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Determinants of physical function in community dwelling old people

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Background. Poor physical function is associated with disability and mortality in old people.
Objectives. The aim was to find determinants of physical function in old people.
Design. Secondary, cross-sectional analysis.
Setting. Community in the Reykjavik, Iceland.
Participants. 236 old people (73.7 ± 5.7 years, 58.2% female).
Measurements. Timed-up-and-go (TUG), six-minute-walk-for-distance (6MWD), anthropometrics, quadriceps strength, dietary intake, mini-mental-state-examination (MMSE), leisure-time physical activity (LTPA) and blood variables were assessed. Descriptive, bivariate and multivariate statistical analyses were used.
Results. There were differences between men and women in energy intake, body composition and muscular strength, but physical function did not differ between men and women. In bivariate analysis, most of the assessed variables correlated with 6MWD and TUG. Stepwise linear models showed that age, body composition, strength, medication, LTPA and MMSE were predictors of physical function but not hematological variables. The association between MMSE and function disappeared when corrected for strength/body weight. Results were similar for both 6MWD and TUG and the strongest predictors in the final models were age and quadriceps strength/body weight.
Conclusions. In community dwelling old people, physical function decreases with age. However, it is of clinical relevance that there are modifiable determinants of physical function, in particular strength for a given body weight, LTPA and number of medications, which represent potential targets to maintain physical function in this age group. Our results also indicate that neither cognitive function, nor dietary intake nor blood chemical variables were independently associated with physical function.

Key words: physical function, 6-minute-walk-for-distance, timed-up-and-go, community dwelling old people

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INTRODUCTION

There is convincing evidence that poor physical function is associated with adverse health outcomes in old people [1-4], e.g., it has been reported that

physical function is associated with disability in both cross-sectional and longitudinal studies [1,2]. Further, poor function is associated with greater hazards of injurious falls [3] and according to a longitudinal study, physical function predicts mortality in community dwelling old people even after correction for various confounders [4].
Several studies are available that have characterized old people with poor physical function [5-18]. Nutrition status, physical activity and body composition have all been associated with physical function [5,6]. One study reported that calf circumference was positively related to higher functional performance in old people [7]. Muscle quality and relative adiposity were strong and independent predictors of physical function in older women [8], although findings from other studies have been inconsistent [9,10].
Blood chemical variables have also been associated with physical function in old people, e.g., hyperuricemia was associated with poor physical performance in older people, over a follow-up of 4.4 years [11]. Further, chronic inflammation has been proposed as a biological mechanism underlying the decline in physical function that occurs with aging [12]. In a recently published longitudinal study, both IL-6 and CRP had some associations with physical performance at baseline, although they did not predict changes in performance seven years later in older adults [12].
In recent years, numerous studies have investigated physical fitness and cognitive impairment in older people in relation to ageing [13,14], but only a limited number of studies have focused on the association between physical and cognitive function [15]. As such, a recently published study found associations between physical function and cognitive impairment in people over 65 years old. Specifically, results indicated that gait speed is the variable that best represents both the cognitive and physical function in people over 65 years of age [15].
Medications have also been associated with poor physical function and old people with poor physical function tend to use a higher number of medications [16] and pharmacologic burden is significantly and independently associated with falls in that group [17].
Obviously, a large number of variables can be associated with physical function. As many of the above mentioned studies focus mainly on one or few of these factors, and as there is plenty of potential interaction between them, it is not known which variables are independently associated with physical function. Thus, the of the aim of the present study was to find determinants of physical function in old people and to investigate whether body composition and muscular strength can explain observed associations of physical function with cognitive function, blood chemical variables, dietary intake and medication.

This was a secondary data analysis from baseline data of a previously published randomized, controlled trial, designed to examine the effect of post-exercise protein ingestion on the efficacy of strength training in old people [18].

METHODS

Subjects

Participants (N = 236) were 65 years and older (range 65-92 years old) and were recruited by advertisements posted in the Reykjavik area. Exclusion criteria were low cognitive function (Mini-Mental State Examination (MMSE) $\leq$ 19 points) [19], major orthopedic disease and pharmacological interventions with exogenous testosterone or other drugs known to influence muscle mass. Furthermore, participants had to be free of any musculoskeletal disorders or other disorders that could affect their muscle mass. Enrolled subjects were apparently healthy, although some had hypertension, hyperlipidemia or type 2 diabetes [19,20]. The study was approved by the Icelandic National Bioethics Committee (15-139-S1) and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All persons gave their informed consent prior to their inclusion in the study.

Body composition

Body composition (lean body mass = LBM, fat mass = FM, appendicular skeletal muscle = ASM) was assessed by dual energy x-ray absorptiometer (DXA) with Hologic QDR-2000 plus®, Hologic Inc., Waltham, MA, USA. The DXA measurements were conducted at the Icelandic Heart Association, Kopavogur, Iceland. Body weight (BW) was measured in light underwear on a calibrated scale (model no. 708, Seca, Hamburg, Germany) and height was measured with a calibrated stadiometer (model no. 206; Seca, Hamburg, Germany). Body mass index (BMI) was calculated from the recorded height and weight (kg/m^2). Waist circumference was measured halfway between the top of the lateral iliac crest and the lowest rib. All measures were performed twice using a tape measure and recorded to the nearest centimeter.

Muscular strength

Quadriceps strength

Quadriceps strength (maximum voluntary isometric contraction (MVIC)) was tested with an isokinetic dynamometer (Kin-Com® 500H Chattanooga). The participants performed three submaximal trials and then

four MVIC tests for five seconds each, with a 50 second rest between tests. The greatest output was recorded as the peak force expressed in Newton (N).

Physical function

Six Minute Walk for Distance (6MWD)

Gait speed was assessed with 6MWD. The 6MWD was performed indoors in a spacious gym hall and conducted according to the guidelines from the American Thoracic Society [21].

Timed Up and Go test (TUG)

During the TUG test the subject was instructed to rise from a chair with a seat height of 43 cm, walk 3 m, turn around, return and sit down again, wearing ordinary footwear and using customary walking aids if necessary [22].

Questionnaires

Demographic characteristics and medication count were collected using questionnaires.

Dietary assessment

Diet was assessed using a 3-day weighed food record at the start of the study. Participants weighed and recorded their food intake for three consecutive days, two week days and one weekend day. Instructions on how to record the diet were given orally and in writing. The participants were provided with electronic scales (PHILIPS HR 2393) and were asked to record all food items and drinks. The results of the food records were typed into an online food calculation program based on the ISGEM databank, which contains data on the composition of foods on the Icelandic market.

Leisure-time physical activity (LTPA)

Information on LTPA during the last year was collected using a questionnaire [23] based on the Compendium of Physical Activities [24] and the Paffenberger's questionnaire [25]. The LTPA for each subject was evaluated by asking them to report their participation in sports, exercises or other physical activities as time per week. In statistical analysis it is shown as hours/week.

Biochemical measurements

Participants were instructed to avoid strenuous exercise and alcohol consumption the day before the drawing of fasting blood samples at baseline and endpoint. The blood samples were centrifuged and the serum was stored at -80°C for subsequent analysis at the University Hospital in Reykjavik, Iceland. Glucose was analyzed using an enzymatic colorimetric assay and an automated analyzer. HbA1c was measured using a chromatographic-spectrophotometric assay. C-reactive protein was measured with ELISA.

Table I. Characteristics of male and female participants.

	All (n = 236) Mean ± SD			Male (n = 98) Mean ± SD			Female (n=138) Mean ± SD			P-value
Age (years)	73.6	±	5.7	74.6	±	5.9	72.8	±	5.5	0.018
Height (cm)	169	±	10	178	±	8	163	±	6	< 0.001
Body weight (kg)	82.6	±	17.5	93.9	±	16.7	74.6	±	13.1	< 0.001
Waist circumference (cm)	99.8	±	14.4	108.5	±	12.1	93.6	±	12.6	< 0.001
BMI (kg/m^2)	28.8	±	4.8	29.7	±	4.6	28.1	±	4.9	0.012
Fat mass (kg)	38.2	±	7.3	32.3	±	10.4	31.4	±	9.5	0.515
Appendicular skeletal muscle (kg)	24.4	±	5.4	29.6	±	3.9	20.9	±	2.6	< 0.001
Quadriceps strength (N)	464	±	124	538	±	124	409	±	90	< 0.001
6MWD (m)	453	±	80	456	±	86	452	±	76	0.708
TUG (sec)	7.9	±	2.2	8.0	±	2.1	7.9	±	2.3	0.595
CRP (mg/L)	7.1	±	4.6	7.4	±	5.4	6.9	±	4.0	0.487
Glucose (mmol/L)	5.0	±	1.0	5.2	±	1.1	4.8	±	0.9	0.020
HbA1c (%)	5.7	±	0.6	5.8	±	0.7	5.6	±	0.5	0.014
MMSE (score)	27.5	±	2.1	27.1	±	2.1	27.8	±	2.0	0.021
Number of drugs	2.1	±	1.5	2.3	±	1.4	1.9	±	1.6	0.067
LTPA** (h/week)	342	±	342	323	±	341	356	±	343	0.462
Energy intake (kcal/d)	1679	±	481	1886	±	528	1531	±	382	< 0.001
Protein intake (g/kg BW/d)	0.95	±	0.27	0.96	±	0.26	0.94	±	0.28	0.587

*Differences between genders according to an independent samples t test (normally distributed variables) and Mann Whitney U test (not normally distributed variables);
** Leisure time physical activity

Table II. Correlation table*.

Variables		Pearson r	P-value
Age (years)	6MWD	-0.502	< 0.001
	TUG (sec)	0.508	< 0.001
BMI (kg/m^2)	6MWD	-0.245	< 0.001
	TUG (sec)	0.151	0.023
Fat mass (kg)	6MWD	-0.238	< 0.001
	TUG (sec)	0.139	0.040
Lean body mass (kg)	6MWD	0.037	0.581
	TUG (sec)	0.002	0.979
ASM (kg)	6MWD	0.077	0.245
	TUG (sec)	-0.039	0.562
ASM (%)	6MWD	0.328	< 0.001
	TUG (sec)	-0.219	0.001
Quadriceps strength (N)	6MWD	0.416	< 0.001
	TUG (sec)	-0.365	< 0.001
Quadriceps strength/body weight (N/kg)	6MWD	0.537	< 0.001
	TUG (sec)	-0.480	< 0.001
HbA1c (%)	6MWD	-0.246	< 0.001
	TUG (sec)	0.224	0.001
CRP (mg/L)	6MWD	-0.155	0.018
	TUG (sec)	0.050	0.454
MMSE (score)	6MWD	0.400	< 0.001
	TUG (sec)	-0.431	< 0.001
Number of medications	6MWD	-0.303	< 0.001
	TUG (sec)	0.250	< 0.001
Physical activity (h/week)	6MWD	0.364	< 0.001
	TUG (sec)	-0.296	< 0.001
Energy intake (kcal/day)	6MWD	0.039	0.585
	TUG (sec)	-0.007	0.919
Protein intake (g/d/body weight)	6MWD	0.086	0.223
	TUG (sec)	-0.127	0.072

*Spearman 's correlation coefficient rho.

Statistical analysis

Statistical analysis was conducted using SPSS for Windows version 22.0 (SPSS, Chicago, IL, USA) and the level of significance was set at $P < 0.05$. Data were checked for normality using the Kolmogorov-Smirnov test and are shown as mean ± standard deviation (SD). Comparisons between groups, e.g., men and women, were done using independent samples' t-test (normally distributed variables) or Mann-Whitney-U test (not normally distributed variables). Correlations between variables were calculated using Spearman 's correlation coefficient rho. Linear models with various degrees of statistical correction were used to find variables associated with 6MWD and TUG. Model 1 included sex, age and factors related to chronic conditions; model 2 additionally included lifestyle factors; model 3 additionally body composition; model 4 additionally included muscular strength.

RESULTS

Baseline data and differences between genders can be seen in Table I. Not unexpected, there were differences between men and women in energy intake, body composition and muscular strength. However, physical function (6MWD, TUG) did not differ between men and women.

Table II shows correlations of physical function with body composition, strength, LTPA, medication, hematological variables, MMSE, energy and protein intake. With the exception of CRP, variables that were significantly associated with 6MWD and TUG were identical.

The multivariate linear models in Table III and IV show that age, number of medications and habitual physical activity are consistently associated with physical function rather independently from other covariates. Hematological variables were not associated with physical function in the models and the association between gender and MMSE

Table III. Determinants* of 6MWD (m).

	Model 1 Age, gender + chronic conditions				Model 2 Additional: lifestyle				Model 3 Additional: body composition				Model 4 Additional: strength			
	B	95% CI		P-value	B	95% CI		P-value	B	95% CI		P-value	B	95% CI		P-value
Intercept	674	466	882	**< 0.001**	666	462	869	**< 0.001**	623	376	869	**< 0.001**	629	382	876	**< 0.001**
Age (years)	-5.3	-6.9	-3.7	**< 0.001**	-5.0	-6.5	-3.4	**< 0.001**	-5.7	-7.2	-4.1	**< 0.001**	-5.1	-6.6	-3.6	**< 0.001**
Male**	23.7	6.7	40.8	**0.007**	22.5	5.9	39.2	**0.008**	7.7	-16.8	32.2	0.535	9.5	-13.7	32.7	0.421
HbA1c (%)	-12.7	-26.8	1.3	0.075	-11.0	-24.8	2.7	0.115	-5.2	-18.5	8.2	0.446	-1.2	-13.9	11.5	0.851
CRP (mg/L)	-0.8	-2.6	1.0	0.394	-0.5	-2.3	1.3	0.571	-0.4	-2.1	1.4	0.689	-1.1	-2.8	0.6	0.198
MMSE (score)	9.3	5.0	13.6	**< 0.001**	7.4	3.0	11.9	**0.001**	5.8	1.4	10.3	**0.010**	1.8	-2.5	6.2	0.414
Number of drugs	-8.3	-14.1	-2.5	**0.005**	-7.3	-12.9	-1.6	**0.012**	-7.1	-12.6	-1.6	**0.012**	-8.1	-13.3	-2.9	**0.003**
Smoking (yes)					-17.3	-52.2	17.6	0.330	-14.6	-47.7	18.4	0.383	3.0	-30.0	35.9	0.859
Alcohol (yes)					7.1	-14.9	29.0	0.527	5.4	-15.6	26.3	0.615	0.0	-20.5	20.4	0.997
Physical activity (h/ week)					3.1	1.7	4.6	**< 0.001**	2.2	0.8	3.6	**0.002**	2.2	0.8	3.5	**0.001**
Fat mass (kg)									-0.9	-2.2	0.4	0.162	-0.2	-1.4	1.1	0.789
ASM (%)									4.88	0.44	9.32	**0.031**	2.68	-1.58	6.95	0.216
Quadr. strength/ BW (N/kg)													16.2	9.0	23.5	**< 0.001**

*using linear models; **as opposed to female

with physical function disappear after correction for body composition and strength. The results also indicate that fat mass *per se* is not associated with function, but ASM is. Results were similar for both 6MWD and TUG and the strongest variables in the final models were age (eta squared = 18 and 21%, respectively) and strength/body weight (eta squared = 10 and 8%, respectively).

DISCUSSION

The present study aimed to find determinants of physical function in community dwelling old people. Not unexpected, age was the variable strongest related to physical function, however, we found a number of other associated variables that were modifiable. Given the importance of physical function in old people [1-4], these variables represent potential targets for future interventions.

In our study LTPA, body composition and muscular strength were related to physical function. According to the multivariate models, a strong association between lower extremity strength per kg body weight and lower extremity function was observed. In order to investigate causality or the direction of this relation, increasing strength and/or reducing body weight could represent the target for future longitudinal, interventional studies. Others have reported similar results, i.e., that muscle quality (strength for a given amount of lean mass) rather than absolute lean mass is the most important predictor of function [8]. Interestingly, in the statistical analysis LTPA remained significantly associated with physical function although we corrected for body composition and strength. This might potentially be related to better

Table IV. Determinants* of TUG (sec).

	Model 1 Age, gender + chronic conditions				Model 2 Additional: lifestyle				Model 3 Additional: body composition				Model 4 Additional: strength			
	B	95% CI		P-value	B	95% CI		P-value	B	95% CI		P-value	B	95% CI		P-value
Intercept	3.08	-2.88	9.05	0.310	2.72	-3.19	8.63	0.365	4.66	-2.83	12.15	0.221	1.44	-5.51	8.38	0.683
Age (years)	0.15	0.10	0.20	**< 0.001**	0.15	0.10	0.19	**< 0.001**	0.16	0.11	0.21	**< 0.001**	0.16	0.11	0.20	**< 0.001**
male**	-0.41	-0.90	0.08	0.099	-0.36	-0.84	0.13	0.146	0.10	-0.64	0.83	0.796	0.07	-0.57	0.72	0.823
HbA1c (%)	0.29	-0.11	0.68	0.159	0.23	-0.17	0.62	0.263	0.10	-0.30	0.50	0.630	-0.02	-0.38	0.33	0.897
CRP (mg/L)	-0.02	-0.08	0.03	0.411	-0.03	-0.08	0.02	0.271	-0.04	-0.09	0.02	0.167	-0.02	-0.06	0.03	0.446
MMSE (score)	-0.28	-0.41	-0.16	**< 0.001**	-0.23	-0.36	-0.10	**0.001**	-0.20	-0.33	-0.06	**0.004**	-0.05	-0.17	0.07	0.417
Number of drugs	0.16	-0.01	0.32	0.063	0.14	-0.03	0.30	0.102	0.14	-0.02	0.30	0.095	0.17	0.03	0.32	**0.021**
Smoking (yes)					1.11	0.11	2.11	**0.030**	1.06	0.07	2.05	**0.036**	-0.02	-0.94	0.89	0.964
Alcohol (yes)					-0.24	-0.88	0.40	0.467	-0.15	-0.79	0.49	0.647	0.06	-0.51	0.64	0.828
Physical activity (h/week)					-0.06	-0.10	-0.02	**0.005**	-0.04	-0.09	0.00	**0.042**	-0.04	-0.08	-0.01	**0.024**
Fat mass (kg)									0.01	-0.03	0.05	0.611	0.00	-0.04	0.04	0.981
ASM (%)									-0.12	-0.26	1.09	0.071	-0.41	-0.16	0.08	0.495
Quadr. strength/ BW (N/ kg)													-0.41	-0.61	-0.20	**< 0.001**

*using linear models; **as opposed to female

balance of physically active people, another important components of physical function [26].

We found a significant negative association between the number of medications and physical function, although median medication count was low or around 2 in our participants. With each additional drug 6MWD decreased by around 7 m and TUG increased by around 0.15 sec according to the statistical model. Similar associations have been reported previously in humans [16]. These associations were independent from body composition or muscular strength, as effect size B did hardly change after correction for fat mass, ASM or quadriceps strengths. However, our study cannot answer whether the drugs were directly associated with lower physical health or if the number of drugs taken by a participant were a proxy of his/her overall health, because the number of chronic diseases were not recorded in the present study.

In a recently published study cognitive function has been reported to be associated with physical function [15]. In our study we assessed cognitive function using the simple screening tool MMSE. We found that MMSE score was related to both TUG and 6MWD, although the distribution of MMSE score was limited due to inclusion criteria in our study. In the multivariate analysis, it turned out that the relationship between MMSE and function was largely explained by muscular strength. In a separate analysis (data not shown) we found that the lowest MMSE quartile had significantly lower quadriceps strength corrected for body weight than the highest quartile. A similar difference between MMSE quartiles in ASM was not seen. Accordingly, results from a recent review on this topic suggest an influence of cognitive function on the muscular strength of old people, which can, according to the authors, affect aspects of their functional capacity and therefore agree with our results [27].

Poorer physical function has been reported in women compared with men [28], which was consequently explained by their higher fat mass, but also by other body composition differences. Although we also found sex specific

differences in body composition and in lower extremity muscle strength, these differences did not translate into poorer lower extremity function in women according to descriptive statistics. Taking into consideration quadriceps strength for each kg of body weight, the numbers were similar for men (5.7 N/kg) and women (5.5 N/kg), potentially explaining why we observed similar function. However, as men were significant older than women in our study, this age difference could affect the comparison between genders. In a simple age corrected comparison (data not shown), there was a tendency for better 6MWD in men compared to women (P = 0.08), however there were no differences observed for TUG. This can be explained by greater height (leg length) in men, which matters less in the 3 m TUG distance, but each step (stride length) starts to matter in a 6MWD in which a tall person will walk further than a short person given the same cadence.

Energy intake, protein intake and blood chemical variables were not associated with physical function in study participants. Although energy and protein intake play undoubtly an important role in the maintenance of lean body mass [29], their associations with physical function are difficult to confirm. Assessment of dietary intake is difficult, especially in old people and the quality of food records depends on the motivation and cognitive function of the old participant [30]. Further, inclusion of lean body mass in statistical analysis will most likely make any potential association between dietary intake and function disappear. Blood chemical variables were associated with function in bivariate analysis, but these associations disappeared in multivariate analysis. Several studies have proposed how deteriorated blood chemical variables can explain poor function [11,12], but our results indicate that they are not independently associated with physical function.

STRENGTH AND LIMITATIONS

It is a strength of this study, that information on many potential variables related to physical function was available, which exceeds previously published studies on this topic. This made it possible to gain a wider understanding on which variables were independently associated with physical function. However, this was a cross-sectional study and it lies in the nature of such study design that it can not differentiate between cause and consequence of an observed association. Longitudinal and intervention studies have to confirm present findings.

CONCLUSIONS

In community dwelling old people, physical function decreases with age. However, there are modifiable determinants of physical function, in particular strength for a given body weight, LTPA and number of medications, which might give the possibility to maintain or improve physical function in this age group. Our results also indicate that neither cognitive function, nor dietary intake nor blood chemical variables were independently associated with physical function.

Ethical consideration

This manuscript is based on a study which was classified as a low risk investigation because the intervention was supervised physical activity with minimal invasive blood sampling. These ethical considerations are based on the decission from the Icelandic National Bioethics Committee (15-139-S1).

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Conflict of interest

The Authors declare no conflict of interest.

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