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Gait speed as a mediator of the effect of sarcopenia on dependency in activities of daily living

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Abstract

Background Sarcopenia in older adults is strongly associated with an increase in dependency in activities of daily living (ADL) and with a decline in gait speed. Interestingly, gait speed has been shown to independently predict mortality. In this context, our study aimed to explore the mediator role of gait speed on the relationship between sarcopenia and dependency in ADL.
Methods A cross-sectional study was conducted in Colombia, 19 705 older adults with a mean age of 70 years, 55.6% women, 16.1% with sarcopenia, and 14.7% mild, moderate, or severe dependency in ADL, according to 'SABE Survey 2015'. Sarcopenia was assessed by calf circumference and ADL dependence through the Barthel Index. Gait speed was measured over a distance of 3 m. The association between sarcopenia condition and gait speed and dependency level was analysed by linear regression adjusted by covariates. To examine whether gait speed mediated the association between sarcopenia and dependence components of physical function, simple mediation models were generated using ordinary least squares with the macro PROCESS version 3.2, adjusted for age, sex, and body mass index (BMI).
Results Significant differences ($P < 0.05$) were found in gait speed and dependency in ADL between the sarcopenia and non-sarcopenia groups after adjusting for age, sex, and BMI. BMI was significantly higher in the non-sarcopenia group whereas dependency was significantly higher in the sarcopenia group (19.6% vs. 13.8%). Results from mediation model regression analysis indicated a significant and direct detrimental effect of sarcopenia on dependency in ADL ($\beta = -0.05$; $P < 0.001$), and a significant indirect effect of gait speed on the direct effect (-0.009 to -0.004).
Conclusions The negative effect of sarcopenia on functional dependence was mediated by the gait speed. Therefore, gait speed may positively influence the detrimental effect of sarcopenia for dependency, after adjusting for age, gender, and BMI. Consequently, physical exercise should be promoted and focused to circumvent the gait speed decline associated with age in older people with sarcopenia.

Keywords Gait speed; Sarcopenia; Elderly; Functional Capacity; Latin-American

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Introduction

Sarcopenia is an age-related loss of muscle mass and function in older adults and may favour the appearance of cardiovascular complications or neurodegenerative disorders[1,2]. While its prevalence is variable depending on its localization and the method of evaluation, it is estimated that 29% of older persons in community-dwelling populations and 14–33% in long-term care populations are affected by sarcopenia.[3] In Colombia, recent results from SABE Bogota study estimated that sarcopenia affects 11.5% of the older population.[4] Sarcopenia is related to several functional comorbidities including mobility disorders, risk of falls and fractures, and a loss of physical independence in activities of daily living (ADL).[5,6] It seems that sarcopenia depends on several coadjuvant factors such as inflammatory processes related to aging, nutritional status, intramuscular fat, and genetics, in addition to the reduction of physical activity, which is a crucial precursor of sarcopenia.[2,7] In the context of the aforementioned factors, there is evidence to indicate that both aerobic and resistance training promote a healthy anti-inflammatory milieu largely through the release of muscle-derived myokines,[8] mitigate mitochondria-related dysfunction,[8] and ameliorates age-related loss of muscle mass and strength[9] as well as functional capacity and physical performance.[10]

As a locomotor capacity, gait speed is representative of neuromuscular quality (morphological and neuronal)[1] and a critical determining factor for healthy aging. Indeed, the European Working Group on Sarcopenia in Older People has developed an algorithm including gait speed measurement as the easiest and most reliable way to determine sarcopenia in clinical practice,[11] and also this has been used to diagnose functional disability and dependence in older adults.[11–13] Correspondingly, the loss of muscle mass and consequently the declining of gait speed are age associated; for example, in a 4-year follow-up of older Chinese, the percentage decline in gait speed was −8.2% and −9.0% in men and women, respectively.[14]

On the other hand, sarcopenia, resulting from reduced skeletal muscle mass, is associated with aging.[15] Based on the need for a simpler method of assessing muscle mass in community-based, and large-scale epidemiological contexts, several regions (Europe, USA, and Asia) and organizations incorporated the use of calf circumference (CC), as a marker of muscle mass in elderly people in primary care setting[11,16–18]. In a Japanese study including 526 participants, CC was positively correlated with appendicular skeletal muscle and as a surrogate marker of muscle mass for diagnosing sarcopenia.[19]

In addition, the sarcopenia and the impairment of gait speed are strongly associated to loss of independence in ADL.[20–22] Therefore, these have three factors related to sarcopenia → declining of gait speed → loss of independency in ADL; and between them, a vicious circle is formed. Consequently and taking into account the previous studies, [23,24] the gait speed seems to be the key factor that can worsen this vicious circle or on the contrary improve it. This possible role of gait speed is known as a mediator role and can be explore through mediation analysis. Statistical mediation analysis allows us to understand how an independent variable 'X' affects a dependent variable 'Y' through the indirect effect of the mediating variable 'M'.[15] For instance, mediation analysis could identify if gait speed do and do not mediate these adverse effects of sarcopenia on dependency. This knowledge could help to adjust physical activity program in older adults, emphasizing the improvement of gait speed. Accordingly, the mediator variable 'M' (gait speed) may play a role as the mediator of the relationship between the antecedent variable 'X' (sarcopenia) and the outcome variable 'Y' (loss of independence)[25] (Figure 1).

While it is known that the level of physical fitness affects independence and that exercise can counteract the detrimental effects of sarcopenia, to our knowledge, no studies have addressed the role of the gait speed in the relationship between sarcopenia and loss of functional independence. Here, we hypothesized that gait speed could have an attenuating effect on the relationship between sarcopenia and loss of independence.

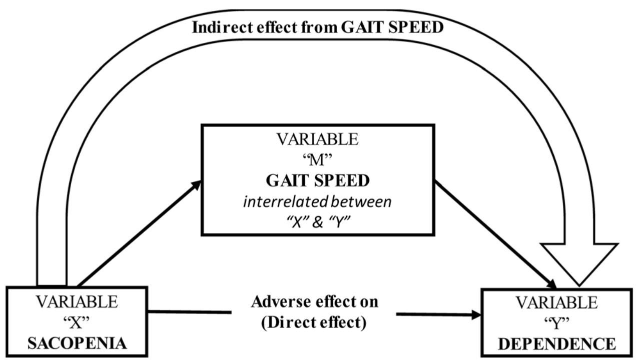
Method

Study design and sample population

The present study is part of the 2015 SABE study survey on health, well-being, and aging in Latin America and the Caribbean. SABE is a multicentre project originally conducted by the Pan-American Health Organization and supported by the Epidemiological Office of the National Health Ministry in Bogotá, Colombia (https://www.minsalud.gov.co/). Details of the survey have been published elsewhere.[26]

In brief, data collection took place between April and September 2015, and the response proportion ranged from ~62% in urban areas to 77% in rural sites.[26] The estimated sample size was 24 553 individuals, and assuming an 80% response the target sample was 30 691 individuals.[26] The estimated sample size was 24 553 individuals, and assuming an 80% response the target sample was 30 691 individuals. However, at fieldwork after implementing several strategies to achieve the overall sample and prevent nonparticipation, response proportion was about 70% and varied by region and urban/rural distributions. The final sample size achieved, including 244 municipalities (*n* = 23 694 older adults) across

Figure 1 Statistical mediation simple diagram.



all departments (i.e. states) of the country. Of the 23 694 participants who took part in SABE Survey, a total of 19 705 remained in the present analysis after excluding participants without a BMI (*n* = 1684), ADL (*n* = 1281), and CC (*n* = 1024) values.

Institutional review boards at the two universities involved in developing the SABE Colombia study [University of Caldas (ID protocol CBCS-021-14) and University of Valle (ID protocol 09-014 and O11-015)] reviewed and approved the study protocol, and written informed consent was obtained from each individual before inclusion and completion of the first examination (including permission to use secondary data and blood samples). Permission was obtained from the National Health Ministry in Bogotá, Colombia, to use the publicly available data for research and teaching purposes (Pontificia Universidad Javeriana). The study protocol to the secondary analysis was approved by the Human Subjects Committee at the Pontificia Universidad Javeriana (ID 20/2017-2017/180, FM-CIE-0459-17). Further details can be obtained from the website of the National Health Ministry in Bogotá, Colombia-SABE (https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/GCFI/doc-metodologia-sabe.pdf).

Data collection

Body measurement assessments were collected by investigators trained in standardized measurement methods, previously trained by research staff from the coordinating centres (Universities of Caldas and Valle). All information collected were obtained through face-to-face interviews conducted at each site on mobile capture devices (tablets) or with printed versions of the questionnaire.

Body mass was measured using weighing scales to the nearest 0.1 kg; height was measured using a stadiometer to the nearest 0.1 cm, with the body mass index (BMI, kg/m^2) was subsequently derived. We defined sarcopenia according to CC, as proposed by Rolland *et al.*,[27] as a 'proxy' measure for assessing muscle mass and early identification of sarcopenia in clinical practice, due to the low cost and ease of application. As described,[27] a CC $<$31 cm is considered to be indicative of low muscle mass. This cut-off has been recommended for use in older individuals by the WHO Expert Committee.[28] Thus, CC measures are practical have acceptable accuracy for estimating sarcopenia when compared with dual-energy X-ray absorptiometry, the gold standard for body composition assessment.[27] CC was measured at a plane perpendicular to the long axis of the calf while the participant was sitting on chair or standing with foot flat on the floor using an inelastic tape measure. Thus, the CC values presented here combine the results of left-foot and right-foot subjects, without consideration for lower body dominance. Gait speed over a distance of 3 m was measured three times, and the analysis used the shortest time of the three attempts.

Functional impairment was assessed with an ADL evaluation using a Spanish-adapted version of the physical level ADL (Barthel Index).[29] The items are weighted: a maximum score of 100 indicates independence, 91–99 minimal dependence, 75–90 mild dependence, 50–74 moderate dependence, 25–49 severe dependence, and 0–24 total dependence.[30] The socio-economic level (I to VI), ethnic group (indigenous, black 'mulato' or Afro-Colombian, white, and others, mestizo, gitano, etc.), and tobacco smoking (patients were categorized as those who do not smoke, those who have never smoked, those who currently smoke, or those who previously smoked) were recorded. A 'proxy physical activity' was evaluated by the following questions: (i) 'Have you regularly exercised, such as jogging or dancing, or performed rigorous physical activity at least three times a week for the past year?' (ii) 'Do you walk at least three times a week between 9 and 20 blocks (1.6 km) without resting?' And (iii) 'Do you walk at least three times a week 8 blocks (0.5 km) without resting?' Those participants who responded affirmatively to two of the three questions were considered physically active. Finally, nutritional status was assessed by using the longer, original version of the Mini-Nutritional Assessment and mobility disability was defined as having difficulty in walking 400 m or climbing a flight of stairs without resting.[26]

Statistical analysis

Before statistical analysis was performed, the normality of variables was tested using the Kolmogorov–Smirnov test. The variables that presented non-uniformity were transformed via natural logarithm or reciprocal transformation (1/x) depending on positive or negative skew.[31] For the descriptive analysis of the sample, we used percentages and frequency distributions for categorical variables, and mean with standard deviation for continuous quantitative variables. The characteristics of the participants with and without sarcopenia were compared with the chi-squared test for categorical variables and Student's *t*-test for continues variables. The association between sarcopenia condition and gait speed and dependency level was analysed by linear regression using three separate models. We entered sarcopenia as predictor variable and gait speed and dependency categories as outcome variables and three separate models: Model 1 adjusted by sex, gender, and BMI; Model 2 adjusted by Model 1 + nutritional status; Model 3 adjusted by Model 2 and mobility disability.

To examine whether gait speed mediated the association between sarcopenia and dependence components of physical function, simple mediation models were generated using ordinary least squares with the macro PROCESS version 3.2, adjusted for age, sex, and BMI. Mediation hypotheses were tested using the bias-corrected bootstrap method with 5000

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samples to calculate confidence intervals (95%). An indirect effect was considered significant when the confidence interval did not include zero.[25]

Results

The descriptive characteristics and differences between the sarcopenia and non-sarcopenia groups are shown in Table 1 . The classification of sarcopenia according to the CC criterion categorized 16.1% of older adults with sarcopenia, with a higher prevalence of sarcopenia in women than in men. Regarding sociodemographic covariates, the results indicated a higher prevalence of sarcopenia with advanced age and with low socio-economic level. In total, 80.7% of the participants with sarcopenia did not achieve the minimum level of recommended physical activity *proxy*. Finally, BMI was significantly higher in the non-sarcopenia group whereas dependency was significantly higher in the sarcopenia group (19.6% vs. 13.8%).

Table 2 shows the associations between sarcopenia and gait speed and dependency level. The results from regression analysis indicate a significant association between sarcopenia and gait speed independently of age, gender, BMI, nutritional status, and mobility disability. Likewise, the association between sarcopenia and dependency level is significant when adjusted the regression by age, gender, BMI, and nutritional status; however, this association is not significant when included in the model the mobility disability.

Table 1 Sample characteristics stratified by sarcopenia status

Sample characteristics	Sarcopenia (*N* = 3168)	Non-sarcopenia (*N* = 16 537)	Total (*N* = 19 705)	*P*-value
Female, *n* (%)	2021 (18.4)	8943 (81.6)	10 964 (55.6)	<0.001
Male, *n* (%)	1147 (13.1)	7594 (86.9)	8741 (44.4)	
Age group, *n* (%)				
60–64	621 (10.3)	5393 (89.7)	6014 (30.5)	<0.001
65–69	640 (12.8)	4360 (87.2)	5000 (25.4)	
70–74	644 (17.3)	3076 (82.7)	3720 (18.9)	
75–79	585 (21.7)	2107 (78.3)	2692 (13.7)	
80–84	392 (26.5)	1086 (73.5)	1478 (7.5)	
85+	286 (35.7)	515 (64.3)	801 (4.1)	
Socio-economic level, *n* (%)				
1	1714 (54.1)	6971 (42.2)	8685 (44.1)	<0.001
2	1073 (33.9)	6420 (38.8)	7493 (38.0)	
3	309 (9.8)	2654 (89.6)	2963 (15.0)	
4	57 (1.8)	383 (2.3)	440 (2.2)	
>5	15 (0.5)	109 (0.7)	124 (0.6)	
Ethnic group, *n* (%)				
Indigenous	236 (10.3)	1124 (7.8)	1360 (8.1)	<0.001
Black	288 (12.6)	1701 (11.8)	1989 (11.9)	
White	546 (23.9)	4002 (27.7)	4548 (27.1)	
Others (mestizo, gitano/gypsy, etc.).	1212 (53.1)	7646 (52.8)	8858 (52.9)	
Smoking status, *n* (%)				
Yes	526 (16.6)	1695 (10.3)	2221 (11.3)	<0.001
No	2642 (83.4)	14 840 (89.7)	17 482 (88.7)	
Physical activity 'proxy', *n* (%)				
Yes	3190 (19.3)	375 (11.8)	3565 (18.1)	<0.001
No	13 327 (80.7)	2790 (88.2)	16 117 (81.9)	
Mobility disability, *n* (%)				
No	2120 (66.9)	11 810 (71.4)	13 930 (70.7)	<0.001
Barely	502 (15.8)	2505 (15.1)	3007 (15.3)	
Some problems	275 (8.7)	1138 (6.9)	1413 (7.2)	
A lot of problems	249 (7.9)	1008 (6.1)	1257 (6.4)	
Cannot walk 400 m, or climb a flight of stairs without rest.	17 (0.5)	63 (0.4)	92 (0.4)	
Body mass index, mean (SD)	22.4 (3.7)	27.9 (4.6)	27.0 (4.9)	<0.001
Nutritional status, *n* (%)				
Malnutrition	282 (8.9)	413 (2.5)	650 (3.3)	<0.001
Risk of malnutrition	1603 (50.6)	5325 (32.3)	6838 (34.7)	
Normal nutritional status	1283 (40.5)	10 782 (65.2)	12 217 (62.0)	
Dependency levels, *n* (%)				
Dependency	1 (0.0)	0 (0.0)	1 (0.0)	<0.001
Severe	13 (0.4)	6 (0.1)	19 (0.1)	
Moderate	250 (7.9)	836 (5.1)	1086 (5.5)	
Mild	357 (11.3)	1433 (8.7)	1790 (9.1)	
Non-dependency	2547 (80.4)	14 262 (86.2)	16 809 (85.3)	

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Table 2 Associations between sarcopenia and gait speed and dependency in older adults

Outcome variable	β	*P*-value	95% CI
Gait speed			
Model 1	−0.040	<0.001	(−0.038 to −0.017)
Model 2	−0.021	0.001	(−0.033 to −0.009)
Model 3	−0.017	0.006	(−0.029 to −0.005)
Dependency			
Model 1	−0.066	<0.001	(−0.088 to −0.044)
Model 2	−0.017	0.007	(−0.055 to −0.009)
Model 3	−0.019	0.101	(−0.041 to 0.004)

Model 1 = adjusted by sex, age, and body mass index; Model 2 = adjusted by Model 1 + nutritional status; Model 3 = adjusted by Model 2 + mobility disability.

Figure 2 shows the mediation models used to determine whether the performance in physical function could mediate the adverse effect of sarcopenia on dependency. In Figure 2, the regression a (β = −0.02; *P* = 0.001) indicated that sarcopenia leads to lower gait speed, and b (β = 0.25; $P < 0.001$) shows a significant direct relationship between higher gait speed and less functional dependence. Also, a direct effect (β = −0.05; $P < 0.001$) was observed for the adverse outcome of sarcopenia on functional dependence. Our mediational hypothesis was confirmed because the confidence intervals did not include zero (−0.009 to −0.004); therefore, gait speed has a mediation effect on the relationship between sarcopenia and functional dependence.

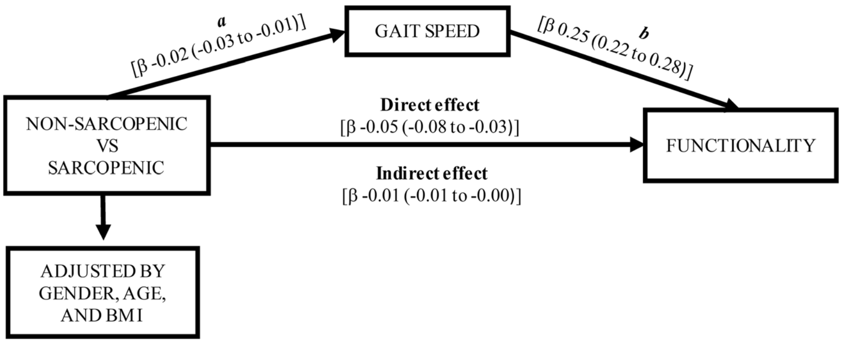
Discussion

The major findings of our analysis were that sarcopenia may negatively influence the independence in ADL in older adults, but this adverse association could be counteracted if physical function performance does not decline. Therefore, gait speed may positively influence the detrimental effect of sarcopenia for dependency, after adjusting for age, gender, and BMI. Older adults who present characteristics of sarcopenia but have a better gait speed than their fewer fit peers will show better functional dependency in ADL, because the association between sarcopenia and dependence was mediated for this physical fitness component. Our results thus contribute to the current knowledge by providing evidence that presenting a better profile in gait speed may ameliorate the negative impact of sarcopenia on dependency.

CC is an anthropometric parameter that is closely related to whole body muscle mass and is known to be associated with the nutrition status of the elderly population.[22] Our findings indicate that lower CC, a valid predictor of sarcopenia,[18,19] might increase the risk of dependency in older adults. This result is similar to previous cross-sectional studies in which lower CC was associated with poor functioning in basic ADL, indicating the high dependency of these patients and a high necessity of care.[20,32] Our results also suggest that sarcopenia induces a lower gait speed. Indeed, it is well documented that the deterioration of gait speed related to sarcopenia during aging is due to quantitative and qualitative changes in muscle structure and function.[1] We also found that the lower the gait speed, the greater dependency, which is in accord with the literature on this topic,[6,33] in which a lower gait speed is related to more problems in ADL. Accordingly, physical activity focused on counteracting the decline in gait speed could prevent functional dependency. Overall, our findings are consistent with previous studies presenting strong evidence on the preventive role of gait speed on all-cause mortality.[24] Consequently, the mediator role of gait speed between sarcopenia and dependence has robustness.

Our results clearly show the differences between older adults with sarcopenia and non-sarcopenia in the performance in gait speed and the level of dependence. As shown in previous studies, our findings confirm that sarcopenia results in lower gait speed[18,34] and independence in daily living.[6,35] Consequently, the promotion of physical activity in older adults is key to maintain the muscle mass to prevent the deterioration of gait speed. In this line, it seems that preventing the deterioration of gait speed is crucial, because it has been shown to be the physical function component more related to sarcopenia, functional independence, vitality, and frailty[22,35–37] and is used as a significant predictor of frailty and all-cause mortality.[22,38] Furthermore, recent studies have

Figure 2 Gait speed as mediator of the effect of sarcopenia on dependency in activities daily living. BMI, body mass index.



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related a decline in gait speed, sarcopenia, pro-inflammatory biomarkers, and functional dependence,[39,40] fostering a vicious cycle that may be broken with physical exercise.[9]

There are several plausible explanations for our finding. First, there was a close relationship between sarcopenia, physical performance (gait speed), and dependency. Muscle mass is a metabolic tissue and endocrine organ, and the construction of muscle mass releases several endocrines called myokines, produced, expressed, and released by muscle fibres under contraction, and exerts both local and pleiotropic effects.[39] In this line, reports of a previous cross-sectional study show a greater proportion of low muscle density in older people with a lower CC scores; moreover, an association was found between high BMI and increased functional disability and the presence of comorbidities and coexisting factors of disability. In addition, reduced muscular strength is known to be significantly and independently associated with functional impairment, walking speed, mobility tasks, physical performance, and all-cause mortality in the elderly population.[39,40] Accordingly, gait speed performance, which is related to muscle mass quality, may be one mechanism for the mediator role between sarcopenia and dependence.

Our study has several limitations that warrant consideration. First, the cross-sectional design of the study limits the causality of the findings and only associations can be drawn, providing hypotheses that can be verified in future studies. A second limitation is the criteria used to establish sarcopenia and non-sarcopenia groups, since the European Working Group on Sarcopenia in Older People proposes an algorithm for sarcopenia case-finding and not only CC; however, it seems that CC is a valid and reliable method to diagnose sarcopenia.[18,19] Another limitation that could affect the results of this study is the level of functional dependence, because this was assessed through a self-reported questionnaire.[41]

To the best of our knowledge, this is the first study aimed at investigating the possible role of gait speed performance in the relationship between sarcopenia and functional dependence. As previously discussed, there is an adverse effect of sarcopenia on functional dependence in older adults, and depending on the level of gait speed, this adverse effect could be aggravated or improved. Thus, gait speed plays a mediator role between sarcopenia and dependence in ADL.

Conclusions and implications

The relationship between sarcopenia and functional dependence is mediated by gait speed, which can attenuate this negative impact. Accordingly, promoting physical exercise in older adults with sarcopenia focused on improving gait speed should counteract the loss of functional independence associated with sarcopenia.

Acknowledgements

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Conflict of Interest

None declared.

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