



Association between baseline handgrip strength and cognitive function assessed before and after a 12-week resistance exercise intervention among community-living older adults

Milan Chang^{a,b,*}, Olof G. Geirsdottir^c, Hrafnhildur Eymundsdottir^a, Inga Thorsdottir^c, Palmi V. Jonsson^{a,d}, Alfons Ramel^c

^a The Icelandic Gerontological Research Institute, National University Hospital of Iceland, Reykjavik, Iceland

^b Norwegian Institute of Public Health, Department of Physical Health and Ageing, Oslo, Norway

^c Unit for Nutrition Research, National University Hospital of Iceland & Faculty of Food Science and Nutrition, University of Iceland, Reykjavik, Iceland

^d Faculty of Medicine, University of Iceland, Reykjavik, Iceland

ARTICLE INFO

Keywords:

Handgrip strength
Cognitive function
Resistance exercise
Community-living older adults

ABSTRACT

Background: Physical activity (PA) is beneficial for the improvement of both physical and cognitive functions for older adults. Handgrip strength is strongly associated with cognition in cross-sectional studies, however, whether handgrip strength is associated with cognitive function in exercise intervention has not been well investigated. The purpose of the study was to investigate whether baseline handgrip strength is associated with cognitive function measured at baseline and after the intervention among community-living older adults.

Methods: A 12-week resistance exercise program (3 times/week; 3 sets, 6–8 repetitions at 75–80% of the 1-repetition maximum) was designed to increase strength and muscle mass of major muscle groups. At the end of the study, 201 out of 237 completed the study (mean age 73.0 ± 5.5 years, 57.0% female). Body composition, PA, handgrip strength, cardiovascular risk factors, and Mini-Mental State Examination (MMSE) were measured at baseline and endpoint. The linear regression analysis was used to examine the association.

Results: Baseline handgrip strength was 28.7 ± 8.7 (kg) and mean MMSE score was 27.6 ± 2.0 at baseline. We found that baseline handgrip strength was significantly associated with the MMSE score measured before the intervention adjusting basic characteristics and cardiovascular risk factors at baseline. Baseline handgrip strength was also significantly associated with MMSE measured after the intervention. One kg higher baseline handgrip strength was significantly associated with a 0.63 and 0.33 higher MMSE score measured at baseline and after the 12-week resistance exercise intervention.

Discussion: Our study found that baseline handgrip strength was strongly associated with cognitive function measured before and after the resistance training intervention. Handgrip strength could be an indicator for cognition among healthy independent older adults.

1. Introduction

Cognitive decline is one of the typical age-related changes among older adults [1,2] and dramatic increase of dementia among older population is one of the most important public health concern in the society [3,4]. Previous research suggested several biomarkers for the cognitive decline among older adults which includes reduced muscle strength [3], fatigue [5], and slower walking speed [6]. These biomarkers are used as predictors for mild cognitive impairment (MCI) and dementia [7,8]. Cognitive decline is also strongly associated with motor

task performances such as handgrip strength [9], gait [10], and balance [11]. The mechanism behind this association could be the decline of nervous function with aging which may compromise the coordinating of cognitive and motor activity [9].

Muscle strength is one of the main factors for maintaining physical function in old age [12]. Preserving a sufficient level of muscle mass and strength can delay the decline of physical function of older adults [13]. There is evidence that physical activity (PA) helps to maintain both physical [14] and cognitive function in late life [15]. Exercise has been suggested as one of the alternative treatment to improve neurocognitive

* Corresponding author at: The Icelandic Gerontological Research Institute, National University Hospital of Iceland, Reykjavik, Iceland.

E-mail addresses: changmilan@gmail.com, milan.changgudjonsson@fhi.no (M. Chang).

<https://doi.org/10.1016/j.ahr.2022.100092>

Received 21 February 2022; Received in revised form 19 July 2022; Accepted 20 July 2022

Available online 22 July 2022

2667-0321/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

function for the older population [16]. Generally, exercise intervention studies reported that both physical and cognitive function had improved after the intervention period among the older population [17,18]. Further, it is well known that both cognitive function and physical function are strongly related with the level of functional limitation in old age [10,19]. Ability to perform ordinary activities is critical for maintaining independent life, but it has been shown that cognitive impairment among older people increases the risk of functional limitation in daily life [20].

Handgrip strength is considered as an overall indicator for general muscle strength, and the most popular method of measurement [9,13]. Measurement of handgrip strength is a simple, fast, and inexpensive way to assess maximum muscle strength in the older population [9]. The direction of the association between handgrip strength and cognition among older adults is still in debate [8,21,22]. To understand the causality of the association, it should be examined on longitudinal design. Previous studies that reported associations between handgrip strength and cognitive function relied on cross-section designs [22], while few longitudinal studies reported significant association [22,23]. A longitudinal study of 12 years reported significant association between handgrip strength and incidence of MCI among older population [24]. Particularly, low handgrip strength is reported to be associated with an increased risk of developing Alzheimer's disease [25], cognitive decline [26,27], and lower quality of life [28]. On the other hand, high handgrip strength at baseline was protective for cognitive function after 7 years of follow-up [29]. A possible mechanism behind this association is that nervous system deficiencies among older adults may limit the muscle force which is due to poor neuromuscular activation and motor unit recruitment [30,31]. The decline of function in the neural and motor systems due to aging could be linked to the declines in handgrip strength which may also influence the progressing cognitive impairment [32]. In general, most exercise intervention studies for older adults look at the improvement of both cognitive [18,33] and physical function [34] after the exercise intervention. However, there is limited information on the association in the exercise intervention study. Considering the strong association between PA, handgrip strength, and cognitive function among older adults, baseline handgrip strength may have an effect on cognitive changes after the exercise intervention. Therefore, the purpose of the study was to investigate whether baseline handgrip strength is associated with cognitive function measured at baseline and whether baseline handgrip strength is still associated with cognitive function measured after the 12-week resistance exercise intervention among community-living Icelandic older adults.

2. Methods

2.1. Study and intervention

At baseline, 237 healthy community-living older adults (aged 62–92) participated in structured exercise program. PA and dietary intake information were collected at baseline and at the end of the intervention. The details of study design and intervention protocol have been published previously [35,36]. In short, the current study was a 12-week resistance exercise intervention study. The study was structured to increase muscle strength and muscle mass of all major muscle groups for older adults. Data was obtained from the measurement at baseline and after a 12-week exercise period. Participants were excluded if they had low cognitive function (Mini-Mental State Examination (MMSE) \leq 19), major orthopedic disease, or use of pharmacological interventions with exogenous testosterone or other drugs known to influence muscle mass. Further, participants were free of any musculoskeletal disorders or other disorders that could affect their muscle mass. Among the total of 237 participants at baseline, 201 (87 men, and 114 women) completed the resistance exercise intervention. All participants were recruited by advertisement in the Reykjavik area. The study was approved by the Icelandic National Bioethics Committee (VSNb2008060007/03–15.

Informed consent was obtained from all participants.

2.1.1. Resistance exercise intervention

The current study adjusted the difficulty level of the resistance exercise program to fit the level of individual physical fitness, as well as to maximize the improvement in physical performance. Each participant received updated personalized exercise prescription during the exercise intervention training. The exercise program was conducted in groups (20 to 30 participants) for one and half hour on three non-consecutive days per week for 12 weeks. All sessions were supervised by study staff, a professional exercise trainer and a physical therapist following the same training protocol. All participants were advised not to make other changes of daily lifestyle.

2.1.2. Exercise education and fitness assessment

Two weeks before the initiation of the intervention, exercise education training was conducted. All participants received personalized exercise prescription during exercise intervention training. The 1-repetition maximum (1-RM) was determined with weight adjustment on each exercise machine for all individuals (Life Fitness, IL, USA).

Training protocol: The training started with 10 to 15 min warm-up routine consisting of activities such as stretching, twisting, and shoulder and ankle rotations. All sessions were supervised by 4–5 staff members.

Resistance training: Each training session included 10 different muscle group exercises using weight machines: (1) leg extension, (2) leg curl, (3) leg press, (4) chest fly, (5) row, (6) pull-down, (7) biceps curl, (8) triceps curl, (9) lower back extension, and (10) abdominal curl. Exercise was performed based on the prescribed weights at the first fitness assessment. After the exercise of each muscle group, the participants had a resting time until they are ready to train the next muscle group.

The frequency and intensity: Each exercise is composed with 3 sets of 6–8 repetitions, starting with a 60% load of their 1-RM measured at first week. During the first week, the participants were instructed on correct exercise techniques. After the first week, each participant increased the load to 75–80% of 1-RM. The progressive exercise load protocol was set to increase 5–10% weekly. After finishing all muscle group exercises, participants performed stretching exercises to end the training.

2.2. Measurements

2.2.1. Exposure measurement: handgrip strength

The handgrip strength was measured for all participants during a personal interview at baseline and after the exercise intervention was terminated with hydraulic hand dynamometer (Baseline Evaluations Corporation). The maximal handgrip strength in kg was measured three times and the average was used for the analysis.

2.2.2. Outcome measurement: cognitive function

The cognitive function was assessed with MMSE [37]. Cognitive function was measured during a personal interview at baseline and after the exercise intervention was terminated. Before the initiation of the exercise intervention, participants who had MMSE 19 or below at baseline measurement were excluded from the study.

2.2.3. Covariates

Covariates and potential confounders were assessed at baseline and end point of the 12-week resistance exercise intervention. Baseline covariates were included in the statistical analysis to examine the associations to compare the outcomes of baseline handgrip strength with two MMSE scores measured before and after the intervention. Information on demographical characteristics was collected during a personal interview at baseline and after the resistance exercise intervention which included age, gender, and education. Education was categorized

into non-formal education, elementary school, secondary school, vocational school (professional skill training school), and university. Blood pressure was measured in sitting position. Participants were instructed to avoid strenuous exercise and alcohol consumption the day before the drawing of fasting blood samples at baseline and endpoint [36,38]. Blood measurement included serum cholesterol, trygliceride, diabetes and c-reactive protein. Body weight was assessed with light underwear on a calibrated scale (model no. 708; Seca, Hamburg, Germany) and we used a calibrated stadiometer (model no. 206; Seca) to measure height. Lean body mass was assessed at the Icelandic Heart Association, Kópavogur, Iceland by a dual-energy x-ray absorptiometer (DXA, Hologic QDR-2000 plus, Hologic Inc., Waltham, MA). BMI was calculated with height and weight (kg/m^2). We used BMI classification defined by World Health Organization as normal ($18.5 \leq \text{BMI} < 25$), overweight ($25.0 \leq \text{BMI} < 30.0$), and obese ($\text{BMI} \geq 30.0$). PA was assessed by self-reports with the first question asking Do you practice regular physical activity? with yes/no option. Then, those who reported regular PA answered minutes per week with various sports or PA type. Kilo-calories per week for all PA data were calculated by multiplying the kilo-calorie score based on metabolic equivalent of the task values for each of the activities [39]. Total PA was the sum of the activity as converted to metabolic equivalent (MET) reported on the questionnaire for walking, and other moderate and vigorous exercise activities.

2.3. Statistical analysis

Analysis of variance for continuous variables and χ^2 test for categorical variables were used to compare subject characteristics by groups. To examine whether the baseline handgrip strength was associated with cognitive function measured before and after the resistance exercise intervention, we used multiple linear regression analysis. The multiple linear regression analyses were performed with 4 models for the association between baseline grip strength and MMSE (measured at baseline and end of the intervention). Model 1 was adjusted for baseline covariates including age, gender, and education. Model 2 was additionally adjusted for BMI, and lean body mass. Model 3 further included systolic blood pressure, total cholesterol, diabetes and PA. The final model 3-1 was performed to examine the association between baseline grip strength and MMSE measured at the end of intervention. To take into account the relevant changes of handgrip strength during the resistance exercise training, the final model 3-1 was adjusted for the difference of handgrip strength measured before and after the intervention. Analyses were performed with STATA software, version 10 (Statacorp, Texas, USA).

3. Results

The characteristics of study participants are shown in Table 1. The mean age of the study participants was 73.0 ± 5.5 years old ($n = 201$). The average and standard deviation of MMSE was 27.6 ± 2.0 at baseline, and 28.0 ± 2.2 after the 12-week of resistance exercise intervention. The average handgrip strength was 28.7 ± 8.7 kg at the baseline, and 30.1 ± 8.9 kg after the intervention. Table 2 presents the average of MMSE and handgrip strength before and after the intervention, and changes after the intervention in both handgrip strength and MMSE were significant.

Table 3 presents results of the multiple linear regression between handgrip strength and cognitive function. Model 1 was adjusted for age, gender, and education and baseline grip strength was significantly associated with pre-MMSE (coefficient = 0.60, 95% confidence interval (CI) 0.25- 0.95, $p = 0.001$) as well as with post-MMSE measured at the end of the intervention (coefficient = 0.30, 95% CI -0.03-0.63, $p = 0.064$). The coefficient in the model 1 indicates that 1 kg of higher handgrip strength at baseline corresponded to 0.6 higher baseline MMSE, and 0.3 higher MMSE measured after the intervention. Both associations were attenuated in model 2 after the additional adjustment

Table 1

Health characteristics of study participants at baseline according to gender.

	Total (N = 201)		Men (N = 87)		Women (N = 114)	
Age, years, Mean (SD) *	73.0	(5.5)	74.1	(5.7)	72.1	(5.3)
Education, n (%) *						
Primary school	24	(11.9)	8	(9.2)	16	(14.0)
Secondary or vocational school	97	(48.3)	37	(42.5)	60	(52.6)
University	37	(18.4)	21	(24.1)	16	(14.0)
Non-formal school	43	(21.4)	21	(24.1)	22	(19.3)
BMI,kg/m ² , Mean (SD)	28.7	(4.9)	29.6	(4.5)	28.2	(5.1)
Total cholesterol, mg/dl, Mean (SD) *	5.6	(1.2)	5.1	(1.1)	6.0	(1.1)
Total Triglyceride, mg/dl, Mean (SD)	1.3	(0.7)	1.3	(0.8)	1.2	(0.6)
C-reactive protein, mg/dl, Mean (SD)	6.8	(3.4)	6.8	(3.1)	6.8	(3.7)
SBP, mm Hg, Mean (SD)	143.6	(18.9)	151.0	(17.9)	138.1	(17.8)
Diabetes, n (%)	12	(6.0)	7	(8.1)	5	(4.4)
PA, MET, Mean (SD)	28.7	(28.9)	26.0	(26.7)	30.7	(30.5)
Handgrip strength, Kg, Mean (SD)						
Baseline handgrip strength*	28.7	(8.7)	36.9	(6.2)	22.4	(3.8)
Endpoint handgrip strength	30.1	(8.9)	38.2	(6.8)	23.9	(4.0)
Changes of handgrip strength	3.0	(5.7)	2.9	(6.1)	3.0	(5.4)
MMSE, Mean (SD)						
Baseline MMSE	27.6	(2.0)	27.3	(2.1)	27.9	(1.9)
Endpoint MMSE	28.0	(2.2)	27.7	(2.2)	28.3	(2.1)
Changes of MMSE	0.4	(1.9)	0.4	(1.9)	0.5	(1.8)

Note. SD = standard deviation, MMSE = Mini Mental State Examination, BMI= Body Mass Index, HDL=High-Density Lipoprotein, DBP= Diastolic Blood Pressure, SBP= Systolic Blood Pressure, Physical activity= PA, MET=Metabolic Equivalent. Age adjusted * $p < 0.05$.

for baseline health related risk factors (pre-MMSE coefficient = 0.64, CI: 0.16–1.03, $p = 0.001$; post-MMSE coefficient = 0.31, CI: 0.02–0.64, $p = 0.064$). The Model 3 was adjusted with additional variables including total lean body mass and PA, and the associations were slightly attenuated (pre-MMSE coefficient = 0.63, 95% confidence interval (CI) 0.26-1.00, $p = 0.001$; post-MMSE coefficient = 0.31, 95% CI 0.02 - 0.64, $p = 0.065$). The finding from the model 3 with pre-MMSE means that 1 kg higher baseline handgrip strength was associated with a 0.63 higher score of baseline MMSE, and 0.31 higher score of MMSE measured after the intervention. In the Model 3-1 looking at the association between baseline handgrip strength and follow-up MMSE, we added handgrip strength measured after the intervention to take into account for changes in handgrip strength after the 12-week resistance exercise intervention. However, the results of model 3-1 remained the same (post-MMSE coefficient = 0.33, CI: 0.008–0.66, $p = 0.044$). The final model 3-1 revealed that the association was strong even after the adjustment for the changes of handgrip strength during the 12-week exercise intervention, meaning that 1 kg higher baseline handgrip strength was associated with a 0.33 increased MMSE score measured after the intervention.

4. Discussion

The current study investigated the association between handgrip strength and cognitive function with a 12-week resistance exercise intervention among community-living older adults in Iceland. Our study found that baseline handgrip strength was significantly associated with cognitive function measured at baseline and at the end of the intervention after adjusting for various covariates and the changes of handgrip strength during the intervention. Our results suggest that handgrip strength is strongly associated with cognitive function in cross-sectional analysis as well as cognitive function measured after the 12-week

Table 2

Baseline health characteristics of study participants according to baseline handgrip strength (group is defined by 50 percentile of low and high handgrip strength in each gender).

	Total (N = 201)		Low Handgrip (N = 118)		High Handgrip (N = 83)	
Age, years, Mean (SD)	73.0	(5.5)	74.3	(6.0)	71.2	(4.1)
Gender, women, n (%)	114	(57.6)	70	(59.3)	44	(53.0)
Education, n (%) *						
Primary school	24	(11.9)	15	(12.7)	9	(10.8)
Secondary or vocational school	97	(48.3)	49	(41.5)	48	(57.8)
University	37	(18.4)	21	(17.8)	16	(19.3)
Non-formal school	43	(21.4)	33	(28.0)	10	(12.1)
BMI, kg/m ² , Mean (SD)	28.8	(4.9)	28.7	(4.7)	29.0	(5.1)
Total cholesterol, mg/dl, Mean (SD)	5.6	(1.2)	5.6	(1.3)	5.6	(1.0)
Total Triglyceride, mg/dl, Mean (SD)	1.3	(0.7)	1.2	(0.6)	1.3	(0.8)
C-reactive protein, mg/dl, Mean (SD)	6.8	(3.4)	6.7	(3.3)	6.9	(3.6)
SBP, mm Hg, Mean (SD)	143.6	(18.9)	143.9	(21.3)	143.2	(14.9)
Diabetes, n (%)	12	(6.0)	8	(6.8)	4	(4.8)
PA, MET, Mean (SD)	28.7	(28.9)	25.9	(25.9)	32.7	(32.5)
Handgrip strength, Kg, Mean (SD)						
Baseline handgrip strength*	28.7	(8.7)	25.1	(6.7)	33.9	(8.7)
Endpoint handgrip strength*	30.1	(8.9)	26.6	(7.0)	35.0	(9.2)
Changes of handgrip strength	3.0	(5.7)	3.4	(6.0)	2.5	(5.2)
MMSE, Mean (SD)						
Baseline MMSE *	27.6	(2.0)	27.2	(2.3)	28.1	(1.2)
Endpoint MMSE	28.0	(2.2)	27.8	(2.4)	28.4	(1.8)
Changes of MMSE	0.4	(1.9)	0.5	(2.0)	0.3	(1.7)

Note. SD = standard deviation, MMSE = Mini Mental State Examination, BMI= Body Mass Index, HDL=High-Density Lipoprotein, DBP= Diastolic Blood Pressure, SBP= Systolic Blood Pressure, Physical activity= PA, MET=Metabolic Equivalent. *p < 0.05.

Table 3

Association between baseline handgrip strength and MMSE assessed before and after the intervention (N = 201).

		Baseline handgrip strength		
		Coefficient (SE)	95% CI (Low ~ High)	p-value
Pre-MMSE	Model 1	0.60 (0.18)	(0.25 ~ 0.95)	0.001
	Model 2	0.63 (0.18)	(0.27 ~ 1.00)	0.001
	Model 3	0.63 (0.19)	(0.26 ~ 1.00)	0.001
Post-MMSE	Model 1	0.30 (0.17)	(-0.03 ~ 0.63)	0.071
	Model 2	0.31 (0.16)	(-0.02 ~ 0.64)	0.064
	Model 3	0.31 (0.17)	(-0.02 ~ 0.64)	0.065
	Model 3-1	0.33 (0.16)	(0.008 ~ 0.66)	0.044

SE = Standard errors, CI = Confidence interval, BMI = Body Mass Index, physical activity = PA.

Model 1= Adjusted for age, gender & education.

Model 2= model 1 + BMI, systolic blood pressure, total cholesterol, Triglyceride, C-reactive protein, and diabetes.

Model 3= model 2 + PA.

Model 4= model 3 + difference in grip strength measured at baseline and end of the intervention.

resistance exercise training among community-living older adults.

Older adults with low physical performance had significantly lower cognitive scores as compared to those with higher physical performance [34,40]. Decline of both physical and cognitive abilities is one of the most critical consequences of aging [9] which is related to an increased risk of dementia and adverse health outcomes [8,41]. Regular exercise is strongly recommended for older adults [42] because low PA level is highly associated with low physical and cognitive function [17].

Epidemiological studies reported that older adults who practiced regular PA compared to those who reported no regular PA in early life had significantly better physical function [14] and cognitive function after more than 20 years [15,43,44]. Muscle mass and muscle strength decrease with aging as a result of hormonal changes and decreased PA [45]. The significant associations of decreased muscle strength, muscle mass with physical function and cognitive function have been consistently reported [43,46]. Muscle strength plays a critical role in maintaining physical function because of its broad physiological and functional roles in daily life among older adults [47]. Therefore, resistance training is suggested as an effective type of exercise for older adults to improve muscle mass [48], and physical function [49].

While age-related declines in muscle strength are due to physiological changes [50], muscle weakness could also be more a product of diminished neural system functioning [51]. Evidences suggest that changes in the brain and nervous system is strongly associated with handgrip strength [52] as well as mobility [53]. The cortical and subcortical regions of the brain regulating hand dexterity are related to cognitive functions [7]. Health-promoting behavior such as PA is also associated with self-regulation ability [54] which is an executive function explained by the neural network functions in the prefrontal cortex [55]. Handgrip strength is a valid and reliable measure of upper limb muscles and it is used as an indicator of health status, muscle strength, and frailty of older adults [9,13]. In cohort studies, baseline handgrip strength also predicted future cognitive function [25], mobility [56], and mortality [24]. It is suggested that handgrip strength is a valuable marker of well-being which could indicate the level of independence in activities of daily living (ADL) among older adults who are at risk of developing disability [57]. Handgrip strength is largely due to neuromuscular activation and motor unit recruitment [58]. Age-related neurodegeneration contributes to decreased handgrip strength which may be further linked to lower cognitive function. Although many studies have investigated the age related association between handgrip strength and cognitive function among older adults [22,26,56,59], the association is often debated as it is bidirectional [40]. The longitudinal association was examined to see whether baseline handgrip strength is associated with cognitive decline over time in observational studies [8, 60]. Most intervention studies also reported mainly the changes in either only handgrip strength or only cognitive function [18,34]. Therefore, it is difficult to determine whether there is also an association after both handgrip strength and cognitive function changed with an exercise intervention for older adults.

The current study is based on the 12-week resistance exercise intervention for older adults. The resistance training intervention program was originally constructed to improve physical function among community-living older adults and all participants were progressively trained during the intervention period according to their fitness level as measured at baseline. The results of the study show whether handgrip strength and cognitive function assessed at baseline changed after 12-week resistance training and the study findings suggest that baseline handgrip strength is significantly associated with cognitive function measured before and after the intervention. The participants in our study were community-living older adults who had no disability or cognitive impairment at the time of admission for the intervention. Meaningful cognitive changes in MMSE among older adults have not been clearly identified, but a recent study reported -0.09 MMSE score decline in 6 months among older adults who had no cognitive impairment [61]. The mean change of MMSE in the current study after the 12-week exercise intervention compared to the baseline MMSE was 0.6, and 1 kg higher handgrip strength at baseline was associated with 0.3 higher MMSE after the intervention. Overall, our findings indicate that MMSE was changed positively after the resistance exercise intervention. The current study found that baseline handgrip strength was associated with the cognitive function before and after the exercise intervention.

Although both handgrip strength and cognitive function changed during the intervention in the current study, the time to effect its

changes to one another could be different. A recent longitudinal study reported that more than 5 kg decrease in handgrip strength over a period of 8 years significantly increased the likelihood of cognitive impairment [56]. In the current study, the handgrip strength increased by 1,4 kg after the resistance exercise intervention was terminated. The 28% (1.4 kg) increase in handgrip strength during the 12-week strength training period means that the normal handgrip strength decline during aging can be reversed. Our findings suggest that it is possible to prevent the decline of muscle strength among older adults, which further could delay the cognitive impairment due to aging process.

Our study has several limitations. The reported amount of PA or exercise did not include the activities that the participant possibly performed outside of the study intervention. All participants were advised to maintain usual lifestyle and PA during the intervention period. However, it is possible that their PA level increased while they participated in the exercise program. When the data is being interpreted it should be considered that those with higher MMSE could have been highly active during the study while those with lower MMSE were not when interpreting the data. The issue of the personalized exercise prescription according to the individual physical fitness could also be a limitation of the study, because participants with lower handgrip strength may have been assigned a lower level of exercise. Therefore, it is difficult to distinguish the effect between low handgrip strength and a low dose of exercise.

Further, it is possible that there was a short-term practice effect on the measurement of MMSE since the intervention period was rather short (12-week). Although all confounding variables were statistically adjusted for in the final analysis, these limitations should be taken into consideration when interpreting the study outcome. The positive cross-sectional and longitudinal association between handgrip strength and cognitive function in the current study could possibly be due to the fact that our study participants were healthier than most of the previous intervention study participants.

5. Conclusion

In conclusion, we found that baseline handgrip strength was strongly associated with cognitive function before and after the 12 weeks of resistance exercise intervention among community-living older adults. Our study suggests that handgrip strength could be a strong indicator for cognitive function among healthy community-living older adults in exercise intervention. Baseline handgrip strength is an important factor in determining the effectiveness of physical activity programs for physical function as well as cognitive function among community-living older adults. Multidisciplinary approaches combined with cognitive training and resistance exercise training for older adults particularly targeting lower handgrip strength could enhance cognitive function and prevent cognitive impairment and disability.

Declaration of Competing Interest

The authors declare that they have no competing interests. All authors are responsible for the reported research.

Funding

This study was part of the IceProQualita project, which was funded by Only the Icelandic Technology Development Fund has provided No 071323008, Research Fund of the University of Iceland, a grant from Landspítali National University Hospital Research Fund and the Helga Jonsdottir and Sigurlídi Kristjánsson Geriatric Research Fund.

Author contribution

M.C worked on study design, planning, and the statistical analysis and wrote the first draft of the manuscript. All co-authors provided

critical revision of the article and read and approved the final manuscript.

Acknowledgment

This study does not necessarily reflect the views of the sponsors, and the sponsors in no way anticipate future policy in this area. The trial is registered at the US National Library of Medicine (Nr. NCT01074879)

References

- [1] Callisaya ML, Blizzard CL, Wood AG, et al. Longitudinal relationships between cognitive decline and gait slowing: the tasmanian study of cognition and gait. *J Gerontol Ser A* 2015;70:1226–32.
- [2] Kojima G, Iliffe S, Walters K. Frailty index as a predictor of mortality: a systematic review and meta-analysis. *Age Ageing* 2018;47:193–200.
- [3] Barnes DE, Covinsky KE, Whitmer RA, et al. Predicting risk of dementia in older adults. *Neurology* 2009;73:173–9.
- [4] Winblad B, Amouyel P, Andrieu S, et al. Defeating Alzheimer's disease and other dementias: a priority for European science and society. *Lancet Neurol* 2016;15:455–532.
- [5] Aedes PA, Savage PD, Brochu M, et al. Resistance training increases total daily energy expenditure in disabled older women with coronary heart disease. *J Appl Physiol* 2005;98:1280–5.
- [6] Welmer A-K, Rizzuto D, Qiu C, et al. Walking speed, processing speed, and dementia: a population-based longitudinal study. *J Gerontol Ser A* 2014;69:1503–10.
- [7] Buchman AS, Bennett DA. Loss of motor function in preclinical Alzheimer's disease. *Expert Rev Neurother* 2011;11:665–76.
- [8] Auyeung TW, Lee JSW, Kwok T, et al. Physical frailty predicts future cognitive decline—a four-year prospective study in 2737 cognitively normal older adults. *J Nutr Health Aging* 2011;15:690–4.
- [9] Fritz NE, McCarthy CJ, Adamo DE. Handgrip strength as a means of monitoring progression of cognitive decline – a scoping review. *Ageing Res Rev* 2017;35:112–23.
- [10] Al-Yahya E, Dawes H, Smith L, et al. Cognitive motor interference while walking: a systematic review and meta-analysis. *Neurosci Biobehav Rev* 2011;35:715–28.
- [11] Callisaya ML, Ayers E, Barzilai N, et al. Motoric cognitive risk syndrome and falls risk: a multi-center study. *J Alzheimers Dis* 2016;53:1043–52.
- [12] Maeda K, Takaki M, Akagi J. Decreased skeletal muscle mass and risk factors of sarcopenic dysphagia: a prospective observational cohort study. *J Gerontol Ser A* 2017;72:1290–4.
- [13] Volaklis KA, Halle M, Thorand B, et al. Handgrip strength is inversely and independently associated with multimorbidity among older women: results from the KORA-age study. *Eur J Intern Med* 2016;31:35–40.
- [14] Chang M, Saczynski JS, Snaedal J, et al. Midlife physical activity preserves lower extremity function in older adults: age gene/environment susceptibility-Reykjavik study. *J Am Geriatr Soc* 2013;61:237–42.
- [15] Chang M, Jonsson PV, Snaedal J, et al. The effect of midlife physical activity on cognitive function among older adults: AGES-Reykjavik study. *J Gerontol A Biol Sci Med Sci* 2010;65:1369–74.
- [16] Erickson KI, Voss MW, Prakash RS, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci USA* 2011;108:3017–22.
- [17] Chang Y-K, Pan C-Y, Chen F-T, et al. Effect of resistance-exercise training on cognitive function in healthy older adults: a review. *J Aging Phys Act* 2012;20:497–517.
- [18] Williamson JD, Espeland M, Kritchevsky SB, et al. Changes in cognitive function in a randomized trial of physical activity: results of the lifestyle interventions and independence for elders pilot study. *J Gerontol A Biol Sci Med Sci* 2009;64:688–94.
- [19] Falbo S, Condello G, Capranica L, et al. Effects of physical-cognitive dual task training on executive function and gait performance in older adults: a randomized controlled trial. *BioMed Res Int* 2016:e5812092. 2016.
- [20] Wang T, Wu Y, Li W, et al. Weak grip strength and cognition predict functional limitation in older Europeans. *J Am Geriatr Soc* 2019;67:93–9.
- [21] Charles LE, Burchfiel CM, Fekedulegn D, et al. Occupational and other risk factors for hand-grip strength: the Honolulu-Asia aging study. *Occup Environ Med* 2006;63:820–7.
- [22] Zammit AR, Piccinin AM, Duggan EC, et al. A coordinated multi-study analysis of the longitudinal association between handgrip strength and cognitive function in older adults. *J Gerontol Ser B* 2021;76:229–41.
- [23] Zammit AR, Robitaille A, Piccinin AM, et al. Associations between aging-related changes in grip strength and cognitive function in older adults: a systematic review. *J Gerontol Ser A* 2019;74:519–27.
- [24] Boyle PA, Buchman AS, Wilson RS, et al. Physical frailty is associated with incident mild cognitive impairment in community-based older persons. *J Am Geriatr Soc* 2010;58:248–55.
- [25] Buchman AS, Wilson RS, Boyle PA, et al. Grip strength and the risk of incident Alzheimer's disease. *Neuroepidemiology* 2007;29:66–73.
- [26] Taekema DG, Ling CHY, Kurlle SE, et al. Temporal relationship between handgrip strength and cognitive performance in oldest old people. *Age Ageing* 2012;41:506–12.

- [27] Kim H, Kim SH, Jeong W, et al. Association between change in handgrip strength and cognitive function in Korean adults: a longitudinal panel study. *BMC Geriatr* 2021;21:671.
- [28] Farina N, Tabet N, Rusted J. The relationship between habitual physical activity status and executive function in individuals with Alzheimer's disease: a longitudinal, cross-lagged panel analysis. *Aging Neuropsychol Cogn* 2016;23:234–52.
- [29] Rijk JM, Roos PR, Deckx L, et al. Prognostic value of handgrip strength in people aged 60 years and older: a systematic review and meta-analysis. *Geriatr Gerontol Int* 2016;16:5–20.
- [30] Shinohara M, Latash ML, Zatsiorsky VM. Age effects on force produced by intrinsic and extrinsic hand muscles and finger interaction during MVC tasks. *J Appl Physiol* 2003;95:1361–9.
- [31] Shinohara M, Li S, Kang N, et al. Effects of age and gender on finger coordination in MVC and submaximal force-matching tasks. *J Appl Physiol* 2003;94:259–70.
- [32] Bishop NA, Lu T, Yankner BA. Neural mechanisms of ageing and cognitive decline. *Nature* 2010;464:529–35.
- [33] Brasure M, Desai P, Davila H, et al. Physical activity interventions in preventing cognitive decline and alzheimer-type dementia: a systematic review. *Ann Intern Med* 2018;168:30–8.
- [34] Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. *JAMA* 2014;311:2387–96.
- [35] Geirsdottir OG, Arnarson A, Ramel A, et al. Muscular strength and physical function in elderly adults 6–18 months after a 12-week resistance exercise program. *Scand J Soc Med* 2015;43:76–82.
- [36] Geirsdottir OG, Arnarson A, Briem K, et al. Effect of 12-week resistance exercise program on body composition, muscle strength, physical function, and glucose metabolism in healthy, insulin-resistant, and diabetic elderly icelanders. *J Gerontol Ser A* 2012;67:1259–65.
- [37] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98.
- [38] Ramel A, Arnarson A, Geirsdottir OG, et al. Glomerular filtration rate after a 12-wk resistance exercise program with post-exercise protein ingestion in community dwelling elderly. *Nutrition* 2013;29:719–23.
- [39] Jetté M, Sidney K, Blümchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clin Cardiol* 1990;13:555–65.
- [40] Sternäng O, Reynolds CA, Finkel D, et al. Grip Strength and cognitive abilities: associations in old age. *J Gerontol Ser B* 2016;71:841–8.
- [41] Sáez de Asteasu ML, Martínez-Velilla N, Zambom-Ferraresi F, et al. Role of physical exercise on cognitive function in healthy older adults: a systematic review of randomized clinical trials. *Ageing Res Rev* 2017;37:117–34.
- [42] Vallance JK, Eurich DT, Lavalley CM, et al. Physical activity and health-related quality of life among older men: an examination of current physical activity recommendations. *Prev Med* 2012;54:234–6.
- [43] Best JR, Nagamatsu LS, Liu-Ambrose T. Improvements to executive function during exercise training predict maintenance of physical activity over the following year. *Front Hum Neurosci* 2014;8:353.
- [44] Rovio S, Kåreholt I, Helkala E-L, et al. Leisure-time physical activity at midlife and the risk of dementia and Alzheimer's disease. *Lancet Neurol* 2005;4:705–11.
- [45] Rizzoli R, Reginster J-Y, Arnal J-F, et al. Quality of life in sarcopenia and frailty. *Calcif Tissue Int* 2013;93:101–20.
- [46] Eggermont LH, Gavett BE, Volkens KM, et al. Lower-extremity function in cognitively healthy aging, mild cognitive impairment, and Alzheimer's disease. *Arch Phys Med Rehabil* 2010;91:584–8.
- [47] Wolfe RR. The underappreciated role of muscle in health and disease. *Am J Clin Nutr* 2006;84:475–82.
- [48] Stewart VH, Saunders DH, Greig CA. Responsiveness of muscle size and strength to physical training in very elderly people: a systematic review. *Scand J Med Sci Sports* 2014;24:e1–10.
- [49] Cadore EL, Pinto RS, Bottaro M, et al. Strength and endurance training prescription in healthy and frail elderly. *Aging Dis* 2014;5:183–95.
- [50] Frontera WR, Zayas AR, Rodriguez N. Aging of human muscle: understanding sarcopenia at the single muscle cell level. *Phys Med Rehabil Clin N Am* 2012;23:201–7. xiii.
- [51] McGrath R, Vincent BM, Hackney KJ, et al. The longitudinal associations of handgrip strength and cognitive function in aging Americans. *J Am Med Dir Assoc* 2020;21:634–9. e1.
- [52] Christensen H, Mackinnon AJ, Korten A, et al. The "common cause hypothesis" of cognitive aging: evidence for not only a common factor but also specific associations of age with vision and grip strength in a cross-sectional analysis. *Psychol Aging* 2001;16:588–99.
- [53] Rosso AL, Studenski SA, Chen WG, et al. Aging, the central nervous system, and mobility. *J Gerontol A Biol Sci Med Sci* 2013;68:1379–86.
- [54] Hall PA, Fong GT. Temporal self-regulation theory: a neurobiologically informed model for physical activity behavior. *Front Hum Neurosci* 2015;9:117.
- [55] Salami A, Rieckmann A, Fischer H, et al. A multivariate analysis of age-related differences in functional networks supporting conflict resolution. *Neuroimage* 2014;86:150–63.
- [56] McGrath R, Robinson-Lane SG, Cook S, et al. Handgrip strength is associated with poorer cognitive functioning in aging Americans. *J Alzheimers Dis* 2019;70:1187–96.
- [57] Cooper R, Kuh D, Cooper C, et al. Objective measures of physical capability and subsequent health: a systematic review. *Age Ageing* 2011;40:14–23.
- [58] Parker K, Rhee Y, Tomkinson GR, et al. Handgrip weakness and asymmetry independently predict the development of new activity limitations: results from analyses of longitudinal data from the us health and retirement study. *J Am Med Dir Assoc* 2021;22:821–6. e1.
- [59] Clouston SAP, Brewster P, Kuh D, et al. The dynamic relationship between physical function and cognition in longitudinal aging cohorts. *Epidemiol Rev* 2013;35:33–50.
- [60] Stessman J, Rottenberg Y, Fischer M, et al. Handgrip strength in old and very old adults: mood, cognition, function, and mortality. *J Am Geriatr Soc* 2017;65:526–32.
- [61] Scharre DW, Chang S, ing Nagaraja HN, et al. Self-Administered Gerocognitive Examination: longitudinal cohort testing for the early detection of dementia conversion. *Alzheimers Res Ther* 2021;13:192.