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Original Article

Identification of Probable sarcopenia based on SARC-F and SARC-CalF in older adults from a low-resource setting.

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Abstract

Objectives: We aimed to investigate the frequency of probable sarcopenia and to compare the performance of SARC-F and SARC-CalF for detecting this condition in outpatient older adults from a low-resource setting. **Methods**: We conducted a retrospective, cross-sectional study in outpatient older adults aged ≥60 years attending a hospital in Peru, between August 2019 and February 2020. Probable sarcopenia was defined as low handgrip strength (<27 kg in men and <16 in women). We used SARC-F and SARC-CalF with their standard cut-off points (≥4 and ≥11, respectively). Low calf circumference was defined as ≤33 cm in women and ≤34 cm in men. We performed sensitivity and specificity analyses. **Results**: We included 206 older adults, 102 (49.5%) aged ≥75 years old and 140 (67.9%) females. Probable sarcopenia was present in 36.40% of the participants. SARC-F ≥4 was observed in 29.61% and SARC-CalF ≥11 in 41.26% of the population. SARC-F≥4 showed 41.33% sensitivity and 77.10% specificity, whereas SARC-Calf ≥11 had 50.67% sensitivity and 64.12% specificity. **Conclusion**: We found that one out of three of the population had probable sarcopenia. SARC-Calf showed superior but still low sensitivity than SARC-F, while both had moderate specificity and thus may be useful for ruling out the disease in clinical practice.

Keywords: Low-resource setting, Probable sarcopenia, SARC-F, SARC-CalF, Sarcopenia

Introduction

Sarcopenia has been defined as the progressive and generalized loss of muscle mass and functional capacity[1]. Currently, it is considered a major public health issue because it is associated with adverse outcomes such as functional decline, frailty, hospitalization, poor quality of life and a threefold higher risk of mortality[2-5]. According to a recent meta-analysis, the global prevalence of sarcopenia ranges from 10 to 27% in adults aged 60 years or over[6]. However, in low- and middle-income countries (LMICs) such as Peru, sarcopenia prevalence is expected to be particularly high, and it is projected to further increase over the next few years due to the rapidly rising aging population[7].

Although sarcopenia has long been associated with aging, it is now recognized that skeletal muscle mass and muscle strength begin to decline from the 4th decade of life[8,9], which broadens the possibilities for implementing early detection strategies. In 2019, the European Work Group of Sarcopenia in Older People (EWGSOP2) published an updated algorithm for diagnosing sarcopenia and recommended incorporating the SARC-F tool as a screening measure[2]. The SARC-F is the pioneer screening tool for sarcopenia and is an acronym of 5 domains: strength, assistance with walking, rising from a chair, climbing stairs, and falls (Malmstrom 2013). It has been reported to have low sensitivity (4-35%), despite

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high specificity (80-98%), which may affect its screening accuracy[10]. Consequently, modified versions have been developed, such as the SARC-CalF, which results from the incorporation of calf circumference. SARC-CalF has shown higher sensitivity than SARC-F (66.7 vs 33.3%, respectively) while maintaining comparable specificity (82.9% vs 84.2%, respectively)[11,12]. SARC-F and SARC-CalF are expected to be suitable tests in low-resource settings as they are inexpensive, rapid, and easy to use in primary care[2,11].

Probable sarcopenia has been defined by the EWGSOP2 as the presence of low muscle strength determined by handgrip strength or the chair stand test. This is one of the most relevant updates of the EWGSOP2, since adverse outcomes from sarcopenia are better predicted by low strength rather than low muscle mass[13-15]. In addition, measuring muscle mass is challenging in primary care since it requires expensive and less accessible tools such as computed tomography (CT), magnetic resonance (MR), and dual energy X-ray absorptiometry (DXA)[2,16], which are not widely available in LMICs. Probable sarcopenia is clinically relevant since it is considered to be enough to trigger the assessment of causes and initiate interventions[2]. However, diagnosing probable sarcopenia in low-resource settings can also be challenging when required training and equipment (hand dynamometer) cannot be implemented. Some studies suggest that the SARC-F may be useful in identifying patients with low muscle strength[17,18], but evidence regarding the accuracy of SARC-F and SARC-CalF for detecting probable sarcopenia is sparse as this term has been recently introduced in the literature. In this context, the aim of this study was: 1) to determine the frequency of probable sarcopenia and 2) to compare the performance of SARC-F and SARC-CalF for detecting probable sarcopenia cases in outpatient older adults from a low-resource setting in Lima, Peru.

Materials and Methods

Study design and setting

Peru is a middle-income country in Latin America where older adults represent 13% of the national population[19]. We conducted a retrospective, cross-sectional study in the Cayetano Heredia Hospital (HCH). The HCH is a tertiary care referral healthcare center located in San Martin de Porres, a low-socioeconomic status district of Lima, the capital of Peru.

Study population

We included data from older adults who attended the outpatient geriatrics clinic at the HCH and underwent a Comprehensive Geriatric Assessment (CGA) between August 2019 and February 2020. CGA involved the evaluation of functionality, cognition, depressive symptoms, nutritional status, social functioning, and physical performance through validated tools and was performed by geriatricians.

The inclusion criteria for this study were as follows: i) older adults aged ≥60 years, ii) patients presenting with stable vital signs and free of acute disorders including fever, decompensated chronic conditions, acute organ failure, acute cerebrovascular or cardiovascular events, active bleeding, and conditions causing acute pain; and iii) patients with complete data on muscle strength assessment, SARC-F score and calf-circumference on their medical records. The exclusion criteria were: i) severe cognitive impairment, defined as 8-10 errors in the Pfeiffer Short Portable Mental Status Questionnaire (SPMSQ) (as it may affect their ability to answer the SARC-F and their performance in the handgrip strength test), ii) patients who were unable to perform grip strength measurement due to specific morbidities, including previous stroke, neuropathy, hand osteoarthritis, and hand or wrist fractures during the last year; and iii) patients presenting with lower extremity edema, as it may mask low calf circumference.

Sampling and Study size

Patients were recruited by convenience sampling in the geriatric outpatient clinic according to the inclusion and exclusion criteria. We assumed the prevalence of probable sarcopenia to be 46.5% based on the results reported by Perez-Sousa et al. in Colombia[35]. A sample size of at least 195 participants was calculated for a statistical power of 80%, a 95% confidence interval, and a precision of 7%. The sample size was calculated with the Epidat 4.2 program.

Data collection and measurements

Data were collected from face-to-face interviews, physical examinations, and medical records.

CGA measurements

Functionality was assessed using the Barthel index, which is a sum score across ten domains of activities of daily living (ADL). We considered a cutoff of <100 to indicate functional dependency[20]. The SPMSQ was used to assess cognition, classifying cognitive impairment as no impairment (0-2 errors), mild (3-4 errors), moderate (5-7 errors), and severe (8-10 errors)[21]. We analyzed cognitive status as a dichotomic variable, with a ≥3 error score indicating cognitive impairment. The 15-item Geriatric Depression Scale (GDS-15) was used to assess the presence of depressive symptoms, defined by a ≥5 score[22]. Social functioning was evaluated through the Gijon social-familial scale (SFES), which assesses family conditions, social contacts, and assistance from the social network[23]. Nutritional assessment was performed using the Spanish-language version of the Mini-Nutritional Assessment (MNA), which consists of 18 items including a 6-items initial screening part[24]. Patients who obtained ≥12 points in the screening section were considered as having normal nutritional status, and those who scored <12 points continued with the remaining questions to complete the full questionnaire. Patients were then classified as malnourished (<17 points) or at risk of malnutrition (17-23.5 points). Gait speed was measured with a stopwatch and was defined as

	Total population (N=206)	Male (n=66)	Female (n=140)
	n (%)	n (%)	n (%)
Age			
60-74 years	104 (50.49)	22 (33.3)	82 (58.57)
≥75 years	102 (49.51)	44 (66.77)	58 (41.43)
Years of education			
None	18 (8.74)	0 (0)	18 (13.14)
1-6 years	103 (50.00)	25 (37.88)	78 (56.93)
7-11 years	66 (32.03)	33 (50.00)	33 (24.09)
≥12 years	16 (7.77)	8 (12.12)	8 (5.84)
Marital status			
Single	36 (17.48)	8 (12.5)	28 (20.14)
Married	96 (46.60)	43 (65.15)	53 (36.80)
Divorced	59 (28.64)	11 (17.19)	48 (34.53)
Widowed	12 (58.25)	2 (3.13)	10 (7.19)
Comorbidities			
Hypertension	115 (55.82)	33 (50.00)	82 (58.57)
Knee and/or hip arthrosis	90 (43.68)	19 (28.79)	71 (50.71)
Diabetes mellitus	39 (18.93)	12 (18.18)	27 (19.29)
COPD	10 (4.85)	3 (4.55)	7 (5.00)
Cardiovascular diseases	35 (16.99)	8 (12.12)	27 (18.75)
Hypothyroidism	32 (15.53)	7 (10.61)	25 (17.86)
Osteoporosis	42 (20.38)	4 (6.06)	38 (27.14)
Others	12 (5.83)	4 (6.06)	8 (5.56)
Multimorbidity			
No	145 (70.38)	58 (87.88)	87 (62.14)
Yes (≥2 comorbidities)	61 (29.61)	8 (12.12)	53 (37.86)
Polypharmacy			
No	167	54 (83.08)	113 (80.71)
Yes (≥5 daily medications)	38 (18.44)	11 (16.92)	27 (19.29)

COPD: Chronic obstructive pulmonary disease

Table 1. Sociodemographic and clinical characteristics of the study population.

the time used by the patient to walk on a flat surface for a distance of 8 meters at their usual pace, without considering the first or the last meter traveled. The shortest time of two consecutive measurements was chosen as the final value. A cut-off point of <1.0 meters per second defined low gait speed[25]. Frailty was assessed using the FRAIL scale, and we classified individuals as frail (≥3 points) or non-frail (which included robust and prefrail patients, corresponding to 0 points and 1-2 points, respectively)[26].

SARC-F and SARC-CalF

The SARC-F is a self-reported symptom-based questionnaire that comprises 5 items: strength, assistance in walking, rising from a chair, climbing stairs, and falls. Total scores range from 0 to 10 points, with a score of ≥4 suggesting risk of sarcopenia[27]. We used the Spanish-language version, which was adapted and validated in Mexican community-dwelling older adults[28] and has shown low to moderate sensitivity (35.6%), high specificity (82.2%), and adequate reliability (Cronbach alpha=0.641).

The SARC-CalF is a 6-item tool produced by adding calf circumference (CC) to the SARC-F. This tool has been shown to significantly improve SARC-F sensitivity (from 33.3 to 66.7%) and diagnostic accuracy for detecting confirmed sarcopenia[29]. The score ranges from

	Total population (N=206)	Males (n=66)	Female (n=140)
	n (%)	n (%)	n (%)
BMI (kg/m²)			
Underweight (≤23.0)	75 (36.40)	29 (43.94)	46 (32.86)
Normal (23.1-27.9)	39 (18.9)	13 (19.70)	26 (18.57)
Overweight (28-31.9)	51 (24.75)	17 (25.76)	34 (24.29)
Obesity (≥32.0)	41 (19.90)	7 (10.61)	34 (24.29)
Calf circumference (cm)			
Normal	102 (49.51)	40 (60.61)	62 (44.29)
Low (≤34-men, ≤33-women)	104 (50.49)	26 (39.39)	78 (55.71)
Physical activity			
Active	60 (29.12)	26 (39.39)	34 (24.46)
Inactive (<150 minutes/week)	145 (70.38)	40 (60.61)	105 (75.54)
Gait speed (m/s)			
Normal (≥1.0)	107 (51.94)	44 (75.86)	63 (50.81)
Low (<1.0)	75 (36.40)	14 (24.14)	61 (49.19)
Handgrip strength (kg)			
Normal	131 (63.59)	32 (48.48)	99 (70.71)
Low (<27-men, <16-women)	75 (36.40)	34 (51.52)	41 (29.29)
Functionality (Barthel index)			
Independent	184 (89.32)	61 (92.42)	123 (88.49)
Dependent (<100 points)	21 (10.19)	5 (7.58)	16 (11.51)
Cognition (SMPSQ)			
No impairment (0-2 errors)	161 (78.15)	55 (83.33)	106 (76.26)
Cognitive impairment (≥3 errors)	44 (21.35)	11 (16.67)	33 (23.74)
Nutritional status (MNA)			
Normal	158 (76.69)	54 (81.82)	104 (74.29)
At risk or malnourished	48 (23.30)	12 (18.18)	36 (25.71)
Frailty (FRAIL)			
Robust or prefrail	191 (92.71)	62 (93.94)	129 (92.81)
Frail	14 (6.79)	4 (6.06)	10 (7.19)
Social risk (SFES)			
No social risk	31 (15.04)	7 (10.61)	24 (17.14)
Social risk	165 (80.09)	56 (84.85)	109 (77.86)
Social problem	10 (4.85)	3 (4.55)	7 (5.00)

BMI: Body mass index, SPMSQ: Short Mental Portable Questionnaire, GDS-15: 15-items Geriatric depression scale, MNA: Mini Nutritional Assessment, SFES: Socio-Familiar Evaluation Scale (Gijon).

Table 2. Anthropometric measures and CGA results of the study population.

0 to 20 points, with a score of ≥11 suggesting risk of sarcopenia. CC is scored 10 points if it is decreased, and 0 point if it is normal. In our study, we considered CC cut-off points of ≤33 centimeters (cm) for women and ≤34 cm for men, based on previous reports from Latin America[11,29]. CC was measured using a tape measure at the level of the maximum circumference below the knee of the non-dominant leg, with the patient in a sitting position, the knees bent at 90 degrees and the feet at ground level.

Age group	Probable sarcopenia*		Total population (N=206)
	Yes, n (%)	No, n (%)	n (%)
60-74 years	24 (32.00)	80 (61.07)	104 (50.49)
≥ 75 years	51 (68.00)	51 (38.93)	102 (49.51)

**Defined as the presence of low handgrip strength (<27 kg for men and <16 kg for women).*

Table 3. Frequency of probable sarcopenia according to age groups.

Tool	Probable sarcopenia*		Total population (N=206)
	Yes	No	
SARC-F ≥4			
Yes	31	30	61
No	44	101	145
SARC-CalF ≥11			
Yes	38	47	85
No	37	84	121

**Defined as the presence of low handgrip strength (<27 kg for men and <16 kg for women)*

Table 4. Performance of the SARC-F and SARC-CalF for probable sarcopenia.

Probable sarcopenia

Probable sarcopenia was defined as a low handgrip strength according to the EWGSOP2 criteria (<27 kg for men and <16 kg for women)[2]. We used a Baseline Hydraulic Hand Dynamometer ® (Fabrication Enterprises, White Plains NY, USA) to measure handgrip strength with the patient seated in an upright position at an armless chair with elbow flexed at 90 degrees. Patients were asked to apply maximal pressure for 3 seconds. Two measurements were performed on each hand, and the maximum grip strength was considered as the final value.

Other variables

Sociodemographic and clinical data included age, gender, years of education, comorbidities, number of medications and anthropometric measures. Multimorbidity was defined as the presence of ≥2 comorbidities[30]. Polypharmacy was defined as the use of ≥5 daily medications[31]. BMI was calculated as weight in kilograms (kg) divided by the square of height in meters (m^2), and was categorized as underweight (≤23 kg/m^2), normal (>23 to <28 kg/m^2), overweight (≥28 to <32 kg/m^2) and obesity (≥32 kg/m^2)[32]. Physical activity was assessed following the World Health Organization (WHO) recommendations for older adults[33]. Patients were asked if they performed any type of aerobic exercise (e.g. walking or tai chi) for a minimum of 150 minutes throughout the week. Based on their responses, participants were categorized into physically active or inactive.

Statistical analysis

Statistical analysis was performed using Stata Statistical Software 14.0 (StataCorp., Texas, USA). Categorical variables were reported as percentages and frequencies, and continuous variables were expressed as mean and standard deviation or medians with interquartile range (IQR), depending on the statistical distribution. The Shapiro-Wilk test was performed to assess normality. The accuracy of the SARC-F and SARC-CalF tools were evaluated using sensitivity-specificity analysis. Positive and negative predictive values (PPV and NPV, respectively) were also calculated.

Results

Two hundred six participants fulfilled the inclusion criteria. The majority of participants were female (67.9%, n=140) and half were over 75 years old and completed between 1 to 6 years of education (49.5%, n=102 and 50.00%, n=103; respectively). The most frequent comorbidities were hypertension (55.82%), knee and/or hip arthrosis (43.68%), osteoporosis (20.38%) and diabetes mellitus (18.93%). Multimorbidity was present in 29.61% (n=61) and polypharmacy in 18.44% of participants (Table 1). Regarding anthropometric measures and physical performance, one third of the participants were in the underweight range (36.40%, n=75), half presented low CC (50.49%, n=104) and most of them were physically

	SARC-F ≥4	SARC-CalF ≥11
Sensitivity (%) (95% CI)	41.33 (34.61-48.06)	50.67 (43.84-57.49)
Specificity (%) (95% CI)	77.10 (71.36-82.84)	64.12 (57.57-70.67)
PPV (%) (95% CI)	50.82 (43.99-57.65)	44.71 (37.92-51.50)
NPV (%) (95% CI)	69.66 (63.38-75.93)	69.42 (63.13-75.71)

Table 5. Sensitivity, specificity and predictive values of SARC-F and SARC-CalF tools for probable sarcopenia.

inactive (70.38%, n=145). According to the CGA measures, 10.19% (n=21) were dependent for ADL, 21.35% (n=44) had cognitive impairment, 23.30% (n=48) were at risk of malnutrition or malnourished, 6.79% (n=14) were frail, and 84.95% (n=175) were classified as having social risk or social problems (Table 2).

Probable sarcopenia was present in 36.40% (n=75) of the participants, with higher frequency among male patients (51.52%, n=34) (Table 2). When analyzing the distribution of probable sarcopenia according to age groups, 68.00% (n=51) of cases were found in older adults aged 75 years and over (see Table 3). SARC-F≥4 and SARC-CalF≥11 were found in 29.61% (n=61) and 41.26% (n=85) of the older adults, respectively (Table 4). The SARC-F cut off ≥4 showed 41.33% sensitivity and 77.10% specificity for detecting probable sarcopenia, with a PPV of 50.82% and NPV of 69.66%. On the other hand, the SARC-Calf ≥11 showed a 50.67% sensitivity, 64.12% specificity, 44.71% PPV and 69.42% NPV (Table 5).

Discussion

In the present study, we aimed to describe the frequency of probable sarcopenia and to investigate the performance of SARC-F and SARC-CalF for detecting this condition in outpatient older adults from a low-resource setting. We found that probable sarcopenia was present in one out of three of the study population according to the EWGSOP2 definition. The SARC-F showed low sensitivity (41.33%) and moderate specificity (77.10%), whereas the SARC-CalF showed higher sensitivity (50.67%) at the expense of specificity (64.12%). Our findings suggest that probable sarcopenia may be a common condition in our context, and specific attention should be given to low-income populations for identifying this disease through accurate tools in regular geriatric care.

Overall, we identified that 36.40% of the participants had probable sarcopenia. To date, some studies have assessed the frequency of probable sarcopenia in older adults, with reports ranging between 5.3% to 73%[15,34-44]. This frequency varies depending on several factors such as age range, ethnicity, socio-economic conditions, comorbidities and lifestyle. In line with several studies, we found the frequency of probable sarcopenia to be two-fold higher for patients aged 75 years and over[15,42], which highlights the need for targeting prompt interventions to this vulnerable group. Nevertheless, very few studies have been conducted in low- and middle-income settings such as Latin America. Mazocco et al. reported a prevalence of probable sarcopenia of 28.5% in community-dwelling older women from Brazil[34], whereas Perez-Sousa et al reported a prevalence of 46.5% in a representative sample of Colombian older adults[35]. Other authors have reported similar prevalence rates, but in populations with evident risk factors for developing sarcopenia, such as advanced age or Parkinson's disease[15,40]. In contrast, Sacar et al reported that 12.7% of a group of outpatient older adults from Turkey had probable sarcopenia, whereas our findings showed a threefold higher proportion[36]. In addition, Dodds et al. showed a prevalence of 7% based on weak handgrip strength among the 1964 British birth cohort aged 69 years[37].

It is evident that our results showed a higher frequency of probable sarcopenia than most of the aforementioned reports, which highlight the relevance of incorporating muscle strength assessment in the mainstream of CGA. Our findings may be attributed to several factors. First, we studied a population with low socio-economic characteristics, which has previously been recognized as a main contributor for developing sarcopenia[45,46]. Furthermore, the vast majority of participants reported poor social functioning (e.g. living alone, having poor social support and/or little participation in community activities), which directly impacts on diet quality and lifestyle. It should be noted that almost one quarter of the population was at risk of malnutrition or malnourished, and over half were physically inactive, which are well-known risk factors for sarcopenia[2]. Further studies should be performed in our context to identify factors associated with low muscle strength in order to prioritize specific groups for interventions.

Regarding SARC-F and SARC-CalF performance, we found the SARC-CalF to have a slightly better sensitivity than the SARC-F for identifying patients with probable sarcopenia. However, sensitivity of both tests was low, which brings limitations to their clinical application. Low sensitivity indicates that a high proportion of older adults with sarcopenia may be overlooked when using these instruments. On the other hand, the moderate specificity values of both tests represent their ability to determine the absence of probable sarcopenia. This is clinically relevant because it enables

avoiding unnecessary testing in terms of time, radiation exposure and cost[12]. Our results are in line with previous reports showing that the SARC-F has low to moderate sensitivity (15-75%) and moderate to high specificity (66.6-99%) for detecting probable sarcopenia[12,17,36,37,47]. A study conducted by Sacar et al. in Turkish older adults found the SARC-F to have 40.3% sensitivity and 88.2% specificity[36], which approximates to our findings. Nevertheless, they also observed that the SARC-F showed a better performance when a cut-off point of ≥1 was used, whereas we found the score of ≥4 to show the best balance between sensitivity and specificity. In contrast, there is limited evidence regarding the diagnostic performance of SARC-CalF for detecting low muscle strength. Our results suggest that measuring CC might improve the ability of SARC-F for finding older adults with low muscle strength, which may be due to its correlation with muscle mass[48].

Our study has some limitations. First, since patients were recruited from the outpatient clinic at one hospital in Peru, the study sample was not representative of the general population and may not be extrapolated to other settings. Second, the confirmation of sarcopenia could not be performed through objective body composition measures due to the lack of advanced diagnostic tools in a resource-limited setting. Third, the lack of national cut-off values for handgrip strength and CC is also a limitation that reflects the need for further studies in Peru and Latin America. However, it is worth mentioning that we used the CC cut-off points suggested by a Brazilian study performed in community-dwelling older adults (≤34 cm for men and ≤33 cm for women) instead of the standard cut-off (≤31 cm)[12]. According to the authors, these results may be extrapolated to the rest of South America since they were obtained from a representative population of the region[29].

On the other hand, this is the first study comparing SARC-F and SARC-CalF performance to detect probable sarcopenia as defined by the EWGSOP2, whereas their accuracy to identify confirmed sarcopenia has been widely described elsewhere[34,47]. Using the EWGSOP2 criteria makes our results comparable to the most recent literature and builds on the existing evidence of probable sarcopenia in Latin America, which is still sparse. This is important because homogeneous data is needed to estimate the magnitude of sarcopenia in LMICs in future studies. It is also relevant because risk factors for sarcopenia such as poor socioeconomic status, malnutrition, food insecurity, and multimorbidity are largely prevalent in these countries[45,46]. Our study contributes to the international literature by highlighting the burden of sarcopenia in older adults from resource-limited settings and the need for further research to standardize cut-off points and identify vulnerable groups in the regular geriatric care. Since probable sarcopenia may be significantly prevalent in these countries, this study encourages the incorporation of muscle strength assessment in the CGA through inexpensive and reproducible tools in primary healthcare.

We conclude that a high proportion of outpatient older adults from a low-resource setting in Peru had probable sarcopenia, suggesting that muscle strength should be assessed in regular geriatric care. The SARC-CalF showed higher but still low sensitivity than the SARC-F for detecting probable sarcopenia. Both tools may be useful for ruling out probable sarcopenia, whereas their ability to identify this condition appears to be limited. Further research is needed in Peru and Latin America to determine the prevalence of probable sarcopenia among older adults and the accuracy of SARC-F and SARC-CalF for detecting this condition in low-resource settings, in order to implement early detection strategies.

Ethical approval

The present study was approved by the Ethics Committee of the Universidad Peruana Cayetano Heredia (Code: 205202). Informed consent was obtained prior to performing the CGA in the outpatient geriatrics clinic.

Authors' contributions

All the authors contributed to the conceptualization and design of the present study. Methodology and data collection: Pamela Ayamamani-Torres, Toshio Yazawa, Guiliana Mas, Tania Tello; Formal analysis and investigation: Claudia L. Vidal-Cuéllar, Guiliana Mas, Tania Tello; Writing - original draft preparation: Claudia L. Vidal-Cuéllar, Guiliana Mas; Writing - review and editing: Guiliana Mas, Pamela Ayamamani-Torres, Toshio Yazawa, Oscar Rosas-Carrasco, Tania Tello. Guiliana Mas and Tania Tello accept responsibility for the integrity of the data analysis. All the authors approved the final version of the manuscript.

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