Relative Handgrip Strength is Inversely Associated with the Presence of Type 2 Diabetes in Overweight Elderly Women with Varying Nutritional Status

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Abstract

Background and Aims

We aimed to investigate cross-sectional relationships of relative handgrip strength (RHGS) with presence of diabetes and hypertension in a community setting.

Methods and Results

Between 2016 and 2018, we enrolled 601 consecutive women with an average age of 70.7 ± 6.9 years (mean $\pm$ SD). Nutritional status was evaluated by the Mini Nutritional Assessment (MNA) score. Muscular strength and level of fitness were assessed by handgrip strength (HGS) and other standardized physical functional tests. The majority of participants were overweight or obese (80% with BMI > 25). Prevalence of diabetes and hypertension was 13 and 60%, respectively. Participants in the lowest quartile of HGS adjusted for BMI (RHGS) had significantly higher prevalence of diabetes and hypertension compared with those in the lower quartile (20.7 vs. 5.3% and 49.3 vs. 39.3%, respectively, $p < 0.01$ for both), whereas differences in nutritional status were not observed. Likelihood of having diabetes was significantly reduced in women with higher RHGS values (OR 0.77; 0.59–0.86 CI95%; p=0.002), independently of age, abdominal adiposity and presence of hypertension. RHGS was positively correlated with most of the physical functional tests performed.

Conclusion

RHGS is an easy-to-obtain and inexpensive measure of muscular strength, independently associated with presence of diabetes in overweight elderly women. Prospective studies are required to assess its predictive value in individuals at risk of new onset or progression of diabetes.

Keywords: nutrition status; muscle strength; diabetes; handgrip; insulin resistance; functional tests

Main text

Introduction

Diabetes mellitus (DM) often induces functional deterioration leading to loss of whole-body homeostasis and deterioration in physical function (1).

Sarcopenia is a physiological process consisting of both loss of muscle mass and muscle function that occurs in the elderly. Sarcopenia is a major driver of frailty and has emerged as one of the strongest predictors of disability (2, 3). Frailty is a dynamic process which progresses from a robust condition to a pre-frail stage, then frailty and eventually disability. DM is characterized by a progressive decline in muscle mass, strength and function (4) resulting from the detrimental effects of diabetic peripheral neuropathy and insulin resistance on skeletal muscles (5). Accordingly, muscle weakness has been consistently linked with DM, even amongst well-nourished subjects (6).

Handgrip strength (HGS) is a low-cost assessment tool and an easy indicator of the overall muscular strength of the body. There is likely a direct relationship between muscle strength and functional decline in DM subjects (7, 8), with further potential implications on the underlying disease driven by protein-calorie malnutrition (9).

Many recent studies have established that low HGS is connected with different health outcomes including metabolic and cardiovascular risk factors. However, rather than absolute HGS, relative HGS (RHGS) adjusted for body mass index (BMI) has been proposed as an easy instrument for assessing metabolic health and cardiovascular risk in public health and clinical practice (10–13).

According to this background, aim of this study was to examine potential associations between presence of DM and muscle health by using RHGS and some other functional balance ability tests, in elderly women enrolled in general living.

Methods

Study design

This is a community-based cross-sectional study carried out from January 2016 to December 2018. Participants were adult Caucasian women, enrolled from those routinely attending one of the twenty-seven Senior Centres in the area of Rome and Viterbo (Italy), who gave their own written informed consent to participate. The study protocol was approved by the local Ethical Committee, and the investigation was conducted in accordance with the Declaration of Helsinki. Exclusion criteria were as follows: a history of pacemaker implantation, heart failure, valvular or congenital disease, osteo-articular disorders and use of glucocorticoids, oestrogens and anti-convulsant medications. Given these criteria, 601 Caucasian women over 60 years of age were finally included in the analysis.

Data collection

Participants were asked to report their age and whether they had ever been diagnosed with or treated for DM or hypertension. Standardized questionnaires were used to collect medical history, including former or current use of medications. Nutritional status of participants was evaluated using the standardized Mini Nutritional Assessment (MNA) questionnaire (14). The MNA scale is structured with anthropometric measurements and questions about dietary habits, global health and social assessment, and subjective assessment of health and nutrition. The sum of the MNA score distinguishes elderly patients in: (1) adequate nutritional status, MNA $\geq$ 24; (2) at risk of malnutrition, MNA between 17 and 23.5; and (3) protein-calorie malnutrition, MNA < 17.

Anthropometric measurements were collected from subjects wearing light clothing and barefoot. Weight was measured using a high-precision digital scale. Height was measured using a high-precision digital stadiometer. BMI was calculated as weight (kg) divided by height (m^2). A standard cloth tape measure was used to record arm, waist, hip and calf circumferences. Waist circumference (WC) was evaluated at the midpoint between the lateral iliac crest and lowest rib. Arm circumference (AC) was measured at the midpoint between theacromion and theolecranon with the person seated with the arm hanging loosely at his side with the elbow bent at a 90-degree angle. Hip circumference (HC) measure was taken at the widest portion of the buttocks. Calf circumference was measured at

the calf's greatest girth with the subject standing upright with feet apart to shoulder width and body weight evenly distributed between both legs. All of these parameters were assessed twice, and the resulting average values were used for subsequent analysis.

Functional tests

The 30-Second Chair Stand Test (CST) was implemented for the evaluation of lower limb strength (15). The subject, sitting in the middle of a standard chair (high 43 cm), with arms crossed at his chest and hands on his shoulders, was invited to get up from a chair up to the complete extension of legs and to repeat the movement. The total number of repetitions performed in a 30-second duration was recorded. All trials were performed using the same chair and with similar ambient conditions as previously described (16). The Reverse Crunch Test (RCT) was used for the assessment of abdominal muscle strength (17). The subjects from the decubitus supine position with feet on the ground moved their knees to their chest and back to the starting position. The total number of repetitions performed in a 30-second duration was recorded. Subjects performed the One-legged Stance Test (OLST) with open eyes and their hands gripped on their iliac crests, while staying, without assistance, on one foot with the other leg flexed forward. The number of seconds that the position was properly kept was recorded (18). The Fingertip-to-floor (FTF) test was used to assess the degree of flexibility in elderly subjects. The subjects were asked to flex their trunks forward while extending their arms forward with joined hands. The distance between the middle finger of the subject and the floor was measured with a standard measuring tape (19).

Hand-grip strength

The European Working Group on Sarcopenia in Older People (EWGSOP) consent document (20) has proposed the HGS measurement as an indicator of overall muscular strength and risk of frailty. HGS was measured in each hand three times with a digital grip strength dynamometer (Takei TKK 5710, Takei Scientific Instruments, Tokyo, Japan). Trained staff instructed the participants to stay with their feet hip width apart and toes pointing forward while holding the dynamometer with the distal interphalangeal finger joints of the dominant hand at 90° to the handle and to squeeze the handle as

hard as they could until they could not squeeze any harder. Subjects were asked to take a breath in and then blow out while squeezing. A resting interval of 30 seconds was allowed between each measurement. A measure of three times was reported as an average. RHGS was estimated as the average value for maximum grip strength of the dominant hand divided by BMI, as previously reported (10-13).

Statistical analysis

Statistical analysis was performed with the SPSS 25.0 software (SPSS, Chicago). The means ± SD with 95%CI or percent proportions were used as descriptive statistics. Linear trends in continuous variables across quartile categories of RHGS were assessed with a generalized linear model including age as a covariate. Differences in proportions of discrete traits were assessed using the chi-square test. The relationship between RHGS and selected quantitative measures of muscular strength were evaluated using bivariate correlation analysis, and resulting Spearman's rank coefficients (rho) were provided to assess the strength of the associations. Relationship between quartile categories of RHGS (quartile IV vs quartile I) and presence of DM (yes/no) was evaluated by logistic multivariate regression analysis adjusted for potential confounding variables by adding them to the regression model. Two models were constructed accordingly. In model 1, we entered age as a potential confounder determined a priori. In model 2, presence of HT, WC and hip circumference were additionally included, since these anthropometrics appeared to significantly change across categories of RHGS. For all analyses, a *p*-value < 0.05 based on a two-sided test was considered statistically significant.

Results

Table 1 shows the main clinical characteristics of the study population. Mean age was 70.7±6.9 years. Out of the total participants, 339 (56.3%) belonged to the age group of over 70 years. The majority of participants were overweight or obese, with nearly 80% of the subjects recorded with a BMI over 25 and predominant abdominal obesity according to WC measurements (91.9 ± 13.2 cm). Presence of DM and hypertension were reported by 13 and 60% of participants, respectively.

According to MNA score, 498 (82.8%) subjects were well nourished (MNA >24), whereas 103 subjects (17.2%) were reported to be at risk of malnutrition (MNA 17-23.5). No subjects were identified as being malnourished (MNA <17).

Measures of muscular strength included the mean absolute HGS at 23±4.8 kg and the average RHGS at 0.81±0.21 kg/BMI. We observed significant associations of RHGS with all selected physical functional tests. As shown in the regression plots (Fig 1a–d), Spearman's rank correlation coefficients revealed a trend toward a significant positive relationship between RHGS and CST (Rho=0.208, p<0.001), RCT (Rho=0.179, p<0.001) and OLST (Rho=0.122, p=0.01), whereas an inverse association was observed with FTF (Rho=-0.215, p<0.001).

When RGHS was further analysed as a categorical variable (Table 2), individuals in the lowest quartile, compared with those in the highest category, were significantly older (p<0.001) and basically more overweight according to most selected anthropometric measures (namely arm, waist and hip circumference, p<0.002 for all). Of note, no inter-quartile differences were observed in MNA mean values as well as in the proportion of patients with adequate nutritional status or at risk for malnutrition. Prevalence of DM was significantly higher in subjects with lower RHGS values (20.7%), with a significant decreasing trend across RHGS categories (p<0.001) (Table 2). Similar figure was observed for the prevalence of hypertension.

We finally tested the strength of association between categories of RHGS and presence of DM. As shown in Table 3, higher RGHS values were associated with a 36% reduced probability of being affected by DM (OR 0.64; CI95% 0.49–0.83), compared to subjects with lower RGHS values. The final adjusted model, including age, WC, HC and presence of hypertension, further confirmed the

relevance of the independent association between the presence of DM and RHGS (OR 0.77; IC95% 0.59–0.86; p = 0.002).

Discussion

In recent years, new therapies for DM have facilitated the ability to achieve measures of good disease control in most cases (21). The same cannot be said for the diagnosis of DM, and especially for type 2 diabetes which is often asymptomatic in the early stage. Accordingly, 3- and 6-years delay in the diagnosis and treatment of type 2 diabetes has been estimated in Europe, mostly because of physicians clinical inertia or patients difficulties to access to health care system screening programs (22). It is therefore necessary that diagnostic tools are developed as simple and easily reproducible as possible, especially in primary care setting.

In this study we showed in first that RHGS can be an easy-to-perform measure of muscle health, significantly related with other physical functional tests commonly used by specialists to evaluate muscle strength, flexibility and balance in elderly people. Handgrip strength is known to be associated with overall strength, which itself reflects the balance of an individual. Low strength has already been associated with a history of falls in both sexes (12). This study's findings thus highlight the opportunity of using RHGS as a health biomarker, realizing that reduced levels of muscle strength may lead to disability and functional limitations, particularly among older individuals (23, 24).

Noteworthy, assessing RHGS in routine practice could be useful and may additionally help identifying elderly subjects with or at risk of DM. Accordingly, women in the top quartile (i.e., those with a demonstrated greater strength in the HG test) had a 36% lower probability of having DM than those in lowest quartile (independently of age, abdominal fat and presence of hypertension). Therefore, through the use of simple additive tools, it could be possible to better identify subjects with a higher risk profile for DM, with individuals reporting lower RHGS values identified as those requiring more intensive action to prevent the disease. These data are in line with those provided by previous studies, showing that HGS is lower in patients with type 2 diabetes than in controls, and that reduced muscle strength is a risk factor for incident type 2 diabetes, with 1 SD higher muscular strength associated with a 13% lower risk of developing type 2 diabetes in near future (25).

The pathophysiological process for the observed link of RHGS with DM may be due to impaired insulin sensitivity and inflammation, since these two factors are both associated with low muscular fitness (26). Fat infiltration in the muscle may also play a role, causing impaired muscular function. (26). Alternatively, low RHGS might be associated with low cardiorespiratory fitness, which in turn has been demonstrated to increase the risk of developing type 2 diabetes (27).

Interestingly, no significant relationships were seen between RHGS values and MNA scores in our population study. This is somewhat surprising, since reduced muscle health is likely to be more frequently detected in subjects with concomitant evidence of malnutrition. It was not the case of women enrolled in this study, as those in the lowest quartile of RHGS did not report MNA scores consistent with higher risk of malnutrition, compared with the top quartile. Such a discrepancy could be attributable to inherent limitations of self-administered questionnaires, as MNA is, whose results are necessarily affected by certain risk of misclassification. Alternatively, this lack of association might be attributable to the fact that the majority of individuals reported to be well nourished, without any of them in the MNA-derived category of malnutrition, even among those with lowest values of RHGS. However, we believe these data cannot be firmly conclusive and more precise criteria (e.g. biochemical criteria) of malnutrition are needed to better assess potential relationship between RHGS and nutritional status.

Interestingly, RHGS might be an useful and inexpensive tool to also indirectly assess cardiovascular health in elderly obese women. In this sense, it has been previously demonstrated that older women with lower RHGS present an impaired heart rate recovery following a treadmill exercise test (11). In accordance, in our study, women with lower RHGS had concomitantly higher prevalence of hypertension, with significant decreasing trend across quartiles of RHGS, irrespective of age. These results are also in line with previous findings from the database of the National Health and Nutrition Examination Survey, revealing an inverse relationship between grip strength and hypertension in adults with healthy BMI and no history of cardiovascular disease (28).

We have to recognize some limitations of our study. First, we included only elderly women, who decided to participate on a voluntary basis. Therefore, these results cannot be generalized to both genders. Second, due to the cross-sectional design of the study, we are unable to draw conclusions

about the causality of the associations observed between reduced RHGS and DM. Appropriate longitudinal studies will be needed to confirm our results. Finally, both DM and hypertension were only self-reported by patients themselves or assessed by researchers on the basis of medications taken, therefore with not negligible risk for underestimation. However, prevalence rates of both conditions in our study were in line with those reported for elderly population in Italy.

In conclusion, our results show that RHGS can provide a valid estimate of muscular strength and physical efficiency in overweight elderly women, with significant relationship with presence of diabetes and hypertension. Future longitudinal researches could explore the predictive value of RHGS in the risk assessment of diabetes in elderly populations.

Acknowledgments

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Tables

Table 1. Main clinical characteristics of the study group ($n = 601$)

Age (yrs.)	70.7 ± 6.9
Age *n* (%)	
< 60 yrs.	33 (5.5)
60–69.9 yrs.	229 (38.1)
70–79.9 yrs.	282 (46.9)
> 80 yrs.	57 (9.4)
BMI (kg/m^2)	29.9 ± 4.7
BMI *n* (%)	
< 25	119 (19.8)
25.1–29.9	254 (42.3)
>30	228 (37.9)
Arm circumference (cm)	30.8 ± 11.3
Waist circumference (cm)	91.9 ± 13.2
Hip circumference (cm)	107.3 ± 11.2
W/H ratio	0.87 ± 0.35
Calf circumference (cm)	35.8 ± 4.9

Diabetes *n* (%)	78 (13)
Hypertension *n* (%)	363 (60.4)
MNA	25.9 ± 1.9
MNA *n* (%)	
Adequate (>24)	498 (82.9)
At risk (17–23.5)	103 (17.1)
Malnutrition (< 17)	0 (0)
HGS (kg)	23 ± 4.8
RHGS (kg/BMI)	0.81 ± 0.21

Abbreviations: BMI, body mass index; MNA, Mini Nutritional Assessment; HGS, Handgrip strength;

RHGS, relative handgrip strength (HGS/BMI). Continuous variables are expressed as means ± SD.

Discrete traits are expressed as *n* (%).

Table 2. Main clinical features of the study group by quartile categories of relative handgrip strength (RHGS)

	Quartile I	*Quartile II*	*Quartile III*	*Quartile IV*	*p*-value[1]
Age (yrs)	73.1±6.5 (72.1-74.2)	71.9±6.1 (70.9-72.8)	69.9±6.5 (68.8-70.1)	67.9±7.2 (66.8-69.1)	<0.001
AC (cm)	32.79±13.78 (30.59-35.00)	31.96±13.85 (29.74-34.17)	30.47±8.77 (29.07-31.87)	28.22±6.84 (27.13-29.31)	0.002
WC (cm)	98.1±14.03 (95.77-100.26)	93.65±13.06 (91.56-95.74)	92.46±9.81 (90.89-94.03)	83.87±11.26 (82.07-85.66)	<0.001
HC (cm)	113.86±12.16 (111.88-115.85)	107.81±9.42 (106.27-109.35)	106.49±11.86 (104.57-108.41)	101.23±7.06 (100.09-102.36)	<0.001
W/H ratio	0.86±0.09 (0.84-0.87)	0.86±0.12 (0.84-0.88)	0.92±0.68 (0.81-1.03)	0.83±0.99 (0.81-0.84)	ns
Calf (cm)	36.35±3.94 (35.72-36.98)	36.23±5.60 (35.33-37.12)	35.67±2.98 (35.19-36.14)	35.21±6.23 (34.21-36.20)	ns
MNA	25.85±1.18 (25.52-26.19)	25.7±2.14 (25.32-26.09)	26.06±1.84 (25.72-26.40)	25.93±1.95 (25.59-26.27)	ns
HGS (Kg)	17.75±3.67 (17.16-18.33)	22.05±2.81 (21.60-22.5)	24.8±3.32 (24.26-25.33)	27.38±2.87 (26.92-27.84)	<0.001
RHGS (Kg/BMI)	0.55±0.08 (0.54-0.57)	0.74±0.04 (0.73-0.75)	0.87±0.04 (0.87-0.88)	1.09±0.12 (1.07-1.11)	<0.001
Diabetes n (%)	31 (20.7)	18 (12)	21 (14)	8 (5.3)	<0.001

Hypertension n (%)	74 (49.3)	73 (48.7)	58 (38.7)	59 (39.3)	0.004
Adequate Nutritional state (MNA >24) n (%)	30 (20)	29 (19.3)	23 (15.3)	28 (18.5)	ns
At risk for malnutrition (MNA 17-23.5) n (%)	120 (80)	121 (80.7)	127 (84.7)	123 (81.4)	ns

Abbreviations: AC, arm circumference; WC, waist circumference; HC, hip circumference; W/H, waist/hip ratio; MNA, Mini Nutritional Assessment; HGS, Handgrip strength; RHGS, relative handgrip strength (HGS/BMI). Continuous variables are expressed as means ± SD and (95% CI). Discrete traits are expressed as *n* (%). [1]Test for linear trend (continuous variables) or for proportions (discrete traits) adjusted for age.

Table 3. Multivariable logistic regression analysis for categories (quartiles) of RHGS vs. presence of

diabetes

Quartile 4 vs. Quartile 1	OR	CI 95%	*p-value*
Unadjusted	0.64	0.49-0.83	0.001
Model 1 (adjusted for age)	0.66	0.50-0.86	0.002
Model 2 (adjusted for age, WC, HC, hypertension)	0.77	0.59-0.86	0.002

Abbreviations: WC, waist circumference; HC, hip circumference.
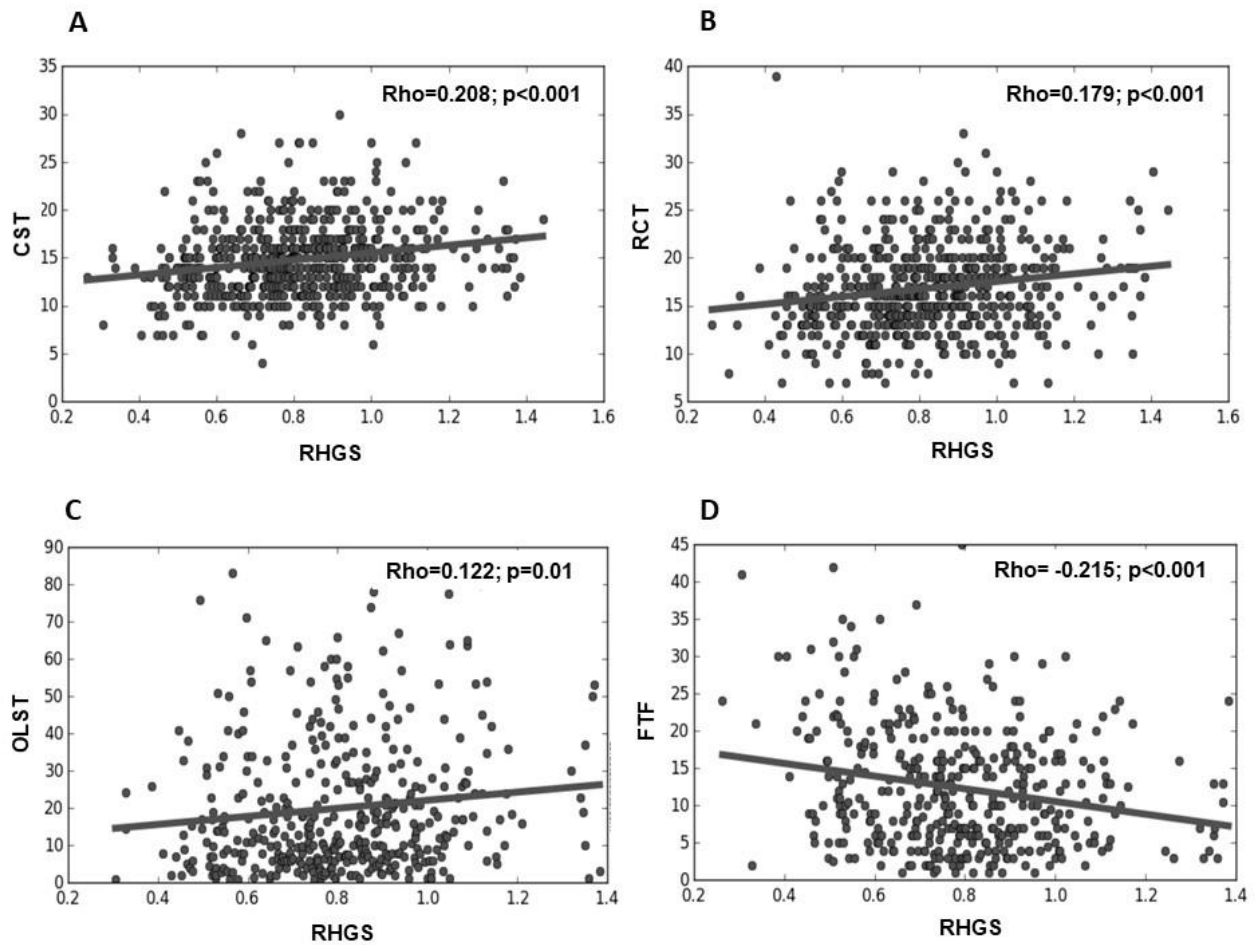
Figure

Figure 1 (a-d): Bivariate correlation analysis between RHGS and selected physical functional tests

(CST, RCT, OLST and FTF, respectively)

Abbreviations: CST, 30-Second Chair Stand Test; RCT, Reverse Crunch Test; OLST, One-legged

Stance Test; FTF, Fingertip-to-floor test; RHGS, relative handgrip strength (HGS/BMI).

Abbreviations:

HGS, Handgrip strength; RHGS, relative handgrip strength (HGS/BMI); MetS, metabolic syndrome;

MNA, Mini Nutritional Assessment; WC, waist circumference; AC, arm circumference; HC, hip

circumference; W/H, waist/hip ratio; CST, 30-Second Chair Stand Test; RCT, Reverse Crunch Test;

OLST, One-legged Stance Test; FTF, Fingertip-to-floor test.