J. Phys. Ther. Sci. 32: 657–662, 2020

The Journal of Physical Therapy Science

Original Article

The exercise intensity of square-stepping exercise in community-dwelling late elderly females

Ryota Uchida, RPT, MS[1)], Shigeharu Numao, PhD[2)], Takashi Kurosaki, BS[1)], Ayaka Noma, RD, MS[3)], Masaki Nakagaichi, PhD[2)*]

[1)] *Graduate School of Physical Education, National Institute of Fitness and Sports in Kanoya: 1 Shiromizu-cho, Kanoya, Kagoshima 891-2393, Japan*
[2)] *Department of Sports and Life Science, National Institute of Fitness and Sports in Kanoya, Japan*
[3)] *Nonprofit Organization Wellspo Kanoya, Japan*

Abstract. [Purpose] Square-stepping exercise is recommended for elderly people, as it has a positive effect on cognitive and physical functions; however, few studies have examined the exercise intensity of square-stepping exercise. Therefore, we aimed to examine the exercise intensity of square-stepping exercise in community-dwelling late elderly females. [Participants and Methods] Study 1: The participants, constituting 12 community-dwelling late elderly females (age: 78.7 ± 3.8 years), performed the three target step patterns. Exhaled gas, heart rate, and rating of perceived exertion using the Borg Scale were measured during square-stepping exercise. Study 2: Participants were 57 community-dwelling elderly females (81.2 ± 4.3 years old). The exercise intensity, heart rate, and rating of perceived exertion using the Borg Scale during square-stepping exercise were measured. [Results] Study 1: The average METs of the 3 target step patterns was 3.6 ± 0.7, and the %heart rate reserve and rating of perceived exertion were 54.3 ± 20.0% and 11.4 ± 1.9%, respectively. Study 2: The average METs during the square-stepping exercise program was 2.1 ± 0.2, and the %heart rate reserve and rating of perceived exertion were 19.6 ± 10.2% and 11.3 ± 1.4%, respectively. [Conclusion] Square-stepping exercise was confirmed to be a low to moderate intensity exercise program and is expected to improve health and physical fitness.

Key words: Square-stepping exercise, METs, Late elderly females

(This article was submitted May 13, 2020, and was accepted Jul. 17, 2020)

INTRODUCTION

In Japan, where aging is a social problem, the total population is expected to decrease, and the proportion of elderly people, especially those aged ≥75 years, will increase. According to the Ministry of Health, Labor and Welfare, the population aged ≥65 years in 2018 was 35.58 million, accounting for 28.1% of the total population[1)]. The population aged >75 years is 17.98 million, accounting for 14.2% of the total population, exceeding those aged 65–74 years for the first time[1)]. As a result, the number of people requiring care has also increased, from approximately 4.378 million in 2007 to approximately 6.187 million in 2016, an increase of 1.89 million in 10 years[2)]. In 2012, the number of elderly people with dementia was 4.62 million, about one in seven elderly people aged >65 years. This is estimated to be 7.3 million by 2025, up to one-fifth[3)]. Based on these data, an effective strategy to address problems caused by an aging society should be established.

The importance of physical activity for preventing illness, nursing care, and dementia in elderly people has already been pointed out. According to the World Health Organization, deaths from physical inactivity account for 6% of deaths worldwide, the fourth risk factor following hypertension (13%), smoking (9%), and hyperglycemia (6%)[4)]. According to the Health Japan 21, rates of mortality, ischemic heart disease, hypertension, diabetes, obesity, osteoporosis, and colorectal cancer have

*Corresponding author. Masaki Nakagaichi (E-mail: gaichi@nifs-k.ac.jp)

declined in people with high activity levels. In addition, exercise has also been reported to improve mental health and quality of life[5]. Even in elderly people, increased physical activity in daily life reduces bedridden status and even deaths[5]. Based on these facts, the Ministry of Health, Labor and Welfare, as a basic policy of the Health Japan 21, aims to increase people's awareness of, and attitude toward, physical activity and exercise to increase the amount of physical activity[5]. Elderly people should exercise with the proper setting conditions, such as the type, intensity, time, and frequency in order to prevent daily living movement disorders effectively[5].

In such social situations, many activities using exercise to prevent nursing care and dementia are being implemented in various parts of Japan. The Square-Stepping Exercise (SSE) aims to maintain and improve elderly people's physical and cognitive functions[6]. SSE is an exercise that involves continuous movement in the forward, backward, left/right, and diagonal directions (stepping). The participant uses a mat that is 100 cm wide and 250 cm deep and is separated into 25 cm square spaces. Studies show that participating in SSE class for three months has a positive effect on physical and cognitive functions of community-dwelling, late elderly (individuals ≥75 years) females[7]. Shigematsu et al. assessed SSE's effects on adherence and functional fitness in a long-term, observational setting after a randomized controlled trial[8]. They reported that SSE had the same level of continuity as walking and that it improved physical fitness as well as, or better than, walking[8]. Furthermore, the practice of SSE has also been reported to greatly improve subjective effects, such as "increased laughter" and "increased community interaction"[9].

Thus, SSE is recommended for elderly people because it has a positive effect on cognitive and physical functions. However, few studies have examined SSE's exercise intensity in detail. Safe and effective exercise should be provided to promote exercise for elderly people in the future. Physical function is significantly lower in the late elderly people than in the early elderly people[10]. Therefore, exercise intensity should be determined to provide an appropriate exercise program for elderly people.

SSE consists of various types of step patterns. For understanding the exercise intensity of SSE, it is important to evaluate the exercise intensity of representative SSE step pattern. First purpose was to examine the transient exercise intensity during SSE in community-dwelling late elderly females. In addition, the SSE is not an individual exercise program, but group exercise program. Therefore, it is necessary to confirm whether the transient exercise intensity of the SSE corresponds to the exercise intensity of the SSE group program. Second purpose was to examine the exercise intensity during the SSE class in community-dwelling late elderly females.

PARTICIPANTS AND METHODS

In this study, the following two measurements were performed to evaluate the transient SSE exercise intensity and the exercise intensity during the SSE class.

In Study 1, the participants were 12 community-dwelling, late elderly females (age: 78.7 ± 3.8 years, height: 143.5 ± 7.6 cm, weight: 47.6 ± 6.1 kg). They participated in an SSE class, one of the K City Elderly Exercise Salon Projects conducted by K City, Kagoshima Prefecture. SSE classes have been conducted without exercise instructors once a week for about 90 min. Those who have orthopedic, respiratory, and circulatory disorders that may affect SSE performance, those who need nursing care, and those who cannot perform the measurement of target step pattern were excluded.

This study was performed with the approval of the National Institute of Fitness and Sports in Kanoya Ethics Review Committee (No. 11-35). The study protocol adhered to the Helsinki Declaration and the National Institute of Fitness and Sports in Kanoya of Health Sciences Research Ethics Guidelines (Studies on People). After explaining the study's purpose, the researchers explained the voluntary nature of research cooperation, the freedom of withdrawal, and the benefits, disadvantages, and risks that could arise from participating in this study. Only individuals who provided written consent to participate were targeted.

Figure 1 shows the protocol. Participants performed the three target step patterns. Exhaled gas, heart rate (HR), and rating of perceived exertion (RPE) using the Borg Scale during SSE were measured.

Step 1 (step forward / left / right), step 2 (step diagonally), and step 3 (backward step) were the three target step patterns of this measurement (Fig. 2). Participants were instructed to be aware of the points such as "stepping at the correct position", "according to the music rhythm of 80 bpm", and "swinging of the limbs". Each step pattern was performed for 160 s, referring to the method by Kozey et al[11]. Each participant performed the three target step patterns alone, and the order was randomly determined by drawing lots. Participants were required to sit in a chair between each step pattern until the HR returned to resting after a break. If they committed an error while performing the target step pattern, they were prompted to restart the step immediately. The parts where the target step pattern failed was excluded from the analysis.

Participants were required to put on masks before starting the step to measure the exhaled gas. The nose and mouth were covered tightly with a mask, and care was taken to prevent exhalation and inhalation from leaking. After wearing, a breath gas analyzer (COSMED K4b2)[12, 13] was connected. A HR sensor (Polar A370) was attached to the wrist of the non-dominant hand. After wearing the exhaled gas analyzer and HR sensor, participants sat on a chair, and the exhaled gas and HR were measured continuously from the start to the end of the protocol. RPE was measured immediately after each step pattern.

In Study 2, the participants were 57 community-dwelling late elderly females (age: 81.2 ± 4.3 years) who were divided into two groups: those who participated in the SSE class, one of the K City Elderly Exercise Salon Projects conducted in K

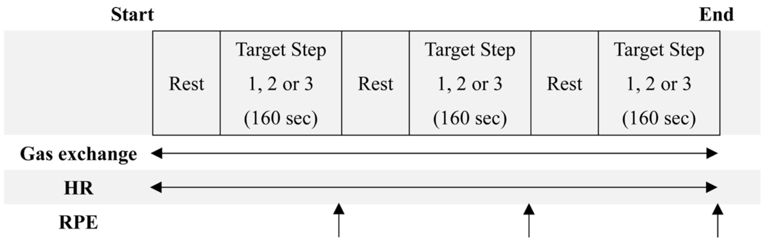

Fig. 1. Protocol of Study 1.
Each participant performed the three target step patterns (the order was randomly determined). Each step pattern was performed for 160 s. Participants were required to sit on a chair between each step pattern until the heart rate (HR) returned to resting value. Exhaled gas, HR, and rate of perceived exertion (RPE) using the Borg Scale during SSE were measured.

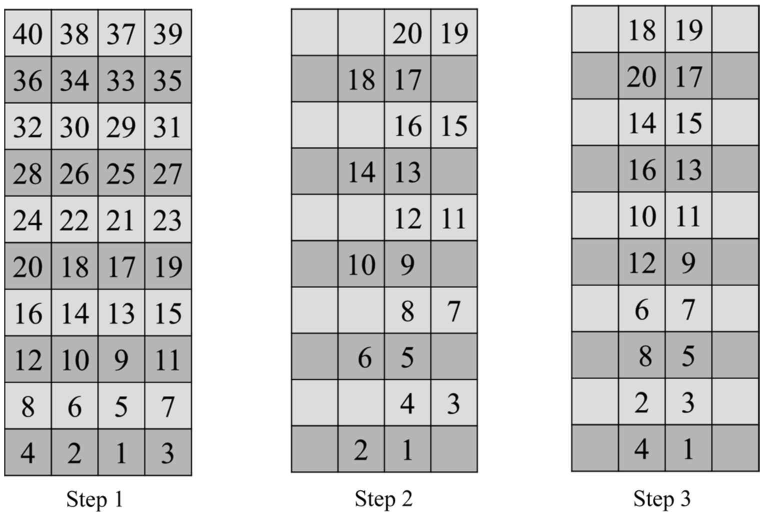

Fig. 2. Target step pattern in Study 1.
Step 1 (step forward / left / right), step 2 (step diagonally), and step 3 (backward step) were used as representative Square-stepping exercise step pattern. Participants stepped alternately on the right and left feet in numerical order.

City, Kagoshima Prefecture, and those who participated in the SSE class held in K town, Miyazaki Prefecture. The exclusion criteria and ethical considerations were the same as in Study 1.

The exercise intensity and HRs were measured during the SSE class. The SSE class consisted of 5-min preparation or warm-up exercises, 70-min SSE (including a 10-min break), 10-min strength training while sitting in a chair, and 5-min stretching. The SSE step patterns are as follows: forward and left and right steps, diagonal steps, and backward steps. In addition, there was also a dual task exercise that combined upper limb movement with a step pattern (Fig. 3). Among them, the step pattern that the exercise class participant chose voluntarily was performed for 70 min with a 10-min break. In SSE class, 5–10 people are lined up on one mat, and the steps are performed consecutively. Before starting the SSE class, participants wore activity meters (Active style Pro HJA-750C)[14] and an HR sensor (Polar A370). The activity meter was attached to the waist, such as a trouser belt or rubber cord. The HR sensor was attached to the wrist of the non-dominant hand. After wearing the activity meter and HR sensor, they sat on a chair, and the resting HR was measured. Then, during SSE, both activity and HR were continuously measured. RPE was measured immediately after the end of the 70-min SSE.

In Study 1 and Study 2, metabolic equivalents (METs), HR, % HR reserve using the Karvonen's method (% HRR), and RPE were used as indices of exercise intensity. In Study 1, METs were calculated based on the oxygen uptake obtained by the expiratory gas analysis; in Study 2, METs were calculated from the activity meter values. In addition, 207 − (age × 0.7) was used to predict the maximum HR for calculating %HRR was 207 − (age × 0.7)[15].

In Study 1, the method by Kozey et al.[11] was used. The average METs were calculated for 30 s, excluding the first 120 s and the last 10 s out of 160 s of continuous recording, of oxygen uptake recorded by the breath gas analyzer during each step pattern. The % HRR was calculated from the HR recorded immediately after the end of each target step pattern, and the resting HR measured before performing the step.

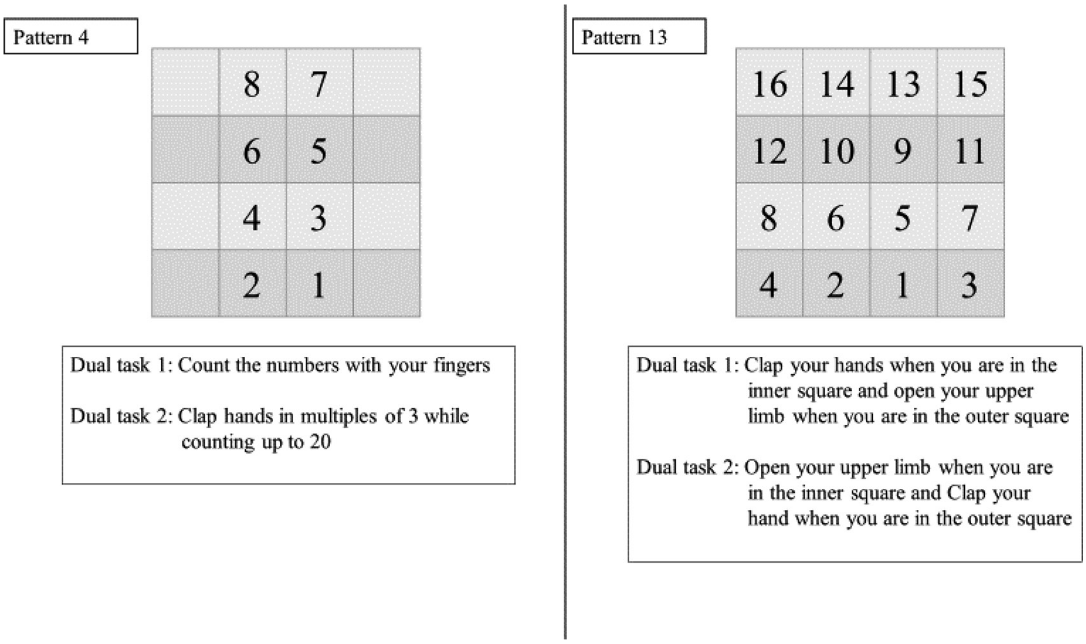

Fig. 3. Examples of dual task step pattern in SSE.
These show the first 4 × 4 square of each step patterns. These patterns are dual task exercises that combined upper limb movement with a step pattern. In these examples, each pattern contains two types of dual tasks.

In Study 2, it was analyzed only during the 70-min SSE, except during the preparation or warm-up exercises, strength training while sitting in a chair, stretching, and a 10-min break. Using the METs recorded on the activity meter every minute, the average METs during SSE were calculated. Using the HR recorded on the HR monitor, %HRR was calculated from the average HR during SSE, and the resting HR measured before starting the exercise class.

IBM SPSS Statistics 21 was used for statistical analyses. One-way analysis of variance was used to compare METs and HR among the three target step patterns in Study 1, and t-test was used to compare METs between Study 1 and Study 2. A significance level was set at less than 5%.

RESULTS

The results of Study 1 are shown in Table 1. The mean METs of the three target step patterns were 3.9 ± 0.8, 3.2 ± 0.7, and 3.5 ± 0.6 in Steps 1, 2, and 3, respectively. The HR after exercise was 122.5 ± 16.4, 114.8 ± 13.9, and 114.8 ± 13.9 bpm in steps 1, 2, and 3, respectively. The %HRR e of the three target step patterns were 60.2 ± 24.6%, 51.4 ± 16.2%, and 51.3 ± 15.8% in Steps 1, 2, and 3, respectively. RPE of the three target steps were 11.7 ± 1.2, 11.5 ± 1.9, and 11.0 ± 1.9 in Steps 1, 2, and 3, respectively. Differences in METs, %HRR, and RPE were not significant among the step patterns.

The results of Study 2 are shown in Table 2. The mean METs, resting HR, average HR, %HRR, and RPE during the SSE program were 2.1 ± 0.2, 79.0 ± 9.9 bpm, 91.8 ± 10.2 bpm, 19.6 ± 10.2%, and 11.3 ± 1.4 in Steps 1, 2, and 3, respectively. The METs of Study 2 were significantly lower than those of Study 1 ($p<0.01$).

DISCUSSION

In this study, two measurements were performed to evaluate the transient SSE exercise intensity and exercise intensity during the SSE class.

In Study 1, all METs of the three target step patterns were 3.0 to 4.0. According to reports from the American College of Sports Medicine (ACSM) and Centers for Disease Control, low-, moderate-, and high-intensity physical activities are defined as <3.0, 3.0–6.0, and >6.0 METs, respectively[16)]. Walking on flat ground (4.8 km/h) is 3.0 METs[17)]. According to the 2013 Physical Activity Standards for Health Promotion in Japan, adequate physical fitness for elderly people aged ≥65 years is defined as performing physical activities of ≥3.0 METs in daily life[18)]. In addition, previous studies reported that aerobic exercise is beneficial for improving cognitive function[19)], and that the effect is large in low- to moderate-intensity exercise[20)]. This study's results show that SSE is equivalent to moderate-intensity exercise, and that exercise intensity may improve cognitive function effectively. Next, RPE of the three target step patterns were 11.7 ± 1.2, 11.5 ± 1.9, and 11.0 ± 1.9 in Steps 1, 2, and 3, respectively. In the exercise prescription for elderly people by ACSM, activities based on perceived exercise intensity are recommended to suit individual physical fitness requirements[17)]. The RPE in SSE was "fairly light" during each

Table 1. The transient SSE exercise intensity

	Step 1	Step 2	Step 3	p
Height (cm)		143.5 ± 7.6		—
Weight (kg)		47.6 ± 6.1		—
Body Mass Index		23.1 ± 2.6		—
Resting HR (bpm)		76.9 ± 13.0		—
HR after exercise (bpm)	122.5 ± 16.4	114.8 ± 13.9	114.8 ± 13.9	0.380
METs	3.9 ± 0.8	3.2 ± 0.7	3.5 ± 0.6	0.097
%HRR (%)	60.2 ± 24.6	51.4 ± 16.2	51.3 ± 15.8	0.469
RPE	11.7 ± 1.2	11.5 ± 1.9	11.0 ± 1.9	0.683

Values indicate mean ± standard deviation.
HR: heart rate; METs: metabolic equivalents; %HRR: % heart rate reserve; RPE: rating of perceived exertion by Borg Scale.

Table 2. The SSE exercise intensity in an exercise classroom

METs	2.1 ± 0.2
Resting HR (bpm)	79.0 ± 9.9
Average HR (bpm)	91.8 ± 10.2
%HRR (%)	19.6 ± 10.2
RPE	11.3 ± 1.4

Values indicate mean ± standard deviation.
METs: metabolic equivalents; HR: heart rate; %HRR: % heart rate reserve; RPE: rating of perceived exertion by Borg Scale.

step pattern. The average intensity of the relative exercise intensity by %HRR was high only in Step 1 and moderate in the other two step patterns. According to Study 1, SSE is found as a simple exercise in terms of perceived exercise intensity, and a moderate-intensity exercise like walking on level ground. Thus, these results suggest that SSE is an effective exercise intensity to promote physical activity in elderly people.

The %HRRs of the three target step patterns were 60.2 ± 24.6%, 51.4 ± 16.2%, and 51.3 ± 15.8% in Steps 1, 2, and 3, respectively. According to reports from ACSM, low-, moderate-, and high-intensity physical activities are defined as <20%, 40–59%, and 60–84%, respectively. Moderate-intensity (%HRR 40–60%) exercise has been known as an effective exercise intensity to improve the health and physical fitness of adults in all ages, including the elderly people[21)]. SSE was an exercise that met this intensity criterion. Conversely, METs, HR after exercise, %HRR, and RPE did not show a significant difference between each step pattern; however, some step patterns included high-intensity exercise with %HRR of >60%. Maximal aerobic capacity usually decreases with age[22)]. Excessive exercise intensity can lead to cardiac accidents, such as arrhythmias and sudden death[23)]. Since SSE includes high-intensity step patterns, risk management during SSE is required for elderly people with weakened physical function.

In Study 2, the average METs are 2.1 ± 0.2 and %HRR was 19.6 ± 10.2%. These values were classified as low-intensity exercises based on ACSM[17)]. METs in Study 2 were significantly lower than those in Study 1. In SSE, it is necessary to wait when others are stepping. In this study, the wait time could not be ruled out, and the average METs and %HRR, including the time, were calculated. Therefore, it is possible to underestimate the exercise intensity of Study 2. However, many health benefits from physical activity can be achieved at even low-intensity physical activity if frequency and duration of exercise are increased appropriately[22)]. Dishman et al. examined the effects of regular low intensity physical activity on oxidative stress markers in older adults, and they suggested that low-intensity physical activity may be useful to prevent the decline of antioxidants linked with aging[24)]. In addition, Byun et al. reported that short low-intensity exercise session on a cycle ergometer improved executive function[25)]. As SSE consists of low- to moderate-intensity steps exercise, a regular SSE program may be effective to improve health related factors.

In Study 1 and Study 2, the SSE exercise intensity was confirmed, and the SSE was confirmed as an exercise program that focuses mainly on low- to moderate-intensity exercise and can be expected to improve health and physical fitness. According to the WHO, elderly people should perform 150 min of moderate-intensity aerobic exercise per week, 75 min of high-intensity aerobic exercise per week, or combination of moderate- to high-intensity aerobic exercise[4)]. Increasing moderate-intensity aerobic exercise to 300 min a week or converting 150 min a week to high-intensity aerobic exercise provides further health benefits[4)]. In one exercise salon or class, SSE implementation time is approximately 60 min; therefore, participating in the exercise salon promotes performing low- to moderate-intensity aerobic exercise for approximately 60 min.

In contrast, the ACSM also recommends that elderly people perform 12–13 moderate-intensity exercise or 14–15 high-intensity exercise in RPE[17, 26]. In addition to aerobic exercise, combining multiple types of exercise programs, such as strength training and flexibility exercise, is recommended.

This study has implications for creating more effective strategies to address the problems caused by an aging society. However, there are several limitations. First, our participants were females; therefore, our findings may not be applicable to males. Second, our participants were recruited in two rural area in Japan. Third, sample size in Study 1 is small. Further studies in other population and large sample are warranted to generalize our results. Finally, the educational level and cognitive function of participants were not measured in this study. These may affect our results.

In conclusion, SSE was confirmed as low- to moderate-intensity exercise program and be expected to improve health and physical fitness. In other words, SSE may be a program that can be recommended actively for future care and dementia prevention activities.

Funding and Conflict of interest

None.

REFERENCES

1) Cabinet Office: Annual Report on the Ageing Society. https://www8.cao.go.jp/kourei/whitepaper/w-2019/zenbun/pdf/1s1s_01.pdf (Accessed Dec. 25, 2019)
2) Cabinet Office: Annual Report on the Ageing Society. https://www8.cao.go.jp/kourei/whitepaper/w-2019/zenbun/pdf/1s2s_02_01.pdf (Accessed Dec. 25, 2019)
3) Cabinet Office: Annual Report on the Ageing Society. https://www8.cao.go.jp/kourei/whitepaper/w-2017/html/zenbun/s1_2_3.html (Accessed Dec. 25, 2019)
4) World Health Organization: Global recommendations on physical activity for health. https://www.who.int/dietphysicalactivity/factsheet_recommendations/en/ (Accessed Dec. 25, 2019)
5) Ministry of Health, Labor and Welfare: Health Japan 21 Physical activity / Exercise. https://www.mhlw.go.jp/www1/topics/kenko21_11/b2.html (Accessed Dec. 25, 2019)
6) Shigematsu R, Okura T: A novel exercise for improving lower-extremity functional fitness in the elderly. Aging Clin Exp Res, 2006, 18: 242–248. [Medline] [CrossRef]
7) Nakagaichi M, Hamahara K, Tanizaki S et al.: Effects of Square-Stepping Exercise on physical function, cognitive function, and subjective health in community-dwelling Japanese older female. Health science research, 2014, 26: 1–6.
8) Shigematsu R, Okura T, Nakagaichi M, et al.: Adherence to and effects of multidirectional stepping exercise in the elderly: a long-term observational study following a randomized controlled trial. J Phys Fit Sports Med, 2013, 2: 127–134. [CrossRef]
9) Nakagaichi M, Nonaka M, Hikiji Y, et al.: Influence on participation motivation and subjective health effect by the difference of the main activity contents in the elderly salon in remote island area. Hokenfu Zasshi, 2018, 74: 412–418.
10) Saito Y, Suganuma K, Saito T, et al.: Motor function of young-old and old-old subjects. J Phys Ther Sci, 2016, 31: 57–60.
11) Kozey SL, Lyden K, Howe CA, et al.: Accelerometer output and MET values of common physical activities. Med Sci Sports Exerc, 2010, 42: 1776–1784. [Medline] [CrossRef]
12) Doyon KH, Perrey S, Abe D, et al.: Field testing of VO2peak in cross-country skiers with portable breath-by-breath system. Can J Appl Physiol, 2001, 26: 1–11. [Medline] [CrossRef]
13) Duffield R, Dawson B, Pinnington HC, et al.: Accuracy and reliability of a Cosmed K4b2 portable gas analysis system. J Sci Med Sport, 2004, 7: 11–22. [Medline] [CrossRef]
14) Ohkawara K, Oshima Y, Hikihara Y, et al.: Real-time estimation of daily physical activity intensity by a triaxial accelerometer and a gravity-removal classification algorithm. Br J Nutr, 2011, 105: 1681–1691. [Medline] [CrossRef]
15) Gellish RL, Goslin BR, Olson RE, et al.: Longitudinal modeling of the relationship between age and maximal heart rate. Med Sci Sports Exerc, 2007, 39: 822–829. [Medline] [CrossRef]
16) Haskell WL, Lee IM, Pate RR, et al.: Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. Med Sci Sports Exerc, 2007, 39: 1423–1434. [Medline] [CrossRef]
17) American College of Sports Medicine: ACSM's Guidelines for Exercise Testing and Prescription, 8th ed. Tokyo: Nankodo, 2011.
18) Ministry of Health, Labor and Welfare: Physical Activity Reference for Health Promotion 2013. https://www.mhlw.go.jp/stf/houdou/2r9852000002xple-att/2r9852000002xpqt.pdf (Accessed Dec. 25, 2019)
19) Ando S, Hatamoto Y, Sudo M, et al.: The effects of exercise under hypoxia on cognitive function. PLoS One, 2013, 8: e63630. [Medline] [CrossRef]
20) Chang YK, Labban JD, Gapin JI, et al.: The effects of acute exercise on cognitive performance: a meta-analysis. Brain Res, 2012, 1453: 87–101. [Medline] [CrossRef]
21) Howley ET: Type of activity: resistance, aerobic and leisure versus occupational physical activity. Med Sci Sports Exerc, 2001, 33: S364–S369, discussion S419–S420. [Medline] [CrossRef]
22) Michael LP, Janus DB, Rod KD, et al.: American College of Sports Medicine Position Stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. Med Sci Sports Exerc, 1998, 30: 975–991. [Medline]
23) Nakajima T: Optimal exercise pattern for heart disease patients: exercise intensity, exercise time, exercise pattern. HEART's Selection, 2012, 44: 279–285.
24) Dishman RK, Sallis JF, Orenstein DR: The determinants of physical activity and exercise. Public Health Rep, 1985, 100: 158–171. [Medline]
25) Byun K, Hyodo K, Suwabe K, et al.: Positive effect of acute mild exercise on executive function via arousal-related prefrontal activations: an fNIRS study. Neuroimage, 2014, 98: 336–345. [Medline] [CrossRef]
26) Nelson ME, Rejeski WJ, Blair SN, et al. American College of Sports Medicine American Heart Association: Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Circulation, 2007, 116: 1094–1105. [Medline] [CrossRef]