535	0.689
Normal									
Total	34 (56.7)	29 (48.3)	31 (51.7)	33 (55.0)	31 (51.7)	34 (56.7)	0.960	0.324	
Frail	0 (0.0)	1 (10.0)	1 (10.0)	2 (20.0)	2 (20.0)	2 (20.0)	0.198	0.069	
Prefrail	13 (44.8)	12 (41.4)	11 (37.9)	15 (51.7)	12 (41.4)	14 (48.3)	0.696	0.117	
Not frail	21 (100.0)	16 (76.2)	19 (90.5)	16 (76.2)	17 (81.0)	18 (85.7)	0.749	0.410	
Walking speed, m/s									
Total	0.9±0.2	1.0±0.3	0.9±0.2	1.0±0.2	1.0±0.2	1.0±0.2	0.519	0.027	0.032
Frail	0.7±0.2	0.7±0.2	0.8±0.2	0.8±0.2	0.8±0.2	0.8±0.2	0.246	0.026	0.655
Prefrail	1.0±0.2	0.9±0.2	0.9±0.1	1.0±0.2	0.9±0.2	0.9±0.2	0.822	0.725	0.020
Not frail	1.1±0.1	1.1±0.2	1.0±0.1	1.1±0.2	1.1±0.2	1.1±0.2	0.760	0.027	0.317
Normal									
Total	49 (81.67)	46 (76.67)	50 (83.33)	53 (88.33)	47 (78.33)	52 (86.67)	0.910	0.015	
Frail	4 (40.0)	3 (30.0)	4 (40.0)	7 (70.0)	5 (50.0)	6 (60.0)	0.612	0.005	
Prefrail	24 (82.8)	22 (75.9)	25 (86.2)	26 (89.7)	22 (75.9)	26 (89.7)	0.796	0.034	
Not frail	21 (100.0)	21 (100.0)	21 (100.0)	20 (95.2)	20 (95.2)	20 (95.2)	0.282	0.544	

Data are from two-way repeated-measures ANOVA and generalized estimating equations. Data are *n* (%) or mean±standard-deviation values.
GDS-SF: short form of the Geriatric Depression Scale, IPAQ: International Physical Activity Questionnaire, MMSE-DS: Mini Mental State Examination for dementia screening, VAS-FOF: Visual Analogue Scale for fear of falling, WHOQOL-BREF: World Health Organization Quality of Life Assessment.

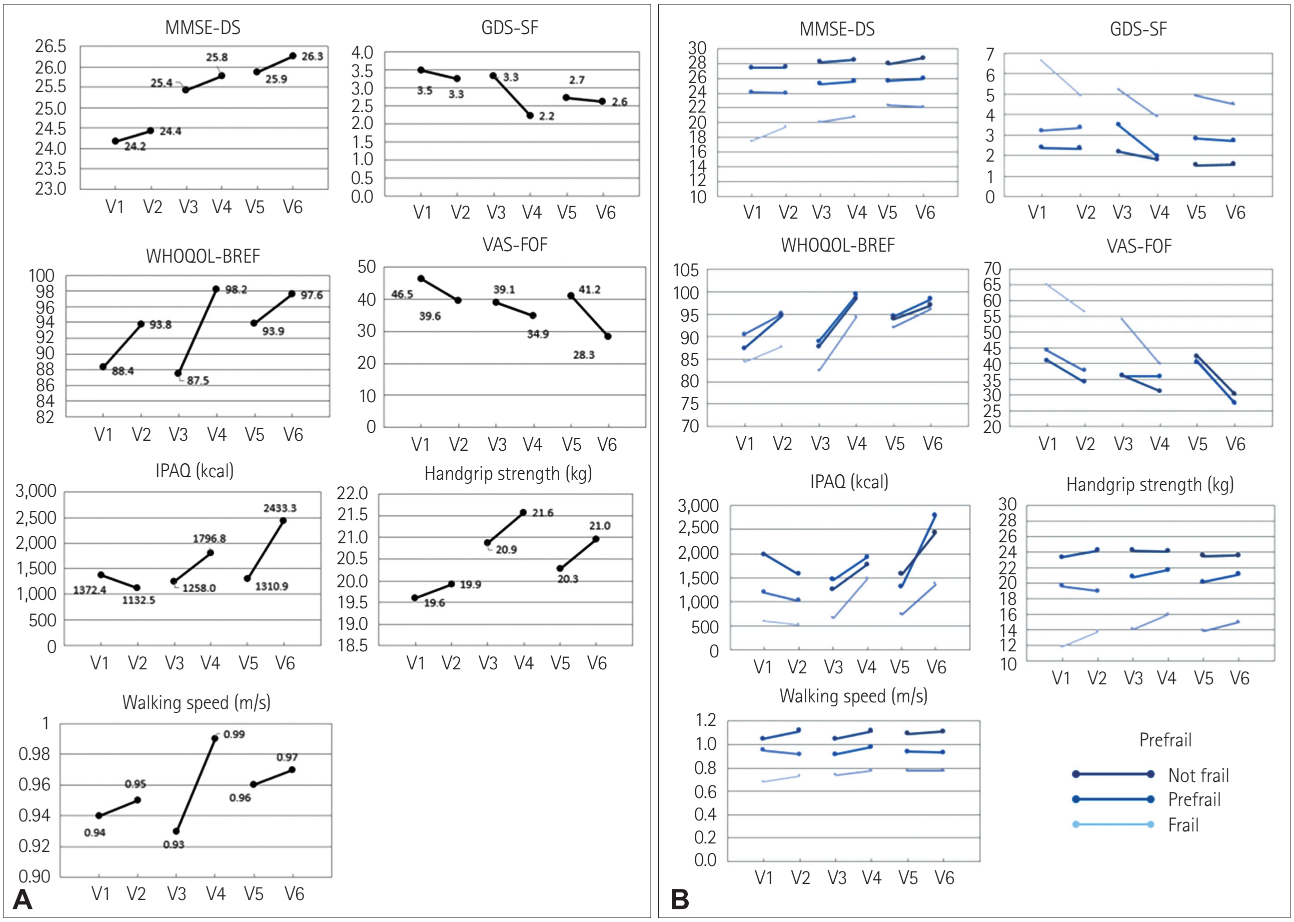

Fig. 2. Effects of multicomponent exercise according to the degree of frailty. A: All participants. B: According to the degree of frailty. GDS-SF: short form of the Geriatric Depression Scale, IPAQ: International Physical Activity Questionnaire, MMSE-DS: Mini Mental State Examination for dementia screening, VAS-FOF: Visual Analogue Scale for fear of falling, WHOQOL-BREF: World Health Organization Quality of Life Assessment.

tervention), and walking speed (p=0.027 for intervention), while the GDS-SF score, IPAQ value, and handgrip strength did not change significantly (Table 3 and Fig. 2).

DISCUSSION

Multicomponent exercise exerted significant beneficial effects on cognitive function, depression, quality of life, physical activity, fear of falling, handgrip strength, and walking speed in this study. Long-term effects were observed for cognitive function, depression, and handgrip strength, and short-term effects were observed for depression, quality of life, fear of falling, handgrip strength, and walking speed.

Many studies have investigated the effects of exercise on cognitive function, depression, and quality of life. There is a growing body of evidence from epidemiological studies showing that exercise and physical activity can delay the onset and progression of dementia in older adults.[30,31] Aerobic exercise is known to be associated with reduced cardiovascular risk factors, resulting in a reduced risk of vascular dementia or small-vessel disease of the brain, and enhancing neurogenesis and neuroplasticity of the hippocampus by increasing the regional blood volume in the hippocampal dentate gyrus,[32] brain-derived neurotrophic factors,[33,34] and the volume of the hippocampus. Although less clear than the effects of aerobic exercise, muscle-strengthening exercise is considered to have a positive effect on cognitive function by promoting the secretion of insulin-like growth factor 1[35,36] in the brain. The results of the present study may be interpreted in the same context.

The effects of multicomponent exercise and the mechanisms of action on cognitive function are not well known. Few studies have investigated multicomponent exercise, and each of them has used a different exercise program. For example, only aerobic and muscle-strengthening exercises were performed in the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability.[37] Another example is a review study reported on in 2015[38] that analyzed six previous randomized controlled studies on the effects of multicomponent exercise on frailty. None of the six studies used a combination of aerobic and muscle-strengthening exercises, and those authors suggested that while frail older adults seemed to benefit from exercise interventions, the optimal exercise program remained unclear.

The present study is noteworthy due to its use of a well-balanced multicomponent exercise program. This program included various types of exercise (e.g., aerobic, muscle-strengthening, flexibility, and balance exercises) with different intensities and frequencies that depended on the degree of frailty of individual participants. We were able to confirm the effect of multicomponent exercise over a 27-month period, during which the subjects participated in repeated sessions of exercise training.

Our analysis of the different frailty groups showed that all of the evaluated outcomes other than depression were significantly improved with short- or long-term effects in the frail group. Multicomponent exercises showed a tendency to protect against cognitive decline and depression in the frail group. One of the particularly interesting results of the present study is that while depression was protected against during the exercise period, the depressive symptoms tended to deteriorate after the exercise period. This suggests that it is very important to maintain exercise programs when attempting to prevent depression, particularly in frail subjects.

Several epidemiological studies have found that frailty increases the risk of cognitive decline and that cognitive impairment increases the risk of frailty, with this cycle being associated with aging.[15,39-41] Although further experimental data are needed to elucidate the mechanisms linking frailty to cognitive impairment,[42-44] possible mechanisms include underlying Alzheimer's disease,[45] hormonal effects,[46,47] nutritional problems, and sarcopenia.[15] In the present study, the frail group showed lower MMSE-DS scores and higher rates of cognitive impairment compared with the other groups (Table 2). The handgrip strength was weak in the frail group, suggesting that sarcopenia was more likely to be involved in the frail group than in the other groups. This in the frail group might already have had Alzheimer's disease, which is the most common cause of dementia, or sarcopenia, which has adverse effects on both frailty and cognition. Furthermore, the age of the participants—which is an important risk factor for frailty—obviously increased during the 27-month study period.

Frailty is a multidimensional concept that influences several domains, such as gait, mobility, balance, muscle strength, motor processing, cognition, nutrition, endurance, and physical activity.[48] Therefore, a multidimensional approach may be needed for the management of frailty. A few studies of the management of frailty[49,50] have led to improvements in the cognitive function of frail subjects. In addition to exercise therapy, these studies have controlled frailty by applying multidomain interventions, including diet, cognitive interventions, and the management of cardiovascular risk factors. As in the present study, the frail subjects were old, and many of them had a low socioeconomic status and lived alone. Considering these unique characteristics of frail subjects, the management of this population may require attention to various risk factors for frailty, including by applying exercise therapy.

This study was conducted in the community based on public projects, and it was subject to some limitations. First, we had to rely on voluntary participation, and so the follow-up periods were not consistent and there was a high rate of dropouts (i.e., not completing the first postexercise assessment). At the end of 27-month follow-up, the remaining subjects were additionally analyzed based on their frailty, which involved a relatively small sample. There is a possibility of attribution bias due to small number of subjects who completed the 27-month follow-up. However, considering that no significant differences were found between the remaining 1-year follow-up subjects and the 27-month follow-up subjects, it is unlikely that the attribution bias was large. We unfortunately did not investigate the cause of participant dropout or whether participants had kept performing multicomponent exercises during the intervention period. However, to encourage participation, we promoted exercise as a lifestyle habit by distributing posters in stages, organizing training sessions before and after the exercise programs to improve the awareness of the relationship between dementia and exercise, preparing self-evaluation sheets, and regularly following up individuals after each exercise period. The second limitation was that the study was conducted without a control group. However, we can infer the effects of multicomponent exercise by performing comparisons with elderly subjects who do not exercise by referring to other studies. Although there was no control group, this study is still meaningful since we compared the effects of multicomponent exercise among the frail, prefrail, and not-frail groups. We also provided multicomponent exercise in various stages according to the degree of frailty in individual subjects. Finally, we did not analyze the change in frailty after the exercise program. The effects of multicomponent exercise should therefore be confirmed more precisely by future studies addressing these limitations and conducting larger-scale investigations.

This study evaluated the effects of long-term exercises on cognition, depression, and the quality of life using a well-balanced multicomponent exercise pyramid that was consistent with the degree of frailty of individual participants. The application of individually customized, multicomponent exercise programs led to improvements in cognitive function, depression, and quality of life in the elderly subjects, especially among those who were more frail.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2020.16.4.612.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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