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### MUSCLE QUALITY IS ASSOCIATED WITH HISTORY OF FALLS IN OCTOGENARIANS

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> Abstract: Objectives: The aim of this study was to compare muscle quality (MQ) between octogenarians classified as non-fallers, fallers and recurrent fallers and identify confounding intrinsic and extrensic factors that impact likelihood for falls. Design: This observational, descriptive, cross-sectional study included older adults (N=220) aged 80 years or older. Measurements: The Short Physical Performance Battery (SPPB) was used to evaluate physical function and MQ was calculated using the ratio of grip strength to arm muscle mass (in kilograms) quantified by DXA. Variables related to sociodemographic, clinical, cognitive function, and falls were evaluated using a questionnaire and symptoms of depression were evaluated by the Geriatric Depression Scale (GDS). A Kruskal-Wallis H test was used to verify differences between groups. Binomial logistic regression was performed to determine the impact of age, depression, polypharmacy, balance, MQ, and sex on participants having more than four falls in their history. Results: Increasing MO was associated with reduced likelihood of more than four falls in their history. Non-fallers were statistically younger (p = 0.012) and took more medications (p = 0.023) than recurrent fallers. Recurrent fallers had lower MQ when compared with fallers (p = 0.007) and non-fallers (p = 0.001) and had a lower GDS score when compared with fallers (p = 0.022). Finally, fallers presented lower scores for balance when compared to non-fallers (p = 0.013). Conclusion: A higher MQ is associated with a reduction in the likelihood falls in octogenarians. Therefore, it may be advantageous for clinicians to evaluate MQ when the screening of the risk of falls in older adults.

Key words: Muscle quality, physical function, handgrip strength, aging, falls.

#### Introduction

Countries are facing a rapid growth in aging populations; for example, Brazil estimates that individuals classified as older adults (> 60 years old) will reach 66 million by 2050 (33.7%) compared to 13.7% in 2014 (1, 2). This transition will be impacted by the growing number of octogenarians, also known as the oldest of older adults. These changes raise important demands for governmental services as risk for disability and falls only increase with aging. This loss of function increases risk for hospitalization and deaths among older individuals (2, 3).

According to the World Health Organization, 50% of the elderly over 85 years living in the community will fall at least once a year, thus constituting a growing public health problem due to population aging and increased longevity (4, 5). Fractures occur in 5-10% of falls and it is estimated that 52% of elderly individuals who suffer hip fracture had fallen at least once in the year prior to the fracture (6). Fractures disproportionality result in mortality in octogenarians. These individuals experience significant losses in locomotor function which ultimately antecedes falls and potentially a terminal life event (7). The prophylactic investigation of factors associated with falls in this age group is clear (6).

Compounding the high prevalence, falls are multifactorial and result from an interaction of multiple risk factors making them more difficult to study. However, these variables can be grouped into intrinsic (age-related) and extrinsic (environmental) elements (3, 8, 9). Important risk factors include: sex (female sex), living alone, physical disability, need of walking aid, vertigo, Parkinson's disease, lower-extremity weakness, diabetes, various pathologies, fear of falling, use of sedatives, antiepileptics, vision and/or hearing impairment (3, 8, 9). Another important fall risk factor is the progressive decline of strength and muscle mass related to aging, also termed sarcopenia (10). The combination of these factors can play an important role fall risk.

Investigators are describing the relationship between strength and muscle mass as muscle quality (MQ; strength per unit of mass) (11). The MQ may provide an estimate of the contribution of neuromuscular factors affecting muscle strength, as well as determine the loss of muscle strength with aging (12, 13). MQ has also been considered an important determinant of muscle function, which in turn has been linked to health outcomes like physical function and development of metabolic disease in older adults (12, 14-16). Furthermore, agerelated changes in MQ might be a better indicator for physical performance than independent metrics of strength (17). Many regard MQ as a more reasonable indicator of the contractile function of skeletal muscle than absolute muscle strength, which is largely dependent on the quantity of muscle mass (18).

Risk for falls is intrinsically linked to MQ in older adults

(19, 20). A recent study found that poor MQ was associated with a higher incidence of falls in women aged 65 to 85 years old (11). A population-based study of 1,099 participants aged 50 years or older found that all muscle performance measures, including MQ, were associated with increased risk of falls within the next ten years (21). These and other studies have previously identified the association of MQ with performance in functional tests in older women (22), with the development of disabilities, self-reported mobility difficulty and hospitalization (15). A decline in MQ has also been connected with chronic diseases like osteoarthritis (23) and type 2 diabetes mellitus (24) when compared to healthy older adults.

Understanding the changes in MQ with advancing age is complicated due to the interaction between MQ and intrinsic and extrinsic factors. Considering this complicated scenario, the impact of MQ on the prevention of falls in octogenarians often debated. It is postulated, however, that maintaining healthy MQ may preserve neuromuscular structure prevents falls may illuminate the relationship between MQ and falls in the oldest of older adults.

The primary purpose of the present study was to compare MQ between non-fallers, fallers and recurrent fallers in octogenarians. A secondary aim was to determine possible confounding intrinsic and extrinsic factors on the likelihood for falls in the same age group. It was hypothesized that MQ, have an impact have an impact on history of falls in octogenarians and that recurrent fallers would have lower MQ when compared with non-fallers and fallers.

#### Methods

#### Study structure and participants

This observational, descriptive, cross-sectional study also gathered secondary data from population research and multicentric «Patterns of physical, cognitive and psychosocial aging in long-lived elderly living in different contexts», conducted from 2016 to 2018, with older participants aged 80 years or older in Brasília (DF). The research was approved by the UCB Research Ethics Committee (protocol: 50075215.2.0000.0029).

Participants were recruited to participate from geriatric outpatient clinics and medical clinics. The present article analyzed the sample from Brasília, which was composed of individuals 80 years or older (N=220). Individuals were excluded from analyses if data from Dual Energy X-Ray Absorptiometry (DXA), handgrip strength, or information about falls were missing.

#### Measures

#### Sociodemographic, clinical, and functional data

The sociodemographic and clinical data were collected through face-to-face interviews guided by a questionnaire divided into the following blocks: chronic non-communicable diseases (heart disease, lung disease, systemic arterial hypertension, stroke, diabetes mellitus, cancer, osteoporosis, osteoarthritis) and polypharmacy (considering the use of 5 or more medications) (25, 26). Cognitive function was assessed by the Mini-Mental State Examination (MMSE) (27). The MMSE score can range from 0 to 30 points, with 30 points corresponding to a best cognitive ability (27). Depressive symptoms were evaluated by the Geriatric Depression Scale (GDS) (28), using a range from 0 to 15. The total score of zero for GDS was considered free of depressive symptoms and  $\geq 6$ identified the presence of depressive symptoms (28).

The Short Physical Performance Battery (SPPB) was used to assess physical function via: static balance; gait speed, and lower limb strength through the test of lifting and sitting from the chair (29). A total score lower than eight was indicative of poor physical performance (10, 29).

#### Falls

Information about falls was also collected in the interview. The question "Did you fall in the last six months? If so, how many times have you fallen?» It was used to categorize «nonfallers» (participants reporting no falls), «fallers» (one to three falls) and «recurrent fallers» (four or more falls).

#### Body composition

The lean muscle mass of the dominant upper limb was measured using the gold standard tool for older adults, DXA (Lunar brand, model DPX-IQ [GE Lunar Corporation], type pencilbeam, software version 4.7) (10). The DXA was calibrated and operated by a technically trained professional. The test included a full body scan with participants in the following position: supine and with legs secured by nonelastic straps at the knees and ankles, and arms aligned along the trunk with the palms facing the thighs. All metal objects were removed from the participant before the scan.

#### Handgrip strength

A hydraulic dynamometer was used to evaluate the handgrip strength of the dominant upper limb (Jamar, Model 5030J1). The elbow was maintained in 90° flexion and standardized verbal encouragement was used. Three consecutive measurements were performed, interspersed with one minute of rest. Three measures on the dominant hand were obtained and the highest value was recorded (30).

#### Muscle quality

The MQ was calculated according to the equation: MQ = muscle strength (kg) / muscle mass (kg). The MQ in this study used the ratio of grip strength to the entire arm muscle in kilograms measured by DXA. The validity and reliability of the MQ measure have been previously reported (12, 31-33).

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#### Statistical Analysis

A Kruskal-Wallis H test for continuous variables was used to verify differences between non-fallers, fallers, and recurrent fallers. When a difference was observed, pairwise comparisons using Dunn's procedure with a Bonferroni correction for multiple comparisons were performed. For dichotomous dependent variables, a chi-square test of homogeneity (2 X C TABLE) was used to determine if a difference exists between the binomial proportions between non-fallers, fallers, and recurrent fallers. When expected cell counts were less than five, Fisher's exact test (2 x c) was applied. When a difference was observed for a chi-square test of homogeneity, a post hoc analysis involving pairwise comparisons using the z-test of two proportions with a Bonferroni correction was used.

Binomial logistic regression was also performed to ascertain the effects of age, depression (no vs. yes), polypharmacy (no vs. yes), balance, MQ, and gender (women vs. men) on the likelihood that participants have more than four falls of history. All the independent variables were chosen based on previous studies that evaluated risk factors for falls among the elderly (3, 9). Only six independent variables were introduced in the logistic regression because a minimum of 20 cases per independent variable is necessary as the regard minimum sample size. Including more than six independent variables would reduce the reliability of estimates (34). The Linearity of the continuous variables concerning the logit of the dependent variable was assessed via the Box-Tidwell procedure and all continuous independent variables were found to be linearly related to the logit of the dependent variable (34).

The logistic regression model was statistically significant, 29.74, p = 0.001. The model explained 48.0% (NagelkerkeR2) of the variance in more than four falls of history and correctly classified 92.9% of cases (34). Sensitivity was 60%, specificity was 100%, positive predictive value was 100% and the negative predictive value was 92.10%34. The area under the ROC curve was 0.85 (95% CI, 0.73 to 0.96), which is at an excellent level of discrimination according to Hosmer et al. (2013) (35). All analyses were conducted using Statistical Package for the Social Sciences (SPSS) software version 20.0 (SPSS Inc., New York).

#### Results

Participants not meeting inclusion criteria or with missing values were excluded from the analysis (Figure 1).

The descriptive characteristics of the participants are shown in Table 1. Non-fallers were statistically younger than recurrent fallers (adj. sig. of p = 0.012, Table1). No differences between groups were observed for handgrip strength after a Bonferroni correction.

Recurrent fallers presented a statistically lower MQ when compared fallers (adj. of = 0.007, Table 1) and non-fallers (adj. sig. of p = 0.001, Table 1). Non-fallers took more medications than recurrent fallers (adj. sig. of p = 0.023, Table 1). Regarding the class of medications, 67.7% of non-fallers used antihypertensive drugs and 12.3% of antidepressants; among the recurrent fallers this proportion was 27.3% and 4.5%, respectively.





Recurrent fallers presented a lower GDS score (adj. sig. of p = 0.022, Table1) and balance when compared to non-fallers (adj. sig. of p = 0.013, Table1). In the non-faller group, 81.5% (n=44) of the participants and 78.1% (n=25) of individuals in the faller groups had a higher prevalence of hypertension when compared with recurrent fallers (p< 0.05; Table1). No other differences were observed (Table1).

Of the six predictor variables, only MQ was considered statistically significant (as shown in Table 1). Increasing MQ was associated with a reduction in the likelihood of being in the recurrent faller group (Table 2).

#### Discussion

The current study provides the following novel findings: 1) Of the six variables, a higher MQ was associated with a reduction in the likelihood of being a recurrent faller. 2) Nonfallers were statistically younger than recurrent fallers. 3) Non-fallers took more medications than recurrent fallers. 4) Non-fallers and fallers were more likely to have a hypertension diagnosis when compared with recurrent fallers. These results should support studies (11, 22) that seek to evaluate and maintain MQ in older adults in order to preserve physical function and avoid negative outcomes associated with aging.

These results are consistent with previous studies that pointed to an association between increased risk of falls with diminished lower extremity MQ in older women (36) and older women classified as obese (37). Balogun et al (21) agrees with the current investigation that upper extremity MQ was associated with the risk of falls. However, only handgrip strength was consistently associated with an increased risk of falls and fractures over 10 years.

Another cross-sectional study with a sample older men (N=1,705; aged 70 years or older) found relationships between

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## Table 1 Main participants characteristics

	Fall	ers	Recurren	nt Fallers	Non-Fa	llers	Р
Age, years	83.88 ± 4.35		86.68 ± 5.43		83.01 ± 2.90		0.014
Body mass index, kg/m <sup>2</sup>	$4.07 \pm 1.59$		$2.42 \pm 1.60$		$5.17 \pm 2.38$		0.930
Fat, %	$33.48 \pm 10.16$		$32.68 \pm 11.36$		$33.87 \pm 9.22$		0.917
Education, years	$5.05 \pm 5.19$		$5.52 \pm 6.20$		$4.33 \pm 4.37$		0.938
Handgrip strength, kg	$18.97 \pm 7.27$		$18.54 \pm 6.44$		$22.36 \pm 7.91$		0.048
Muscle quality, kg/kg	$4.07 \pm 1.59$		$2.42 \pm 1.60$		$5.17 \pm 2.38$		0.001
MMSE	$19.22 \pm 7.82$		$20.47 \pm 5.48$		$20.77 \pm 5.04$		0.829
Geriatric depression scale, score	$4.83 \pm 3.52$		$2.85 \pm 2.53$		$4.05 \pm 3.00$		0.026
Walk, score	$2.69 \pm 1.28$		$2.89 \pm 1.18$		$3.23 \pm 0.92$		0.115
Chair stands, score	$1.34 \pm 1.09$		$1.67 \pm 1.23$		$1.66 \pm 0.99$		0.368
Standing balance, score	$2.53 \pm 1.29$		$2.88 \pm 1.31$		$3.31 \pm 0.92$		0.016
SPPB, score	$6.59 \pm 3.08$		$7.47 \pm 3.08$		$8.16 \pm 2.23$		0.075
Medications, number	$3.97 \pm 3.34$		$3.38 \pm 2.97$		$5.15 \pm 2.81$		0.011
	Fallers		<b>Recurrent Fallers</b>		Non-Fallers		Р
Gender	Female	Male	Female	Male	Female	Male	
	23 (65.7)	12 (34.3)	14 (63.6)	8 (36.4)	39 (63.9)	22 (36.1)	0.981
	Fallers		<b>Recurrent Fallers</b>		Non-Fallers		Р
	Yes	No	Yes	No	Yes	No	
Cardiopathy	7 (23.3)	23 (76.7)	10 (50)	10 (50)	12 (24.5)	37 (75.5)	0.074
Hypertension	25 (78.1)	7 (21.9)	8 (15.7)	14 (63.6)	44 (81.5)	10 (18.5)	0.001
Stroke*	1 (4.0)	24 (96.0)	5 (25)	15 (75)	7 (14.6)	41 (85.4)	0.124
Diabetes*	8 (26.7)	22 (73.3)	3 (15.8)	16 (84.2)	13 (26)	37 (74)	0.675
Cancer*	5 (20)	20 (80)	4 (21.1)	15 (78.9)	7 (15.9)	37 (84.1)	0.817
Arthritis*	5 (21.7)	18 (78.3)	3 (15.8)	16 (83.2)	14 (30.4)	32 (69.6)	0.491
Pulmonary disease*	2 (8.3)	22 (91.7)	4 (21.1)	15 (78.9)	8 (17.4)	38 (82.6)	0.503
Depression	9 (31)	20 (69)	9 (47.4)	10 (52.6)	10 (22.2)	35 (77.8)	0.133
Osteoporosis	7 (30.4)	16 (69.6)	8 (50)	8 (50)	18 (37.5)	30 (62.5)	0.462
Polypharmacy	13 (39.4)	20 (60.6)	14 (66.7)	7 (33.3)	33 (62.3)	20 (37.7)	0.064

Note: data presented as frequency and percentage values; \*Fisher exact test; MMSE = mini-mental state examination; SPPB = short-physical performance battery.

upper and lower limb MQ and functional outcomes (38). The prevalence ratio for MQ of the lower limbs, limitation, and physical disability was stronger than that of the upper limbs. In their study, handgrip strength was associated with physical disability in instrumental activities of daily living (38). Presently, handgrip strength of the non-fallers was higher when compared to fallers and recurrent fallers. Admittedly, MQ might be a better indicator for physical performance in older adults than strength or mass alone (17, 39). These findings are corroborated by further findings that lower MQ is an important contributing factor to the age-related decline in handgrip strength (40). It is well known that handgrip strength is a powerful predictor of disability and negative outcomes in older

adults (40), further supporting our findings of an association of upper limb MQ with the risk of falls.

Not all fall risk literature aligns with the current results. Anderson et al (41) found no impact on the risk of falls and predictive ability of muscle size (cross sectional area) and density in the trunk. The results showed that the high muscle density of the trunk is associated with better balance. However, this finding does not immediately translate into a lower probability of falling and the authors suggested that the balance depends more on MQ than on muscle size (41).

A potential reason for the diverging results is the sampled population in each study. The current study recruited only those 80 years or older, but Anderson et al. (41) recruited across the

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#### Table 2

Logistic regression predicting likelihood of exhibiting more than four falls of history based on age, depression, polipharmarcy, balance, muscle quality and gender

	В	SE	Wald	df	Р	Odds Ratio	95% CI for Odds Ratio	
							Lower	Upper
Age	,125	,103	1.496	1	,221	1.134	,927	1.386
Depression	1.202	,882	1.857	1	,173	3.326	,590	18.741
Polipharmarcy	-,231	,811	,081	1	,776	,794	,162	3.894
Balance	,443	,338	1.716	1	,190	1;557	,803	3.019
Muscle quality	-,892	,300	8.874	1	,003	,410	,228	,737
Gender (M/F)	,560	,870	,414	1	,520	1;751	,318	9.634
Constant	-10.988	9.392	1.369	1	,242	,000		

Note: Depression and polipharmarcy is for no compared to yes; Gender is for women compared to men.

adult age continuum. The association between balance and risk of falls may not be as pronounced in the oldest of older adults, who are likely equilibrium deficient (36), have functional limitation(s) (38) and are at greater risk for falls (4, 5). This hypothesis is supported by our findings that non-fallers were significantly younger than recurrent fallers and presented a higher score in the balance test compared to fallers, evidencing the influence of age on risk for falls (9).

We may assume that older adult fallers may have a decline in contractile function that is more pronounced when compared to non-fallers (42). This physiological consequence would affect postural balance and ultimately the risk of falls (36, 43).

Despite the growing evidence (21, 38, 44), there is no consensus to standardize the use of MQ in clinical evaluation practice. The EWGSOP (10) recommends the use of highly sensitive imaging tests, such as Magnetic Resonance Imaging (MRI) and CT, in addition to MQ calculated using DXA or bioimpedance analysis (BIA). However, MRI and CT scans may be more cost prohibitive than DXA and BIA. If MQ proves to be predictive of fall risk in octogenarians, there needs to be further investigation to solidify the association between risk of falls and MQ.

Outside of the current study, polypharmacy is not typically associated with falls (45, 46). Studies often include a wide range of ages when defining an older adult sample (typically 60 years and older), which may washout the potential to detect a polypharmacy effect on fall risk in the oldest samples. Non-fallers had a significantly higher prevalence (67.7%) of hypertension compared to recurrent fallers. However, hypertension was not include in the logistic regression because the use of antihypertensive medications is associated with a lower risk of injurious falls among older adults (47).

The present study also found that older fallers presented a higher GDS score than the recurrent fallers; that is, the elderly who had one to three episodes of falls had higher depressive symptoms. Other articles, with samples composed of elderly people aged 65 years or older, also described an association between depressive symptoms and more than two episodes of falls (48). Based on our findings that recurrent fallers (four or more episodes of falls) presented significantly lower GDS scores. We speculate that the absence or low GDS scores make the older adults more willing to perform activities in home and community, thus making them at greater risk for falls.

It is important to point out that the present study has some limitations. Because this is a study with secondary data from a population survey, the data were collected by several evaluators, and not only by a single evaluator. To minimize the effect of this limitation, all evaluators were properly trained. Falls were evaluated through interviews and the response was conditional to the memory of the participant or his/her companion. The sample of the present study was composed only of older individuals aged 80 years or older, so the results may not apply to a sample of younger individuals. In addition, our findings are limited to a relatively small (N = 122) convenience sample of octogenarians. Finally, the crosssectional nature of this study prevents the capacity to identify any causal relationship between study variables and outcomes.

#### Conclusion

In conclusion, MQ was lower in recurrent fallers and the improvement of MQ was associated with a reduction in the likelihood of recurrent falls. Because of this, it is important to evaluate MQ when screening for risk of falls and establish fall risk prevention protocols aimed at increasing MQ, not simply strength or muscle mass.

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