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Original Article

New Outlook on the Clinical and Laboratory Determinants of Handgrip Strength in Older Adults

Paulina Fatyga [a *], Agnieszka Pac [b], Małgorzata Fedyk-Łukasik [c], Tomasz Grodzicki [c], Anna Skalska [c]

[a] *Department of Toxicology and Environmental Diseases, Jagiellonian University Medical College, Krakow, Poland,* [b] *Chair of Epidemiology and Preventive Medicine, Jagiellonian University Medical College, Krakow,* [c] *Department of Internal Medicine and Gerontology, Jagiellonian University Medical College, Krakow, Poland*

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SUMMARY

Background: Handgrip strength (HGS) is one of the main methods for assessing physical ability. It is a predictor of poor patient outcomes such as longer hospital stay, increased functional limitations, poor health-related quality of life, and increased mortality. Low muscle strength is also a primary indicator of sarcopenia. The aim of this study was to identify the determinants of low HGS in outpatient older adults.
Methods: This cross-sectional study included individuals aged ≥ 60 years followed in the Geriatric Outpatient Clinic from October 2010 to February 2014. Handgrip strength was recorded using a hydraulic hand dynamometer. Participants were divided into 2 groups: with low muscle strength (< 27 kg for men and < 16 kg for women) and with normal muscle strength. Mood was assessed using the 30-point Geriatric Depression Scale (GDS). The risk of malnutrition was evaluated using the Mini Nutritional Assessment. Body composition was measured by dual-energy X-ray absorptiometry. The following laboratory parameters were also assessed: high-sensitivity C-reactive protein, N-terminal pro-hormone of brain natriuretic peptide (NT-proBNP), vitamin D, interleukins IL-6, IL-8, and IL-18, pentraxin 3, and osteoprotegerin.
Results: The study included 102 patients (61.8% men) at a mean age of 72.3 ± 8.9 years. According to the logistic regression model adjusted for age and sex, HGS was negatively associated with the GDS score (odds ratio [OR], 1.103; 95% CI, 1.004–1.212) and NT-proBNP levels (OR, 1.046; 95% CI, 1.007–1.085, per 100 units). Moreover, HGS was negatively (but not significantly) associated with the number of medications taken (OR, 1.342; 95% CI 0.997–1.806).
Conclusion: The study showed that the GDS score and NT-proBNP levels have a negative effect on HGS and may also affect the prognosis of sarcopenia.

1. Introduction

Low muscle strength, also known as dynapenia, is a significant problem among the elderly. Reduced muscle strength is associated with poor current and future health outcomes including an increased risk of falls,[1] osteoporosis and fracture,[2] coronary heart disease, and stroke,[3] longer hospital stays,[4] reduced health-related quality of life,[5] and increased all-cause mortality.[6] Handgrip strength (HGS) is a key component of the diagnosis of sarcopenia, which is a common progressive and generalized loss of skeletal muscle mass and strength.[7]

Low muscle strength was used as the primary parameter of sarcopenia in a 2018 definition proposed by the European Working Group on Sarcopenia in Older People (EWGSOP2). Muscle strength is currently the most reliable measure of muscle function. Specifically, low muscle strength may indicate sarcopenia. The diagnosis of sarcopenia is confirmed if there is low muscle quantity or quality, and the condition is considered severe if low muscle strength, low muscle quantity or quality, and low physical performance are simultaneously present.[4]

The use of HGS as a biomarker of the current health status is most directly supported by studies showing a cross-sectional association between handgrip strength and the strength of other muscle actions in both healthy individuals and adults with a pathology.[8] Based on these studies and the practicality of hand-grip dynamometry, the measurement of handgrip strength has been widely adopted as a singular indicator of overall strength.[9] Importantly, the measurement of handgrip strength is simple and inexpensive. For this reason, handgrip strength testing is advised for routine use in hospital practice, in specialty clinical settings, and in community geriatric healthcare. However, the value of this tool was considered insufficient by some investigators.[10]

In order to develop the hypothesis and rationale for this study, available literature data on HGS were analyzed. The search revealed conflicting results regarding the prognostic markers of low HGS. The rationale for the study was based on the evidence that factors such as low body weight,[11] diabetes,[12] chronic obstructive pulmonary disease,[13] physical inactivity,[14] and vitamin D deficiency[15] are associated with poor muscular strength in middle-aged and older adults.

* Corresponding author. Department of Toxicology and Environmental Diseases, Jagiellonian University Medical College, Krakow, Poland.
E-mail address: paulina.fatyga@uj.edu.pl (Paulina F.)

Another study showed that poor muscle strength was associated with age above 75 years and malnutrition, but not with chronic obstructive pulmonary disease or diabetes.[16] Cognitive function and functional status were also reported to affect HGS.[17] To the best of our knowledge, only one study investigated the association between N-terminal pro-hormone of brain natriuretic peptide (NT-proBNP) and HGS.[18] Our previous research showed that, apart from an inverse relationship between NT-proBNP levels and the Mini Nutritional Assessment (MNA) score, increasing NT-proBNP levels[19] were associated with the degree of malnutrition risk, which might suggest a negative link between NT-proBNP and muscle strength. Moreover, high-sensitivity C-reactive protein (hsCRP), interleukins IL-6, IL-8, IL-18, pentraxin 3, and osteoprotegerin were shown to be associated with inflammation, which is a significant factor in the pathophysiology of sarcopenia and low muscle strength.[20–22]

We hypothesized that age, malnutrition, cognitive function, diabetes, chronic obstructive pulmonary disease, physical inactivity, vitamin D deficiency, and chronic inflammation may affect HGS. In the current study, we aimed to identify new clinical and laboratory determinants of HGS in elderly outpatients.

2. Patients and methods

This cross-sectional study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Bioethical Committee of Jagiellonian University (Krakow, Poland), and all individuals signed written informed consent to participate in the study. Patients aged 60 years or older followed in the Geriatric Outpatient Clinic of University Hospital from October 2010 to February 2014 were included in the survey, as described in a previous study.[19] We enrolled consecutive patients who signed an informed consent form and who did not meet the exclusion criteria. These participants constituted a representative group of geriatric outpatients.

The most significant exclusion criteria were as follows: an active inflammatory state (e.g. pneumonia, arthritis, or urinary tract infection), immobility, and a Mini Mental State Examination (MMSE) score below 10. In all patients, data on demographic characteristics, smoking status, past and current medical history, and medication use were obtained from medical records. If patients had dementia or cognitive impairment (but an MMSE score minimum 10), the interview was completed by a proxy.

Handgrip strength was measured with a hydraulic hand dynamometer (SH5001; Saehan Corporation, Masan, Korea). Each participant was asked to sit on a chair comfortably, with the elbow flexed at 90 degrees and the forearm in semi-pronation lying on an arm rest. Then, participants were instructed to squeeze the dynamometer with their hand with maximum strength. There were 3 measurements of HGS in the dominant hand, and the maximum value was included in the analysis. We divided participants into 2 groups: with low and with normal muscle strength. Based on EWGSOP2, the cut-off points for low strength by HGS were below 27 kg for men and below 16 kg for women.

Body composition was examined using a dual-energy X-ray absorptiometry (Lunar Prodigy, General Electric Medical Systems). Weight (kg) and height (m) were measured, and the body mass index (BMI; kg/m^2) was calculated. Mental status was evaluated using the MMSE score,[23] while mood was assessed by means of the 30-point Geriatric Depression Scale (GDS), in which a higher score indicates a more depressed state.[24]

The following medical comorbidities were considered: coronary heart disease/myocardial infarction, chronic heart failure, hypertension, valve defect, diabetes, stroke, osteoarthritis, chronic obstructive pulmonary disease, past and current smoking, and falls.

Functional status was assessed by the Katz Index of Independence in Activities of Daily Living (ADL).[25] To assess more complex activities necessary for functioning in community settings, the Lawton's Instrumental Activities of Daily Living (IADL) Scale was also used.[26] The risk of malnutrition was evaluated using the MNA score, in which higher scores indicate better nutritional status.[27]

Serum NT-proBNP and vitamin D levels were measured by an electrochemiluminescence immunoassay with a Roche immunoassay analyzer. Serum IL-6 and IL-8 levels were assessed using Human IL-6 Immunoassay Quantikine® HS ELISA and Human CXCL8/IL-8 Immunoassay Quantikine® ELISA kits (R&D Systems, Inc., Minneapolis, MN, USA). Serum IL-18 levels were measured using Human IL-18 ELISA Kit (Medical & Biological Laboratories CO., Ltd, Japan). Osteoprotegerin concentrations were determined using a sandwich enzyme immunoassay, RD194003200 Human Osteoprotegerin ELISA kit (BioVendor – Laboratorni medicina a.s., Brno, Czech Republic). Finally, pentraxin 3 levels were assessed by Human Quantikine Pentraxin 3/TSG-14 Immunoassay by R&D Systems (ELISA Reader ELX 808, BIO-TEK® Instruments, Inc., Winooski, VT, USA).

2.1. Statistical analysis

The statistical analysis was carried out in SPSS 27 (PS IMAGO PRO 7.0, Predictive Solutions Sp. Zo.o., Krakow, Poland), licensed to Jagiellonian University. In all analyses, 2-sided tests were used. A p value of less than 0.05 was considered significant. The distribution of variables was verified using the Shapiro-Wilk test. Descriptive statistics included means and standard deviations (SD) for normally distributed variables, and median with interquartile range (IQR; upper–lower quartile) for variables that did not follow the normal distribution. Moreover, qualitative data were presented with relative frequencies. A multivariable binary logistic regression model was used to assess the predictors of low HGS. Because of the relatively small number of cases, different models were built, and the final optimal model was selected. The results were expressed as an odds ratio (OR) with 95% confidence interval (95% CI).

3. Results

3.1. Baseline characteristics

Of all patients treated in the Geriatric Outpatient Clinic, 102 individuals with all data available were included in the study. The mean age of participants was 72.3 ± 8.9 years (61.8% men). Based on the ADL and IADL scores, we determined that our study group was well organized and fit in daily living (median ADL, 6 [IQR, 6–6]; median IADL, 25 [IQR, 22–27]). Malnutrition or the risk of malnutrition (MNA score < 24/30) was diagnosed in 29.3% of the study population. The median number of comorbidities was 5 (IQR, 4–7). The most common comorbidity was hypertension (87.3%), followed by coronary heart disease (78.4%), chronic heart failure (69.6%), osteoarthritis (53.9%), and diabetes (31.4%). Chronic obstructive pulmonary disease was rare (4.9%) and present only in patients with low HGS. A comparison of patients with low and normal HGS is shown in Table 1.

The groups did not differ in terms of BMI (p = 0.225), MNA score (p = 0.129), number of comorbidities (p = 0.832), prevalence of hypertension (p = 0.762), chronic heart failure (p = 0.490), diabetes (p = 0.396), and osteoarthrosis (p = 0.840), IADL score (p = 0.083), ADL score (p = 0.134), and the levels of albumin (p = 0.318), creatinine (p = 0.090), vitamin D < 30 ng/ml (p = 0.052), and hsCRP (p = 0.991).

Table 1
Characteristics of the study groups with normal and low handgrip strength.

Variable	Handgrip ≥ 27 (M) ≥ 16 (F) kg (n = 38)	Handgrip < 27 (M) < 16 (F) kg (n = 64)	p value
Handgrip max (kg), median [IQR]			
Men	33.3 [30–40]	20 [16.7–22]	
Women	20 [18–22]	10.9 [6.7–12.6]	
Age (years), median [IQR]	68.5 [63–72]	74 [67.5–82.5]	< 0.001
Male sex, n (%)	31 (81.6)	32 (50)	0.002
No. of medications, median [IQR]	7 [6–8]	7 [6–9]	0.137
MMSE (points), median [IQR]	28 [26–30]	27 [25–29]	0.012
GDS (points), median [IQR]	7 [4–10]	10 [7–16]	0.001
GDS ≥ 10 (points), n (%)	11 (29.7)	32 (51.6)	0.034
CHD, n (%)	34 (89.5)	46 (71.9)	0.037
COPD, n (%)	0 (0)	5 (7.8)	0.154*
Active smoking, n (%)	4 (10.8)	8 (12.7)	1*
Past smoking, n (%)	23 (62.2)	31 (49.2)	0.209
ALM/BMI, median [IQR]	0.75 [0.63–0.87]	0.72 [0.59–0.82]	0.470
LBM (kg), median [IQR]	51.1 [42.2–54.9]	47.8 [40.8–54.0]	0.173
LBM/BMI, median [IQR]	1.79 [1.50–1.96]	1.72 [1.44–1.93]	0.571
Trunk fat (g), median [IQR]	16329 [14345–19584]	15809 [10813–18730]	0.195
Hemoglobin (g/dl), median [IQR]	14.2 [13.3–14.9]	13.6 [12.8–14.7]	0.037
Vitamin D (ng/ml), median [IQR]	20.3 [10.1–28.4]	11.4 [5.8–16.1]	0.003
Pentraxin 3 (ng/ml), median [IQR]	0.46 [0.38–0.63]	0.69 [0.44–0.96]	0.028
Osteoprotegerin (pmol/l), median [IQR]	7.1 [6.1–8.6]	8.8 [6.4–11.4]	0.022
IL-18 (pg/ml) median [IQR]	410.86 [294.86–471.19]	417.60 [317–558.64]	0.377
IL-6 (pg/ml) median [IQR]	3.67 [2.32–4.69]	3.88 [2.49–6.57]	0.303
IL-8 (pg/ml) median [IQR]	13.77 [9.22–27.81]	12.78 [8.19–19.68]	0.247
NT-proBNP (pg/ml) median [IQR]	497.1 [140.9–1658]	554.9 [137.1–3191]	0.458

* p value calculated using the Fisher's exact test.
Abbreviations: ALM, appendicular lean mass; BMI, body mass index; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; GDS, Geriatric Depression Scale; IL-6, interleukin 6; IL-8, interleukin 8; IL-18, interleukin 18; LBM, lean body mass; MMSE, Mini Mental State Examination; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

3.2. Multiple regression analyses

First, the association between potential predictors and low HGS (adjusted for age and sex) was assessed. We found that the risk of low HGS was associated with a higher number of medications taken, higher GDS score, as well as higher pentraxin 3, osteoprotegerin, NT-proBNP, and IL-18 levels. Higher vitamin D levels were associated with a lower risk of reduced HGS. Data are presented in Table 2.

The other parameters did not show any significant effect on HGS: BMI (OR, 0.953; 95% CI, 0.853–1.065); MNA score (OR, 0.881; 95% CI, 0.731–1.062); MMSE score (OR, 0.862; 95% CI, 0.725–1.024); hemoglobin (OR, 0.870; 95% CI, 0.644–1.176); albumin (OR, 0.968; 95% CI, 0.829–1.131); creatinine (OR, 1.004; 95% CI, 0.987–1.022); vitamin D < 30 ng/ml (OR, 2.613; 95% CI, 0.673–10.148); hsCRP (OR, 0.986; 95% CI, 0.911–1.066); IL-6 (OR, 1.078; 95% CI, 0.952–1.221), and IL-8 (OR, 1.005; 95% CI, 0.961–1.051). Moreover, there was no significant relationship between HGS and hypertension (OR, 1.585; 95% CI, 0.350–7.166), coronary heart disease (OR, 0.445; 95% CI, 0.118–1.681), chronic heart failure (OR, 3.037; 95% CI, 0.776–11.885), diabetes (OR, 1.924; 95% CI, 0.717–5.166), osteoarthrosis (OR, 0.579; 95% CI, 0.222–1.510), past smoking (OR, 0.590; 95% CI, 0.258–1.349), active smoking (OR, 0.833; 95% CI, 0.233–2.984), the number of diseases (OR, 1.082; 95% CI, 0.880–1.331), as well as IADL score (OR, 0.885; 95% CI, 0.765–1.025) and ADL score (OR, 0.496; 95% CI, 0.106–2.314).

Excessive alcohol consumption as another potential confounder was excluded in all patients.

From among the significant predictors, a set of independent variables were selected to create the most optimal logistic regression model with low HGS as a dependent variable (Table 3). Vitamin D, pentraxin 3, osteoprotegerin, and IL-18 were no longer significant in the multivariable logistic regression model.

Table 2
Logistic regression models for the relationship between potential predictors and low handgrip strength (each adjusted for age and sex).

Variable	OR (95% CI)
Number of medications	1.373 (1.098–1.717)
GDS (points)	1.120 (1.024–1.225)
GDS ≥ 10 points	2.785 (1.043–7.435)
ALM (kg)	1.015 (0.891–1.156)
ALM/BMI	0.707 (0.066–7.558)
LBM (kg)	1.021 (0.959–1.088)
LBM/BMI	1.051 (0.362–3.051)
Vitamin D (ng/ml)	0.955 (0.913–0.999)
Pentraxin 3 (ng/ml)	6.600 (1.211–35.977)
Osteoprotegerin (pmol/l)	1.289 (1.016–1.634)
NT-proBNP (pg/ml; per 100)	1.046 (1.014–1.080)
IL-18 (pg/ml)	1.005 (1.001–1.008)

Abbreviations: ALM, appendicular lean mass; BMI, body mass index; GDS, Geriatric Depression Scale; IL-18, interleukin-18; LBM, lean body mass; NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

4. Discussion

In our study, we identified the determinants of low HGS in the Polish outpatient population of elderly people. The main findings of our research were that age, GDS score, and NT-proBNP levels negatively influenced HGS. There was also a trend towards a negative effect of a greater number of medications taken on HGS, but the association was not significant.

Table 3
Multivariable regression model with low handgrip strength as a dependent variable.

Variables	OR (95% CI)
Age (years)	1.097 (1.022–1.178)
Male sex	0.070 (0.014–0.356)
No. of medications	1.342 (0.997–1.806)
GDS score (points)	1.103 (1.004–1.212)
NT-proBNP (per 100 pg/ml)	1.046 (1.007–1.085)

Abbreviations: GDS, Geriatric Depression Scale; NT-proBNP, N-terminal prohormone of brain natriuretic peptide (expressed per 100, pg/ml).

4.1. Handgrip strength and age

According to the pathophysiology of aging and the results of other studies, muscle strength decreases with age. In line with our research, Riviati et al. showed that age above 75 years increased the risk of low HGS.[16] Moreover, Lu et al. revealed that HGS declined with age in both men and women.[28]

4.2. Handgrip strength and depressive symptoms

Our study showed that low muscle strength is related to depression. This is consistent with numerous previous studies,[29–32] although some conflicting findings were also reported.[33]

First, in a cross-sectional study by Wang et al. on older Chinese community-dwelling individuals, sarcopenia was found to be significantly associated with depressive symptoms (OR, 2.23; 95% CI, 1.06–4.92).[29] Additionally, in a prospective cohort study, Fukumori et al. reported that lower HGS (per 1-SD decrease) was associated with the longitudinal development of depressive symptoms after 1 year (OR, 1.13; 95% CI 1.01–1.27; p = 0.036).[30] Their results suggest that lower HGS, adjusted for age and sex, was both cross-sectionally and longitudinally associated with depressive symptoms. Also, a cross-sectional study by Wu et al. on 1046 elderly people in China revealed that both muscle mass and muscle strength were negatively associated with depressive symptoms.[31] Moreover, Brooks et al. showed that depression was associated with reduced HGS in unadjusted and fully adjusted models (B = -0.26 $\pm$ 0.79 and B = -0.19 $\pm$ 0.08, respectively; p < 0.001).[32] However, in contrast to our study and some previous research, Byeon et al. showed that sarcopenia was not associated with depressive symptoms or the prevalence of depression in any age group (20–39, 40–59, and $\geq$ 60 years).[33]

4.3. Handgrip strength and NT-proBNP

Although in our patients none of the chronic diseases had a significant effect on muscle strength and there was no significant difference in the incidence of heart failure in patients with normal and low muscle strength, higher NT-proBNP levels turned out to be a significant factor negatively affecting HGS. To the best of our knowledge, the relationship between NT-proBNP levels and HGS was previously reported only by Markus et al. in the SHIP study (The Sedentary's Heart The Study of Health in Pomerania), which revealed that lower HGS was associated with higher NT-proBNP levels.[18] This is consistent with our results.

Interestingly, Duarte et al. stated that HGS is independently associated with the severity of chronic heart failure (assessed by the New York Heart Association classification) and ejection fraction, even after adjustment for other confounding variables.[34] NT-proBNP levels correspond with the severity of chronic heart failure, although higher levels of NT-proBNP can also occur in other diseases. Importantly, muscle wasting connected with reduced muscle strength is a common comorbidity among patients with chronic heart failure.[35,36]

4.4. Handgrip strength and polypharmacy

In our study low HGS was not related to the number of medications taken. In line with our findings, Volaklis et al. reported that there was no significant association between muscle strength and polypharmacy (OR, 1.04; 95% CI, 0.66–1.63; p = 0.873) after multivariable adjustment.[37]

4.5. Handgrip strength and inflammatory markers

In addition, considering that moderate chronic inflammation is one of the pathogenetic factors of sarcopenia, we assessed the relationship between muscle strength and selected proinflammatory cytokines. While higher concentrations of IL-18, pentraxin 3, and osteoprotegerin were significant factors of reduced muscle strength in the age- and sex-adjusted analysis, they were no longer significant in the multivariable analysis. Literature data on the links between IL-18, osteoprotegerin, pentraxin 3 and HGS are scarce. Can et al. reported that there was no significant difference in serum pentraxin-3 levels between patients with and without sarcopenia.[38] Moreover, osteoprotegerin was shown to improve muscle strength in the mouse models of Duchenne's muscular dystrophy and denervation-induced atrophy.[39] To our knowledge, no studies have assessed the association between IL-18 and HGS. On the other hand, a correlation between vitamin D deficiency and low muscle strength was previously described,[15,40] although this finding was not supported by the multivariable analysis in our study.

5. Conclusion

This study presents data for the Polish population of elderly outpatients. In addition to old age, higher NT-proBNP levels and a higher GDS score may serve as determinants of reduced muscle strength and an increased risk of sarcopenia. This indicates that it is important to include HGS testing in routine screening of older adults, particularly patients with symptoms of depression and chronic heart failure. Identifying the predictors of HGS in older people might be valuable for developing alternative preventive and therapeutic strategies.

6. Limitations

Our study has several limitations. First, the number of patients included in the analysis was relatively small, which limited the statistical power and precluded a separate analysis of men and women. Second, the study had a cross-sectional design, so we were unable to assess the causative relationship between HGS and other other analyzed parameters. Finally, the study population was not homogeneous and had comorbidities, which – although typical of the Polish geriatric population – may have influenced the results.

Declaration of any potential financial and non-financial conflicts of interest

None.

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