ORIGINAL ARTICLE

Relationship between hand grip strength and peak VO_2 in community-dwelling elderly outpatients

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This work was performed at the Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology.

Abstract

Background Hand grip strength and peak oxygen uptake (VO_2) are important components of frailty. However, the relationship between these two variables among community-dwelling elderly people is still unclear. The present study aimed to investigate this relationship.

Methods Participants were 190 Japanese community-dwelling elderly outpatients (61 men and 129 women, mean age 78.0 years). Hand grip strength of participants' was measured using a Smedley-type hand dynamometer. Peak VO_2 levels were assessed with a cardiopulmonary exercise test. Skeletal muscle mass index (SMI) and usual walking speed were assessed physiologically and physically. Sample size was calculated using G*Power 3.1.9.2.

Results There were significant correlations between hand grip strength and age (r = −0.22), peak VO_2 (r = 0.40), SMI (r = 0.51), and usual walking speed (r = 0.29). There were significant differences in age, peak VO_2 and SMI after participants were divided into normal and low hand grip strength groups according to the Asian Working Group for Sarcopenia threshold, whether both sexes were combined or considered separately. Multiple logistic regression analysis showed that peak VO_2, SMI and age were independent determinants of hand grip strength after adjusting for potential confounders (Exp(B) = 0.871; 0.475; 1.065). Longitudinal analysis after 6 months of exercise training showed the percentage of change in hand grip strength and peak VO_2 were correlated positively (r = 0.22) for 92 participants.

Conclusion Peak VO_2 is independently associated with hand grip strength among community-dwelling elderly outpatients.

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Introduction

Hand grip strength (HGS) is one of the important components of frailty, as is peak oxygen uptake (VO_2) [1]. HGS is known to be related to disability [2] and mortality [3], and has received much clinical attention in cardiology recently because it has been identified as a predictor of risk of cardiovascular (CV) disease [4] and coronary heart disease (CHD) [5]. Peak VO_2 is also known as an index of exercise capacity [6] and

life expectancy [7]. Recently, it has been reported that peak VO_2 is related to cardiovascular risk factors [8]. However, the relationship between HGS and peak VO_2 among community-dwelling elderly people is still unclear. Clarifying the relationship between these two variables might be useful for understanding why HGS is a predictor of cardiovascular events.

In this study, therefore, we investigated the relationship between HGS and peak VO_2 in community-dwelling elderly outpatients.

Methods

Participants

Participants were 190 community-dwelling people (61 men and 129 women) aged 65 to 97 years (mean age 78.0 years) who lived in the Tokyo metropolitan area. None of the participants were hospitalized at the time of the study, but all were receiving outpatient treatment at the Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology. Exclusion criteria were: age younger than 65 years, impaired vision, impaired hearing, musculoskeletal impairments that might interfere with the ability to perform the symptom-limited exercise test, a clinically unstable condition, a diagnosis of congestive heart failure, dementia, and Parkinson's disease. Potential participants who performed habitual exercise training were also excluded from the study. Habitual exercise training is defined as the performance of repetitive activity more than three times a week for the purpose of improving and/or maintaining physical performance such as aerobic training (i.e. walking, swimming), resistance training, and/or a combination of these methods (i.e. cycling). All willing participants were assigned to the study after application of the exclusion criteria. Participants' clinical characteristics are summarized in Table 1.

A 6-month follow-up assessment was conducted with 92 participants who consented to join an exercise program and could engage in it successfully for 6 months.

Cardiopulmonary exercise test

All participants underwent a symptom-limited cardiopulmonary exercise test (CPET) using an upright, electromagnetically-braked cycle ergometer (Aerobike Strength Ergo-8, Mitsubishi Electronic, Tokyo, Japan), a metabolic analyser (Aeromonitor AE-310S, Minato Medical Science, Osaka, Japan), and an electrocardiogram (Stress test system ML-9000, Fukuda Denshi, Tokyo, Japan) and automatic-cuff blood pressure manometer (FB-300, Fukuda Denshi, Tokyo, Japan). Resting blood pressure and heart rate were measured before the CPET started. The CPET began with a 3-min rest on the ergometer followed by a 4-min warm-up at 0 watts (W) at 60 rpm. The load was then increased incrementally by 15 W per min during the test. All CPET parameters were measured from the beginning of the initial rest on the cycle ergometer until the end of the exercise session.

The CPET was terminated in response to any of the following conditions: the participant requested to stop or was unable to continue to perform the pedalling exercise correctly; or abnormal physiological responses occurred [9]. VO_2, carbon dioxide output (VCO_2), minute ventilation, tidal volume, and frequency of respiration were smoothed with an 8-breath moving average. Peak VO_2 was defined as the highest VO_2 value obtained during the last minute of the CPET. Peak W was defined as the power at measured peak VO_2 with CPET. VO_2/heart rate (HR) (oxygen pulse) was calculated by dividing the moving average VO_2 by the HR. When the respiratory exchange ratio (VCO_2/VO_2) was less than 1.0 at peak exercise, the test was considered insufficient because of the participant's poor effort, and these peak exercise data were not used in the analyses. Of the CPET cardiac parameters, we paid particular attention to peak VO_2 and peak VO_2/HR, because there is a significant linear

correlation between peak VO_2 and peak CO [10], and between peak VO_2/HR and SV [11].

Skeletal muscle mass index and body mass index

Appendicular skeletal muscle mass was measured using total body dual-energy X-ray absorptiometry (DEXA, Lunar iDXA, GE Healthcare, Tokyo, Japan). The sum of the muscle mass of the four limbs was considered the appendicular skeletal muscle mass, and the skeletal muscle mass index (SMI) was calculated as appendicular skeletal muscle mass divided by height in meters squared (kg/m^2). Body mass index was calculated as body weight divided by height in meters squared (kg/m^2)

Table1

Participant characteristics (n=190)			Mean (range)
Male n (%)			61 (32.1%)
	Age (years)	All	78.0 ± 6.5
		Male	78.7 ± 7.3
		Female	77.6 ± 6.2
	Body Mass Index (kg/m^2)	All	22.8 ± 3.6
		Male	22.8 ± 3.2
		Female	22.7 ± 3.7
Physiological Assessment			
	Resting heart rate (beat/min)		70.9 ± 11.7
	Resting systolic blood pressure (mmHg)		136.4 ± 20.7
CardioPulmonaryExcercise Test			
	Peak VO_2 (ml/min/kg)		16.4 ± 4.3
	Peak VO_2/heart rate (ml/bpm)		7.3 ± 2.1
	Peak watts		68.2 ± 25.1
	Peak metabolic equivalent		4.7 ± 1.3
	$\Delta VO_2/\Delta$Work load (ml/watt)		8.6 ± 2.5
	VE/VCO_2 slope		34.3 ± 9.9
	Peak heart rate (beat/min)		122.5 ± 22.0
	Peak systolic blood pressure (mmHg)		181.1 ± 27.5
Physical Assessment			
	Skeletal muscle mass index (kg/m^2)	All	6.2 ± 0.9
		Male	6.8 ± 0.9
		Female	5.9 ± 0.7
	Hand grip strength (kg)	All	19.6 ± 6.4
		Male	25.6 ± 6.5
		Female	16.9 ± 4.2
	Usual walking speed (m/sec)	All	0.9 ± 0.2
		Male	0.9 ± 0.3
		Female	1.0 ± 0.3
Type of Illness			[n (%)]
	Hypertension		107 (53%)
	Dyslipidemia		79 (39%)
	Diabetes mellitus		45 (22%)
	Atrial fibrillation		12 (6%)
	Coronary artery disease		37 (18%)
	Chronic heart failure		10 (5%)
	Sarcopenia	All	43(23%)
		Male	22(12%)
		Female	21(11%)
Medications			
	Calcium channel blocker		83 (41%)
	Angiotensin-converting-enzyme inhibitor		16 (8%)
	Angiotensin II receptor blocker		55 (27%)
	Beta blocker		37 (18%)
	Statin		63 (31%)

VO_2: oxygen uptake, V_E vs. VCO_2 slope: minute ventilation versus carbon dioxide output slope.

Physical performance evaluation

Handgrip strength was assessed two times on each hand alternately using a Smedley-type hand dynamometer (JAMAR, Sammons Preston Rolyan, IL, USA). The highest value of two trials was used in the analyses. We divided participants into low and normal hand grip groups, according to the Asian Working Group for Sarcopenia (AWGS; the cut-off thresholds of HGS for

sarcopenia were 26 kg for males and 18 kg for females)[12]. We also used the AWGS criteria to diagnose sarcopenia.

To test usual walking speed, we asked participants to walk along a straight 11-m walkway on a flat floor, once, at their usual speed. Walking speed was measured over a 5-m distance between markers placed 3-m and 8-m from the start of the walkway. Two trials were conducted per person, with the shorter time used in the analyses.

All physical performance parameters were assessed for each participant by trained research assistants.

Exercise training program

Each exercise session included warm-up, cool down, and flexibility exercises, along with 30 minutes of submaximal aerobic exercise in the form of cycling training at 50–70% of peak VO_2 and 15 minutes of submaximal resistance training (knee extension, hip abduction, rowing, leg press) at 50–70% of the one-repetition maximum. Participants underwent one exercise session 2 days per week over a 6-month period. Training was performed according to the American Heart Association's guidelines [13].

Statistics

Sample size of 160 patients was calculated for 95% power, $\alpha = 0.05$, $\beta = 0.05$, and anticipated effect size = 0.15 using sample size software (G*Power 3.1.9.2. Germany). Pearson's correlation analysis was performed to examine the relationship between HGS and physiological assessment, cardiac functional parameters of CPET, and physical functional assessments.

Comparisons of the clinical characteristics of patients in the low and normal HGS groups were performed using unpaired Student's t-tests.

Multiple logistic regression analysis to predict low HGS with peak VO_2 was adjusted for age, hypertension, diabetes mellitus, dyslipidaemia, coronary artery disease, chronic heart failure and SMI. Pearson's correlation analysis was performed to examine the relationship between the percentage change in HGS and the percentage change in CPET and physiological parameters. All statistical analyses were performed using SPSS Version 22 (IBM Japan, Tokyo, Japan). The significance level was set at $p < 0.05$ for all tests.

Ethical considerations

This study was approved by the Ethics Committee of the Tokyo Metropolitan Geriatric Hospital and Institute of Gerontology (Authorization Number: 240301), and conforms with the principles outlined in the Declaration of Helsinki. All participants gave their written informed consent before data collection.

Results

Table 2(A) shows the correlation between HGS and other indices in this study. Significant positive correlations were found with peak VO_2 ($r = 0.40$, $p < 0.001$), peak VO_2/HR ($r = 0.55$, $p < 0.001$), peak HR ($r = 0.24$, $p < 0.01$), peak W ($r = 0.56$, $p < 0.001$), peak metabolic equivalent ($r = 0.39$, $p < 0.001$), $\Delta VO_2/\Delta$work load ($r = 0.39$, $p < 0.001$), SMI ($r = 0.51$, $p < 0.001$), and usual walking speed ($r = 0.29$, $p < 0.001$). Similarly, significant negative correlations were found with age ($r = -0.22$, $p < 0.01$) and resting systolic blood pressure ($r = -0.18$, $p < 0.05$).

Table 3 shows the difference between the normal and low hand grip groups overall and by sex. Significant differences were seen in age, peak VO_2, peak VO_2/HR, peak watts, peak metabolic equivalents and SMI in overall and both of sex.

Table 4 shows the multiple logistic regression analysis for predicting low HGS with peak VO_2. There

were significant independent relationships between HGS and peak VO_2 (Exp(B) = 0.871, $p < 0.01$), SMI (Exp(B) = 0.475, $p < 0.001$) and age (Exp(B) = 1.065, $p < 0.05$), after adjustment for potential confounders (hypertension, diabetes mellitus, dyslipidemia, coronary artery disease and chronic heart failure).

Table 2(B) shows the correlation between percentage change in HGS and percentage change in other indices after the 6-month exercise training. A significant correlation was seen between these two variables ($r = 0.22$, $p < 0.05$).

Table2

(A) Univariate correlations between hand grip strength and other indices (n = 190)		
	Correlation	**p**
Age	-0.22	0.002
Body mass index	0.09	0.206
Resting heart rate	0.05	0.516
Resting systolic blood pressure	-0.18	0.028
Peak VO_2	0.40	<0.0001
Peak VO_2/heart rate	0.55	<0.0001
Peak watts	0.56	<0.0001
Peak metabolic equivalent	0.39	<0.0001
$\Delta VO_2/\Delta LOAD$	0.39	<0.0001
VE/VCO_2 slope	-0.12	0.098
Peak heart rate	0.24	0.001
Peak systolic blood pressure	-0.01	0.949
Skeletal muscle mass index	0.51	<0.0001
Usual walking speed	0.29	<0.0001
(B) After 6 months of exercise (vs. % change in hand grip strength) (n = 92)		
% change in body mass index	-0.09	0.403
% change in peak VO_2	0.22	0.037
% change in peak VO_2/heart rate	0.21	0.055
% change in peak watts	0.12	0.268
% change in $\Delta VO_2/\Delta LOAD$	0.02	0.882
% change in VE/VCO_2 slope	-0.14	0.190
% change in skeletal muscle mass index	-0.06	0.640

VO_2: oxygen uptake, V_E vs. VCO_2 slope: minute ventilation versus carbon dioxide output slope.

Table 3

Comparison of clinical characteristics between normal hand grip group and low hand grip group

	All Participants (n = 190)			Males (n = 61)			Females (n = 129)		
	Normal hand grip group (Mean±SD) (n = 90)	Low hand grip group (Mean ± SD) (n = 100)	p	Normal hand grip group (Mean ± SD) (n = 31)	Low hand grip group (Mean ± SD) (n = 30)	p	Normal hand grip group (Mean ± SD) (n=59)	Low hand grip group (Mean ± SD) (n=70)	p
Age (years)	76.37 ± 5.89	79.46 ± 6.73	0.001	76.59 ± 6.53	80.76 ± 7.45	0.020	76.06 ± 5.57	78.89 ± 6.36	0.007
Body mass index (kg/m^2)	23.32 ± 3.19	22.33 ± 3.84	0.049	23.75 ± 2.77	21.83 ± 3.43	0.017	22.97 ± 3.40	22.55 ± 4.00	0.519
Resting heart rate (beat/min)	70.96 ± 11.81	70.81 ± 11.58	0.934	72.81 ± 11.26	70.72 ± 13.76	0.522	69.93 ± 12.24	70.85 ± 10.62	0.651
Resting systolic blood pressure (mmHg)	135.74 ± 19.79	136.92 ± 21.51	0.724	126.14 ± 20.83	131.04 ± 21.12	0.428	139.53 ± 18.38	139.45 ± 21.36	0.983
Peak VO_2 (ml/min/kg)	17.69 ± 3.83	15.14 ± 4.41	<0.0001	18.04 ± 3.55	14.97 ± 4.29	0.003	17.57 ± 3.96	15.21 ± 4.50	0.002
Peak VO_2/heart rate (ml/bpm)	8.01 ± 2.07	6.57 ± 1.93	<0.0001	9.33 ± 2.50	7.51 ± 2.14	0.003	7.35 ± 1.51	6.16 ± 1.69	<0.0001
Peak watts (watts)	77.39 ± 22.46	59.54 ± 24.48	<0.0001	86.90 ± 20.01	64.80 ± 22.33	<0.0001	72.80 ± 22.95	57.29 ± 25.17	<0.0001
Peak metabolic equivalent	5.09 ± 1.15	4.33 ± 1.26	<0.0001	5.15 ± 1.02	4.28 ± 1.23	0.004	5.07 ± 1.21	4.35 ± 1.28	0.001
$\Delta VO_2/\Delta LOAD$ (ml/watt)	9.03 ± 2.21	8.14 ± 2.60	0.011	9.92 ± 1.74	8.99 ± 2.23	0.078	8.56 ± 2.28	7.80 ± 2.67	0.089
VE/VCO_2 slope	33.38 ± 8.09	35.23 ± 11.25	0.193	34.25 ± 8.07	37.47 ± 11.97	0.223	32.79 ± 8.24	34.27 ± 10.88	0.392
Peak heart rate (beat/min)	126.52 ± 22.09	118.78 ± 21.36	0.014	125.74 ± 22.95	114.27 ± 22.42	0.053	127.10 ± 22.08	120.71 ± 20.76	0.093
Peak systolic blood pressure (mmHg)	184.23 ± 26.75	178.23 ± 28.02	0.129	177.03 ± 30.54	166.27 ± 29.98	0.170	187.34 ± 24.02	183.36 ± 25.68	0.368
Skeletal muscle mass index (kg/m^2)	6.47 ± 0.88	5.90 ± 0.83	<0.0001	7.19 ± 0.77	6.30 ± 0.87	<0.0001	6.06 ± 0.68	5.73 ± 0.75	0.012
Usual walking speed (m/sec)	1.01 ± 0.21	0.86 ± 0.25	<0.0001	0.95 ± 0.22	0.84 ± 0.27	0.088	1.05 ± 0.21	0.87 ± 0.25	<0.0001

VO_2: oxygen uptake, V_E vs. VCO_2 slope: minute ventilation versus carbon dioxide output slope.

Table4

Multiple logistic regression analysis to predict Sarcopenic group					
	B	p	Exp(B)	LCI	UCI
Peak VO_2	-0.138	0.004	0.871	0.792	0.958
Skeletal muscle mass index	-0.743	<0.0001	0.475	0.319	0.709
Age	0.063	0.018	1.065	1.011	1.123

Model chi-square p < 0.001; Hosmer-Lemeshow p = 0.873; Accuracy 70.0%

Adjusted for Hypertension, Diabetes mellitus, Dyslipidemia, Coronary artery disease, Chronic heart failure

VO_2: oxygen uptake

Discussion

This study examined the relationship between HGS and peak VO_2 among community-dwelling elderly outpatients.

In this study, 30 male participants (49%) and 70 female participants (54%) were below the threshold for HGS, according to the AWGS criteria [12]. Furthermore, the prevalence of sarcopenia according to the AWGS criteria [12] was 12% for males and 11% for females in this study (Table1). Recently, it has been reported that the prevalence of sarcopenia ranged from 2.5 to 28.0% in Japanese males and 2.3 to 11.7% in Japanese females, with muscle mass measured by dual-energy X-ray absorptiometry [14]. Therefore, the prevalence of sarcopenia in this study was similar to the previous report.

This study showed that peak VO_2 was an independent determinant of HGS in multiple logistic regression analysis, and also showed the correlation between percentage change in HGS and percentage change in peak VO_2 after 6-month exercise training in community-dwelling elderly outpatients. Peak VO_2 is known as an index not only of exercise capacity [6] and life expectancy [7], but also of cardiac output (CO) [10]. Similarly, our study showed that peak VO_2/HR, which is also known as the index of stroke volume (SV) [11], is bi-directionally related to SMI [15]. Therefore, it seems reasonable that HGS would show a bi-directional relationship to the index of CO (=SV x HR) during exercise in this study.

However, despite a previous study's report of a relationship between HGS and CV events [4, 5], our study showed no association between HGS and chronic heart failure or coronary artery disease (Table 4). Similarly, Gubelmann et al. reported that the association disappeared after adjustment for CV risk, although there was an observed relationship between low HGS and CV events [16]. They suggested that the effect of low HGS on incident CV events is mediated by CV risk [16].

Recently, it was reported that 1-metabolic equivalent decrement in peak VO_2 corresponded to 57% and 67% higher likelihood of clustering of cardiovascular risk factors (i.e., 3 of the following: hypertension, high blood glucose level, large waist circumference, low high-density lipoprotein cholesterol level, or high triglyceride level) among community-dwelling older women and men, respectively [17]. Similarly, a systematic review has established that peak VO_2 has a significant association with metabolic syndrome [18]. Thus, decreased peak VO_2 might be a phenotype of cardiovascular risk factors.

Additionally, it has been reported that cardio-metabolic disease risk is robustly associated with HGS in U.S. and Chinese aging adults [19], and that metabolic syndrome is also strongly associated with low HGS [20]. These findings may indicate that there is cross-triangle association among HGS, peak VO_2 and cardiovascular risk factors, but the potential mechanism

among these triangle associations is still unclear. A previous study suggested that myostatin, which is one of the factors in the ubiquitin proteasome system, might be a potential mechanism of this triangle association. First, higher serum myostatin is associated with lower HGS [21], and lower myostatin is associated with higher HGS [22]. Furthermore, it is known that inhibition of myostatin increases skeletal muscle mass and strength in mice [23], and recently it was reported in a placebo-controlled, double-blind, parallel, multicentre, phase 2 study that myostatin antibody treatment increases skeletal muscle mass and may improve muscle power [24]. Second, Brandt et al. have shown that muscle myostatin mRNA is negatively related to peak VO_2 in healthy subjects [25]. They also reported that muscle myostatin mRNA is positively correlated with fasting insulin, HOMA2-IR, fat mass and triglyceride levels in a healthy group [25]. Furthermore, they found that muscle myostatin mRNA correlated positively with TNF-α, IL-6 [25], which is an important muscle catabolic factor in the ubiquitin proteasome system [26]. Thus, myostatin is associated with double cascades of cardio-metabolism, and of muscle metabolism, and myostatin also has an association with peak VO_2.

Finally, Table 2(B) shows the positive correlation between percentage change in HGS and the percentage change in peak VO_2 after 6 months of exercise intervention. This result may indicate the importance of peak VO_2 on HGS longitudinally. Cunha et al. reported that exercise training not only improves exercise capacity (i.e., peak VO_2), but also inhibits over-activity of the ubiquitin proteasome system, which is related to skeletal muscle atrophy [27]. Interestingly, Takahashi et al. reported that femoral muscle mass influenced both peak VO_2 and HGS in community-dwelling older people [28], which may suggest an important role of training to increase femoral muscle mass in the improvement of HGS.

There are several limitations to this study. We did not evaluate the factors related to the ubiquitin proteasome system, particularly myostatin. Similarly, we didn't evaluate cardio-metabolic profiles such as blood glucose level, high-density lipoprotein cholesterol level, low-density lipoprotein cholesterol level, triglyceride level, or large waist circumference. Thirdly, there is no control group in this study to evaluate the effect of exercise. Finally, the participants of this study were based on hospital sample, and based on chronic disease(s); therefore, there is a limitation to applicate to general elderly population.

HGS is one of the important components of frailty, as is peak VO_2 [1]. In conclusion, this study showed the relationship between these variables in community-dwelling elderly outpatients.

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Declaration of Conflict of interests

The authors declare that we have no conflict of interest.

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