DOI: 10.4025/jphyseduc.v33i1.3351

Original Article

POLIMORFISMO DO GENE *ACTN3* E OS FATORES ASSOCIADOS AO DESEMPENHO FUNCIONAL DE IDOSAS ATENDIDAS NA ATENÇÃO PRIMÁRIA EM SAÚDE

ACTN3 GENE POLYMORPHISM AND FACTORS ASSOCIATED WITH FUNCTIONAL PERFORMANCE IN ELDERLY WOMEN ASSISTED IN PRIMARY HEALTH CARE

Leandro César Teixeira Machado[1], Mateus Medeiros Leite[1], Marina Morato Stival[1], Yuri Gustavo de Sousa Barbalho[1], Filipe Dinato de Lima[2], Luciano Ramos de Lima[1], Alessandro de Oliveira Silva[2], Izabel Cristina Rodrigues da Silva[1], and **Silvana Schwerz Funghetto[1]**

[1]University of Brasília, Brasília-DF, Brazil.
[2]University Center of Brasília, Brasília-DF, Brazil.

RESUMO

Objetivo: analisar as potenciais influências do polimorfismo genético R/X do gene *ACTN3* e das características antropométricas e metabólicas no desempenho funcional de mulheres idosas atendidas na atenção primária em saúde. *Método:* Cento e quarenta e uma idosas foram avaliadas em relação as características antropométricas, metabólicas, funcionais, aspectos clínicos, cognitivos e demográficos. Foram determinadas as frequências de alelos e genótipos do polimorfismo do gene *ACTN3*. *Resultados:* 141 idosas (68,30 ± 6,18 anos) foram avaliadas. Não foram observadas diferenças significativas ($p > 0,05$) entre os genótipos RR e RX/XX no desempenho funcional, características antropométricas ou metabólicas das idosas. O tempo de realização do TUG apresentou correlações positivas com idade, índice de massa corporal, circunferência da cintura e percentual de gordura (s = 0,315; $p < 0,001$; s = 0,238; $p = 0,005$; s = 0,174; $p = 0,039$; s = 0,207; $p = 0,014$) respectivamente. Correlações negativas foram observadas entre o TUG com força de preensão manual absoluta (s = - 0,314; $p < 0,001$) e relativa (s = - 0,380; $p < 0,001$). *Conclusão:* Em nosso estudo, não foram observadas influências dos polimorfismos do gene *ACTN3* no desempenho funcional das idosas, sendo este, influenciado por outros fatores.

Palavras-chave: Desempenho funcional. Variação genética. Envelhecimento. Força muscular.

ABSTRACT

Objective: To analyze potential influences of the R/X genetic polymorphism of the *ACTN3* gene, as well as of anthropometric and metabolic characteristics on the functional performance of elderly women assisted in primary health care. *Method*: One hundred and forty-one elderly women were assessed in terms of anthropometric, metabolic and functional aspects, in addition to clinical, cognitive and demographic characteristics. Allele and genotype frequencies of *ACTN3* gene polymorphism were determined. *Results*: 141 elderly women (68.30 ± 6.18 years) were evaluated. No significant differences ($p > 0.05$) were observed between the RR and RX/XX genotypes in the elderly women's functional performance, anthropometric or metabolic characteristics. The TUG test completion time showed positive correlations with age, body mass index, waist circumference, and fat percentage (s = 0.315; $p < 0.001$; s = 0.238; $p = 0.005$; s = 0.174; $p = 0.039$; s = 0.207; $p = 0.014$), respectively. Negative correlations were found between the TUG test with absolute handgrip strength (s = - 0.314; $p < 0.001$) and relative handgrip strength (s = - 0.380; $p < 0.001$). *Conclusion*: In our study, there were no influences from *ACTN3* gene polymorphisms on the functional performance of the elderly women, which is influenced by other factors.

Keywords: Functional performance. Genetic variation. Aging. Muscle strength.

Introduction

The growth in the number of individuals over 60 years of age is a global trend. In Brazil, demographic and epidemiological data point to a population of 37.7 million elderly people. Of these, about 58% have comorbidities[1]. Forecasts point to an increase in the elderly population from 14.7% in 2021 to 32.2% in 2060[2]. This rise in longevity comes along with substantial physical changes, such as progressive loss of muscle mass, strength and power, balance and cardiometabolic functions[3]. Such facts contribute to a higher prevalence of the development of

chronic diseases, such as obesity, cancer, diabetes mellitus[4,5], increased sarcopenia, and loss of functional capacity[6].

This clinical condition consequently represents an increase in morbimortality in this population. Simple and low-cost measures are important in order for health professionals to predict impaired mobility in the elderly, as well as to track sarcopenia and associated factors[6]. The timed up and go (TUG) test associated with the handgrip strength (HGS) test is an example of effective tool for tracking frailty and consequent functional dependence in older adults[7–10].

Functional performance in the elderly can be influenced by the natural consequences of age and by several factors, such as anthropometry and body composition. In elderly women, age, shorter stature, heavier weight, higher body mass index (BMI), low level of physical activity, impaired cognitive performance and a greater number of comorbidities are associated with worse performance on the TUG test[11]. In addition to these factors, genetic aspects are related to the speed at which these changes occur, which can directly influence the other risk factors for several diseases prevalent in the elderly[12,13].

For instance, it is possible to perceive the influence of the *ACTN3* gene, which encodes the α-actinin-3 protein, a structural protein of the Z disk of muscle cells, with main function in helping in and maintaining the myofibrillar arrangement, contributing to the muscle contraction process[14]. Although it is not considered a disease, deficient production of the α-actinin-3 protein is associated with loss of function and reduced muscle volume[15,16], with a marked decrease as one ages[17].

The *ACTN3* gene is involved in the genetics of physical fitness, being explored in professional and amateur elite athletes[18,19], as well as in health outcomes in the general population. Individuals with the RR genotype fully express the α-actinin-3 protein, with better capacity for muscle contractions. However, those who have both XX mutant alleles present total absence of the protein and lower physical performance[19].

Although the association of the *ACTN3* gene with anthropometric parameters in elderly women has not been confirmed[20], the influence of the XX genotype has been reported as a protective potential against obesity in animal models[21]. Nonetheless, regarding metabolic parameters, Barrón-Cabrera et al. (2021) observed a metabolic dysregulation, with the presence of high levels of fasting glucose, dyslipidemia, hypertriglyceridemia, and insulin resistance in adult women with XX genotype[22].

Some studies suggest the influence of *ACTN3* gene polymorphisms in the elderly when it comes to loss of muscle function, maintenance of bone mineral density, and risk of metabolic disorders[23,24]. However, in elderly women, this gene is still little explored with regard to physical fitness and performance, and results are conflicting[12,24]. The XX genotype is associated with lower muscle volume in older adults with sarcopenia[25]. On the other hand, studies have verified greater handgrip strength and better muscle strength responses after training in the elderly[17,20]. The presence of the R allele may be associated with a higher risk of sarcopenia compared to the X allele in active elderly women[20], while a decreased prevalence of sarcopenia is observed in elderly Koreans carrying the R allele[26].

In this sense, studies that explore more evidence of the effects of the *ACTN3* gene on functional performance and other associated factors, especially in elderly Brazilian women, are relevant. Therefore, the present study aimed to analyze potential influences of the R/X genetic polymorphism of the *ACTN3* gene, as well as of anthropometric and metabolic characteristics on the functional performance of elderly women assisted in primary health care. Based on the information presented, our initial hypothesis was that elderly women with the RR genotype would present better functional performance.

Methods

This is a cross-sectional study, with a quantitative approach, conducted with elderly female users of a Basic Health Unit (BHU) in the Federal District, from June to August 2019. The project was submitted to the Research Ethics Committee (REC) of the Federal District's Health Department [*Secretaria de Saúde do Distrito Federal*] (SES/DF) and approved with opinion No. 1.355.211 and CAAE 50367215.5.0000.5553. All of them received information about the research, in accordance with Resolutions No. 466/2012 and No. 510/2016 of the National Health Council, and signed the Free and Informed Consent Form (FICF).

Study participants and design

Sampling was set by convenience. The elderly women were recruited by telephone, whose number was taken from their records in the BHU's Family Health Strategy. Those who met the following inclusion criteria were included: female sex, age ≥ 60 years, being assisted at the BHU during the data collection period, accepting to participate in the research and having completed all laboratory tests and anthropometric measurements proposed by the study. Elderly women with inflammatory, rheumatic, autoimmune or chronic diseases that made it impossible to perform the tests were excluded. Initially, 150 elderly women were selected, but 9 did not complete the data collection, totaling a sample with 141 elderly women.

The elderly female participants received guidance on the necessary preparation to undergo the tests, measurements and blood exams. Data collection took place from June to August 2019 on two occasions: at the University and at the BHU. On the first occasion, at the university, questionnaires and anthropometric measurements were applied, and the Dual-energy X-ray Absorptiometry (DEXA) was performed. On the second occasion, at the BHU, blood was collected, and performance and muscle strength tests were carried out.

Procedures, tests and measurements

Initially, a structured questionnaire was applied to verify demographic data (age, education and marital status), presence of self-reported pathologies, such as Systemic Arterial Hypertension (SAH) and Diabetes *Mellitus* (DM), as well as health-related behavior (sedentary lifestyle). To assess cognitive function, the Mini Mental State Examination (MMSE) was used, which evaluates orientation, memory and attention. The test has a maximum score of 30 points, and the following score was considered to classify cognitive deficit: 20 points for illiterates; 25 points for elderly people with 1 to 4 years of schooling; 26.5 for 5 to 8 years old; 28 for those aged 9 to 11 years old, and 29 for those aged over 11[27].

To measure anthropometric characteristics and body composition, the women's body mass, height and waist circumference (WC) were measured. Their Body Mass Index (BMI) was obtained through weight (kg) and height (m) measurements using the equation: BMI = [(Weight(kg)/Height(cm)^2)]. Body fat percentage (BF%) was determined by DEXA (General Electric-GE, 8548 BX1L, 2005, Lunar DPX type - Encore 2005)[28].

Subsequently, the elderly women were scheduled to go to the BHU for blood collection after a 12-hour fast. The collection was performed by means of venipuncture, preferably in the antecubital fossa. The concentrations of glycated hemoglobin (HbA1c), Glycemia, Cholesterol, Triglycerides, high-density lipoprotein (HDL-C) and low-density lipoprotein (LDL) were performed in a clinical analysis laboratory funded by the research project.

Functional performance was assessed using the Timed Up and Go (TUG) test. Prior to the evaluation, two tests were run for familiarization with the protocol. Performance was evaluated in seconds, and timing started right after the signal with the word "go", while the

elderly woman was still seated, and ended immediately when she sat down again. A colored mark was fixed to demarcate the 3-meter walk, starting from the chair[10].

Isometric muscle strength was measured using a calibrated JAMAR® hydraulic dynamometer. In the sitting position, holding the dynamometer in a 90-degree elbow flexion, the elderly woman underwent three measurements for both hands, with maximum readings recorded. Absolute handgrip strength (AHGS) was summed from the readings of both hands. Relative handgrip strength (RHGS) was defined as absolute handgrip strength divided by the BMI[29].

Genomic deoxyribonucleic acid (DNA) was extracted from 5 mL blood samples, collected with EDTA anticoagulant using Invitek's Invisorb Spin Blood Minikit (250) (catalog # CA10-0005, batch # 1031100300), with an average concentration of 20 ng/μL. Genotyping for *ACTN3* gene polymorphisms was performed by the polymerase chain reaction (PCR) method with restriction fragment length polymorphism. The PCR product was digested with *Dde*I restriction enzyme (New England Biolabs, Inc., USA). To assemble the digestion system, the following were used: 10.0 μL of PCR; 2.0 μL of 10x NEB3.1 buffer (Biolabs); 1 μL of *Dde*I enzyme (10U/μL), topped up with ultrapure water to a final volume of 20 μL per reaction. The system was maintained at 37˚C for 3 hours. The digestion products were subjected to an electrophoretic run in 3% agarose gel (Invitrogen Life Technologies, USA), with ethidium bromide at a power of 100W for 20 minutes. The R577X allele created a new restriction site, and the 291bp fragment was cleaved into three of 108bp, 97bp and 86bp; the 577R allele was cleaved into 205bp and 86bp[30].

Statistical analysis

All analyses were conducted using the Statistical Package for Social Sciences (IBM SPSS, IBM Corporation, Armonk, NY, USA, 25.0). Descriptive analysis was used to calculate descriptive measures, and absolute and relative frequencies. The Kolmogorov–Smirnov test was applied to verify data normality distribution. Spearman's correlation coefficient was used to verify the correlation between the variables. To compare TUG values in accordance with clinical, demographic and lifestyle characteristics, the Kruskal-Wallis test and the Mann-Whitney U test were employed, when appropriate. To compare the genotypes, the t test for independent samples was used when normality was verified, and the Mann-Whitney U test when normal distribution was not verified. Adherence to the Hardy-Weinberg equilibrium for genotypic frequency in controls was analyzed by the chi-square test with one degree of freedom. $p < 0.05$ was adopted as significance level.

Results

The clinical characteristics of body composition, metabolic parameters, muscle strength and functional performance of the 141 elderly women are presented in Table 1.

Table 1. Anthropometric, metabolic and functional characterization of the elderly women (N=141)

	Minimum	Maximum	Mean ± SD	Median (interquartile range)
Age (years)	60.00	85.00	68.30 ± 6.18	67.00 (63.00 – 73.00)
BMI (kg/m²)	21.50	48.00	30.40 ± 4.30	30.40 (27.80 – 32.30)
Waist (cm)	63.00	141.00	99.02 ± 10.86	99.00 (94.00 – 102.00)
Body fat (%)	32.50	56.30	43.48 ± 4.37	43.17 (40.90 – 46.00)
HbA1c (%)	4.60	12.50	6.33 ± 1.43	5.90 (5.50 – 6.80)
Blood glucose (mg/dL)	56.00	362.00	117.09 ± 49.91	99.00 (87.00 – 125.20)
Cholesterol (mg/dL)	89.00	351.40	198.76 ± 45.06	198.00 (167.00 – 225.00)
Triglycerides (mg/dL)	60.00	441.00	157.85 ± 76.70	137.00 (104.00 – 186.00)
HDL (mg/dL)	23.00	91.70	48.95 ± 9.53	48.00 (43.00 – 54.00)
LDL (mg/dL)	32.00	246.60	118.58 ± 41.71	117.00 (89.40 - 144.00)
AHGS (Kg)	8.00	68.00	35.95 ± 10.29	35.00 (29.00 – 43.00)
RHGS (Kg/BMI)	0.26	2.97	1.21 ± 0.41	1.16 (0.96 - 1.42)
TUG (sec)	6.87	31.62	15.84 ± 4.77	15.49 (12.29 – 18.50)

Note: Values are expressed as minimum, maximum, mean ± standard deviation, median and (interquartile range). BMI = body mass index. HbA1c = glycated hemoglobin. HDL = high density lipoprotein. LDL = low density lipoprotein. AHGS = absolute handgrip strength. RHGS = relative handgrip strength. TUG = timed up and go test
Source: The authors

The allelic and genotypic frequencies for the *ACTN3* gene polymorphisms do not differ in terms of the Hardy-Weinberg equilibrium ($X^2 = 0.136$; degree of freedom = 1; $p = 0.712$). However, there was a higher frequency for the genotype of RR homozygotes (n=65) and a lower frequency for XX homozygotes (n=13). Carriers of the homozygous XX genotype were grouped with those with the heterozygous RX genotype (n=34) for analysis purposes (Table 2).

Table 2. Analysis of the elderly women's ACTN3 allelic and genotypic frequency. Brasília, 2020 (N=141)

		Frequencies	
		n	%
*Allelic frequency**	R	128	90.78
	X	76	9.22
Genotypic frequency	RR	65	46.10
	RX	63	44.68
	XX	13	9.22
	RX + XX	76	53.90

Note: Values are presented in absolute and relative frequencies
Source: The authors.

No significant differences ($p > 0.05$) were observed between the RR and RX/XX genotypes for anthropometric and metabolic characteristics. Likewise, there were no statistical differences between the RR and RX/XX genotypes for the elderly women's AHGS, RHGS and functional performance (TUG) (Table 3).

Table 3. Comparison of anthropometric, metabolic and functional characteristics, in accordance with the elderly women's *ACTN3* genotypes (N=141)

	ACTN3		
	RR (n=65)	**RX/XX (n=76)**	**p**
Age (years)	67.00 (63.00 – 73.00)	67.00 (63.00 – 72.00)	0.985b
BMI (kg/m²)	30.40 (27.90 – 32.00)	30.40 (27.65 – 33.0)	0.712b
Waist (cm)	99.00 (97.00 – 104.00)	99.00 (91.75 – 101.00)	0.073b
Body fat (%)	43.38 ± 4.45	43.56 ± 4.32	0.810a
HbA1c (%)	5.80 (5.40 – 6.40)	5.95 (5.50 – 7.20)	0.117b
Blood glucose (mg/dL)	97.00 (87.00 – 112.80)	106.50 (88.50 – 139.50)	0.071b
Cholesterol (mg/dL)	197.55 ± 45.74	199.79 ± 44.76	0.770a
Triglycerides (mg/dL)	132.00 (102.00 – 170.00)	142.50 (108.50 – 217.00)	0.146b
HDL (mg/dL)	48.00 (43.00 – 53.00)	48,00 (42,50 – 55,00)	0.895b
LDL (mg/dL)	119.88 ± 43.35	117.48 ± 40.51	0.734a
AHGS (Kg)	36.64 ± 11.63	35.36 ± 9.02	0.462a
RHGS (Kg/BMI)	1.17 (0.99 – 1.45)	1.15 (0.95 – 1.37)	0.546b
TUG (sec)	15.54 (11.87 – 18.48)	15,53 (12,68 – 18,61)	0.415b

Note: Values are presented as mean ± standard deviation or median (interquartile range). BMI = body mass index. HbA1c = glycated hemoglobin. HDL = high density lipoprotein. LDL = low density lipoprotein. AHGS = absolute handgrip strength. RHGS = relative handgrip strength. TUG = timed up and go test. [a] p value obtained by the independent t test. [b] p value obtained by the Mann-Whitney U test

Source: The authors

Regarding the cognitive aspect, 50.4% showed changes in the mini mental state examination. There was a prevalence of 80.9% of systemic arterial hypertension (SAH) and 57.4% of diabetes *mellitus* (DM). A total of 74.5% of the elderly women had completed elementary school, 41.8% were married, and 77.3% reported doing physical exercises (Table 4).

Comparing the values obtained in the TUG test, it was observed that elderly women with normal cognitive aspects performed better on the TUG test ($p = 0.035$), so did those without SAH, who performed better on the TUG test ($p = 0.002$). In addition, better performance was observed with shorter execution time for elderly women with high school level compared to illiterate ones and those with elementary school level ($p = 0.021$; $p = 0.042$, respectively) (Table 4).

Table 4. Functional performance comparison in accordance with the elderly women's clinical, demographic and lifestyle variables (N=141)

		Functional performance (TUG)			
		Minimum	**Maximum**	**Median (interquartile range)**	***p***
MMSE	Altered (n=71)	6.87	31.62	16.27 (12.32 – 19.78)	0.035b
	Normal (n=70)	7.37	30.44	14.71 (12.21 – 17.09)	
SAH	Yes (n=114)	6.87	31.62	16.03 (12.69 – 19.22)	0.002b
	No (n=27)	7.55	20.99	12.90 (11.36 – 15.48)	
DM	Yes (n=81)	7.37	31.62	15.66 (12.68 – 18.71)	0.264b
	No (n=60)	6.87	26.28	14.71 (11.95 – 18.20)	
Education	Illiterate (n=13)	11.48	24.18	16.27 (14.42 – 20.24)	0.045c
	Element. (n=105)	6.87	31.62	15.59 (12.21 – 19.01)	
	High School (n=23)	7.37	18.71	13.67 (11.04 – 16.87)	
Marital status	Single (n=21)	10.56	31.62	15.48 (13.51 – 18.84)	0.230c
	Married (n=59)	6.87	30.44	14.75 (11.92 – 17.92)	
	Divorced (n=14)	9.33	28.19	14.87 (9.65 – 18.50)	
	Widow (n=47)	8.47	25.14	16.71 (14.19 – 18.73)	
Physical Activity	Yes (n=109)	6.87	28.19	15.41 (12.10 – 17.75)	0.058b
	No (n=32)	7.37	31.62	17.09 (12.80 – 22.61)	

Note: Values are shown as minimum, maximum, median and (interquartile range). TUG = timed up and go test. MMSE = Mini Mental State Examination. SAH = systemic arterial hypertension. DM = diabetes mellitus. Element. = elementary school. b p value obtained by the Mann-Whitney U test. c p value obtained by the Kruskal-Wallis test

Source: The authors

No significant correlations were observed between the TUG test and metabolic measures ($p > 0.05$). Figure 1 shows the scatterplots for the correlations that showed significance between the TUG test and the descriptive measures. Positive correlations were observed between the TUG test and age ($s = 0.315$; $p < 0.001$), BMI ($s = 0.238$; $p = 0.005$), waist circumference ($s = 0.174$; $p = 0.039$), and body fat percentage ($s = 0.207$; $p = 0.014$). Negative correlations were found between the TUG test and absolute handgrip strength ($s = -0.314$; $p < 0.001$) and relative handgrip strength ($s = -0.380$; $p < 0.001$).

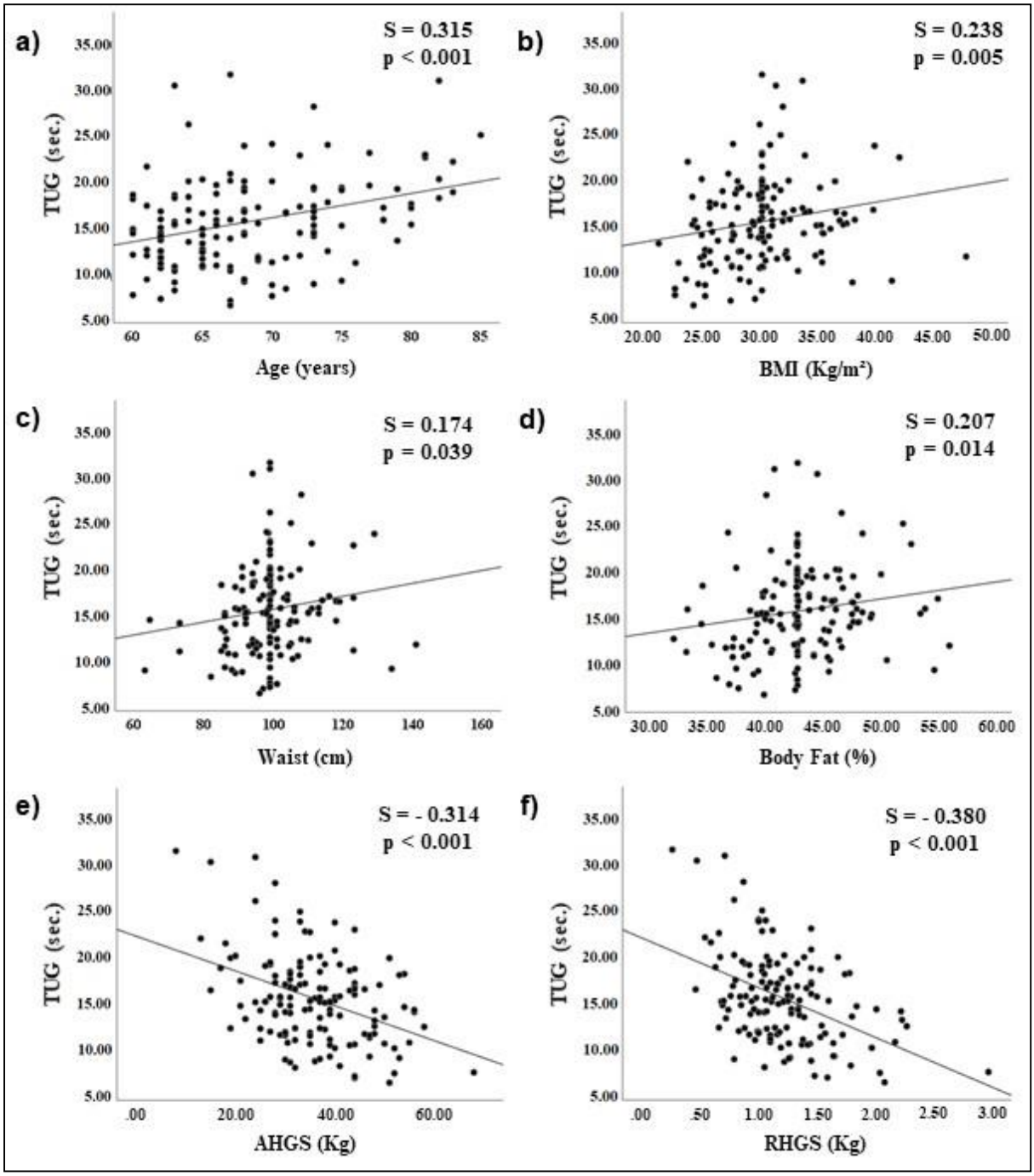

Figure 1. Scatterplots for significant correlations between the elderly women's clinical and functional characteristics with the timed up and go test

Note: a) correlation between TUG and age. b) correlation between TUG and BMI. c) correlation between TUG and waist circumference. d) correlation between TUG and body fat percentage. e) correlation between TUG and AHGS. f) correlation between TUG and RHGS. TUG = timed up and go test. BMI = body mass index. AHGS = absolute handgrip strength. RHGS = relative handgrip strength. Results obtained by Sperman's correlation

Source: The authors

Discussion

This study sought to analyze potential influences of the R/X genetic polymorphism of the *ACTN3* gene, as well as of anthropometric and metabolic characteristics on the functional performance of elderly women assisted in primary health care. The *ACTN3* gene has an effect

on muscle phenotypes, especially in young people and athletes[31], and on capacities related to muscle strength in elderly women[20]. The initial hypothesis that the elderly women's functional performance would be different depending on the *ACTN3* gene polymorphism was not confirmed.

The genetic aspects of aging are associated with strength and functional performance[12]. As for the *ACTN3* gene polymorphisms, a study evidenced a greater peak isokinetic knee torque in elderly women with XX homozygosity compared to those with RR+RX[32]. Also in that study, the authors did not identify differences between the genotypes for handgrip strength and functional performance in the gait speed test. Likewise, in the present study, no differences were observed between the genotypes in the elderly women's muscle strength and functional performance.

One possible factor for this finding may be related to the low frequency of XX homozygotes observed and the unification of this genotype with heterozygous RX genes. The presence of the R allele is related to protection against the development of sarcopenia and its consequences, such as loss of strength and muscle performance[26]. Another influential characteristic refers to ethnicity, in which a higher frequency of the X allele is observed in Asian populations, with the effects of the genotypes on these outcomes being shown[23].

Additionally, *ACTN3* expression is limited to fast-twitch skeletal muscle fibers, especially type II fibers[24]. These fibers are the main ones affected in the aging process, which alters the homeostasis of skeletal muscle, causing sarcopenia, with significant loss of muscle mass and strength[6,33]. Due to the loss of these fibers during the sarcopenic process in aging, it is possible that the effect of the *ACTN3* gene polymorphism is smaller in the elderly, not influencing the capacity to produce strength and functionality, as observed in some previous studies[34,35].

Changes in functional performance and muscle phenotypes, especially during aging, depend on environmental and genetic factors, as well as on gene-environment interactions[36], factors which determine individual variability in musculoskeletal characteristics. Moreover, several genes may be associated with these outcomes in terms of performance[12,37]. In the present study, no significant differences were observed between the genotypes of the *ACTN3* gene for strength and muscle performance. This finding reinforces the idea of a multifactorial and polygenetic approach for the determination of functionality in the elderly[12,32].

With regard to metabolic variables, research still shows an unclear relationship between the latter and the *ACTN3* gene. However, the study by Barrón-Cabrera et al. (2021) observed an association of the XX genotype with metabolic changes in women, implicating this gene in the development of chronic metabolic diseases[22]. Such a fact can be observed in the study by Riedl et al. [38], with an increased frequency of the XX genotype in individuals with DM.

As for the other factors that may influence functional performance, the results of the present study revealed that elderly women with greater age, BMI, waist circumference, and high body fat percentage performed the TUG test over a longer time, which characterizes them with impaired functional performance. Furthermore, altered cognitive aspect, lower level of education, and presence of SAH were associated with a longer time to complete the TUG test.

Increase in the time and decrease in the speed to complete the TUG test are associated with lower functional performance. In the present study, an average of 15.84 (± 4.77) seconds was observed, positively associated with age. Corroborating these results, previous research has indicated that elderly people with advanced age take longer to complete the TUG test, associating this fact with aging-related changes, such as muscle weakness and the very execution of the test, which requires an active and precise control of the central nervous system with different processes that control anticipatory postural adjustments[39–41].

Most of the sample was overweight, with an average BMI of 30.40 (± 4.30) kg/m². Additionally, high values were observed for waist circumference and fat percentage. These measures showed a positive association with TUG completion time. In the elderly population, studies point out that anthropometric parameters and obesity are associated with other dysfunctions, such as higher cardiovascular risk[42], greater inflammation[43], lower muscle strength and function, leading to frailty and difficulties in daily living activities[44,45].

The results showed negative correlations between absolute and relative muscle strength and the time taken to perform the TUG test, which are good markers to identify impaired performance in elderly women[8]. Other factors, such as muscle strength and power in the lower limbs, balance, mobility and aerobic capacity have been shown to determine TUG variability in elderly women[10]. Moreover, low muscle strength associated with impaired functional performance and low muscle mass are the basis for sarcopenia diagnosis[6]. In this sense, the TUG test is related to the classification of this syndrome, especially in elderly people with good physical and cognitive capacity[7].

When it comes to the cognitive aspect, the elderly women with altered cognition had lower functional performance with longer TUG completion time, and so did those with a lower level of education. Other studies also show the association of poor performance on the TUG test in the elderly with cognitive alterations, which indicates a risk factor for this population with regard to impaired functional performance and increased risk of falls[46–48].

Still concerning clinical characteristics, the present study found a SAH prevalence of 80.9%. The latter proved to be a factor associated with lower functional performance, as elderly women with SAH needed more time to execute the TUG test. Hypertensive individuals have slower processing speed, reduced balance, less functional mobility, and greater fear of falling compared to normotensive ones[49]. In this study, DM had a prevalence of 57.4%, which did not prove to be an influential characteristic for the TUG test. Differently, studies report negative effects of DM, with a significant decrease in gait speed, increased frailty and depression, declines in muscle strength, balance and aerobic resistance[50]. Likewise, the consequences of DM, such as diabetic neuropathy, tend to influence TUG time increases and lower functional performance[51].

From a clinical point of view, our results provide relevant information as to using the TUG test as a simple and viable tool in routine clinical practice and in research involving the evaluation of functional performance and associated factors, as well as the need for further investigations for a better understanding about the association of the *ACTN3* gene with functional performance in elderly women. Such findings can thus especially inform health professionals working in primary care. Some limitations of our study must be considered when interpreting the results. In the evaluation of the sample based on the genotypes of the *ACTN3* gene, the low number of elderly women with XX genes did not allow for an isolated analysis of the presence of the R allele. Moreover, we did not evaluate the genotypes considering clinical characteristics of a cognitive aspect, SAH, DM, and the effect of physical activity and other functional performance tests.

It is suggested that future studies consider the evaluation of other functional performance markers in order to identify the relationship between *ACTN3* gene polymorphisms and physical fitness in elderly women. Studies with larger samples and different genders are also needed to increase the statistical power of the analysis of genetic polymorphisms.

Conclusions

In this study, no influence of *ACTN3* gene polymorphisms on the functional performance of elderly women was observed. However, it was found that those of older

age, with higher BMI, waist circumference and body fat percentage took longer to complete the TUG test, which characterizes them with impaired functional performance. On the other hand, elderly women with lower absolute and relative muscle strength executed the TUG test over a longer time. Presence of SAH, altered cognitive aspect and low education were also influential factors for the values verified in the TUG test. In summary, the use of the TUG test proved to be efficient in monitoring the clinical and functional characteristics of elderly women assisted in primary health care, even if independently of the aspects of the *ACTN3* gene.

References

1. Departamento Intersindical de Estatística e Estudos Socioeconômicos (DIEESE). Perfil das pessoas com 60 anos ou mais. [Internet]. SÃO PAULO: DIESE. 2021 [cited 2022 Jul 26]. Available from: https://www.dieese.org.br/outraspublicacoes/2021/graficoPerfil60AnosMais.html
2. IBGE – Instituto Brasileiro de Geografia e Estatística. Projeções da População do Brasil e Unidades da Federação por sexo e idade simples: 2010-2060, revisão 2018. [Internet]. IBGE. 2018 [cited 2022 Jul 26]. Available from: https://www.ibge.gov.br/estatisticas/sociais/populacao/9109-projecao-da-populacao.html?=&t=resultados
3. Santos JL dos, Trennepohl C, Rosa CB, Garces SBB, Myskiw J de C, Costa DH. Impact of sarcopenia, sedentarism and risk of falls in older people's health self-perception. Fisioter em Mov. 2019;32. DOI: https://doi.org/10.1590/1980-5918.032.ao17
4. Vancampfort D, Stubbs B, Firth J, Koyanagi A. Handgrip strength, chronic physical conditions and physical multimorbidity in middle-aged and older adults in six low- and middle income countries. Eur J Intern Med. 2019;61:96–102. DOI: https://doi.org/10.1016/j.ejim.2018.11.007
5. Cunningham C, O' Sullivan R, Caserotti P, Tully MA. Consequences of physical inactivity in older adults: A systematic review of reviews and meta-analyses. Scand J Med Sci Sports. 2020;30(5):816–27. DOI: https://doi.org/10.1111/sms.13616
6. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31. DOI: https://doi.org/10.1093/ageing/afy169
7. Filippin LI, Miraglia F, Teixeira VN de O, Boniatti MM. Timed Up and Go test as a sarcopenia screening tool in home-dwelling elderly persons. Rev Bras Geriatr e Gerontol. 2017;20(4):556–61. DOI: https://doi.org/10.1590/1981-22562017020.170086
8. Souza Saraiva W, Prestes J, Schwerz Funghetto S, Navalta JW, Tibana RA, da Cunha Nascimento D. Relation Between Relative Handgrip Strength, Chronological Age and Physiological Age with Lower Functional Capacity in Older Women. Open Access J Sport Med. 2019;10:185–90. DOI: https://doi.org/10.2147/OAJSM.S227720
9. Lee JE, Chun H, Kim Y-S, Jung H-W, Jang I-Y, Cha H-M, et al. Association between Timed Up and Go Test and Subsequent Functional Dependency. J Korean Med Sci. 2020;35(3). DOI: https://doi.org/10.3346/jkms.2020.35.e25
10. Coelho-Junior HJ, Rodrigues B, Gonçalves I de O, Asano RY, Uchida MC, Marzetti E. The physical capabilities underlying timed "Up and Go" test are time-dependent in community-dwelling older women. Exp Gerontol. 2018;104:138–46. DOI: https://doi.org/10.1016/j.exger.2018.01.025
11. Larsson BAM, Johansson L, Johansson H, Axelsson KF, Harvey N, Vandenput L, et al. The timed up and go test predicts fracture risk in older women independently of clinical risk factors and bone mineral density. Osteoporos Int. 2021;32(1):75–84. DOI: https://doi.org/10.1007/s00198-020-05681-w
12. Pratt J, Boreham C, Ennis S, Ryan AW, De Vito G. Genetic Associations with Aging Muscle: A Systematic Review. Cells. 2019;9(1):12. DOI: https://doi.org/10.3390/cells9010012
13. Oblak L, van der Zaag J, Higgins-Chen AT, Levine ME, Boks MP. A systematic review of biological, social and environmental factors associated with epigenetic clock acceleration. Ageing Res Rev. 2021;69:101348. Available from: https://doi.org/10.1016/j.arr.2021.101348
14. Houweling PJ, Papadimitriou ID, Seto JT, Pérez LM, Coso J Del, North KN, et al. Is evolutionary loss our gain? The role of ACTN3 p.Arg577Ter (R577X) genotype in athletic performance, ageing, and disease. Hum Mutat. 2018;39(12):1774–87. DOI: https://doi.org/10.1002/humu.23663
15. Del Coso J, Moreno V, Gutiérrez-Hellín J, Baltazar-Martins G, Ruíz-Moreno C, Aguilar-Navarro M, et al. ACTN3 R577X Genotype and Exercise Phenotypes in Recreational Marathon Runners. Genes (Basel).

2019;10(6):413. DOI: https://doi.org/10.3390/genes10060413
16. Frattini IR, Ferrari GD, Chiaratto T, Ferezin LP, Hott SC, Bueno Júnior CR. Efeito de polimorfismos genéticos da ECA e da ACTN3 na capacidade e na incidência de quedas em idosas. J Phys Educ. 2016;27(1):2713. DOI: https://doi.org/10.4025/jphyseduc.v27i1.2713
17. Fernández-Araque A, Giaquinta-Aranda A, Rodríguez-Díez JA, Carretero-Molinero S, López-López J, Verde Z. Muscular Strength and Quality of Life in Older Adults: The Role of ACTN3 R577X Polymorphism. Int J Environ Res Public Health. 2021;18(3):1055. DOI: https://doi.org/10.3390/ijerph18031055
18. Weyerstraß J, Stewart K, Wesselius A, Zeegers M. Nine genetic polymorphisms associated with power athlete status – A Meta-Analysis. J Sci Med Sport. 2018;21(2):213–20. DOI: https://doi.org/10.1016/j.jsams.2017.06.012
19. Del Coso J, Hiam D, Houweling P, Pérez LM, Eynon N, Lucía A. More than a 'speed gene': ACTN3 R577X genotype, trainability, muscle damage, and the risk for injuries. Eur J Appl Physiol. 2019 ;119(1):49–60. Available from: https://doi.org/10.1007/s00421-018-4010-0
20. Romero-Blanco C, Artiga-González MJ, Gómez-Cabello A, Vila-Maldonado S, Casajús JA, Ara I, et al. Strength and Endurance Training in Older Women in Relation to ACTN3 R577X and ACE I/D Polymorphisms. Int J Environ Res Public Health. 2020;17(4):1236. DOI: https://doi.org/10.3390/ijerph17041236
21. Houweling PJ, Berman YD, Turner N, Quinlan KGR, Seto JT, Yang N, et al. Exploring the relationship between α-actinin-3 deficiency and obesity in mice and humans. Int J Obes. 2017;41(7):1154–7. Available from: https://doi.org/10.1038/ijo.2017.72
22. Barrón-Cabrera E, Torres-Castillo N, González-Becerra K, Zepeda-Carrillo EA, Torres-Valadez R, Hernández-Cañaveral I, et al. The ACTN3 R577X polymorphism is associated with metabolic alterations in a sex-dependent manner in subjects from western Mexico. J Hum Nutr Diet. 2022; 35:713-21. DOI from: https://doi.org/10.1111/jhn.12948
23. Pickering C, Kiely J. ACTN3, Morbidity, and Healthy Aging. Front Genet. 2018;9:20184. DOI: https://doi.org/10.3389/fgene.2018.00015
24. Kumagai H, Tobina T, Ichinoseki-Sekine N, Kakigi R, Tsuzuki T, Zempo H, et al. Role of selected polymorphisms in determining muscle fiber composition in Japanese men and women. J Appl Physiol. 2018;124(5):1377–84. DOI: https://doi.org/10.1152/japplphysiol.00953.2017
25. Kiuchi Y, Makizako H, Nakai Y, Taniguchi Y, Tomioka K, Sato N, et al. Associations of alpha-actinin-3 genotype with thigh muscle volume and physical performance in older adults with sarcopenia or pre-sarcopenia. Exp Gerontol. 2021;54:111525. DOI: https://doi.org/10.1016/j.exger.2021.111525
26. Cho J, Lee I, Kang H. ACTN3 Gene and Susceptibility to Sarcopenia and Osteoporotic Status in Older Korean Adults. Biomed Res Int. 2017;2017: 4239648. Available from: https://doi.org/10.1155/2017/4239648
27. Brucki SMD, Nitrini R, Caramelli P, Bertolucci PHF, Okamoto IH. Sugestões para o uso do mini-exame do estado mental no Brasil. Arq Neuropsiquiatr. 2003;61(3B):777–81. DOI: https://doi.org/10.1590/S0004-282X2003000500014
28. Lohman TG. Advances in body composition assessment. Champaign [Internet]. IL: Human Kinetics. 1992 [cited 2022 Jul 26]. p. 1–24. Available from: https://typeset.io/papers/advances-in-body-composition-assessment-11s7nqp3cw
29. Byeon JY, Lee MK, Yu M-S, Kang MJ, Lee DH, Kim KC, et al. Lower Relative Handgrip Strength is Significantly Associated with a Higher Prevalence of the Metabolic Syndrome in Adults. Metab Syndr Relat Disord. 2019;17(5):280–8. DOI: https://doi.org/10.1089/met.2018.0111
30. Mills M. Differential expression of the actin-binding proteins, alpha-actinin-2 and -3, in different species: implications for the evolution of functional redundancy. Hum Mol Genet. 2001;10(13):1335–46. DOI: doi.org/10.1093/hmg/10.13.1335
31. Ben-Zaken S, Eliakim A, Nemet D, Meckel Y. Genetic Variability Among Power Athletes. J Strength Cond Res. 2019;33(6):1505–11. DOI: https://doi.org/10.1519/JSC.0000000000001356
32. Boshnjaku A, Krasniqi E, Tschan H, Wessner B. ACTN3 Genotypes and Their Relationship with Muscle Mass and Function of Kosovan Adults. Int J Environ Res Public Health. 2021;18(17):9135. DOI: https://doi.org/10.3390/ijerph18179135
33. Correa-de-Araujo R, Harris-Love MO, Miljkovic I, Fragala MS, Anthony BW, Manini TM. The need for standardized assessment of muscle quality in skeletal muscle function deficit and other aging-related muscle dysfunctions: A symposium report. Front Physiol. 2017;8:87. DOI: https://doi.org/10.3389/fphys.2017.00087
34. Min S-K, Lim S-T, Kim C-S. Association of ACTN3 polymorphisms with BMD, and physical fitness of elderly women. J Phys Ther Sci. 2016;28(10):2731–6. DOI: https://doi.org/10.1589/jpts.28.2731

35. Kahraman M, Ozulu Turkmen B, Bahat-Ozturk G, Catikkas NM, Oren MM, Sahin A, et al. Is there a relationship between ACTN3 R577X gene polymorphism and sarcopenia? Aging Clin Exp Res . 2022;34(4):757–65. DOI: https://doi.org/10.1007/s40520-021-01996-8
36. Kemp GJ, Birrell F, Clegg PD, Cuthbertson DJ, De Vito G, van Dieën JH, et al. Developing a toolkit for the assessment and monitoring of musculoskeletal ageing. Age Ageing. 2018;47(suppl 4):iv1–iv19. DOI: https://doi.org/10.1093/ageing/afy143
37. Zempo H, Miyamoto-Mikami E, Kikuchi N, Fuku N, Miyachi M, Murakami H. Heritability estimates of muscle strength-related phenotypes: A systematic review and meta-analysis. Scand J Med Sci Sports. 2017;27(12):1537–46. Doi: https://doi.org/10.1111/sms.12804
38. Riedl I, Osler ME, Benziane B, Chibalin A V, Zierath JR. Association of the ACTN3 R577X polymorphism with glucose tolerance and gene expression of sarcomeric proteins in human skeletal muscle. Physiol Rep . 2015;3(3):e12314. DOI: https://doi.wiley.com/10.14814/phy2.12314
39. Mangano GRA, Valle MS, Casabona A, Vagnini A, Cioni M. Age-Related Changes in Mobility Evaluated by the Timed Up and Go Test Instrumented through a Single Sensor. Sensors. 2020 Jan 28;20(3):719. DOI: https://doi.org/10.3390/s20030719
40. Ibrahim A, Singh DKA, Shahar S. 'Timed Up and Go' test: Age, gender and cognitive impairment stratified normative values of older adults. PLoS One. 2017;12(10):e0185641. DOI: https://doi.org/10.1371/journal.pone.0185641
41. Zarzeczny R, Nawrat-Szołtysik A, Polak A, Maliszewski J, Kiełtyka A, Matyja B, et al. Aging effect on the instrumented Timed-Up-and-Go test variables in nursing home women aged 80–93 years. Biogerontology. 2017;18(4):651–63. DOI: https://doi.org/10.1007/s10522-017-9717-5
42. Costa MVG da, Lima LR de, Silva ICR da, Rehem TCMSB, Funghetto SS, Stival MM. Risco cardiovascular aumentado e o papel da síndrome metabólica em idosos hipertensos. Esc Anna Nery. 2021;25(1):1–8. DOI: https://doi.org/10.1590/2177-9465-ean-2020-0055
43. Funghetto SS, Silva AO, Dutra MT, Stival MM, Barbalho YGS, Leite MM, et al. Inflammatory parameters in elderly women with and without sarcopenic obesity. Multi-Science J. 2020;3(3):23–8. DOI: https://doi.org/10.33837/msj.v3i3.1306
44. Tanaka M, Ikezoe T, Ichihashi N, Tabara Y, Nakayama T, Takahashi Y, et al. Relationship of low muscle mass and obesity with physical function in community dwelling older adults: Results from the Nagahama study. Arch Gerontol Geriatr. 2020;88:103987. DOI: https://doi.org/10.1016/j.archger.2019.103987.
45. Afonso C, Sousa-Santos AR, Santos A, Borges N, Padrão P, Moreira P, et al. Frailty status is related to general and abdominal obesity in older adults. Nutr Res. 2021;85:21–30. DOI: https://doi.org/10.1016/j.nutres.2020.10.009
46. Melo LM, Ansai JH, Ferreira ACVG, Silva DCP, Vale FAC, Takahashi ACM, et al. Correlation between changes in Timed Up and Go performance and cognition in older people with mild cognitive impairment: A longitudinal study. Clin Biomech. 2022;94:105620. DOI: https://doi.org/10.1016/j.clinbiomech.2022.105620
47. Batko-Szwaczka A, Wilczyński K, Hornik B, Janusz-Jenczeń M, Włodarczyk I, Wnuk B, et al. Predicting Adverse Outcomes in Healthy Aging Community-Dwelling Early-Old Adults with the Timed Up and Go Test. Clin Interv Aging. 2020;15:1263–70. DOI: https://doi.org/10.2147/CIA.S256312
48. Borda MG, Ferreira D, Selnes P, Tovar-Rios DA, Jaramillo-Jiménez A, Kirsebom B-E, et al. Timed Up and Go in People with Subjective Cognitive Decline Is Associated with Faster Cognitive Deterioration and Cortical Thickness. Dement Geriatr Cogn Disord. 2022;51(1):63–72. DOI: https://doi.org/10.1159/000522094
49. Ozaldemir I, Iyigun G, Malkoc M. Comparison of processing speed, balance, mobility and fear of falling between hypertensive and normotensive individuals. Brazilian J Phys Ther. 2020;24(6):503-11. DOI: https://doi.org/10.1016/j.bjpt.2019.09.002
50. Lin C-C, Ou H-Y, Hsu H-Y, Cheng K-P, Hsieh T-J, Yeh C-H, et al. Beyond Sarcopenia: older adults with type II diabetes mellitus tend to experience an elevated risk of poor dynamic balance—a case–control study. BMC Geriatr. 2022;22(1):138. DOI: https://doi.org/10.1186/s12877-022-02826-w
51. Riandini T, Khoo EYH, Tai BC, Tavintharan S, Phua MSLA, Chandran K, et al. Fall risk and balance confidence in patients with diabetic peripheral neuropathy: An observational study. Front Endocrinol (Lausanne). 2020;11:573804. DOI: https://doi.org/10.3389/fendo.2020.573804

Acknowledgements: We would like to thank everyone who accepted to participate in this study. We are also thankful to the Federal District Research Support Foundation [*Fundação de Apoio à Pesquisa do Distrito Federal*] (FAP-DF), the National Council for Scientific and Technological Development [*Conselho Nacional de Desenvolvimento Científico e Tecnológico*] (CNPq), the Coordination for the Improvement of Higher Education Personnel [*Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*] (CAPES) and to the University of Braília [*Universidade de Brasília*],for all the support given to our research

ORCID
Leandro César Teixeira Machado: https://orcid.org/0000-0002-7003-6442
Mateus Medeiros Leite: https://orcid.org/0000-0002-0438-3833
Marina Morato Stival: https://orcid.org/0000-0001-6830-4914
Yuri Gustavo de Sousa Barbalho: https://orcid.org/0000-0002-5584-998X
Filipe Dinato de Lima: https://orcid.org/0000-0001-5748-7540
Luciano Ramos de Lima: https://orcid.org/0000-0002-2709-6335
Alessandro de Oliveira Silva: https://orcid.org/0000-0003-3513-7034
Izabel Cristina Rodrigues da Silva: https://orcid.org/0000-0002-6836-3583
Silvana Schwerz Funghetto: https://orcid.org/0000-0002-9332-9029

Received on Oct 30, 2021.
Reviewed on Jul 14, 2022.
Accepted on Jul 25, 2022.

Correspondence address: Mateus Medeiros Leite. Campus Universitário - Centro Metropolitano, Ceilândia Sul, Brasília-DF. CEP:72220-275. E-mail: leite.mateus@aluno.unb.br