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Factors associated with health and intrinsic capacity domain in older adults: A secondary analysis for Survey on Health, Well-Being, and Aging in Colombia

Doctoral Thesis

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FACTORS ASSOCIATED WITH HEALTH AND INTRINSIC CAPACITY DOMAIN IN OLDER ADULTS: A SECONDARY ANALYSIS FOR SURVEY ON HEALTH, WELL-BEING, AND AGING IN COLOMBIA

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List of Abbreviations

ACSM: American College of Sports Medicine

ADL: Activities of Daily Living

AHA: American Heart Association

BMI: Body mass index

DBP: Blood Pressure, Diastolic

CC Calf circumference

CCI: Charlson Comorbility Index

CIF: Classification International of Functioning, Disability and Health

CIRS-G: Cumulative Illness Rating Scale for Geriatrics

COPD: Chronic Obstructive Pulmonary Disease

CRF: Cardiorespiratory Fitness

CRP: C– Reactive Protein

DNA: Deoxybonucleic acid

ELSA: English Longitudinal Study of Ageing

EABP: Elevated arterial blood pressure

EWGSOP: European Working Group on Sarcopenia in Older People

FA: Functional Ability

GSAP: Global Strategy and Plan of Action on Aging and Health

GDS-15: Geriatric Depression Scale

HAS: Hertfordshire Aging Study

HBP: High blood Pressure

HDL-c: High-density lipoprotein cholesterol

HWC: High waist circumference

HLFBTg: High levels of fasting blood triglycerides

IC: Intrinsic Capacity

ICD: Index of Coexistent Diseases

IL-6: Interleukin-6

KFI: Kaplan-Feinstein Index

LDL-c: Low-density lipoprotein cholesterol

LMS: Least-Mean-Square algorithm

MS: Metabolic Syndrome

MMI: Multi-Morbidity Index

MMSE: Mini Mental State Examination

MNA-SF: Mini-Nutritional Assessment Scale-Short Form

mARN: messenger Robonucleic Acid

MVPA: Moderate Vigorous Physical Activity

NHMS: National Health and Morbidity Survey

NCD: Non-Communicable Diseases

NICE: National Institute for Health and Care Excellence

PAHO: Pan American Health Organization

PA: Physical Activity

PI: Physical Inactivity

RCTs: Randomized Controlled Trial

SABE: Survey on Health, Wellness and Aging

SD: Standard Deviation

SHARE: Survey of Health, Ageing and Retirement in Europe

SMD: Standard Mean Difference

SP: Slow Phenoptosis

SBP: Blood Pressure, Sistolic

SPPB: Short Physical Performance Battery SPPB

TNF-α : Tumoral Necrosis Factor alpha

WHO: World Health Organization

WVT: Whispered Voice Test

Summary (Inglés-Español)

Summary

This research work focuses on the exploration and analysis of the database of the National Study of Health, Well-Being and Aging, SABE Colombia 2015, especially in what has to do with the prevalence of Metabolic Syndrome in the elderly, and its associated factors. The definition of cohort points of handgrip strength, by sex and age in older adults; as well as the probabilities of adverse events for each of the domains of intrinsic capacity. And the mediating role of the speed of gait of the effect of sarcopenia on activities of daily living.

The SABE Colombia 2015 survey aims to investigate the current situation, in the rural and urban environment, of the elderly, from a social determinants of health approach. Within this interest, three secondary studies related to the characteristics concerning the determinants of health, care and of individual, sociodemographic and environmental factors are proposed.

Study 1 (Chapter 2)

The purpose of this study to analyze the prevalence of metabolic syndrome and associated risk factors in older individuals aged ≥60 years in Colombia. The data for this study came from a secondary cross-sectional, nationally representative SABE study Survey on Health, Well-Being, and Aging in Colombia, 2015**.** Setting and participants: A total of 1637 participants (60.7% women, 70.5±7.9 years) from 86 Colombian municipalities participated. A structured questionnaire was used to collect data on socio-demography, lifestyle, and medical conditions. Measurements included anthropometric variables, handgrip strength, high-density lipoprotein cholesterol, triglycerides, fasting glucose, and blood pressure. Univariate and multivariate regression models were established as part of the main analysis. Using the harmonized Joint Scientific Statement criteria, metabolic syndrome was present in 54.9% of the study population, with a higher prevalence among females than males (59.8% vs. 47.3%). Smoking (odds ratio [OR] = 1.59; 95% confidence interval [CI] = 1.03–2.44; p=.034), male gender (OR = 1.38; 95% CI = 1.05–1.82; p=.020) and sarcopenia (OR = 1.63; 95% CI = 1.06–2.52; p=.026) were associated with increased odds of metabolic syndrome. Metabolic syndrome is prevalent in this study population. Smoking, male gender, and sarcopenia are associated with metabolic syndrome. Screening for promotion of healthy lifestyle and nutrition counselling should be offered routinely among this nationally representative sample of Colombian older adults.

Study 2 (Chapter 3)

The purposes of this study were three-fold: (1) to describe handgrip strength in older individuals aged ≥ 60 years in Colombia; (2) to identify sex- and age-specific muscle weakness cut-off points in older adults; and (3) to determine the odds of adverse events for each of the intrinsic capacity domains for individuals with handgrip strength greater than the muscle weakness cut-off points, as compared with their weaker counterparts. Methods: A cross-sectional study was conducted in Colombia, among 5,237 older adults aged ≥60 years old (58.5% women, 70.5±7.8 years), according to "SABE Survey 2015". Handgrip strength data were obtained with a Takei dynamometer. Sociodemographic variables, five domains of intrinsic capacity (i.e., locomotion, vitality, cognition, psychological, and sensory), and medical conditions were assessed and analyzed. Adjustments variables were age, ethnicity, socioeconomic status, urbanicity, body-mass index, smoking status, alcohol intake, drug use, physical activity, and comorbid chronic diseases. Sex-stratified analyses were conducted with logistic regression models. Handgrip strength was greater among men than among women (26.7 ± 8.5 kg vs 16.7 ± 5.7 kg, respectively, p<0.001) at all ages. Weak handgrip strength cut-off points ranged from 17.4 to 8.6 and 10.1 to 4.9 in men and women, respectively. Overall, participants with optimal handgrip strength had better intrinsic capacity (in men, odds ratio [OR]=0.62, 95% confidence interval [CI] 0.53 to 0.71; p<0.001; and in women, OR=0.79, 95%CI 0.68 to 0.92; p=0.002) than their weaker counterparts. Also, men with optimal handgrip strength had a lower risk of hospitalization (OR=0.47, 95%CI 0.29 to 0.78; p=0.004) than their weaker counterparts. This study is the first to describe handgrip strength values and cut-off points for muscle weakness among a nationally representative sample of Colombian older adults by age and sex. After categorizing older adults as weak or not weak based on the handgrip cut-off points, non-weakness was associated with a decreased odds of intrinsic capacity impairments. These cut-off points may be good candidates for clinical assessment of risks to physical and mental health in older Colombian adults.

Study 3 (Chapter 4)

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RESUMEN

El presente trabajo de investigación se centra en la exploración y análisis de la base de datos del Estudio Nacional de Salud, Bienestar y Envejecimiento, SABE Colombia 2015, en especial, en lo que tiene que ver con la prevalencia de Síndrome Metabólico en personas mayores, y sus factores asociados. La definición de puntos de cohorte de la fuerza prensil, por sexo y edad en adultos mayores; así como las probabilidades de eventos adversos para cada uno de los dominios de capacidad intrínseca. Y el papel mediador de la velocidad de la marcha del efecto de la sarcopenia en actividades de la vida diaria.

La encuesta SABE Colombia 2015 tiene como propósito indagar sobre la situación actual, en el entorno rural y urbano, de las personas adultas mayores, desde un enfoque de determinantes sociales de la salud. Dentro de este interés se proponen tres estudios secundarios relacionados con las características concernientes con los determinantes de la salud, el cuidado y de los factores individuales, sociodemográficos y del entorno**.**

Estudio 1 (Capítulo 2)

En este primer estudio se analizó la prevalencia del síndrome metabólico y los factores de riesgo asociados en personas mayores de 60 años o más. Los datos provienen de una encuesta secundaria, representativa a nivel nacional, del estudio SABE, sobre salud, bienestar y envejecimiento en Colombia, 2015. Se incluyeron 1637 participantes (60.7% mujeres, 70.5 ± 7.9 años) de 86 municipios colombianos. Se recopilaron datos sociodemográficos, estilo de vida y condiciones médicas. Las mediciones incluyeron variables antropométricas, fuerza de agarre, colesterol de lipoproteínas de alta densidad, triglicéridos, glucosa en ayunas y presión arterial. Se utilizaron modelos de regresión univariada y multivariada. El síndrome metabólico estuvo presente en el 54,9% de la población del estudio, con una prevalencia más alta entre mujeres que entre hombres (59,8% frente a 47,3%). El Fumar (cociente de probabilidad [OR] = 1.59; intervalo de confianza del 95% [CI] = 1.03–2.44; p = .034), ser de sexo masculino (OR = 1.38; IC del 95% = 1.05–1.82; p = .020) y poseer sarcopenia (OR = 1,63; IC del 95% = 1,06-2,52; p = 0,026) se asociaron con mayores probabilidades de tener síndrome metabólico.

Estudio 2 (Capítulo 3)

El propósito de este segundo estudio fue describir la fuerza prensil en personas mayores de 60 años o más en Colombia; determinando los puntos de corte de la fuerza por sexo y edad en adultos mayores; así como las probabilidades

de eventos adversos para cada uno de los dominios de capacidad intrínseca para individuos con una fuerza prensil mayor, en comparación con sus contrapartes más débiles. Se realizó un estudio transversal con datos de 5237 adultos mayores de 60 años o más (58,5% mujeres, 70,5 ± 7,8 años), según la Encuesta SABE 2015. Los datos de fuerza prensil se obtuvieron con un dinamómetro Takei. Se evaluaron y analizaron las variables sociodemográficas, los dominios de capacidad intrínseca (es decir, locomoción, vitalidad, cognición, psicológica y sensorial) y condiciones médicas. Las variables de ajuste fueron la edad, el origen étnico, el estado socioeconómico, la urbanidad, el índice de masa corporal, el estado de fumador, el consumo de alcohol, el consumo de drogas, la actividad física y las comorbilidades. Se realizaron análisis estratificados por sexo con modelos de regresión logística. La fuerza prensil fue mayor entre los hombres que entre las mujeres (26.7 ± 8.5 vs. 16.7 ± 5.7 kg, respectivamente, P <0.001) en todas las edades. Los puntos de corte de fuerza prensil baja oscilaron entre 17,4 y 8,6 y entre 10,1 y 4,9 en hombres y mujeres, respectivamente. En general, los participantes con una fuerza prensil óptima tenían mejor capacidad intrínseca [en hombres, cociente de probabilidad (OR) = 0,62, 95% de intervalo de confianza (IC) de 0,53 a 0,71; P <0,001; y en mujeres, OR = 0,79, IC del 95%: 0,68 a 0,92; P = 0.002] que sus contrapartes más débiles. Además, los hombres con una fuerza prensil óptima tenían un menor riesgo de hospitalización (OR = 0,47; IC del 95%: 0.29 a 0.78; P = 0.004) que sus contrapartes más débiles. Este estudio es el primero en describir los valores de fuerza prensil y los puntos de corte para la debilidad muscular en una muestra representativa a nivel nacional de adultos mayores colombianos por edad y sexo. Después de clasificar a los adultos mayores como débiles o fuertes según los puntos de corte de la fuerza, la fuerza se asoció con una disminución de las probabilidades de deterioro de la capacidad intrínseca.

Estudio 3 (Capítulo 4)

En el tercer estudio planteamos explorar el papel mediador de la velocidad de la marcha en la relación entre la sarcopenia y la dependencia en las ADL. Un total de 19,705 adultos mayores con una edad media de 70 años, 55.6% mujeres, 16.1% con sarcopenia y 14.7% dependencia leve, moderada o severa en ADL. La sarcopenia se evaluó mediante la circunferencia de la pantorrilla y la dependencia de ADL a través del Índice de Barthel. La velocidad de la marcha se midió en una distancia de 3 m. El análisis de covarianza se utilizó para explorar las diferencias en la velocidad de la marcha y el índice de Barthel entre los grupos de sarcopenia y no sarcopenia. Se realizo una mediación para examinar si la velocidad de la marcha mediaba la asociación entre la sarcopenia y los componentes de dependencia de la función física. Se encontraron diferencias significativas (p <0.05) en la velocidad de la marcha y la dependencia en ADL entre los grupos de sarcopenia y no sarcopenia después de ajustar por edad, sexo e índice de masa corporal. Los resultados del análisis de regresión del modelo de mediación indicaron un efecto perjudicial significativo y directo de la sarcopenia sobre la dependencia en ADL (ß= −0.05; P = 0.000), y un efecto indirecto significativo de la velocidad de la marcha sobre el efecto

directo (−0.009 a −0.004). El efecto negativo de la sarcopenia sobre la dependencia funcional fue mediado por la velocidad de la marcha.

Declaration

Jorge Enrique Correa Bautista, express that doctoral thesis is based on three articles (chapters 2 to 4), which have been published in indexed international journals. In order to meet the requirements of the doctoral program, the structure of the published works has been adjusted to present this document. These modifications do not change the contents of the published articles.

The role I played in each of these publications is presented below.

- Application for public-use data files and documentation to SABE Survey.
- Analysis and interpretation of results.
- Writing of the papers included in this document.

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List of Publications

1. Ramírez-Vélez R, Correa-Bautista JE, Cano CA, Izquierdo M, et al. Metabolic Syndrome and Associated Factors in Older people of Colombia: a secondary analysis of SABE Colombia 2015 (*In elaboration*)

2. Ramírez-Vélez R, Correa-Bautista JE, García-Hermoso A, Cano CA, Izquierdo M. Reference values for handgrip strength and their association with intrinsic capacity domains among older adults. J Cachexia Sarcopenia Muscle. 2019;10(2):278-286.

3. Perez-Sousa MA, Venegas-Sanabria LC, Chavarro-Carvajal, DA., Cano-Gutiérrez, CA, Izquierdo M, Correa-Bautista JE, Ramírez-Vélez R. Gait speed as a mediator of the effect of sarcopenia on dependency in activities of daily living. J Cachexia Sarcopenia Muscle. 2019 May 8. doi: 10.1002/jcsm.12444. [Epub ahead of print]

CHAPTER 1

APPROACHES TO AGING, INTRINSIC CAPACITY, AND MULTIMORBIDITIES

1. Global and regional aging in numbers

Aging is a global phenomenon. It is estimated that the adult population over 60 years of age reached 962-million people in 2017. It is expected for this number to duplicate in the next 30 years, estimating that by 2050 this figure can reach 2.1-billion elderly people throughout the world (1,2). According to global epidemiological analyses, growth of the elderly population is not equal in each of the regions of the world, given that this population growth depends on the economic development in each of the world´s regions. It is estimated that 71-million people (>60 years of age) live in Latin America, which represents 11.2% of the region's population. In the Caribbean, this figure reaches 13.2%. By 2100, the population in Latin America and the Caribbean will be comprised of 32% elderly adults (3,4).

Rapid global epidemiological growth of the elderly population is justified by progress in the control and treatment of chronic disease, pandemic control, reduction of military conflicts, progress in agriculture, technological development, access to better public services, aspects that have contributed to reduced all-cause mortality in the world (5) and a five-year increase in life expectancy of the global population in the last 18 years (6).

2. Aging, health, and wellbeing in Colombia

The 2018 Colombian National Census reported that 13.4% of the population is composed of elderly individuals (>60 years of age); where women represent a higher proportion with 54.2% against men with 45.8%, respectively (7). The trend in Colombia is of rapid elderly population growth, expecting by 2021, to have an elderly individual for every two Colombian adolescents (8). Added to this, it should be considered that Colombia is one of the countries in the region with greater social inequality in this population, which is why conditions to access healthcare services, education, pension, and quality of life are low (9,10).

In response to this situation, the national government has been consolidating the National Policy on Aging and Old Age (8). This policy was formulated in late 2007, seeking to protect, promote, and defend the rights of elderly individuals in compliance with that mandated by Legislation 1151 of 2007 (11). Another important norm is Legislation 1315 of 2009 (12), which determines the minimum conditions to guarantee care and provide quality comprehensive services to the elderly. This normative framework seeks to improve conditions of equality, autonomous life, dignity, and health in the elderly in Colombia (8).

Thereafter, the Ten-Year Public Health Plan for 2012 – 2021 (PDSP, 2012-2021) was proposed (13) in which aging is a priority from an approach of health determinants. One of the strategies proposed by the (PDSP, 2012-2021) is that of designing an information structure that permits characterizing the population aging process at national and territorial levels, given that Colombia needs up-to-date data

and primary sources of information on the situation of the elderly (14). To meet this need, the Ministry of Health and Social Protection and COLCIENCIAS have promoted the SABE Temporary Union, conformed by diverse research groups from Universidad del Valle and Universidad de Caldas, with collaboration from the National Consulting Center (CNC, for the term in Spanish) to develop the Survey on Health, Wellbeing, and Aging (SABE-Colombia) between 2014 and 2015 (14,15).

The SABE-Colombia survey sought to know the current situation, in the rural and urban settings, of the elderly population in Colombia through interdisciplinary in-depth exploration and evaluation of old age and aging, within the framework of the determinants of active aging and from the model of Social Health Determinants (15).

The sample was comprised of 24,553 people and, supposing an 80% response, the objective sample was made up of 30,691 individuals from 32 departments (16). However, during the field work and after implementing various strategies to achieve the general sample, the response proportion was of approximately 70%, which varied according to the regional and urban/rural distribution. The final sample size (including 244 municipalities) was of 23,694 elderly individuals (16).

The survey reported information on socioeconomic aspects, the physical and social environment, behavior, cognition and affect, functionality, mental wellbeing, health conditions, and use and access to health services. Likewise, biochemical tests were taken to measure levels of glucose, lipid profile, and hemoglobin. Anthropometric measurements were taken, like weight, height, circumference of the waist, calf, and arm. In addition, blood pressure was measured and functionality tests were performed, like handgrip strength, gait rate, balance and time of incorporation from a chair (14,15).

The 2015 SABE-Colombia is part of the multicentric project by the Pan American Health Organization (PAHO), the Survey on Health, Wellbeing, and Aging by SABE 2015 in Latin America and the Caribbean (16–18). This project was conducted in seven capital cities of Latin America and the Caribbean (17). The SABE survey becomes a starting point in the systematic study of aging in urban zones in the region of Latin America and the Caribbean (19). This regional effort has permitted achieving specialized databases between countries that are comparative and compatible to each other; likewise, it has permitted development of expertise among professionals from different areas and has favored profound reflection on the conditions of the elderly in the region.

Another antecedent of the 2015 SABE-Colombia is the SABE Bogotá study conducted in 2012, with a sample of 2,000 elderly individuals from urban and rural zones in the city, ranging between 60 and 100 years of age, with this being a representative sample of over 700,000 people 60 years of age or more living in the city (19). The results obtained permitted characterizing conditions of sarcopenia in

adults with COPD/Asthma (20), the frequency of vaccinations in the elderly population, and the association with socioeconomic and health factors (21), prevalence and frailty and sarcopenia and its associated factors (22); along with the report of the prevalence of multi-morbidity and depression symptoms in the elderly in the city (23). This work of SABE Bogotá was considered a preparation exercise for the national survey. This PhD work was based on performing secondary analyses of the data from this national survey.

3. Healthy Aging

Aging has been described as a multifactor phenomenon of decline or progressive, non-linear and irreversible loss of the individual's capacities occurring throughout life (24). This phenomenon is conditioned by different cultural, social, intrapersonal, biological processes and by the life story of each individual, added to the development of risk factors against chronic disease and exposure to environmental conditions. In light of this fact, the aging phenomenon is a process inherent to life itself (25). It can be optimized by improving health and reinforcing social, productive, learning, wellbeing, and quality-of-life opportunities.

Different theoretical and conceptual models of psychosocial and biomedical origin have been proposed to understand and promote a better way of aging (26). Among these, the successful aging model proposed by Rowe and Kahn (27) is highlighted. This is understood as the actions carried out to reach a high level of satisfaction and happiness upon processes of life changes. Therefore, with sufficient levels of physical activity, maintenance of cognitive functions, and preservation of interpersonal relationships, the possibility of getting sick can be reduced (28). Another model is that of Selection, Optimization, and Compensation (SOC) by Baltes & Baltes (29). It centers on the strategies people use to compensate for losses due to aging, generating compensations that permit maintaining a sufficient level of functionality with a high degree of perception of wellbeing. In this same line, there is the model proposed by Kahana & Kahana (30), which is based on the implementation of prior strategies to prevent and control stressful factors or their effects that can alter the perception of wellbeing. Recently, other proposals have emerged, like: the productive aging (31), positive aging (32), optimal aging (33), and independent aging (34). Concepts formulated from the positive view of aging, counteracting the focus of decline or functional loss of the pathological elderly individual, resulting from the disease burden (35).

Based on the aforementioned, since the 1990s, the World Health Organization (WHO) has promoted the concept of Active Aging, proposed from an approach of equality of rights for the elderly, prioritizing independence, participation, dignity, assistance, and performance of their own desires. The concept of healthy aging is understood as a process of development and maintenance of the functional capacity in individuals, which permits achieving wellbeing in old age (36,37), where functionality is the determinant of the interaction with the environment, independent

from the presence or not of disease. What it seeks is to have a higher number of years of life with a good state of health to continue with life's purposes. Hence, healthy aging focuses on an individual's functional capacity, on their physical and mental capacities and how these allow them to interact in the environments they inhabit (38).

From this logic, in 2016, the Global Strategy and Action Plan on Aging and Health (GSAP) was first proposed as a commitment by the member states of the world health assembly to adopt measures to trigger the creation of the next ten-year plan for active and healthy aging, 2020 – 2030 (39). Among the multi-sector actions proposed there is active aging, as a way of recognizing and exalting the capabilities and experience of the elderly in social, economic, cultural, spiritual activities and as a citizen in the possibilities of participating and contributing to society (40). What active aging provides are opportunities of social integration, health, and wellbeing through maintaining and improving the functional and intrinsic capacity in the elderly (34,41).

In contrast to the aforementioned, one of the principal problems the elderly have is physical inactivity (PI), which has been increasing significantly in the last 20 years globally (42). Due to its rapid spread, PI is considered a pandemic, which is strongly associated with the presence of non-communicable diseases (NCD) in adults and in the elderly (43). Within this context, recent cross-sectional studies indicate that the prevalence of PI in the elderly is above 50%, as reported by Chan *et al*.,(44) after analyzing adults ≥60 years of age (n = 3,790) from the National Health and Morbidity Survey (NHMS) in Malaysia, demonstrating 48.8% PI prevalence. Likewise, higher prevalence has been reported, like those in the United States (45) and Brazil (46) with 73% and 62%, respectively. In Europe, (47), PI prevalence is at 12.5%, according to the Survey of Health, Aging, and Retirement in Europe (SHARE), which analyzed people over 55 years of age (n = 19,298) from a total of 58,489 people from 16 countries. The PI prevalence varied among different European countries, ranging between 4.9% in Sweden and 29% in Portugal.

These prevalence studies also suggest various factors associated with PI in the elderly, like gender, where PI is more prevalent in women, in elderly people, in adults with higher income, in people who consume less fruits and vegetables (<5 portions/day), in people who remain mostly seated, and with presence of NCD, like diabetes, and with mobility limitations. Similarly, several authors (48–50) have shown how PI is a risk factor associated with suffering from NCD, like type II diabetes, cardiovascular disease, and premature mortality. Additionally, nearly 92% of the elderly live with a chronic disease (51) and 62% of the elderly live with two or more co-morbidities (52).

3. Benefits of physical activity in the elderly

Physical activity (PA) is considered one of the most important strategies to control and prevent NCD. Organizations, like the American College of Sports

Medicine) (53) and the American Heart Association (54) coincide on recommending for the elderly to engage in at least 150 minutes (2 hours and 30 minutes) to 300 minutes (5 hours) of moderate-intensity PA per week, or 75 minutes (1 hour and 15 minutes) to 150 minutes (2 hours and 30 minutes) of vigorous-intensity PA, or an equivalent combination between both intensities, accompanied by at least two days of muscle strengthening activities per week, as proposed by the Physical Activity Guidelines for Americans (55,56).

Together with the aforementioned, consistent epidemiological and experimental evidence exists on the benefits of PA on health and on the physical and mental function in the elderly (57–61). An example of this is found in a recent meta-analysis proposed by Northey *et al*., (62) which analyzed 39 clinical trials with interventions of aerobic physical exercise, endurance training, multi-component training, and Tai chi in adults over 50 years of age. The exercise interventions were conducted in 45- to 60-min sessions with moderate intensity. The results reported significant association (0.29; 95%CI: 0.17 to 0.41; p <0.01) among the subjects who exercised with improvement in the cognitive function.

Other studies also confirm how PA can delay brain aging (63–66). Raichlen *et al*., (67) examined neuro images from the National Biobank of the United Kingdom in (n = 7,148 subjects; male = 3,062; female = 4,086; age = 62.14 ± 7.40 years), crossing such with variables, like moderate to vigorous physical activity (MVPA) and cardiorespiratory fitness (CRF). These authors reported how MVPA and CRF associated positively with changes in the general volume of grey matter (p = 1.28 E-05). Likewise, when data were adjusted first by CRF, followed by MVPA, these associated positively with changes in the volumes of the left and right hippocampus (p left = 0.01; p right = 0.02), but without changes in the general volume of grey matter. These results suggest that MVPA and CRF are powerful neuro-physiological stimuli that, through different mechanisms, can generate structural changes at brain level in the elderly.

Similarly, other works have centered on understanding the changes caused by PA on some health predictors, like inflammatory markers in the elderly. However, although the results are not completely conclusive, it is considered a promising line of research to understand the effects of PA on the systemic inflammatory response, which is generated by NCD. Recently, Guohua Zheng *et al*., (68) performed a meta-analysis with 11 randomized controlled trials (RCT) in a sample of 1,250 participants. The experimental group engaged in aerobic exercise during four weeks, with three or more exercise sessions per week. The results showed that aerobic exercise reduces significantly the inflammatory markers (C– Reactive Protein (CRP): Standard Mean Difference, SMD = 0.53, 95%CI 0.26–0.11, p = 0.0002; Tumoral Necrosis Factor Alpha (TNF-α): SMD = 0.75, 95%CI 0.31–1.19, p = 0.0007; interleukin 6 (IL-6): SMD = 0.75, 95%CI 0.31–1.19, p = 0.0007), which is why aerobic exercise has a positive effect on reducing CRP, TNF-α, and IL-6 in the elderly.

These findings coincide with another meta-analysis proposed by Sardelli *et al*., (69) who analyzed the effects of endurance training on inflammatory markers of the elderly in 13 RCTs, where endurance training reduced CRP in the elderly [DME] = - 0.61; 95%CI = -0.83; -0.31, p <0,001), tended to reduce IL-6 (SMD = -0.19, 95%CI = -0.42; 0.02, p = 0.07), and reported no changes in TNF-α. Other analyses in the subgroups showed a possible association between muscle mass for changes in CRP and in TNF-α. Reductions in CRP and TNF-α only occurred in the RCTs that carried out a greater number of exercise (> 8), greater weekly frequency (three times/week), and durations over 12 weeks. These results demonstrate the anti-inflammatory effect of aerobic and endurance physical exercise, which depends on the muscle mass and CFR in the elderly.

All these works on the benefits of PA in the elderly reveal its importance within the active aging approach, with multi-component interventions with physical exercise being fundamental to diminish morbidity and delay disability processes in the elderly (70,71).

5. Intrinsic and functional capacity in the elderly

Intrinsic Capacity (IC) is a term proposed recently by the WHO (2). It is conceived as a multi-dimensional indicator of the functional state of people, which is quantifiable throughout life (72). The IC is defined as the sum of all the individual's physical and mental capacities (59). This capacity becomes the base for the Functional Ability (FA). A higher relation between individuals and their environment indicates higher FA degree and independence (58,60).

The IC focuses on the function and not on the deficiencies or losses resulting from disease. It is believed that IC is a holistic approach, proposed to better comprehend the aging process (2). It may be said that IC is a theoretical construct that originates from the International Classification of Functioning, Disability, and Health (ICF) (75), also derives from the results of the English Longitudinal Study of Aging (ELSA) and the Hertfordshire Aging Study (HAS) in the United Kingdom (76).

Figure 1 represents IC as the inner part of a cube, center of FA, determined by the individual's personal and phenotypic characteristics. Likewise, it is conditioned by trends related with age, health habits, traits and abilities, gradual accumulation of biological changes, risk factors, presence of diseases and lesions, and geriatric syndromes.

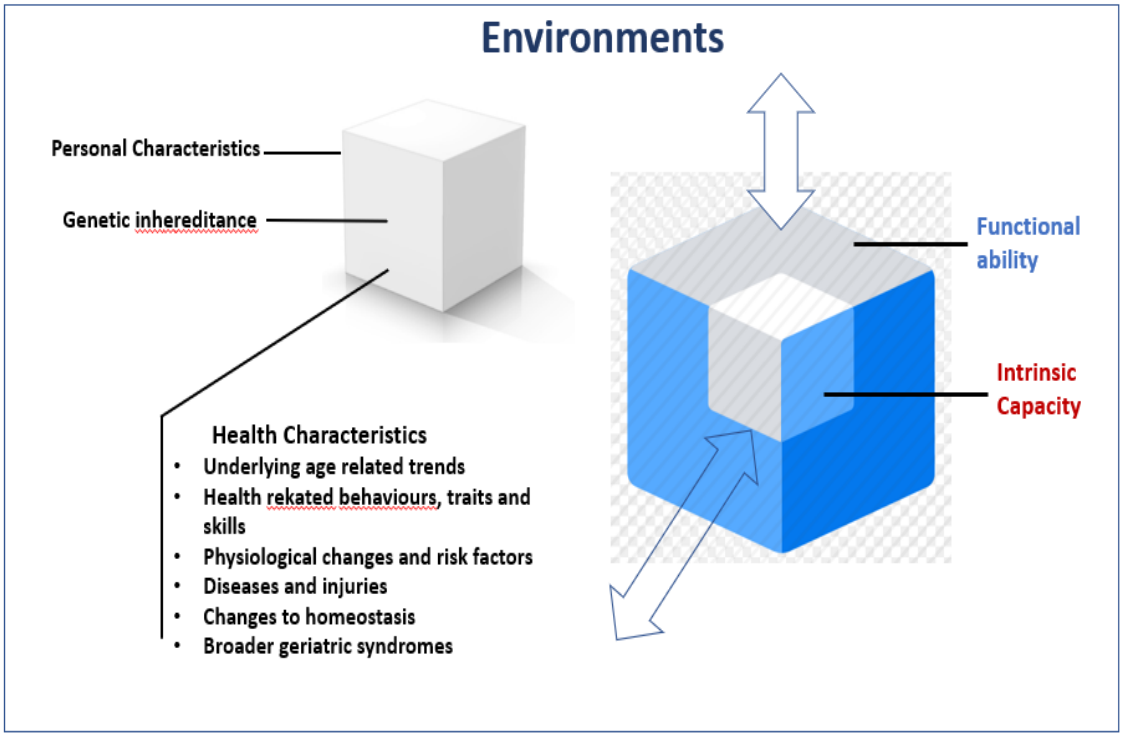

Figure 1. Conceptual model of healthy aging. Modified from reference (2). Reprinted courtesy of the Copyright Holder under a Creative Commons License CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/)

The IC is a dynamic construct that changes throughout life. The Healthy Aging model by the WHO proposes that IC reaches its maximum point during adult age and tends to decline as of middle age. This decline is different in each person, among individuals, and within each IC domain (74). These differences may be observable through continuous evaluations of the IC domains, which permit estimating a course or trajectory of IC over time, independent of the biological aging (2), Figure 2.

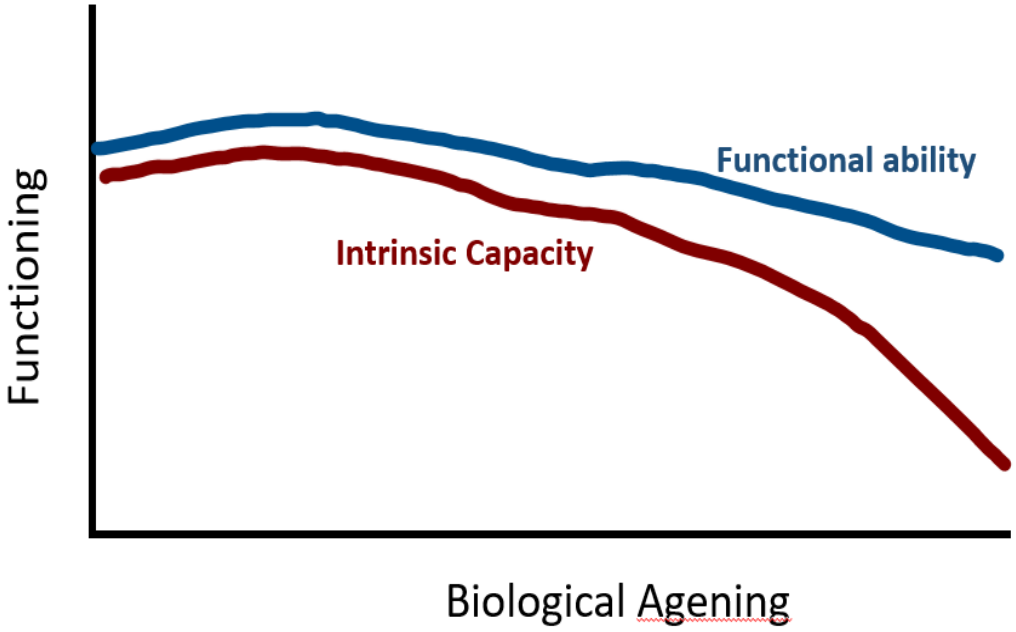

Figure 2. Trajectories of FA and IC. Modified from reference (2). Reprinted courtesy of the Copyright Holder under a Creative Commons License CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/)

Cesari *et al*., (77) refer to five IC domains, which are necessary for its proper screening. These domains are: cognition, psychological aspects, sensory (vision and audition), locomotion, and vitality. It is important, to consider these domains as a cluster of information, which must be studied together from an integrative approach. Measurement and follow up of these domains become important biomarkers to predict health, functionality, quality of life, and dependence in the elderly (78). The following describes each of these aspects.

Regarding the cognitive domain, the decline of the cognitive function is a frequent problem during aging. In recent decades, research has focused on demonstrating the relationship between the decline in the cognitive function as a stage prior to dementia (79), Alzheimer's disease (80), and Parkinson (81). Among the possible mechanisms showing this relationship are changes in the cerebral vascular function during aging (82). The cognitive function is an important indicator of risk of mortality, disability, and of poor quality of life in the elderly (83). Due to this, its measurement is primordial as an indicator of the cognitive domain within the IC. For this, different neuro-psychological tests have been used to measure memory, intelligence, and capacity to solve problems (84). The test used in screening cognitive function is the Mini Mental State Examination (MMSE)(85–87).

In addition, psychological disorders and affective diseases are highly prevalent in the elderly (86). These disorders represent risk of mortality, principally due to cardiovascular disease (88). Similarly, these psychological disorders are

related significantly with the presence of mental diseases, like: depression, schizophrenia, bipolar disease, and anxiety disorders (89). Due to the aforementioned, psychological aspects become an essential domain of IC, which seeks to evaluate the social interactions of the elderly, as well as the emotional vitality and mood state (77). Monitoring the psychosocial aspects permits early detection of mental disease in the elderly. The Geriatric Depression Scale (GDS-15) (90,91) is among the instruments used to identify and distinguish symptoms of depression and dementia.

Sensory deficits are among the principal causes of falls in the elderly (92). Globally, 285-million people have visual impairment. Of these people, the elderly represent from 65% to 82% of these figures (93). Visual impairment affects the cognitive domain and the mobility domain within IC (94), generating a higher risk of hospitalization (95), disability (96), co-morbidities, like psychiatric diseases (97) and mortality (98). The Peek Acuity test (99) is suggested to assess visual acuity in the elderly; it is used in the clinical practice and in the community environment.

Other frequent sensory deficiencies are hearing loss caused by impairment of the vestibular system in the elderly. It is estimated that from 50% to 80% of the population over 80 years of age has between moderate and severe hearing disability (100). Hearing disability is associated with degenerative diseases, like Alzheimer's. It is also associated with poor quality of life (96), depression (101), low mobility (102), and risk of all-cause mortality (103). The instrument to evaluate auditory sensory is the Whispered Voice Test (WVT) (104,105) in adults. These sensory deficiencies are considered another domain to bear in mind within the IC.

The following IC domain is that of locomotion. This domain is fundamental to estimate functionality in the elderly. It is so important that, according to the theory of continuous movement, the existence of life on the planet is strongly tied to movement from the molecular to the macro (106). Locomotion is associated with different states of health (74). Balance, strength, and gait rate are indicators of FA and locomotion in the elderly. Neuromuscular changes affect balance, strength, and gait in the elderly, which is why they are associated with a higher risk of falls (107,108). Hence, low muscle mass and strength is associated with all-cause mortality (109) and physical disability (110) in the elderly. Other associations have been identified, like the association between obesity and decline in gait rate (111).

Regarding gait rate, it is a valid and reliable measure to predict reduction in dependence, mortality due to cancer, and cardiovascular disease (112). The Short Physical Performance Battery (SPPB) tests (113) are used to adequately evaluate the locomotion domain.

Finally, the last domain is that of vitality. This term gathers those functions that guarantee adequate body homeostasis (74), mainly that having to do with energy expenditure, metabolism, nutritional state, and hormone activity. With aging,

changes take place in all these aspects of energy regulation. The capacity of the elderly to maintain adequate nutrient absorption processes, as well as reduction in taste, smell, and changes in hormonal and metabolic mediators are changes related with aging. Energy expenditure and basal metabolic rate are also compromised with aging (114,115). To assess part of these changes in the nutritional and metabolic state in the elderly, the Mini-Nutritional Assessment Scale Short Form (MNA-SF)(116) should be used. This scale provides information on the nutritional state, symptoms of acute disease, psychological stress, weight loss, and food intake. It also provides information on prior conditions of frailty and to the Frailty Syndrome, as well as information on the cognitive function and possible depression states (117).

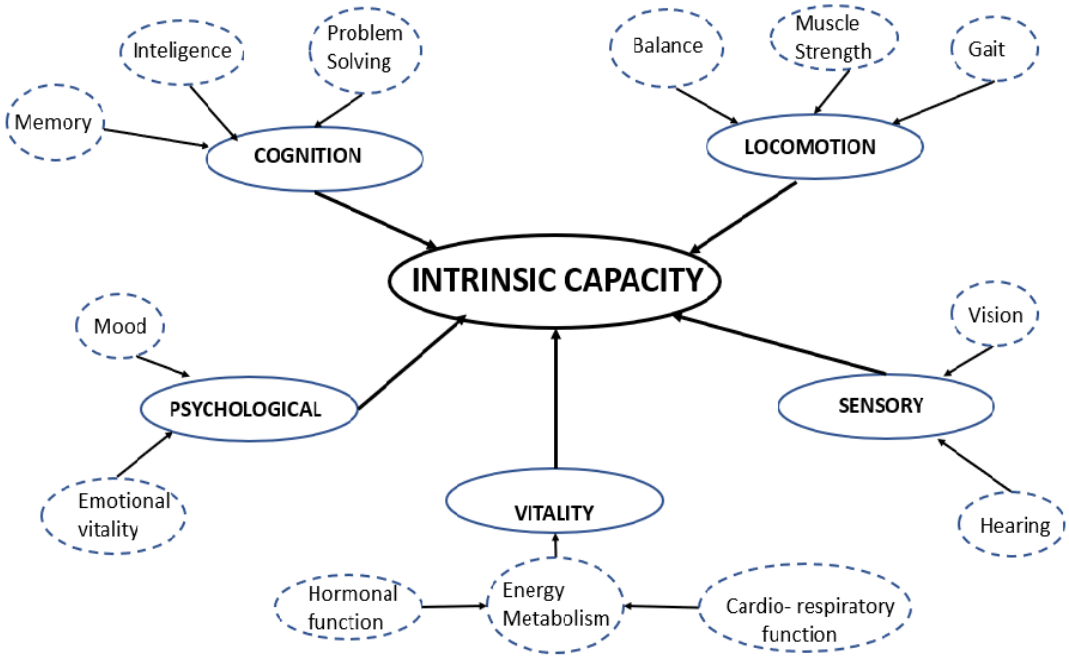

Figure 3. Schematic diagram of the five IC domains. Modified from reference (77). Reprinted courtesy of the Copyright Holder under a Creative Commons License CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/)

As noted, clinical and epidemiological evidence exists that describes the behavior of the five IC domains of cognition, psychological aspects, sensory (vision and audition), locomotion, and vitality. The set of six instruments suggested to measure IC have demonstrated adequate accuracy and sufficient predictive capacity (74). Nevertheless, it is still necessary to advance in understanding the relationships among domains and their indicators with other clinical and subclinical methods to measure health and functionality.

One of the principal barriers confronted by the IC concept is its insertion within health systems and policies, which are centered on identifying and treating the

disease deficits, then on the organism's residual wellbeing. The IC is a theoretical construct in processes of consolidation.

6. Multi-morbidities associated to aging

Aging can be understood as a physiological process of determined change occurring at different levels, from the molecular to the multi-systemic. This process has a plausible explanation from biology as a phenomenon of slow impairment and programmed death at long-term cell level, which is known as "Slow Phenoptosis" (SP) related with age (118,119).

Among the manifestations of SP, we must consider the shortening of chromosome telomeres resulting from the cell division (120), cell apoptosis (121), variations in cell duplicity rates, and epigenetic alterations in the DNA structure (122), or in mRNA intracellular signaling pathways (123). All these changes lead to chronic systemic inflammation, alterations in the energy metabolism, and modifications of the neuromuscular function (124). The prior systemic changes become co-morbidities or multi-morbidities of aging, which are conceived as a condition or grouping of chronic circumstances that predispose to functional and cognitive impairment, frailty, disability, and even mortality in the short term in the elderly.

The most frequent co-morbidities are high blood pressure (HBP); venous insufficiency; metabolic conditions, like diabetes, dyslipidemia; musculoskeletal conditions, like arthritis, osteoarthritis, chronic pain (125); cardiovascular disease; pulmonary disease; and sensory and mental diseases, like schizophrenia(126). These co-morbidities are determining factors in the health and quality of life of the elderly. This is why chronic multi-morbidity has become an important theme in caring for the elderly, so much so that the National Institute for Health and Care Excellence (NICE) in the United Kingdom proposed in 2016 the first recommendation and prioritizing guide of multi-morbidity, its measurement, and clinical management for health professionals (127).

The prevalence of co-morbidities in the elderly population has been well studied, which is why their prevalence in general is between 55% and 98% in individuals over 60 years of age. These co-morbidities increase with age, occur more in women and in low-income individuals. Several combinations can be produced of pathological processes that coexist and make complex the condition of health (128).

Various studies have analyzed in depth multi-morbidities in the elderly; such is the case of the work proposed by Sakib *et al*., (129), which conducted an analysis of the national base of the Canadian longitudinal study, which extracted data from 81,179 participants between 45 and 85 years of age. Through self-report, 27 different morbidities were identified. A multiple regression was performed to determine the association between sociodemographic and lifestyle factors. Of all the participants, 39.6% (99%CI 38.4-40.7) had 3+ chronic morbidities. Prevalence of 4+ to 5+ morbidities was at 14.2% in individuals over 60 years of age; 52% of the elderly had 3+ co-morbidities. Likewise, (ELSA Study) in Brazil, 19 different types of co-

morbidities were identified, classifying the multi-morbidity between ≥ 2 and ≥ 3. From the total of 9,412 individuals, 67.8% (95%CI 65.6-69.9) and 47.1% (95%CI 44.8-49.4) showed ≥ 2 and ≥ 3 diseases, respectively. The most frequent morbidities included back problems and systemic high blood pressure; co-morbidities ≥ 2 were between 11.6% and 23.2%; and morbidities ≥ 3 were between 4.9% and 9.5% (130). The appearance of multi-morbidity in the elderly is high even since middle age.

Multi-morbidity is a fundamental element in the intervention of the elderly, given that with a higher number of morbidities coexisting in the individual, the clinical, therapeutic, and pharmacological management becomes complicated, which increases the demand for more specialized health services, an increase in the risk of frailty and functional and cognitive impairment (131).

Figure 4 presents a schematic diagram of the relation between increased demands on health care resulting from the severity and the complexity of the co-morbidities.

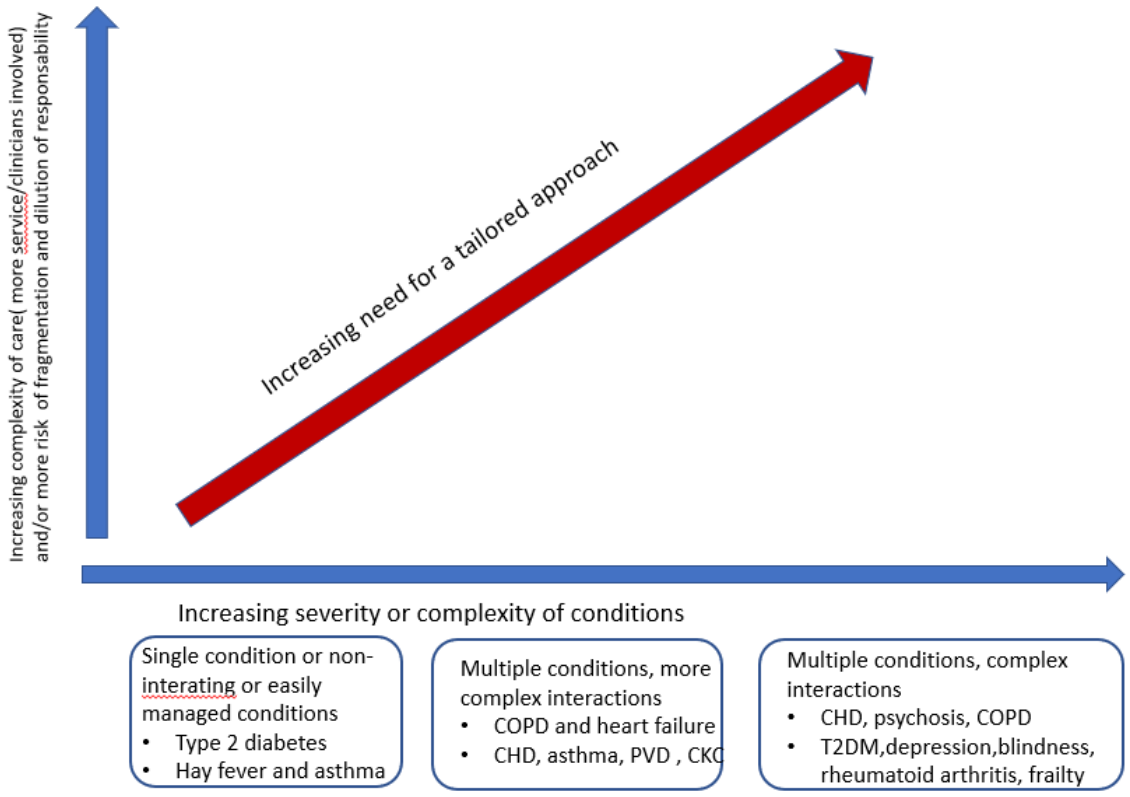

Figure 3. Multi-morbidity model in the elderly. Modified from reference (131). Reprinted courtesy of the Copyright Holder under a Creative Commons License CC BY 2.0 (https://creativecommons.org/licenses/by/2.0/)

In recent years, the spectrum of multi-morbidities has increased, if we bear in mind distinct psycho-social aspects, like depression and complex conditions with

frailty (22,72,126) and sarcopenia (20,110,132). Thereby, multi-morbidities become a growing challenge for the health sector, which requires greater evidence-based knowledge and an effective clinical practice for their control and management (133).

A practical way of predicting the severity in the health condition of individuals in relation with the morbidities is by applying distinct multi-morbidity prediction indices. Among the instruments most commonly used, there is the multi-morbidity index (MMI) (134), which conducts a prognosis of the patients from their clinical chart. Taking each diagnosis as an independent variable and using the International Classification of Disease, the Cumulative Illness Rating Scale for Geriatrics (CIRS-G), which uses a scoring system that includes 14 domains, one for each body system and a severity scale for each domain (40). Additionally, the Charlson Co-morbidity Index (CCI), which helps to predict the risk of mortality due to diabetic neuropathy (136); the Kaplan-Feinstein Index (KFI) evaluates the prognosis of patients with diabetes in relation with their co-morbidities (137); and the Index of Coexistent Diseases (ICD) as strong prediction factor of mortality in kidney patients on dialysis (138)(139). Presence of multi-morbidities is associated with a higher degree of functional loss and disability (140). Profound knowledge of the evolution of multi-morbidities is an essential element to bear in mind when implementing plans and programs of physical activity and physical exercise in the elderly.

Finally, this chapter provides a general view of the principal categories of this PhD thesis work. Initially, it displayed global and regional epidemiological data of aging, and contextualized on the situation of aging, health, and wellbeing of the elderly in Colombia. This was followed by the presentation of the concept of healthy aging, the benefits of physical activity in the elderly, IC and FA, and the multi-morbidities associated with aging. The presentation of these concepts is fundamental for the study and comprehension of IC as multidimensional indicator of functionality and its possible relation with the prevalence of metabolic syndrome, its associated factors, definition of cohort points of handgrip strength, and the mediating role of gait rate in the relationship between sarcopenia and dependence in the elderly in Colombia.

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CHAPTER 2

METABOLIC SYNDROME AND ASSOCIATED FACTORS IN OLDER PEOPLE

1. Introduction

The number of elderly people worldwide is expected to double over the next 50 years [1,2]. Older (> 60 years old) in Latin America and the Caribbean will reach ~101 million (15% of the population) [3]. For Colombia, the mean life expectancy will rise to 77.6 years for women and 69.8 years for men in 2025. Due to this, the Pan American Health Organization (PAHO) and the Merck Institute of Aging and Health called for greater surveillance over the causes of morbidity and mortality in older adults [4].

The Metabolic Syndrome (MS) is a complex cluster of cardiovascular risk factors that are associated with a sedentary lifestyle, poor nutrition, and consequent obesity, and is strongly associated with cardiovascular diseases, include glucose intolerance (type 2 diabetes, impaired glucose tolerance, or impaired fasting glycemia), insulin resistance, abdominal obesity, dyslipidemia, and hypertension [5,6]. Accordingly, MS increases the risk of developing diseases of cardiovascular origin such as acute myocardial infarction [7], ischemic stroke or coronary heart disease [8,9]. Indeed, the prevalence of cardiovascular disease attributable to MS is around 12–17% [10].

Several studies have deepened in the analysis of the presence of MS in Latin America reporting its associated factors such as increasing age, Hispanic or indigenous heritage, physical inactivity, high alcohol intake, smoking, history of hypertension or type 2 diabetes (first-degree family members), and belonging to a low socioeconomic status [11]. Likewise, the general prevalence of MS in Latin-American countries has been established in 24.9% (range: 18.8–43.3%) and is slightly more frequent in women (25.3%) than in men (23.2%). On the other hand, several risk factors for MS have been suggested, such as alcohol/cigarette smoking intake, residence (urban/rural) and inflammatory markers [12], dietary factors, such as intake of total fat or saturated fat [13], physical inactivity, and poor physical fitness [14]. We previously demonstrated in Colombian collegiate students aged 18–30 years that those with the sex (male), age (over 23 years old), weight status (overweight or obese) and having an unhealthy waist to height ratio were more likely to have a prevalence of MS [15]. Additionally, other studies that included diverse Hispanic/Latino populations suggested a marked heterogeneity in risk factor prevalence within this population [16].

Latin America has undergone a well-documented epidemiologic transition fueling a non-communicable disease epidemic [17] and makeable changes in people´s lifestyles that may contribute to greatly increased burden on cluster of cardio-metabolic disease as MS [11]. However, only a few studies have analyzed MS prevalence specifically in older adults, in whom important changes could still be made to their lifestyles to improve independence and quality of life, as well as preventing other lethal diseases. Therefore, the aim of this study were to analyze the prevalence of MS and its influencing factors in Colombian older people from a

sample of the SABE Colombia study. Understanding the MS prevalence in the national level is important to develop the effective programs and strategies to prevent and control MS.

2. Materials and Methods

2.1. Study Design and Sample Population

This study is part of the 2015 SABE study Survey on Health, Well-Being, and Aging in Latin America and the Caribbean, which is a multicenter project conducted by the Pan-American Health Organization (PAHO) 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 [18]. The instrument used was derived from the original SABE study conducted in 5 Latin America capital cities [19]. The estimated sample size was 24,553 individuals, and assuming an 80% response of the target sample was 30,691 individuals [18]. The final sample size achieved, (including 244 municipalities) was 23,694 elderly Colombians. Institutional review boards 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. Written informed consent was obtained from each individual before inclusion and completion of the first examination. Permission and details available in https://www.minsalud.gov.co/. The study protocol to the secondary analysis was approved by the Human Subjects Committee at the Pontificia Universidad Javeriana (ACTA ID 20/2017-2017/180, FM-CIE-0459-17).

The survey included elderly Colombians (≥60 years) using purposive, randomized sampling (urban and rural areas). In this sub-sample, 86 municipalities were defined for blood sampling, and two out of every five people were called to participate. A total of 1637 were included in the present analysis.

2.2. Measurements

Data collection staff was trained by the research teams of the coordinating centers (Universities of Caldas and Valle) for face-to-face interviews and physical measurements. Body mass index (BMI) was estimated in kg/m2 from the measured weight and height. Sarcopenia was defined according to calf circumference (CC) as a "proxy" measure for assessing early identification of sarcopenia in clinical practice, due to the low cost and ease of obtaining [20]. As described by Rolland et al., [20] a CC smaller than 31 cm is considered to be indicative of sarcopenia. This cut-off has been recommended for use in older individuals by the WHO Expert Committee [21].

Handgrip strength was assessed on a Takey dynamometer (Grip Strength Dynamometer Model T.K.K. 5001®, Takei Scientific Instruments Co., Ltd, Niigata, Japan) including the highest value (kg) from two attempts (both hands). Handgrip

strength was categorized into 3 levels by sex (low, moderate and high) according to the KORA-age study [22].

Blood samples were taken by puncturing the capillary vein under standardized conditions, with the participant having fasted at least 10–12 hours beforehand. The biochemical profile included: (i) HDL-cholesterol (HDL-c); (ii) triglycerides; (iii) low-density lipoprotein cholesterol (LDL-c); (iv) total cholesterol; and (v) glucose fasting. Samples were analyzed by standard enzymatic colorimetric methods. Blood Pressure, Diastolic (DBP) and systolic (SBP), was measured with subjects in rest (5-min) with an automated procedure using the OMRON HEM – 705 monitor (Omron® Healthcare Europe BV, Hoofddorp, The Netherlands).

For the lifestyle, personal habits regarding alcohol intake (participants were categorized as those who do not drink and those who drink less than one day per week, two to six days a week, or everyday) and smoking status (participants were categorized as those who do not smoke and those who have never-smoked, those who currently smoke, or those who previously smoked) were recorded. A “proxy physical activity” report was conducted 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?" Participants were considered physically active if they responded affirmatively two of the three questions. Self-reported comorbidities were assessed by asking the participants if they had a diagnosis made by a physician.

2.3. Definitions of MS

MS was defined according to the most recent Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention [23] by adopting the Ethnic Central and South American criteria for waist circumference. Participants were classified as having MS if they had at least 3 of following metabolic risk factors or components (MS-components): abdominal obesity (waist circumference ≥90 cm for Latin-American men and ≥80 cm for Latin-American women; elevated triglycerides (fasting serum triglycerides ≥150 mg/dL or taking medication for abnormal lipid levels); reduced HDL-c (fasting serum HDL-c <40 mg/dL in males; <50 mg/dL in females or specific treatment for this lipid abnormality); elevated blood pressure (SBP ≥130 mmHg or DBP ≥85 mmHg or taking hypertension medication); elevated fasting glucose (serum glucose level ≥100 mg/dL or taking diabetes medication).

2.4. Definitions of potential influencing factors

Potential influencing factors included sex (male/female), sarcopenia status (≤31 cm with sarcopenia or >31 cm without sarcopenia), handgrip strength

categorized into 3 score by sex (low, moderate and high levels), alcohol intake (never or no/current or yes), smoking status now (never or no/current or yes), and physical activity “proxy” levels (physically active/non physically active).

2.5. Statistical Analysis

General characteristics from the study sample are presented as frequency and percentage or as the mean and standard deviation (SD). Two-way analysis of variance or the χ2 test to compare sex and age differences were used. Descriptive analysis of the prevalence of the MS by sex an age stages, as well as, a descriptive analysis of the MS-components have been presented in figures using percentages. Relationships between influencing factors of MS and MS (categorical variables) have been performed by Pearson Chi-square.

Simple logistic regressions were performed individually for each independent variables to analyze the association with MS. MS was included in each simple logistic regression as the dependent variable (reference: to have MS). Sex with males as an indicator, age, BMI, to have sarcopenia, handgrip strength with the high level of strength as an indicator, be a smoker, have alcoholic intake, and be physically inactive, were included as fixed factors.

Then, a multiple logistic regression was used to identify the main predictor or influencing factors associated (clinical characteristic) of MS including at the same model: sex (indicator: male), sarcopenia (indicator: to have sarcopenia), handgrip strength (indicator: high level of handgrip strength) smoking habit (indicator: be smoker), alcoholic habit (indicator: to have alcoholic habit) and physical activity levels (indicator: be physically inactive) as independent variables. Both, simple logistic regression and multiple logistic regression (model) used the intro method. Multiple logistic regression was adjusted by the following confounders: age, ethnicity, socioeconomic status, urbanicity, BMI, medication use, and medical conditions (presence or absence of hypertension, diabetes, respiratory diseases, cardiovascular diseases, stroke, osteoporosis or cancer). The analysis of the data was performed with the SPSS statistical software package, version 24.0 (IBM, Chicago, IL, USA) for Windows.

3. Results

3.1. Characteristics of the study population

The general characteristics of the participants are presented according to the overall sample, sex and aging stages in Table 1. Most of the participants (males=213, females=312) belonged to aging stage III (70–80 years). Social status in level 2 (42.6%), urban area context (83.3%), and other ethnic groups (54.1%) were the most prevalent sociodemographic characteristics. The waist circumference and BMI means in the overall sample were 92.5 cm and 27.3 kg/m2, respectively.

Most of the sample had abdominal obesity (78.6%), and an overweight status (41.3%), but an healthy sarcopenia status (86%). Risky blood parameters for the overall sample were SBP (132.64±23.5 mmHg), Fasting Serum Triglycerides (160.94±83.3 mg/dL), and LDL-c (126.85 ± 35.3 mg/dL). The handgrip strength mean for the overall sample was 32.4 kg, with prevalence at high category (59.4%).

Several statistical differences were observed according to the sex (Table 1). Females showed several highest values compared with males (i.e.: abdominal obesity, BMI, overweight, total cholesterol, HDL-c, LDL-c), whereas males presented higher values regarding waist circumference, blood pressure, and handgrip strength. Additionally, numerous statistical differences were observed between aging stages within the sex groups (Table 1).

Table 1. Characteristic of the sample study according to age group (stage) and sex

	All (n=1637)	Males (n=642)						Females (n=995)						P value Males vs females	
		Overall males	STAGE I (n=166)	STAGE II (n=150)	STAGE III (n=213)	STAGE IV (n=113)	P value (between stages)	Overall females	STAGE I (n=303)	STAGE II (n=245)	STAGE III (n=312)	STAGE IV (n=135)	P value (between stages		
Sociodemographic characteristics															
Age*	70.5 (7.9)	71.1 (8.1)	62.0 (1.38)	66.98 (1.5)	74.1 (2.8)	84.3 (3.6)		70.5 (7.9)	62.0 (1.42)	66.8 (1.4)	74.1 (2.8)	84.7 (4.1)			
Social Status															
Level 1	492 (30.1)	205 (31.9)	50 (30.1)	48 (32.0)	68 (31.9)	39 (34.5)		287 (28.8)	90 (29.7)	73 (29.8)	91 (29.2)	33 (24.4)			
Level 2	697 (42.6)	266 (41.4)	75 (45.2)	58 (38.7)	92 (43.2)	41 (36.3)		431 (43.3)	129 (42.6)	108 (44.1)	132 (42.3)	62 (45.9)			
Level 3	410 (25.0)	158 (24.6)	35 (21.1)	41 (27.3)	51 (23.9)	31 (27.4)	0.352	252 (25.3)	73 (24.1)	62 (25.3)	81 (26.0)	36 (26.7)	0.719		
Level 4	30 (1.8)	10 (1.6)	3 (1.8)	3 (2.0)	2 (0.9)	0 (0.0)		20 (2.0)	10 (3.3)	1 (0.4)	6 (1.9)	3 (2.2)			
Level >5	8 (0.5)	3 (0.5)	3 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)		5 (0.5)	1 (0.3)	1 (0.4)	2 (0.6)	1 (0.7)			
Urbanicity															
Urban	1363 (83.3)	514 (80.1)	138 (83.1)	119 (79.3)	169 (79.3)	88 (77.9)	0.697	849 (85.3)	258 (85.1)	212 (86.5)	263 (84.3)	116 (85.9	0.897		
Rural	274 (16.7)	128 (19.9)	28 (16.9)	31 (20.7)	44 (20.7)	25 (22.1)		146 (14.7)	45 (14.9)	33 (13.5)	49 (15.7)	19 (14.1)			
Ethnic group															
Indigenous	85 (6.1)	50 (9.2)	14 (8.8)	11 (8.0)	22 (12.2)	3 (4.6)		35 (4.1)	12 (4.2)	14 (6.1)	7 (2.7)	2 (2.7)			
Black "mulato" or Afro-Colombian	130 (9.4)	57 (10.5)	16 (10.1)	15 (10.9)	15 (8.3)	11 (16.9)		73 (8.6)	31 (11.0)	16 (7.0)	21 (8.1)	5 (6.7)			
White	422 (30.4)	154 (28.5)	52 (32.7)	39 (28.30)	48 (26.7)	15 (23.1)	0.404	268 (31.7)	87 (30.7)	70 (30.7)	83 (32.0)	28 (37.3)	0.535	<.001	
Others*	750 (54.1)	281(51.8)	77 (48.4)	138 (52.9)	95 (52.8)	36 (55.4)		469 (55.5)	153 (54.1)	128 (56.1)	148 (57.1)	40 (53.3)			
Anthropometric Characteristics															
Waist Circumference*	92.5 (11.0)	93.4 (10.9)	93.3 (10.8)	92.1 (11.5)	93.87 (10.2)	93.5 (11.8)	1.000	91.8 (11.0)	91.7 (11.1)	92.8 (9.8)	92.7 (11.7)	88.4 (10.9)*@	<.030	<.001	

Abdominal Obesity	1285 (78.6)	410 (64.0)	108 (65.1)	95 (63.3)	137 (64.6)	70 (61.9)	0.950	875 (88.0)	265 (87.5)	223 (91.0)	279 (89.7)	108 (80.0)	.010	<.001
Non-Abdominal Obesity	350 (21.4)	231 (36.0)	58 (34.9)	55 (36.7)	75 (35.4)	43 (38.1)		119 (12.0)	38 (12.5)	22 (9.0)	32 (10.3)	27 (20.0)		
BMI*	27.36 (4.6)	26.0 (3.9)	26.5 (3.7) [a]	25.8 (4.1) [a]	26.1 (3.6) [a]	25.2 (4.0)	>1.000	28.2 (4.9)	28.3 (4.7) [a]	28.8 (4.5) [a]	28.6 (5.2) [a]	25.7 (4.3) [$*]	<.001	<.001
Nutritional Status														
Underweight (<18.5 kg/m2)	22 (1.5)	12 (2.0)	3 (1.9)	6 (4.1)	1 (0.5)	2 (2.2)		10 (15.0)	1 (0.4)	1 (0.4)	4 (1.4)	4 (3.9)		
Normal weight (18.5-24.9 kg/m2)	463 (30.9)	237 (39.8)	44 (28.0)	62 (42.8)	85 (42.1)	46 (50.5)	0.011	226 (25.0)	67 (23.5)	52 (22.4)	61 (21.6)	46 (44.7)	<.001	<.001
Overweight (25-29.9 kg/m2)	618 (41.3)	255 (42.9)	83 (52.9)	55 (37.9)	87 (43.1)	30 (33.0)		363 (40.2)	121 (42.5)	85 (36.6)	120 (42.4)	37 (35.9)		
Obese (>30 kg/m2)	395 (26.4)	91 (15.3)	27 (17.2)	22 (15.2)	29 (14.4)	13 (14.3)		304 (33.7)	96 (33.7)	94 (40.6)	98 (34.6)	16 (15.5)		
Sarcopenia status														
No	1393 (86)	551 (87.0)	149 (90.9)	130 (87.2)	183 (87.1)	89 (80.9)	0.122	842 (85.4)	275 (91.1)	224 (92.2)	261 (84.7)	82 (61.7)	<.001	0.350
Yes	226 (14.0)	82 (13.0)	15 (9.1)	19 (12.8)	27 (12.9)	21 (19.1)		144 (14.6)	27 (8.9)	19 (7.8)	47 (15.3)	51 (38.3)		
Blood Parameters														
ASBP (mmHg)*	132.64 (23.5)	134.0 (23.8)	131.6 (22.0) [b,a]	131.4 (24.1)	135.3 (24.3)	138.5 (24.4)	>1.000	131.7 (23.3)	126.51 (21.9) [b,a]	130.8 (22.3)	135.4 (10.4) [$]	136.7 (26.2) [$]	<.001	.024
ADBP (mmHg)*	72.66 (11.7)	74.3 (12.3)	76.95 (12.6) [$,a]	74.4 (11.8)	73.4 (12.0) [b,a]	72.2 (12.8) [b,a]	<0.020	71.6 (11.1)	72.3 (10.4) [a]	73.3 (11.7)	71.3 (10.3) [a]	67.4 (11.9) [$*,a]	<.001	.045
Fasting Glycemia (mg/dL)*	98.34 (26.5)	97.25 (26.3)	95.6 (23.7)	95.1 (21.3)	100.5 (33.1)	96.3 (24.0)	1.000	99.1 (26.3)	99.6 (27.1)	100.2 (32.1)	99.1 (23.6)	95.5 (17.1)	>.050	>.050
Fasting Serum Triglycerides (mg/dL)*	160.94 (83.3)	153.7 (81.6)	175.4 (9.3) [$]	154.1 (16.6)	145.3 (75.5) [b,a]	137.8 (69.8) [$]	<0.004	165.6 (84.1)	166.1 (85.9)	167.7 (89.3)	170.9 (83.3) [a]	148.6 (69.9)	>.050	.001
HDL-Cholesterol (mg/dL)*	45.63 (12.9)	41.8 (11.3)	41.3 (11.7) [a]	42.1 (11.6) [a]	41.9 (11.0) [a]	42.1 (10.9) [a]	1.000	48.1 (13.3)	47.8 (12.5) [a]	47.29 (12.6) [a]	47.46 (13.7) [a]	51.6 (14.5) [$*]	<.020	<.001
LDL-Cholesterol (mg/dL)*	126.85 (35.3)	120.1 (32.7)	122.7 (12.1) [a]	125.4 (33.3) [$]	117.8 (32.8) [a]	113.4 (31.5) [$,a]	0.033	131.2 (36.2)	137.6 (33.2) [b,a]	129.10 (37.1)	129.3 (38.6) [b,a]	125.2 (33.6) [b,a]	<.030	.010
Total-Cholesterol (mg/dL)*	195.32 (41.4)	183.9 (38.6)	189.8 (39.4) [$,a]	189.8 (39.28) [$,a]	180.3 (37.4) [a]	174.5 (36.4) [$,a]	<0.015	202.6 (41.4)	209.0 (39.4) [b,a]	200.8 (42.1) [a]	200.2 (43.6) [b,a]	197.2 (38.1) [b,a]	<.040	.010
Physical Fitness Parameters														
Handgrip strength (kg)	32.4 (12.3)	40.03 (12.6)	44.8 (12.1) [a]	43.3 (10.9) [a]	38.87 (11.7) [a]	30.3 (11.6) [$*,a]	<0.001	27.2 (9.1)	29.1 (9.0) [b,a]	27.9 (8.7) [b,a]	25.8 (9.3) [a]	24.7 (8.6) [b,a]	<.040	<.001
Low**	270 (17.5)	131 (21.2)	15 (9.3)	15 (10.1)	45 (22.3)	56 (52.8)		139 (15.0)	25 (8.7)	32 (13.7	53 (18.3)	29 (25.0)		
Moderate**	357 (23.1)	138 (22.3)	29 (18.0)	33 (22.1)	54 (26.7)	22 (20.8)	<0.001	219 (23.6)	66 (22.9)	52 (22.2)	73 (25.3)	28 (24.1)	<.001	.007
High**	918 (59.4)	349 (56.5)	117 (72.7)	101 (67.8)	103 (51.0)	28 (26.4)		569 (61.4)	197 (68.4)	150 (64.1)	163 (56.4)	59 (50.9)		

Data have been expressed as frequency and percentage for qualitative variables and *mean and standard deviation for quantitative variables. MS: metabolic syndrome

** Low: men, ≤30 (kg); women, ≤18 (kg). Moderate: men, >30 (kg) and ≤38 (kg); women, >18 (kg) and ≤24 (kg). High: men, >38 (kg); women, >24 (kg). ASP: Arterial Systolic Blood Pression; ADBP: Arterial Diastolic Blood Pression; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; WHO: World Health Organization.

3.2. Clinical characteristics and prevalence of MS

The incidence of alcohol consumption (9.2%) and smoking (12.1%) was low but significantly higher in men than in women (smoking: 12.6% vs 6.9%; alcohol: 21.3% vs 6.1%), and mainly were presented at first aging stages. Most of the sample (mainly women at the first aging stages) were not physically active (82.9%). Hypertension was the most common chronic comorbidity (44.2%), following of diabetes (16.4%). Females presented the highest prevalence compared with males (60.8% vs 48%, p<0.001, and 18.3% 13.4%, p=0.009, respectively) at aging stage III and IV, respectively. Finally, cardiovascular diseases and stroke with no differences between sex and aging stages, Table 2.

Table 2. Clinical characteristics and distribution by stage aged group

		Males (n= 642)						Females (n=995)						P valu
Clinical characteristics	**All (n=1637)**	**Overall males**	**STAGE I (n=166)**	**STAGE II (n=150)**	**STAGE III (n=213)**	**STAGE IV (n=113)**	**P value (between stages)**	**Overall Females**	**STAGE I (n=303)**	**STAGE II (n=245)**	**STAGE III (n=312)**	**STAGE IV (n=135)**	**P value (between stages)**	**Males vs female**
Smoking habits														
No smoke	1486 (90.8)	561 (87.4)	138 (83.1)	121 (74.7)	194 (91.1)	108 (95.6)	<0.001	925 (93.1)	276 (91.1)	231 (94.3)	293 (94.2)	125 (92.6)	0.380	**<0.001**
Smokes	150 (9.2)	81 (12.6)	28 (16.9)	38 (25.3)	19 (8.9)	5 (4.4)		69 (6.9)	27 (8.9)	14 (5.7)	18 (5.8)	10 (7.4)		
Alcohol consumption														
Non alcoholic	1438 (87.9)	505 (78.7)	109 (65.7)	112 (74.7)	182 (85.4)	102 (90.3)	<0.001	933 (93.9)	278 (91.7)	227 (93.0)	299 (95.8)	129 (95.6)	0.144	**<0.001**
Alcoholic	198 (12.1)	137 (21.3)	57 (34.3)	38 (25.4)	31 (14.6)	11 (9.7)		61 (6.1)	25 (8.3)	17 (7.0)	13 (4.2)	6 (4.4)		
Physical Activity "proxy"														
Physically active	280 (17.1)	144 (22.4)	53 (31.9)	45 (30.0)	37 (17.4)	9 (8.0)		136 (13.7)	45 (14.9)	40 (16.4)	41 (13.2)	10 (7.4)		
Non-Physically active	1354 (82.9)	498 (77.6)	113 (68.1)	105 (70.0)	176 (82.6)	104 (92.0)	<0.001	856 (86.3)	258 (85.1)	244 (83.6)	269 (86.8)	125 (92.6)	0.093	**<0.001**
Comorbid chronic diseases														
Hypertension	911 (44.2)	307 (48.0)	63 (38.2)	59 (39.9)	116 (54.5)	69 (61.1)	<0.001	604 (60.8)	151 (50.0)	141 (57.6)	215 (69.1)	97 (71.9)	**<0.001**	<.001
Diabetes	268 (16.4)	86 (13.4)	25 (15.2)	24 (16.1)	30 (14.1)	7 (6.2)	0.090	182 (18.3)	45 (14.9)	47 (19.2)	62 (19.9)	28 (20.7)	0.314	0.009
Respiratory diseases	183 (11.2)	64 (10.0)	11 (6.6)	11 (7.3)	22 (10.3)	20 (17.7)	0.013	119 (12.0)	25 (8.3)	27 (11.0)	47 (15.1)	20 (14.8)	**0.043**	0.209
Cardiovascular diseases	233 (14.3)	80 (12.5)	12 (7.2)	18 (12)	30 (14.2)	20 (19.9)	0.052	153 (15.4)	37 (12.2)	33 (13.5)	55 (17.6)	28 (20.7)	0.065	0.104
Stroke	85 (5.2)	39 (6.1)	5 (3.0)	10 (6.7)	18 (8.5)	6 (5.3)	0.169	46 (4.6)	11 (3.6)	11 (4.5)	13 (4.2)	11 (8.1)	0.330	0.316
Osteoporosis	207 (12.7)	33 (5.1)	3 (1.8)	6 (4.0)	15 (7.1)	9 (8.0)	0.054	174 (17.5)	38 (12.6)	37 (15.2)	72 (23.3)	27 (20.0)	**0.004**	<0.001
Cancer	90 (5.5)	37 (5.8)	8 (4.8)	6 (4.0)	13 (6.1)	10 (8.8)	0.367	53 (5.3)	15 (5.0)	14 (5.7)	18 (5.8)	6 (4.5)	0.925	0.710

Data have been expressed as frequency and percentage. P in bold = significant differences

3.3. *Prevalence of MS and its distribution by MS-components*

The overall prevalence of MS in the study sample was 54.9% (95% confidence interval [CI] 52.4–57.3. The prevalence of MS according to sex, and the aging stages is presented in Figure 1. A. MS was more prevalent in females than in males (59.8% versus 47.3%) irrespective of the aging stage. For females, the prevalence of MS was highest in aging stage III (64.6%), whereas for males it was highest in the aging stage I (49.4%). The most prevalent MS-components were abdominal obesity (78.5%), low levels of HDL-c (57.3%), elevated arterial blood pressure (EABP) (53.1%), and high levels of fasting blood triglycerides (HLFBTg) (45.5%). Elevated fasting blood glucose was the least common components of MS (31.1%). Related to the MS-components by sex (Figure 1.B), the greatest differences were observed for high waist circumference (HWC), and low levels of HDL-c (LLHDL), with a higher prevalence in females than in males (HWC: females=88% vs males 64 %, p<0.001 and LLHDL: females=60.7% vs males=51.7%, p<0.001). The prevalence of HLFBTg was also significantly higher in females than in males (females=48.8% vs males=40.8 %, p=0.001). However, males presented a higher prevalence of EABP than females (57.2% vs 50.8 %, p=0.001). The prevalence of MS according to the MS-components was presented in figure 1.C.

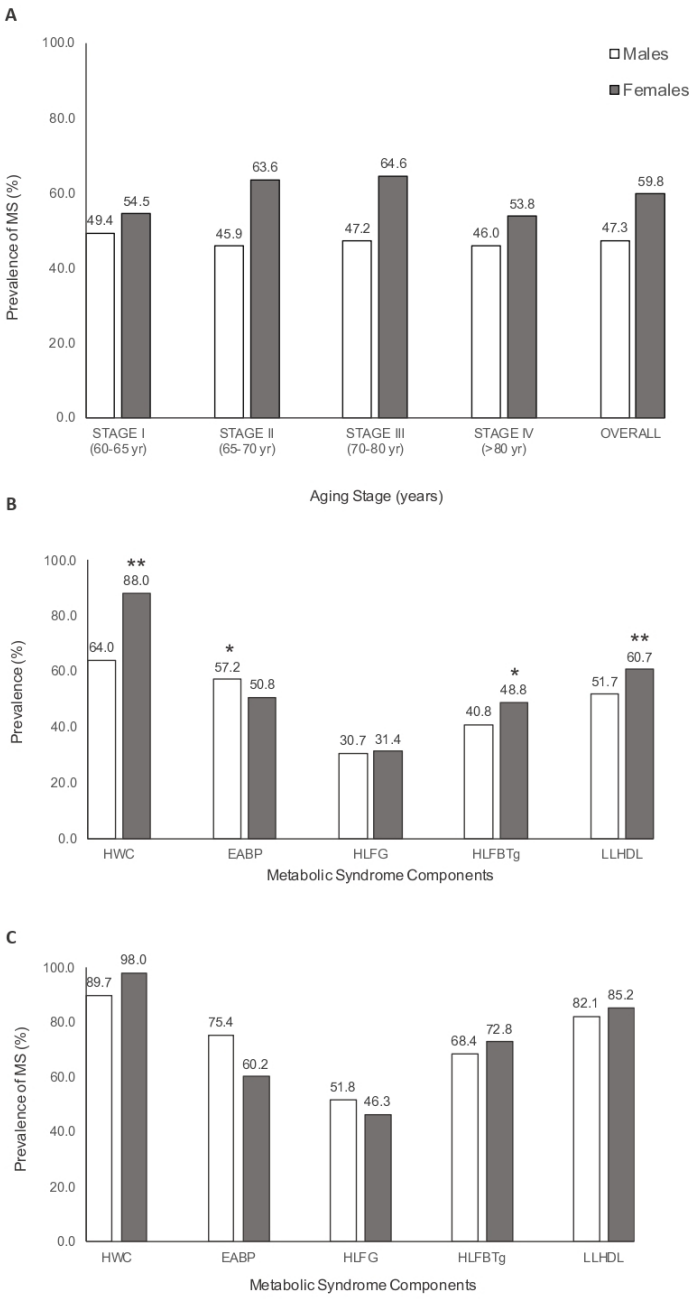

Figure 1. The prevalence of MS according to the MS-components. A: Distribution of the prevalence of metabolic syndrome according to aging stage and sex. B: Prevalence of the MS-components according to sex. (HWC = High Waist Circumference; EABP =Elevated Arterial Blood Pressure; HLFG = High Levels of Fasting Glucose; HLFBTg= High Levels of Fasting Blood Triglycerides; LLHDL = Low Levels of High Density Lipoprotein; C: Prevalence of MS according to metabolic abnormalities. **p<0.001; *p=0.001.

Additionally, we explore the MS prevalence according to the studied comorbid chronic diseases. Participants with MS presented the hypertension as the main comorbid chronic disease with a prevalence of 60.9% of the sample. The rest of participants with MS presented the following prevalence of the comorbid chronic diseases: diabetes (23.1%), cardiovascular disease (16.2%), osteoporosis (14.1%), respiratory diseases (11.1%), stroke (5.1%), and cancer (4.8%), Table 2.

3.4. Relationship between MS status and clinical characteristics

Relationship between MS status and clinical characteristics were presented in table 3. Clinical characteristics such as sex, sarcopenia status and handgrip strength were significantly associated ($p<0.05$).

Table 3. Relationship between MS status and clinical characteristics

Clinical characteristics	Have MS	Not Have MS	Pearson Chi- square P value
Sex			
Men	336	301	**<0.001**
Women	395	588	
Sarcopenia status			
Yes	804	577	**<0.001**
No	78	143	
Handgrip strength			
Low	476	435	
Medium	201	151	**0.025**
High	163	104	
Smoking status			
Yes	76	72	0.108
No	654	817	
Alcohol intake			
Yes	789	633	0.212
No	100	97	
Physical Activity "proxy"			
Physically active	139	139	0.078
Non-Physically active	747	592	

3.5. Influencing factors associated with MS

Table 4 shows the ORs for the influencing factors associated with MS among the Colombian older adults (univariate analysis) were male gender (OR= 1.662, 95%CI= 1.359–2.032; p<0.001), to have a sarcopenia status (OR= 2.55, 95%CI=1.900–3.434; p<0.001), and a low handgrip strength (OR=1.432, 95%CI= 1.084–1.892; p=0.011). Sarcopenia status was the main variable associated with MS, with more than two times the approximate risk of occurrence of MS.

Table 4. Univariate association analysis between MS and clinical characteristics

Clinical characteristics	OR	95% CI		P value
Sex (reference males)	1.662	1.359	2.032	**<0.001**
Sarcopenia status				
Yes (reference No)	2.550	1.901	3.434	**<0.001**
Handgrip Strength (reference Hight)				
Low	1.432	1.084	1.892	**0.011**
Medium	1.216	0.949	1.559	0.121
Smoking status				
Yes (reference No)	1.319	0.940	1.850	0.109
Alcohol intake				
Yes (reference No)	1.209	0.897	1.629	0.212
Physical Activity "proxy"				
Non-Physically active (reference active)	0.793	0.612	1.026	0.078

BMI: Body Mass Index; WHO= World Health Organization. p value in bold = significant association

After the adjustment by the main confounders in the multiple regression model (Figure 2), male gender (OR= 1.388; 95%CI= 1.054–1.828; p=0.020) and a sarcopenia status (OR= 1.637; 95%CI= 1.061–0.525; p=0.026) were again significantly associated with MS. In addition, being a smoker was positively associated with MS (OR= 1.591; 95%CI= 1.036–2.443; p=0.034). Thus, in general, to have a sarcopenia status and smoking were the main risk factors associated with MS in this sample of Colombian older adults, with more than 1.5 times the approximate risk of occurrence of MS.

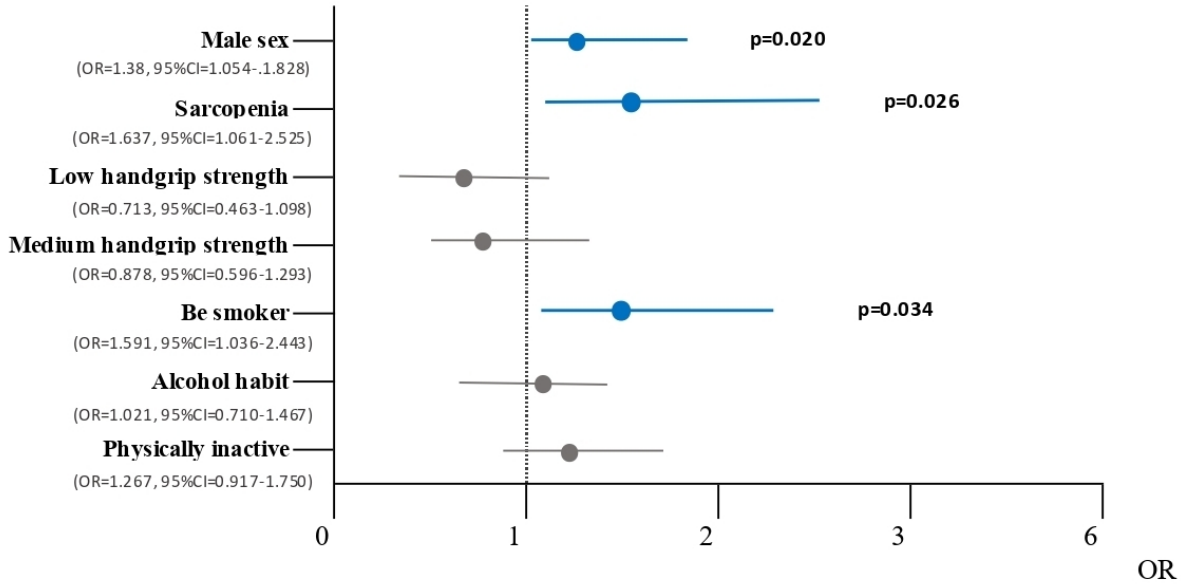

Figure 2. Multiple logistic regression model of the influencing factors associated with MS among Colombian older adults. Multiple logistic regression adjusted for age, ethnicity, socioeconomic status, urbanicity, BMI, medication use, and medical conditions (presence or absence of hypertension, diabetes, respiratory diseases, cardiovascular diseases, stroke, osteoporosis or cancer).

4. Discussion

The main finding of the present study was the considerably high prevalence of MS in the sample (54.9%). The prevalence of MS was more prevalent in females than in males irrespective of the aging stage (females highest prevalence in aging stage III (70–80 years) and in aging stage I (60–65 years for males). The most prevalent MS-components for the overall sample were abdominal obesity (78.5%), low levels of HDL-c (57.3%), EABP (53.1%) and high levels of fasting blood triglycerides (45.5%). Female gender, a poor sarcopenia status, and be smoking were found to be significantly associated with probability of MS (after adjustment).

It should be noted that while the prevalence of MS in the present sample is high (54.9%), it is similar to other Latin American studies in older people, such as Ecuador 59.9% [24], Brazil with 51.5.% [16], Southern Cone of Latin America with 53% [25], in Ecuador elders (≥65 years) with 40% [26],Colombia with 52.2%, [27] and in the CARMELA study with 35.5% [28]. A reasonable explanation for the high prevalence of MS in the present study could be that most of the sample belonged to an urban area (83.3%), where people have a higher risk of MS [29,30]. This might be due to several lifestyle aspects, such as dietary patterns or low physical activity levels, as was found in our study where most of the sample (82.9%) was insufficiently active.

According to our results regarding sex, in the six Latin American studies previously mentioned [16,24–28], females also had a higher prevalence of MS than males in general, and particularly in the older adult groups (when it applied). As previously reported, MS is more common in females in an older North American population of Mexican origin [31]. Many of the typical aspects of MS, such as increased abdominal adiposity and dyslipidemia, hyperglycemia, and hyperinsulinism, are experienced in females along the menopausal transition [31]. The cessation of estrogen secretion at the beginning of menopause accentuates these aspects, decreasing the quality of life [32]. Additionally, it seems that the onset of menopause begins earlier in Latin American countries than in Europe and USA, what may be associated with higher altitude residency and lower educational-economical income [33,34]. In the present study, the overall sample belonged to social status 1-2 (72.7%), and with a residency at high altitude (Bogota, 2680 m), but without significant differences between genders.

Consequently, scientific investigations on Latin American postmenopausal women related to the MS prevalence and its associated factors have increased [35], although little is known about older adult populations. In addition, males presented the highest MS prevalence (49.4%) in aging stage I (60–65 years), but not in the later ones. In agreement with our results, in a cross-sectional analysis of 4289 Taiwanese individuals [36], the male:female MS ratio reversed after the age of 60 (men 30.4% vs women 40.3%). Similarly, in a large population-based project enrolling 36 cohorts from 10 European countries [37], there was an increase in the prevalence of MS from age groups 19–39 years to 60–78 years was nearly two-fold in males, and five-fold in females, resulting in a higher prevalence of MS in women after the age of 50. Again, the typical changes in the hormonal status during and after menopause could explain the significant influence of sex in the age-related increase of MS [38,39]. Other explanation could be due to fluctuations in individual and social behavior, such as modifications in socio-economic status or adoption of an unhealthy lifestyle [40].

Overall, the most prevalent MS-components were abdominal obesity (78.5%), low levels of HDL-c (57.3%), EABP, and high levels of fasting blood triglycerides (45.5%). Likewise, in the study of Davila et al.[27], where 312 (34.7% of the whole sample) older adults (55–64 years) from Medellin (Colombia) were evaluated, the major MS-metabolic risk factor was abdominal obesity with a prevalence of 87.4%, followed by low levels of HDL-c (59.1%), HLFBTg (52.0%) and EABP (44.8%).

Concerning MS-components analyzed by sex in the whole sample, several statistical differences were observed. For instance, females presented a higher prevalence of HWC and LLHDL than males. Moreover, females displayed significantly higher HLFBTg than males, but males presented a higher prevalence of EABP. Accordingly, in a French study conducted in 3508 participants, females presented a higher prevalence of HWC, and low HDL-cholesterol, whereas EABP was the most commonly found metabolic disorder in males; however, the age range

only covered 35–64 years [41]. Alike, a Taiwanese study found a high prevalence of BP and TG in males below 60 years, although without differences in MS-components between genders in the age group above 60 years [42]. Additionally, a large Korean study including 103,763 participants aged 66 years or older revealed that females had a significantly higher percentage of abdominal obesity (+12%) and lower HDL-c levels (−47%) than men, whereas men presented higher rates of EABP (+6%). However, contrary to our results, the Korean study indicated that men had usually high levels of triglycerides (+5%), compared with woman [43]. Unfortunately, gender-related differences are sensitive to social and cultural conducts, dietary behaviors and psychosocial aspects [38].

Finally, the multivariate regression model indicated that the clinical characteristics that were associated with MS were male gender, to have a sarcopenia status, and smoking (after adjustment). In accordance with our results of univariate regression analysis, numerous studies have shown the high prevalence of MS and associated risk in people with a nutritional status of normal weight near the upper range or slightly overweight [44]. Moreover, sarcopenia has been linked to several metabolic disorders, and a recent meta-analysis revealed that it is positively associated with MS in middle-aged and older non-obese people [45]. In our study, sarcopenia status was high (14% for the overall sample) compared with a previous study carried out in the same region [46], where 6.96% of the participants (≥60 years old) presented sarcopenia. Also, our sarcopenia prevalence is higher than most of the studies conducted in older adults in other countries, going from Belgium with 12% to the United States with 5%, but not Japan (24.2%) [45]. However, stratification cut-off values for community-dwelling populations could vary between studies, as well as age range included.

Lastly, regarding the significant association between MS and smoking status, a previous Chinese study showed that active smoking in men was strongly associated with increased CVD risk [47], independent of the presence of MS. Moreover, tobacco smoke exposure (including active and passive smoking) increased the prevalence of coronary heart disease, stroke, and CVD in both genders with or without MS. In the same line, smoking habits could also explain in part the association between MS and male gender, since in the present sample, significantly more smokers were males than females for the whole sample (males = 12.6% vs females = 6.9) and for most of the age stages.

In conclusion, the prevalence of MS is 54.9% among Colombian older adults and females presented the highest prevalence of MS irrespective of the aging stage. High abdominal obesity was the main prevalent MS-components (78.5%). Male gender, sarcopenia status, and being a smoker were found to be significantly associated with the probability of MS. New health policies and prevention strategies focused on the elderly Latin American population should be implemented based on these findings.

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CHAPTER 3

REFERENCE VALUES FOR HANDGRIP STRENGTH AND THEIR ASSOCIATION WITH INTRINSIC CAPACITY DOMAINS AMONG OLDER ADULTS

1. Introduction

Colombia is a country with approximately 48 million inhabitants, with some 5.2 million inhabitants aged 60 years and older [1]. Currently, the life expectancy in Colombia is 72.3 years, and by 2025, life expectancy is expected to be 77.6 years for women and 69.8 years for men. In this context, the World Health Organization (WHO) has published the World Report on Aging and Health [2], which describes healthy aging as the result of the interaction between the physical and mental capacity of an individual (the intrinsic capacity) and the context of each individual's life (the environment) [3]. Accordingly, healthy aging depends upon intrinsic capacity, socioeconomic status and physical environment, and the interactions between these factors [4]. In this vein, the WHO has proposed five domains –locomotion, vitality, cognition, psychological, and sensory –that can be used to evaluate an individual's intrinsic capacity.

Muscular strength as evaluated by handgrip strength has predictive value for assessing declines in physical and mental capacities in older adults [5], which are both components of the intrinsic capacity construct. Recent studies have shown that greater handgrip muscular strength is associated with lower all-cause [6] and cancer mortality [7].

The world's population is rapidly getting older [8]; thus, the preservation of muscle strength and power with advancing age is of considerable clinical significance. Against this background, the development of clinically-viable screening tools for detecting individuals at heightened risk for functional limitations is warranted [7]. Indeed, it has been reported that handgrip strength reference values and muscular weakness cut-off points for older adults are needed [9], but no data have yet been described for the Colombian elderly population. Additionally, several cross-sectional studies have presented different handgrip strength cut-off points in Italian [10], Finnish [11], Chinese [12], and American [13] [14] older adults, thus suggesting that different ethnicities may have different muscle weakness cut-off points for identifying clinically relevant health outcomes.

The results of the Survey on Health, Well-Being, and Aging in Latin America and the Caribbean, (SABE, from the initials in Spanish SAlud, Bienestar & Envejecimiento) have increased our understanding of the aging process and have helped to create public policies aimed at improving the well-being of the Latin American and Caribbean populations. They have also provided a framework for performing a second set of studies in the region.

The purposes of this study were three-fold: (1) to describe handgrip strength in older individuals aged ≥ 60 years in Colombia; (2) to identify sex- and age-specific muscle weakness cut-off points in older adults; and (3) to determine the odds of adverse events for each of the intrinsic capacity domains for individuals with handgrip strength greater than the muscle weakness cut-off points, as compared with their weaker counterparts.

2. Materials and methods

2.1. Study design

This study is part of the 2015 SABE study Survey on Health, Well-Being, and Aging in Latin America and the Caribbean. Of the initial 23,694 elderly Colombians who took part in SABE–Colombia, a total of 5,237 were included in the present analysis after excluding participants without handgrip strength results (n = 18,457). There were no differences in the study key characteristics (i.e., age, body mass, height, body-mass index [BMI], and sex distribution) between the current study sample and the original SABE study sample (all $p>0.05$). The 5,237 elderly Colombians constituted the final analytical sample of the non-institutionalized population. 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).

Details of background and design methods (i.e., characteristics of participants, sample calculation, outcomes, and analysis plan) of the SABE Study have been previously published elsewhere [1]; nevertheless, the most relevant information is briefly described below. All information collected was obtained through face-to-face interviews conducted at each site on mobile capture devices (e.g., tablets) or with printed versions of the questionnaire. During the personal interviews, direct physical measurements were taken, including handgrip strength (absolute and relative; i.e., handgrip strength [kg] /body mass [kg]), measured with a Takei dynanometer (Takei Scientific Instruments Co. Tokyo, Japan), height (standing and sitting) and weight. Five domains of the intrinsic capacity (locomotion, vitality, cognition, psychological, and sensory) were assessed as follows: (i) the cognition domain was assessed by the modified version of the mini-mental state examination (MMSE) [15 16]; (ii) the locomotion domain was defined according to five definitions – sarcopenia [17], prevalence of falls, functional impairments assessed with an activities of daily living (ADL) scale [18], mobility /disability [19], and physical performance assessed by the validated Spanish version of the short physical performance battery (SPPB) [20]; (iii) the psychological domain was assessed by the Yesavage geriatric depression scale (YGDS) and mental problems; (iv) the sensory domain was assessed as hearing and vision problems [21]; and (v) the vitality domain was assessed as loss of appetite [22] and weight loss.

The self -reported comorbidities or medical conditions category was assessed by asking the participants if they had been diagnosed by a physician with hypertension, diabetes, respiratory diseases, cardiovascular diseases, cancer, or osteoporosis. Drug use was evaluated with the following question: "Do you currently take or use any prescription medication"? For the lifestyle domain, personal habits

regarding alcohol consumption and cigarette smoking were recorded. A “proxy physical activity” was also evaluated. Finally, hospitalization > 24 h in the last year was recorded.

2.2. Data analysis

We used SPSS v24.0 software for Windows (SPSS, Chicago, IL, USA), except for the LMS method calculations (see below). The optimal power to obtain normality was calculated for each of a series of age groups and the trend summarized by a smooth (L) curve. Trends in the mean (M) and coefficient of variation (S) were similarly smoothed. The resulting L, M and S curves contain the information to produce any centile curve, and to convert measurements (even extreme values) into exact standard deviation (SD) scores [23]. Anthropometric and handgrip characteristics from the study sample are presented as the mean and SD. Normality for the selected variables was verified using histograms and Q-Q plots. Differences were analyzed by two-way analysis of variance or the Chi-square test (χ^2) to compare sex and age differences.

The LMS method assumes that the outcome variable has a normal distribution after a Box-Cox power transformation is applied, according to the LMS method implemented in the LMS Chart Maker Pro Version 2.54 (Medical Research Council, London, UK). Smoothed and specific curves for each age were obtained *via* a penalized maximum likelihood with the following abbreviations: M (median), L (Box-Cox transformation) and S (coefficient of variation) [24]. The appropriate number of degrees of freedom was selected on the basis of the deviance, Q-tests and worm plots, following the suggestions of Royston & Wright [25]. The 3rd, 10th, 25th, 50th, 75th, 90th, and 97th smoothing centiles were chosen as age- and sex-specific reference values. Statistical significance was assessed with a two-tailed α level of 0.05.

Finally, logistic regression models were used to compare the prevalence of adverse events in the five domains of the intrinsic capacity according to the cut-off for handgrip strength. The analysis was adjusted for age, ethnicity, socioeconomic status, urbanicity, BMI, smoking status, alcohol intake, drug use, physical activity, and medical conditions (presence or absence of osteoporosis, cardiovascular diseases, hypertension, diabetes, cancer, or respiratory diseases).

3. Results

The characteristics of the sample are summarized in Table 1. Age ranged from 60 to 85 years, with a mean of 70.5 ± 7.8 years. Absolute and relative handgrip strength was higher among men than among women ($p<0.001$). In the total sample, self-reported comorbidities were presented in the following proportions of cases: osteoporosis (12.3%), cardiovascular diseases (14.3%), hypertension (55.9%), diabetes (16.6%), cancer (4.9%), and respiratory diseases (10.8%). According to the intrinsic capacity domains, overall, women had more problems with locomotion,

sensory, and psychological parameters than men (p<0.01), except in terms of hearing problems.

Table 1. Characteristics of the study participants (n=5.237)

Characteristics	Men (n=2,172)	Women (n=3,065)	Overall (n=5,237)	*P* for group
	Mean ± SD	Mean ± SD	Mean ± SD	
Anthropometric and handgrip strength				
Age (years)	70.8 ± 8.0	70.2 ± 7.7	70.5 ± 7.8	0.004
Height (cm)	162.9 ± 6.9	150.9 ± 6.3	156.0 ± 8.8	<0.001
Weight (kg)	67.8 ± 12.5	62.7 ± 13.2	64.8 ± 13.1	<0.001
BMI (kg/m^2)	25.6 ± 4.0	27.7 ± 5.3	26.8 ± 4.9	<0.001
Handgrip strength (kg)	26.7 ± 8.5	16.7 ± 5.7	20.9 ± 8.6	<0.001
Handgrip (kg)/weight (kg)	0.40 ± 0.12	0.27 ± 0.10	0.33 ± 0.12	<0.001
Sociodemographic outcomes	n (%)	n (%)	n (%)	
Socioeconomic status				
Level I	807 (37.2)	986 (32.2)	1,793 (34.2)	0.088
Level II	897 (41.3)	1,295 (42.3)	2,192 (41.9)	0.397
Level III	417 (19.2)	662 (21.6)	1,079 (20.6)	0.709
Level IV	38 (1.7)	90 (2.9)	128 (2.4)	<0.001
Level V-VI	13 (0.6)	32 (1.0)	45 (0.9)	0.763
Urbanicity				
Urban	1,602 (73.8)	2,453 (80.0)	4,055 (77.4)	0.589
Rural	570 (26.2)	612 (20.0)	1,182 (22.6)	0.016
Ethnic group				
Indigenous	171 (7.9)	142 (4.6)	313 (6.0)	<0.001
Black “mulato” or Afro-Colombian	202 (9.3)	226 (7.4)	428 (8.2)	0.016
White	540 (24.9)	848 (27.7)	1,388 (26.5)	0.671
Others*	955 (44.0)	1,351 (44.1)	2,306 (44.0)	0.342
Cognition outcome				
Cognitive impairment	304 (14.0)	498 (16.2)	802 (15.3)	0.014
Locomotion outcomes				
Sarcopenia	445 (20.5)	796 (26.0)	1,241 (23.7)	<0.001
Falls	324 (14.9)	560 (18.3)	884 (16.9)	<0.001
Functional impairment	322 (14.8)	677 (22.1)	999 (19.1)	<0.001
Difficulty walking 400 meters	274 (12.6)	423 (13.8)	697 (13.3)	<0.001
SPPB < 6 points	455 (20.9)	1015 (33.1)	1,470 (28.1)	<0.001
Psychological outcomes				
Depression	1,073 (49.4)	1,605 (52.4)	2,678 (51.1)	<0.001
Mental problems	123 (5.7)	342 (11.2)	465 (8.9)	<0.001
Sensory outcomes				
Visual problems	1,187 (54.7)	1,715 (56.0)	2,902 (55.4)	<0.001
Hearing problems	618 (28.5)	682 (22.3)	1,300 (24.8)	<0.001
Vitality				
Weight loss	335 (15.4)	582 (19.0)	582 (11.1)	<0.001
Appetite loss	403 (18.6)	868 (28.3)	1,271 (24.3)	<0.001

Comorbid chronic diseases			
Hypertension	1,040 (47.9)	1,889 (61.6)	2,929 (55.9)	<0.001
Diabetes	306 (14.1)	562 (18.3)	868 (16.6)	<0.001
Respiratory diseases	217 (10.0)	351 (11.5)	568 (10.8)	0.050
Cardiovascular disease	297 (13.7)	452 (14.7)	749 (14.3)	0.145
Osteoporosis	101 (4.7)	543 (17.7)	644 (12.3)	<0.001
Cancer	98 (4.5)	161 (5.3)	259 (4.9)	0.122
Clinical outcomes			
Hospitalized > 24 h last year	249 (11.5)	378 (12.3)	627 (12.0)	0.187
Drug use	1,360 (62.6)	2,424 (79.1)	3,784 (72.3)	<0.001
Lifestyle outcomes			
Alcohol	494 (22.7)	151 (4.9)	645 (12.3)	<0.001
Smoking	329 (15.1)	219 (7.1)	548 (10.5)	<0.001
Meeting PA recommendations	1,683 (77.5)	2,630 (85.8)	4,313 (82.4)	<0.001

Data are presented as mean ± SD or No. (percentage) of participants. SD, standard deviation; BMI, Body mass index; PA, physical activity. * Others (mestizo,gitano/ROM, etc). Significant difference between men and women group were analyzed by t-student or chi-square test.

Table 2 and Figure 1 show smoothed age- and sex-specific percentiles of handgrip strength in men and women. The data showed that men performed better in the test at all ages than women. In men, the 50th centile of handgrip strength ranged from 17.6 kg to 30.5 kg, and in women from 12.4 kg to 18.5 kg. There was a decrease in muscle strength across the age range in both sexes.

Table 2. Smoothed age-and sex-specific percentile of handgrip strength

Sex/age group	n	L	S	P3	P10	P25	P50(M)	P75	P90	P97
Men (n=2,172)										
60–64	562	1.07	0.26	14.0	19.6	25.1	30.5	35.9	41.2	46.4
65–69	535	1.04	0.28	12.6	18.0	23.3	28.6	33.9	39.1	44.3
70–74	423	0.95	0.30	11.0	16.0	21.2	26.3	31.6	36.8	42.1
75–79	304	0.81	0.33	9.4	13.9	18.7	23.8	29.1	34.6	40.3
80–84	201	0.69	0.36	7.5	11.4	15.7	20.4	25.5	30.9	36.6
85 +	147	0.60	0.40	6.0	9.3	13.2	17.6	22.5	27.8	33.6
Women (n=3,065)										
60–64	873	1.00	0.32	6.8	10.7	14.6	18.5	22.4	26.3	30.1
65–69	774	1.10	0.32	6.1	9.8	13.6	17.3	21.1	24.8	28.6
70–74	563	1.02	0.35	5.0	8.7	12.4	16.1	19.8	23.5	27.2
75–79	427	0.99	0.36	4.0	7.6	11.1	14.7	18.3	21.8	25.4
80–84	271	1.14	0.43	1.9	5.8	9.6	13.4	17.2	21.0	24.8
85 +	157	0.98	0.44	1.4	5.1	8.8	12.4	16.1	19.8	23.5

L, power in the Box-Cox transformation for “correcting” the skewness, M, median, S, coefficient of variation; P, percentile.

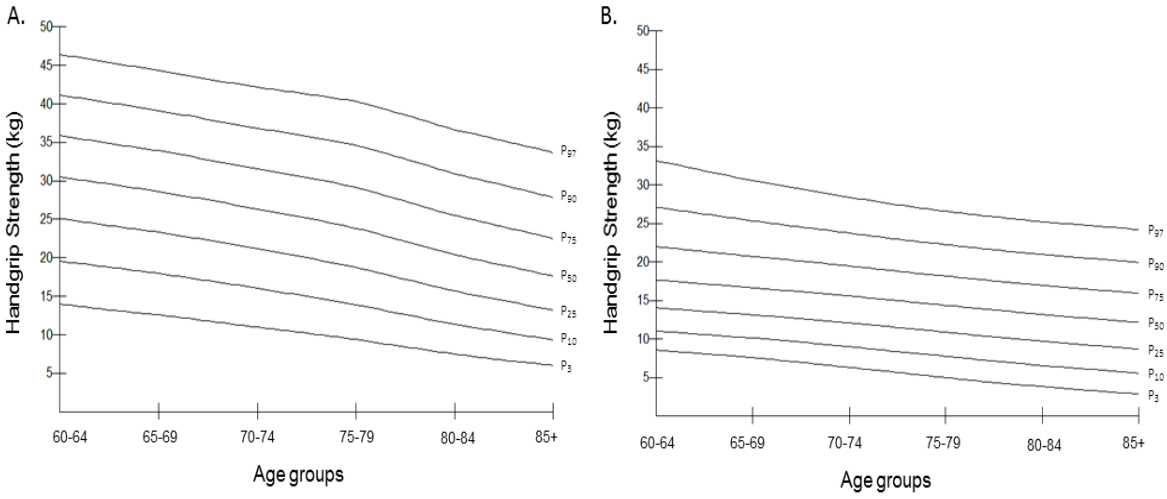

Figure 1. Absolute strength smoothed centile curves for men (A) and women (B) for Colombian aged 60 + years**.** The analysis was adjusted for age, ethnicity, socioeconomic status, urbanicity, BMI, smoking status, alcohol intake, drug use, physical activity, and medical conditions (presence or absence of osteoporosis, cardiovascular diseases, hypertension, diabetes, cancer, or respiratory diseases).* Pooled intrinsic capacity was calculated without hospitalization outcome values.

Weak handgrip cut-off values using <1 SD by sex and age group are shown in Table 3. These cut-off points ranged from 17.4 to 8.6 and 10.1 to 4.9 in men and women, respectively.

Table 3. Weak handgrip cut point values using<1 SD by sex and age group

Sex/age group	Cut point (kg)
Men	Mean
60–64	17.4
65–69	15.7
70–74	14.3
75–79	12.3
80–84	10.1
85 +	8.6
Women	
60–64	10.1
65–69	8.9
70–74	8.2
75–79	6.7
80–84	5.3
85 +	4.9

Finally, Figure 2 shows the association between optimal handgrip strength (kg) with the domains of intrinsic capacity. Overall, participants with optimal handgrip strength had better intrinsic capacity than weak older adults, including both men (odds ratio [OR]=0.62, 95%CI 0.53 to 0.71; p<0.001) and women (OR=0.79, 95%CI 0.68 to 0.92; p=0.002). Regarding the intrinsic capacity domains, older men with optimal handgrip strength had lower odds of having cognition (OR=0.50, 95%CI 0.29 to 0.85; p=0.010), locomotion (OR=0.47, 95%CI 0.37 to 0.59; p<0.001), and vitality (OR=0.68, 95%CI 0.47 to 0.98; p=0.040) than their weaker counterparts. Older women with optimal handgrip strength also had lower odds of having cognition (OR=0.44, 95%CI 0.24 to 0.80; p=0.007), locomotion (OR=0.66, 95%CI 0.51 to 0.85; p=0.001), and psychological (OR=0.57, 95%CI 0.40 to 0.82; p=0.002) problems than their weaker counterparts (Figure 2). Additionally, older men with handgrip strength greater than the muscle weakness cut-off points had lower odds of hospitalization than their weaker counterparts (OR=0.47, 95%CI 0.29 to 0.78; p=0.004).

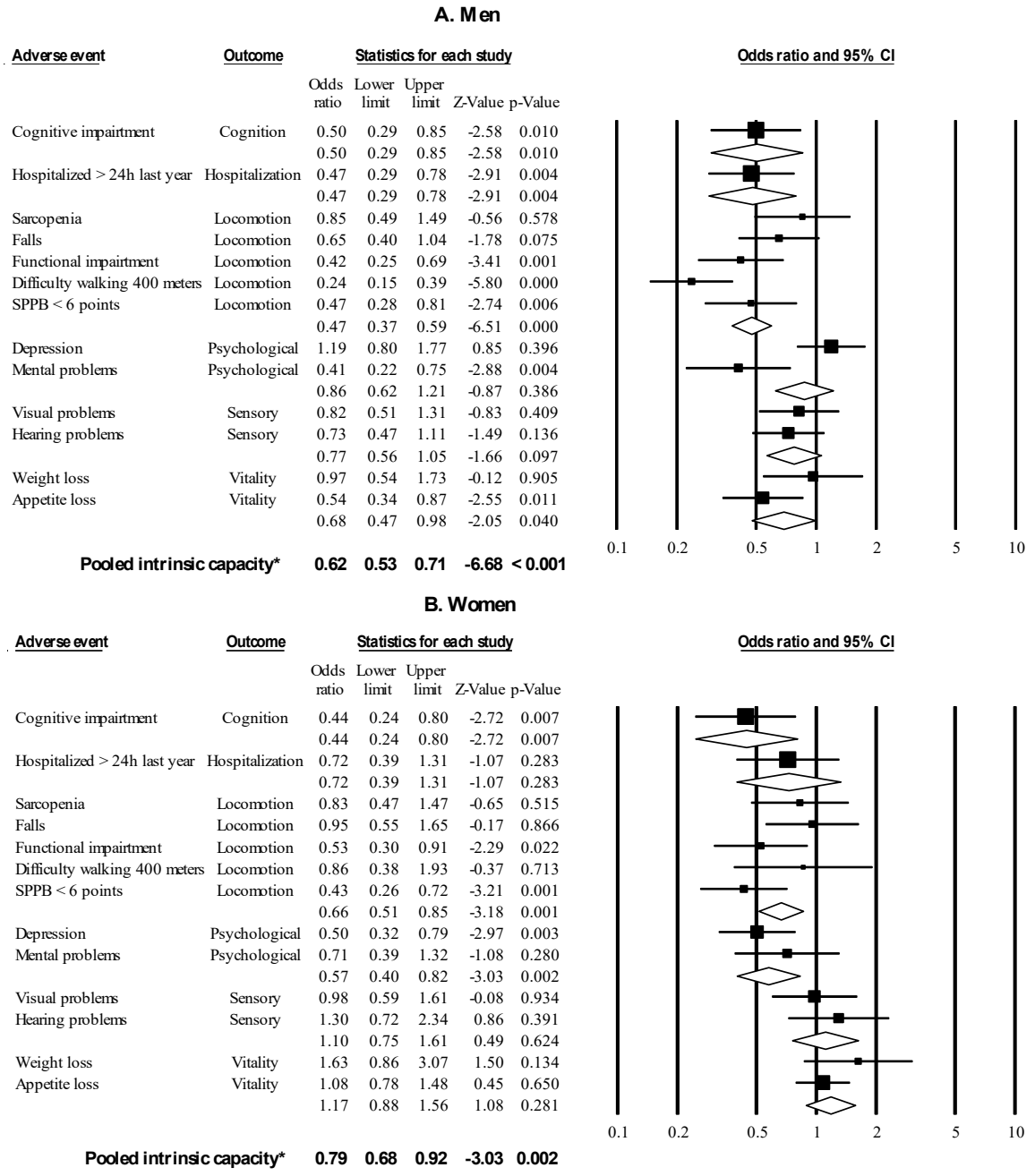

Figure 2. Association between health handgrip strength (Kg) with the components of the intrinsic capacity and hospitalization

4. Discussion

Using a nationally representative sample of older Colombian adults, this study presents normative data for handgrip strength, identifies sex- and age-specific muscle weakness cut-off points, and determines the odds of adverse events for each

intrinsic capacity domain for individuals with handgrip strength greater than the muscle weakness cut-off points. Overall, older adults with handgrip strength greater than the muscle weakness cut-off points had lower odds of adverse events in most of the intrinsic capacity domains (especially in cognition and locomotion domains) and hospitalization (only in men) than their weaker peers. Our results may inform intervention strategies aiming to increase muscle strength and promote healthy aging.

Several handgrip strength normative ranges for older adults from populations with different nationalities and ethnicities have been published in the last several years [26-30], however, to our knowledge, normal handgrip strength values have never been described for the Colombian population. We found that, overall, older Colombian adults have lower handgrip strength values than their peers in other populations [26-29]. Our results showing that gender and age affect handgrip strength are in accordance with the findings of previous studies [26-29]. Thus, the results of this study contribute to the current body of literature by presenting sex- and age-specific weakness cut-off points among the Colombian elderly.

Different handgrip strength mean values have been observed in different countries, as reported previously [20], but the nature of these differences is not known. Differences in handgrip strength mean values between Colombian older individuals from a less-developed country (this study) and individuals in developed countries may be due to a number of factors, although it is uncertain which of the three factors, genetic, environment or biological, are more decisive for handgrip strength results [31]. For instance, biological or environment factors such as health status, lifestyle, and demographic and socioeconomic characteristics vary greatly between countries with different handgrip strength levels. Along this line, education and socioeconomic status are factors that might explain differences in handgrip strength ranges among countries [32]. Also, beyond ethnic differences in height and in skeletal muscle mass and function [33], there are well-recognized differences in dietary protein intake between different countries, and this variation might also explain differences in muscle strength [34]. Absolute strength has also been related to nutrition status and is reported to have positive influence on individuals' grip strength. Another possible reason for the divergence between studies might be methodological differences (i.e., variability in the equipment used and the protocol for measuring handgrip strength) [35].

Several studies have determined absolute [11, 14, 10] and relative handgrip strength cut-off points [12, 13], which are overall higher than our cut-off points. For example, Duchowny et al. [14] determined cut-off points for weakness associated with gait speed (<0.8 m/second) in older American adults, with values of <40 kg and <31 kg in men and women, respectively. Similarly, Cruz-Jentoft et al. [10] found that among community-dwelling older adults in Italy, a handgrip strength <30 kg in men and <20 kg in women was associated with slow gait speed and an inability to walk 1 km without difficulty. Therefore, different cut-off points are observed in different countries; however, while the nature of these differences is unclear [31], as mentioned,

heterogeneous designs, genetic, and environmental factors may explain some of the differences among the studies.

The handgrip strength cut-off points reported in the present study are useful for determining who among older adults may benefit from lifestyle modifications to preserve muscle strength and reduce the odds of physical and mental limitations. In this context, our results reveal that older men with handgrip strength greater than the muscle weakness cut-off points had a lower odds of hospitalization for >24 hours than their weaker counterparts. However, the cross-sectional design of the present study did not allow us to determine whether the measured handgrip strength differed from habitual strength, or if the handgrip was impaired as a result of the presenting condition (see limitations, below). Our results partially confirm those of previous studies that analyzed the prospective association between customary handgrip strength and hospital admission, which showed varying results [9] [36]. The Hertfordshire Cohort Study [9] provided evidence that handgrip strength among community-dwelling men and women in the UK was associated with risk of hospital admission over the following decade. By contrast, a prospective study of 279 older adults aged ≥70 years from Germany who were followed-up for 18 months found no association between handgrip strength and the risk of hospital admission [36]. The differences between these studies may be explained by the thresholds for admission, which likely differ between healthcare systems, and their cross-sectional design.

A recent narrative review reported that weak handgrip strength was associated with reduced cognitive performance over time; therefore, greater handgrip strength may be protective against cognitive decline in older adults [37]. Indeed, recent evidence has shown that weak handgrip strength is associated with an increased risk of psychological problems such as depression [38] [39]. These findings were confirmed by the results of our analysis, which suggested that older adults with handgrip strength greater than the muscle weakness cut-off points had lower odds of cognitive impairment and depression than their weaker peers. Overall, weak handgrip strength, cognition and depression share some risk and pathogenic factors (particularly an increased rate of oxidative stress [40] and inflammation [41], decreased sex hormone levels [42] and maximal voluntary contraction [43]) that may influence the onset of depression and cognitive impairment [44]. Given the strength of the evidence in this area, handgrip strength and our cut-off points are easy to utilize and are clinically useful biomarkers of cognitive decline and mental health across the lifespan of individuals from the Colombian population.

Physical decline, in terms of decreasing muscle weakness and poor mobility, has been repeatedly included as an additional vital sign [45] and a key instrument for the functional assessment of older patients [46]. The present results are also in agreement with those of previous research and suggest that handgrip weakness is associated with measures of functional limitations in older adults [47]. For example, Ishizakiet et al. [48] determined that older adults with weak handgrip strength had difficulty performing many tasks, such as shopping for groceries, preparing meals

and performing housework. Our lower cut-off points appear to have the ability to identify older adults of both sexes with locomotion problems. Therefore, it seems that it is especially important for older adults to preserve muscle strength to avoid functional limitations, such as by participating in muscle strengthening activities to preserve function. Additionally, our results suggest that optimal handgrip strength is associated with a lower odds of experiencing weight loss in older men, and so muscle strength could favor the maintenance of optimal homeostasis [7].

Finally, the only intrinsic capacity domain that did not appear to be related to handgrip strength was hearing impairment. Hearing loss in the elderly is of increasing importance as the global population ages. Disabling hearing negatively affects communication and social engagement and can lead to reduced quality of life in adults [49], and may also underlie cardiovascular risk and diseases (i.e. diabetes, hypertension and history of cerebrovascular accident) [50]. These associations are mainly related to the compromised blood supply to the cochlea under vascular disease conditions [51], as well as other sensor neural, nutritional status and medical comorbidity factors that may accumulate with age and are not a result of normal aging [51]. Peripheral age-related hearing loss is also a possible biomarker and modifiable risk factor for cognitive decline, cognitive impairment, and dementia [50 52]. Our results, however, revealed that an individual with low levels of handgrip strength might not necessarily have a worse hearing status, and suggest that different age-related mechanisms could be underlying this.

The strengths of this study include the large sample size of older adults with a nationally representative proportion of persons aged ≥60 and the objective assessment of muscle strength. This study does, however, have some limitations. First, the cross-sectional design did not allow a definitive conclusion that weak muscle strength precedes adverse events. Second, several measures, such as falls, history of chronic disease, and drug use, were self-reported by participants; therefore, different types of response biases may have been introduced.

5. Conclusion

This study provides reference values for handgrip strength in Colombian individuals 60 years and older. After categorizing participants as weak or not weak based on the handgrip cut-off points, non-weakness was associated with a decreased odds of intrinsic capacity impairments, especially in the cognition and locomotion domains, and of hospitalization (only in men). Therefore, a simple handgrip strength test with the appropriate cut-off points may be a good candidate for clinical assessment of risks to physical and mental health in older Colombian adults.

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Conflicts of Interest: The authors declare no conflict of interest.

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CHAPTER 4

GAIT SPEED AS A MEDIATOR OF THE EFFECT OF SARCOPENIA ON DEPENDENCY IN ACTIVITIES OF DAILY LIVING.

1. Introduction

Sarcopenia is an age-related loss of muscle mass and function in older adults and may favor 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, promotes 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, 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 ageing. Indeed, the European Working Group on Sarcopenia in Older People (EWGSOP) 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 four-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) (REF). 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, have three factors related Sarcopenia, declining of gait speed, loss of independency in ADL; and between them a vicious circle is forms. Consequently and taking into account the

bibliography (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 effect 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.

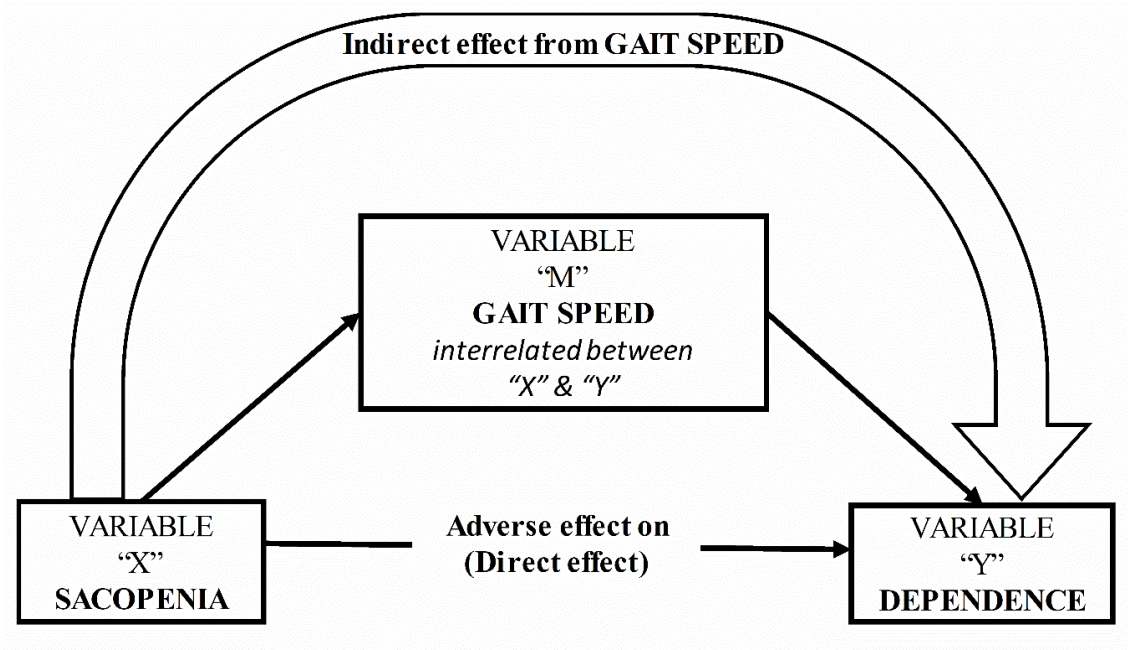

Figure 1. Statistical mediation simple diagram

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.

2. Method

2.1 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 multicenter

project originally conducted by the Pan-American Health Organization (PAHO) 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 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 = 1,684), ADL (n = 1,281) and CC (n = 1,024) 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 (ACTA 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).

2.2 Data Collection

Body measurement assessments were collected by investigators trained in standardized measurement methods, previously trained by research staff from the coordinating centers (Universities of Caldas and Valle). All information collected was 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/m2) 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 with foot flat on the floor using an inelastic tape measure. Thus, the CC values presented here combine the results of left- 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 socioeconomic 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. Finally, 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.

2.4 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 (SD) 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, were 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 model:

Model 1 adjusted by sex, gender and BMI; Model 2 adjusted by model 1 + nutritional status; Model 3 adjusted by model 2 and problems to walk 400-m.

To examine whether gait speed mediated the association between sarcopenia and dependence components of physical function, a 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). Mediation hypotheses were tested using the bias-corrected bootstrap method with 5,000 samples to calculate confidence intervals (CI95%). An indirect effect was considered significant when the confidence interval did not include zero (25).

3. 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 females than in males. Regarding sociodemographic covariates, the results indicated a higher prevalence of sarcopenia with advanced age and with low socioeconomic 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% versus 13.8%).

Table 1. Sample characteristics stratified by sarcopenia status

Sample characteristics	Sarcopenia (N = 3,168)	Non-sarcopenia (N = 16,537)	Total (N = 19,705)	p-value
Female, n (%)	2,021 (18.4)	8,943 (81.6)	10,964 (55.6)	<0.001
Male, n (%)	1,147 (13.1)	7,594 (86.9)	8,741 (44.4)	
Age group, n (%)				
60–64	621 (10.3)	5,393 (89.7)	6,014 (30.5)	
65–69	640 (12.8)	4,360 (87.2)	5,000 (25.4)	
70–74	644 (17.3)	3,076 (82.7)	3,720 18.9)	<0.001
75–79	585 (21.7)	2,107 (78.3)	2,692 (13.7)	
80–84	392 (26.5)	1,086 (73.5)	1,478 (7.5)	
85 +	286 (35.7)	515 (64.3)	801 (4.1)	
Socioeconomic level, n (%)				
1	1,714 (54.1)	6,971 (42.2)	8,685 (44.1)	<0.001
2	1,073 (33.9)	6,420 (38.8)	7,493 (38.0)	

3	309 (9.8)	2,654 (89.6)	2,963 (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)	1,124 (7.8)	1,360 (8.1)	<0.001
Black	288 (12.6)	1,701 (11.8)	1,989 (11.9)	
White	546 (23.9)	4,002 (27.7)	4,548 (27.1)	
Others	1,212 (53.1)	7,646 (52.8)	8,858 (52.9)	
Smoking status, n (%)				
Yes	526 (16.6)	1,695 (10.3)	2,221 (11.3)	<0.001
No	2,642 (83.4)	14,840 (89.7)	17,482 (88.7)	
Physical Activity “proxy”, n (%)				
Yes	3,190 (19.3)	375 (11.8)	3,565 (18.1)	<0.001
No	13,327 (80.7)	2,790 (88.2)	16,117 (81.9)	
Problems to walk 400-m, n (%)				
No	2,120 (66.9)	11,810 (71.4)	13,930 (70.7)	<0.001
Barely	502 (15.8)	2,505 (15.1)	3,007 (15.3)	
Some problems	275 (8.7)	1,138 (6.9)	1,413 (7.2)	
A lot of problems	249 (7.9)	1,008 (6.1)	1,257 (6.4)	
Can not walk 400-m	17 (0.5)	63 (0.4)	92 (0.4)	
BMI, 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	1,603 (50.6)	5,325 (32.3)	6,838 (34.7)	
Normal nutritional status	1,283 (40.5)	10,782 (65.2)	12,217 (62.0)	
Missing data			4090	
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)	1,086 (5.5)
Mild	357 (11.3)	1,433 (8.7)	1,790 (9.1)
Non dependency	2,547 (80.4)	14,262 (86.2)	16,809 (85.3)

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 problems to walk 400-m. 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 problems to walk 400-m.

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 BMI
Model 2 = adjusted by model 1 + nutritional status
Model 3 = adjusted by model 2 + difficulties to walk 400-m

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 since 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.

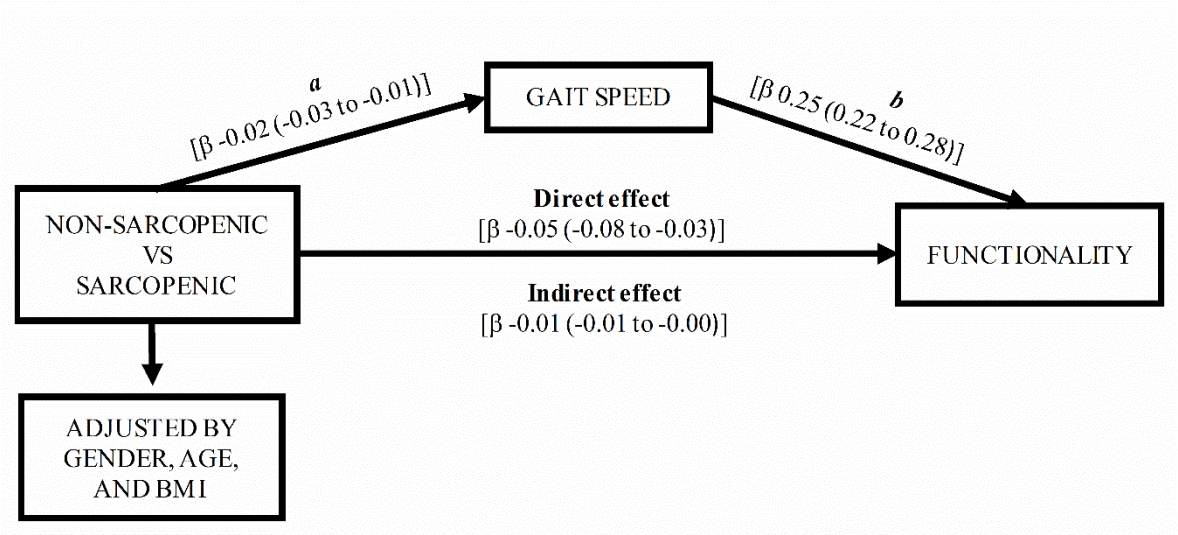

Figure 2. Gait speed as mediator of the effect of sarcopenia on dependency in activities daily living.

4. 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, since 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 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, since 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 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 fibers under contraction and exert 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 EWGSOP proposes an algorithm for sarcopenia case-finding and not only CC; however, it seems that CC is a valid and reliable method to diagnoses sarcopenia (18,19). Another limitation that could affect the results of this study is the level of functional dependence, since 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.

5. 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.

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CHAPTER 5

GENERAL DISCUSSION

General discussion

The most relevant finding of this doctoral thesis work are the interactions between health conditions and the IC domains in a sample of older adults of the 2015 SABE Colombia Survey. Regarding metabolic syndrome (MS)as an abnormal metabolic condition, its prevalence was established along with the associated risk factors in the elderly. Likewise, a description of the values of handgrip strength was made, determining for the first time, the cut-off points of strength by sex and age for this population, and their association with decreased probability of impairment of the IC. Finally, the mediating role of gait rate was explored as an indicator of the locomotion domain between sarcopenia and dependence on activities of daily living.

In this sense, evidence is provided on health conditions associated with losses of IC, responsible for much of the decline in functionality and dependency in the elderly (1). Thus, it can be deducted that if we know how to enhance the IC domains with adequate health conditions, better functionality, healthy aging, and wellbeing in the elderly can be achieved, as proposed by the WHO (2,3). Likewise, variations in health conditions contribute to the diversity found in FA in the elderly in older age with younger groups(4).

Different interactions between health conditions and IC losses can be established, for example, increased metabolic cardio risk determined by the presence of MS, which leads to losses in the vitality domain within the IC. This metabolic alteration is associated with both loss of strength and muscle mass in the locomotion domain and this, in turn, leads to changes in nutritional status.

The analysis of IC, as a multi-dimensional indicator, is complex, but useful for understanding and comparing functional capacity among individuals and population groups, independent of chronological age and multimorbidity (1). That is why, recently, the WHO presented a guide on comprehensive care, focused on measurement and on ways for primary care and care of the elderly, which seeks to provide guidance on the measurement protocols of the elderly, associated with losses in IC: loss of mobility, malnutrition, visual impairment, hearing loss, cognitive decline, symptoms of depression.

Prevalence of MS and associated factors (study 1)

The main finding herein was the considerably high prevalence of MS in the sample (54.9%). The occurrence of MS was more prevalent in females than in males; irrespective of the aging stage (females had the highest prevalence in aging stage III (70–80 years) and in aging stage I (60–65 years for males). The most prevalent MS-components for the overall sample were abdominal obesity (78.5%), low levels of HDL-c (57.3%), EABP (53.1%), and high levels of fasting blood triglycerides (45.5%).

A relationship exists between MS and all-cause mortality and CVD mortality. Recently, Sang-Yhun *et al*., (5) performed a meta-analysis with 20 prospective studies, finding that MS is associated with all-cause mortality and CVD mortality [relative risk (RR), 1.23; 95%CI, 1.15–1.32; I2=55.9%] and CVD mortality (RR, 1.24; 95%CI, 1.11–1.39; I2=58.1%). Risk estimates of all-cause mortality for single components of metabolic syndrome were significant for higher values of waist circumference or body mass index (RR, 0.94; 95% CI, 0.88–1.00), higher values of blood glucose (RR, 1.19; 95% CI, 1.05–1.34), and lower values of high-density lipoprotein (HDL) cholesterol (RR, 1.11; 95% CI, 1.02–1.21). In the elderly population, metabolic syndrome was associated with increased risk of all-cause and CVD mortality. Therefore, having a 54.9% prevalence of MS in older adults in Colombia, presents an increased risk of all-cause and CVD mortality.

It should be noted that while the prevalence of MS in the present sample is high (54.9%), it is similar to that of other Latin American studies in the elderly with 53% (6) and Mexico (7). In relation to gender, the higher prevalence of MS in women is explained by hormonal changes in menopause (8). This higher prevalence in women is associated with a higher risk of knee osteoarthritis (odds ratio (OR) = 1,644, p <0.001; and OR = 1,608, p <0.001) (9). Thereby, MS is associated with displacement of locomotion in adult women.

Similarly, MS, as a health condition, was associated with losses in cognitive functions, dietary patterns, and metabolic health in older adults in New Zealand (10). The foregoing was also demonstrated by Kassam *et al*., in a cross-sectional study in which the prevalence of metabolic syndrome in the elderly with schizophrenia, in individuals 55 years or older (n = 353), almost half of them (n = 77; 51.7%) tested positive, according to the NCEP ATPIII criteria for MS. These findings support that the prevalence of MS among the elderly with morbidities is high, and their diagnosis and prior intervention is essential to improve the wellbeing of the elderly (11).

Finally, MS is a health condition that plays an important role in the inflammatory profile of the elderly, mainly due to increased levels of IL-6 and CRP (12), which entails even greater cardiometabolic risk in the elderly.

Handgrip strength values and their association with IC.

Handgrip strength is a considerably reliable measure, to evaluate muscle strength due to its reproducibility, reliability, and validity (13). Muscular strength, as evaluated by handgrip strength, has predictive value to assess declines in physical and mental capacities in the elderly (14); these are both components of the intrinsic capacity construct. Recent studies have shown that greater handgrip muscular strength is associated with lower all-cause and cancer mortality (15). Other authors have associated low handgrip values with increased waist circumference and body mass index (16), which is why it is considered a predictor

of nutritional status (17) and the presence of chronic diseases, hypertension (HT), diabetes mellitus (DM), coronary heart disease (CHD), and chronic obstructive pulmonary disease (COPD) (18).

The aging process is related to changes in muscle mass and, in its neurophysiological component, to changes that generate loss in the contractile capacity of muscle fiber, so that 57% muscle strength losses in type-II muscle fiber have been reported, as well as 25% decrease in type-I muscle fiber (19). Loss of muscle mass and strength affects physical performance, functional status, and mobility and favors the presence of sarcopenia, understood as a progressive loss of muscle mass and strength that increases the risk of disability and death in the elderly (20.21).

Overall, older adults with handgrip strength greater than the muscle weakness cut-off points had lower odds of adverse events in most of the intrinsic capacity domains (especially in cognition and locomotion domains) and hospitalization (only in men) than their weaker peers. Our results may inform intervention strategies aiming to increase muscle strength and promote healthy aging.

Several papers have published normative reference values of handgrip strength in older people in different populations (22,23,24); however, in Colombia, it is the first time that reference values are reported for this population.

In conclusion, our findings demonstrated the association between an optimal prehensile force with each of the IC domains, mainly with the cognitive, locomotion, and vitality domains. No associations with the auditory sensitivity domain will be established. Low strength values are associated with cognitive change and depression than their weakest peers with reduced cognitive performance (26-28). Given the results obtained, our prehensile force cohort points are useful to predict cognitive risk and mental health in the elderly in Colombia.

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

Sarcopenia is the loss of muscle mass and age-dependent function. It is a common condition among the elderly and is associated with several adverse health outcomes (29). Sarcopenia is associated with falls, frailty, malnutrition, disability, and mortality (30-32) and it is a highly prevalent in the elderly (33). Sarcopenia brings costs to health and social systems; therefore, it is necessary to study its interactions with the IC domains.

Slow walking speed has been used to predict adverse health outcomes, such as hospital admissions, falls, and mortality (34,35). Our findings demonstrated the positive mediating effect of gait rate to decrease the negative

impact that sarcopenia has on ADLs. Older adults with sarcopenia, but who have a better walking speed have a better functional dependence on ADL.

Decreased walking speed has been related to cognitive deficits in the elderly (36). This reflects decreased information processing to respond to orders, standing, and moving the body; it is a complex activity that requires important cognitive processes. In addition, our findings demonstrate how the presence of sarcopenia is associated with low speed in gait and, consequently, in the loss of functionality and independence (37). Gait rate can positively affect the negative effects of sarcopenia on functional dependence.

What is evident is a close relationship between the cognitive domains of vitality and cognition, given that strength, muscle mass, cognitive processes, and functional dependence are related. What is relevant is that for the first time these interrelations with epidemiological evidence are demonstrated, so the compression between the interactions between the biomarkers of each domain is a field of work that must be developed towards the future.

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CHAPTER 6

CONCLUSIONS, AND FUTURE PERSPECTIVES

Study 1 (Chapter 2)
Conclusion

The prevalence of MS is 54.9% among the Colombian elderly and females had the highest prevalence of MS, irrespective of the aging stage. High abdominal obesity was the main prevalent MS component (78.5%). Male gender, sarcopenia status, and being a smoker were found significantly associated with the probability of MS. New health policies and prevention strategies focused on the elderly Latin American population should be implemented based on these findings.

Future perspective 1:

When observing a prevalence of MS in the Colombian elderly, due to the characteristics of the population from each region of the country, the need is clear to conduct regional studies to evaluate the factors associated with the prevalence of MS in the elderly and, therefore, improve the diagnosis and treatment of the disease with cardiovascular risk reduction.

It is important to conduct clinical trials with multicomponent trials to see their effects on each of the components of MS in the Colombian elderly.

The SABE study can be continued in five years to identify patterns of epidemiological trend in long-term MS prevalence.

Research should continue on the interactions of MS with other components of the IC domains.

Study 2 (Chapter 3)
Conclusion

A simple measure, such as prehensile strength, and cohort point deficiency can be good biomarkers for the clinical assessment of physical and mental health risks in the Colombian elderly.

Future perspective 2:

With strength reference values for the elderly population in Colombia, it is necessary to carry out additional studies on the effects of enhancing physical exercise programs in this population to assess the improvements in strength and its effects on the elderly population.

Further research is required on the role of strength as an indicator of the locomotion domain and its interactions with other biomarkers from other domains, such as cognition vitality, visual and auditory impairments, and psychological aspects.

Study 3 (Chapter 4)
Conclusion

The relationship between sarcopenia and functional dependence is mediated by gait rate, which can attenuate this negative impact. Accordingly, promoting physical exercise in older adults with sarcopenia focused on improving gait rate should take into account the loss of functional independence associated with sarcopenia. Gait rate is a clinical marker and an important measure of functional capacity among the elderly.

Future perspective 2:

With respect to gait rate in the relationship between sarcopenia and functional dependence, it is necessary to study this mediation in the elderly with underlying pathological conditions, like COPD and brain diseases, with the proposed identification of possible changes within rehabilitation programs so that they focus on the priority rehabilitation objective

It is suggested to continue studying other possible mediations of gait rate with other health conditions, such as frailty.

Relevant Papers

CHAPTER 7

RELEVANT PAPERS

Metabolic Syndrome and Related Disorders

Metabolic Syndrome and its Influencing Factors in Older People: A Secondary Analysis of SABE Colombia in 2015

Journal:	*Metabolic Syndrome and Related Disorders*
Manuscript ID	Draft
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Keyword:	Aging, Cardiovascular Disease, Clinical, Central Obesity, Dyslipidemia
Manuscript Keywords (Search Terms):	Older adults, Metabolic risk, Cardiovascular diseases, Prevalence, Latinos

Title: Metabolic Syndrome and its Influencing Factors in Older People: A Secondary Analysis of SABE Colombia in 2015

Running Head: Metabolic Syndrome in Older People from Colombia

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Abstract

Background: Understanding the metabolic syndrome prevalence in the national level is important to develop the effective programs and strategies to prevent and control metabolic syndrome. This study aimed to analyze the prevalence of metabolic syndrome and its influencing factors in older individuals aged ≥60 years in Colombia.

Methods: The data for this study came from a secondary cross-sectional, nationally representative SABE study Survey on Health, Well-Being, and Aging in Colombia, 2015. A total of 1637 participants (60.7% women, 70.5±7.9 years) from 86 Colombian municipalities participated. A structured questionnaire was used to collect data on socio-demography, lifestyle, and medical conditions. Measurements included anthropometric variables, handgrip strength, high-density lipoprotein cholesterol, triglycerides, fasting glucose, and blood pressure. Univariate and multiple regression models were established as part of the main analysis.

Results: Using the harmonized Joint Scientific Statement criteria, metabolic syndrome was present in 54.9% of the study population, with a higher prevalence among females than males (59.8% vs. 47.3%). Individuals who were cigarette smoking (odds ratio [OR] = 1.59; 95% confidence interval [CI] = 1.03–2.44; p=0.034), male gender (OR = 1.38; 95%CI = 1.05–1.82; p=0.020) and sarcopenia (OR = 1.63; 95%CI = 1.06–2.52; p=0.026) were more likely to have a higher prevalence estimate of metabolic syndrome.

Conclusions: Overall prevalence of metabolic syndrome among older adults in Colombia is high. Smoking, male gender, and sarcopenia status are associated with metabolic syndrome. These results suggested that metabolic syndrome is still a serious public burden in Colombia, and screening for promotion of healthy lifestyle and nutrition counselling should be offered routinely in old age.

Keywords: Older adults, Metabolic risk, Cardiovascular diseases, Prevalence

1. Introduction

The number of elderly people worldwide is expected to double over the next 50 years [1,2]. Older (> 60 years old) in Latin America and the Caribbean will reach ~101 million (15% of the population)[3]. For Colombia, the mean life expectancy will rise to 77.6 years for women and 69.8 years for men in 2025. Due to this, the Pan American Health Organization (PAHO) and the Merck Institute of Aging and Health called for greater surveillance over the causes of morbidity and mortality in older adults [4].

The Metabolic Syndrome (MS) is a complex cluster of cardiovascular risk factors that are associated with a sedentary lifestyle, poor nutrition, and consequent obesity, and is strongly associated with cardiovascular diseases, include glucose intolerance (type 2 diabetes, impaired glucose tolerance, or impaired fasting glycemia), insulin resistance, abdominal obesity, dyslipidemia, and hypertension [5,6]. Accordingly, MS increases the risk of developing diseases of cardiovascular origin such as acute myocardial infarction [7], ischemic stroke or coronary heart disease [8,9]. Indeed, the prevalence of cardiovascular disease attributable to MS is around 12–17% [10].

Several studies have deepened in the analysis of the presence of MS in Latin America reporting its associated factors such as increasing age, Hispanic or indigenous heritage, physical inactivity, high alcohol intake, smoking, history of hypertension or type 2 diabetes (first-degree family members), and belonging to a low socioeconomic status [11]. Likewise, the general prevalence of MS in Latin-American countries has been established in 24.9% (range: 18.8–43.3%) and is slightly more frequent in women (25.3%) than in men (23.2%). On the other hand, several risk factors for MS have been suggested, such as alcohol/cigarette smoking intake, residence (urban/rural) and inflammatory markers [12], dietary factors, such as intake of total fat or saturated fat [13], physical inactivity, and poor physical fitness [14]. We previously demonstrated in Colombian collegiate students aged 18–30 years that those with the sex (male), age (over 23 years old), weight status (overweight or obese) and having an unhealthy waist to height ratio were more likely to have a prevalence of MS [15]. Additionally, another studies that included diverse Hispanic/Latino populations suggested a marked heterogeneity in risk factor prevalence within this population [16].

Latin America has undergone a well-documented epidemiologic transition fuelling a non-communicable disease epidemic [17] and makeable changes in

people´s lifestyles that may contribute to greatly increased burden on cluster of cardio-metabolic disease as MS [11]. However, only a few studies have analyzed MS prevalence specifically in older adults, in whom important changes could still be made to their lifestyles to improve independence and quality of life, as well as preventing other lethal diseases. Therefore, the aim of this study were to analyze the prevalence of MS and its influencing factors in Colombian older people from a sample of the SABE Colombia study. Understanding the MS prevalence in the national level is important to develop the effective programs and strategies to prevent and control MS.

2. Materials and Methods

2.1. Study Design and Sample Population

This study is part of the 2015 SABE study Survey on Health, Well-Being, and Aging in Latin America and the Caribbean, which is a multicenter project conducted by the Pan-American Health Organization (PAHO) 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 [18]. The instrument used was derived from the original SABE study conducted in 5 Latin America capital cities [19]. The estimated sample size was 24,553 individuals, and assuming an 80% response of the target sample was 30,691 individuals [18]. The final sample size achieved, (including 244 municipalities) was 23,694 elderly Colombians.

Institutional review boards 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. Written informed consent was obtained from each individual before inclusion and completion of the first examination. Permission and details available in https://www.minsalud.gov.co/. The study protocol to the secondary analysis was approved by the Human Subjects Committee at the Pontificia Universidad Javeriana (ACTA ID 20/2017-2017/180, FM-CIE-0459-17).

The survey included elderly Colombians (≥60 years) using purposive, randomized sampling (urban and rural areas). In this sub-sample, 86 municipalities were defined for blood sampling, and two out of every five people were called to participate. A total of 1637 were included in the present analysis.

2.2. Measurements

Data collection staff was trained by the research teams of the coordinating centers (Universities of Caldas and Valle) for face-to-face interviews and physical measurements. Body mass index (BMI) was estimated in kg/m^2 from the measured weight and height. Sarcopenia was defined according to calf circumference (CC) as a "proxy" measure for assessing early identification of sarcopenia in clinical practice, due to the low cost and ease of obtaining [20]. As described by Rolland et al., [20] a CC smaller than 31 cm is considered to be indicative of sarcopenia. This cut-off has been recommended for use in older individuals by the WHO Expert Committee [21].

Handgrip strength was assessed on a Takey dynamometer (Grip Strength Dynamometer Model T.K.K. 5001®, Takei Scientific Instruments Co., Ltd, Niigata, Japan) including the highest value (kg) from two attempts (both hands). Handgrip strength was categorized into 3 levels by sex (low, moderate and high) according to the KORA-age study [22].

Blood samples were taken by puncturing the capillary vein under standardized conditions, with the participant having fasted at least 10–12 hours beforehand. The biochemical profile included: (i) HDL-cholesterol (HDL-c); (ii) triglycerides; (iii) low-density lipoprotein cholesterol (LDL-c); (iv) total cholesterol; and (v) glucose fasting. Samples were analyzed by standard enzymatic colorimetric methods.

Blood Pressure, Diastolic (DBP) and systolic (SBP), was measured with subjects in rest (5-min) with an automated procedure using the OMRON HEM – 705 monitor (Omron® Healthcare Europe BV, Hoofddorp, The Netherlands).

For the lifestyle, personal habits regarding alcohol intake (participants were categorized as those who do not drink and those who drink less than one day per week, two to six days a week, or everyday) and smoking status (participants were categorized as those who do not smoke and those who have never-smoked, those who currently smoke, or those who previously smoked) were recorded. A “proxy physical activity” report was conducted 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?" Participants were considered physically active if they responded affirmatively two of the three

questions. Self-reported comorbidities were assessed by asking the participants if they had a diagnosis made by a physician.

2.3. Definitions of MS

MS was defined according to the most recent Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention [23] by adopting the Ethnic Central and South American criteria for waist circumference. Participants were classified as having MS if they had at least 3 of following metabolic risk factors or components (MS-components): abdominal obesity (waist circumference ≥90 cm for Latin-American men and ≥80 cm for Latin-American women; elevated triglycerides (fasting serum triglycerides ≥150 mg/dL or taking medication for abnormal lipid levels); reduced HDL-c (fasting serum HDL-c <40 mg/dL in males; <50 mg/dL in females or specific treatment for this lipid abnormality); elevated blood pressure (SBP ≥130 mmHg or DBP ≥85 mmHg or taking hypertension medication); elevated fasting glucose (serum glucose level ≥100 mg/dL or taking diabetes medication).

2.4. Definitions of potential influencing factors

Potential influencing factors included sex (male/female), sarcopenia status (≤31 cm with sarcopenia or >31 cm without sarcopenia), handgrip strength categorized into 3 score by sex (low, moderate and high levels), alcohol intake (never or no/current or yes), smoking status now (never or no/current or yes), and physical activity “proxy” levels (physically active/non physically active).

2.5. Statistical Analysis

General characteristics from the study sample are presented as frequency and percentage or as the mean and standard deviation (SD). Two-way analysis of variance or the χ^2 test to compare sex and age differences were used. Descriptive analysis of the prevalence of the MS by sex an age stages, as well as, a descriptive analysis of the MS-components have been presented in figures using percentages. Relationships between influencing factors of MS and MS (categorical variables) have been performed by Pearson Chi-square.

Simple logistic regressions were performed individually for each independent variables to analyze the association with MS. MS was included in each simple logistic

regression as the dependent variable (reference: to have MS). Sex with males as an indicator, age, BMI, to have sarcopenia, handgrip strength with the high level of strength as an indicator, be a smoker, have alcoholic intake, and be physically inactive, were included as fixed factors.

Then, a multiple logistic regression was used to identify the main predictor or influencing factors associated (clinical characteristic) of MS including at the same model: sex (indicator: male), sarcopenia (indicator: to have sarcopenia), handgrip strength (indicator: high level of handgrip strength) smoking habit (indicator: be smoker), alcoholic habit (indicator: to have alcoholic habit) and physical activity levels (indicator: be physically inactive) as independent variables. Both, simple logistic regression and multiple logistic regression (model) used the intro method. Multiple logistic regression was adjusted by the following confounders: age, ethnicity, socioeconomic status, urbanicity, BMI, medication use, and medical conditions (presence or absence of hypertension, diabetes, respiratory diseases, cardiovascular diseases, stroke, osteoporosis or cancer).

The analysis of the data was performed with the SPSS statistical software package, version 24.0 (IBM, Chicago, IL, USA) for Windows.

3. Results

3.1. Characteristics of the study population

The general characteristics of the participants are presented according to the overall sample, sex and aging stages in Table 1. Most of the participants (males=213, females=312) belonged to aging stage III (70–80 years). Social status in level 2 (42.6%), urban area context (83.3%), and other ethnic groups (54.1%) were the most prevalent sociodemographic characteristics. The waist circumference and BMI means in the overall sample were 92.5 cm and 27.3 kg/m^2, respectively. Most of the sample had abdominal obesity (78.6%), and an overweight status (41.3%), but an healthy sarcopenia status (86%). Risky blood parameters for the overall sample were SBP (132.64±23.5 mmHg), Fasting Serum Triglycerides (160.94±83.3 mg/dL), and LDL-c (126.85 ± 35.3 mg/dL). The handgrip strength mean for the overall sample was 32.4 kg, with prevalence at high category (59.4%).

Several statistical differences were observed according to the sex (Table 1). Females showed several highest values compared with males (i.e.: abdominal obesity, BMI, overweight, total cholesterol, HDL-c, LDL-c), whereas males presented

higher values regarding waist circumference, blood pressure, and handgrip strength. Additionally, numerous statistical differences were observed between aging stages within the sex groups (Table 1).

**** Table 1 here ****

3.2. Clinical characteristics and prevalence of MS

The incidence of alcohol consumption (9.2%) and smoking (12.1%) was low but significantly higher in men than in women (smoking: 12.6% vs 6.9%; alcohol: 21.3% vs 6.1%), and mainly were presented at first aging stages. Most of the sample (mainly women at the first aging stages) were not physically active (82.9%). Hypertension was the most common chronic comorbidity (44.2%), following of diabetes (16.4%). Females presented the highest prevalence compared with males (60.8% vs 48%, p<0.001, and 18.3% 13.4%, p=0.009, respectively) at aging stage III and IV, respectively. Finally, cardiovascular diseases and stroke with no differences between sex and aging stages, Table 2.

**** Table 2 here ****

3.3. Prevalence of MS and its distribution by MS-componets

The overall prevalence of MS in the study sample was 54.9% (95% confidence interval [CI] 52.4–57.3. The prevalence of MS according to sex, and the aging stages is presented in Figure 1. A. MS was more prevalent in females than in males (59.8% versus 47.3%) irrespective of the aging stage. For females, the prevalence of MS was highest in aging stage III (64.6%), whereas for males it was highest in the aging stage I (49.4%). The most prevalent MS-components were abdominal obesity (78.5%), low levels of HDL-c (57.3%), elevated arterial blood pressure (EABP) (53.1%), and high levels of fasting blood triglycerides (HLFBTg) (45.5%). Elevated fasting blood glucose was the least common components of MS (31.1%). Related to the MS-components by sex (Figure 1.B), the greatest differences were observed for high waist circumference (HWC), and low levels of HDL-c (LLHDL), with a higher prevalence in females than in males (HWC: females=88% vs males 64 %, p<0.001 and LLHDL: females=60.7% vs males=51.7%, p<0.001). The prevalence of HLFBTg was also significantly higher in females than in males (females=48.8% vs males=40.8 %, p=0.001). However, males presented a higher prevalence of EABP than females (57.2% vs 50.8 %, p=0.001). The prevalence of MS according to the MS-components was presented in figure 1.C.

Additionally, we explore the MS prevalence according to the studied comorbid chronic diseases. Participants with MS presented the hypertension as the main comorbid chronic disease with a prevalence of 60.9% of the sample. The rest of participants with MS presented the following prevalence of the comorbid chronic diseases: diabetes (23.1%), cardiovascular disease (16.2%), osteoporosis (14.1%), respiratory diseases (11.1%), stroke (5.1%), and cancer (4.8%), Table 2.

**** Figure 1 here ****

3.4. Relationship between MS status and clinical characteristics

Relationship between MS status and clinical characteristics were presented in table 3. Clinical characteristics such as sex, sarcopenia status and handgrip strength were significantly associated ($p<0.05$).

**** Table 3 here ****

3.5. Influencing factors associated with MS

Table 4 shows the ORs for the influencing factors associated with MS among the Colombian older adults (univariate analysis) were male gender (OR= 1.662, 95%CI= 1.359–2.032; $p<0.001$), to have a sarcopenia status (OR= 2.55, 95%CI=1.900–3.434; $p<0.001$), and a low handgrip strength (OR=1.432, 95%CI= 1.084–1.892; $p=0.011$). Sarcopenia status was the main variable associated with MS, with more than two times the approximate risk of occurrence of MS.

**** Table 4 here ****

After the adjustment by the main confounders in the multiple regression model (Figure 2), male gender (OR= 1.388; 95%CI= 1.054–1.828; $p=0.020$) and a sarcopenia status (OR= 1.637; 95%CI= 1.061–0.525; $p=0.026$) were again significantly associated with MS. In addition, being a smoker was positively associated with MS (OR= 1.591; 95%CI= 1.036–2.443; $p=0.034$). Thus, in general, to have a sarcopenia status and smoking were the main risk factors associated with MS in this sample of Colombian older adults, with more than 1.5 times the approximate risk of occurrence of MS.

**** Figure 2 here ****

4. Discussion

The main finding of the present study was the considerably high prevalence of MS in the sample (54.9%). The prevalence of MS was more prevalent in females than in males irrespective of the aging stage (females highest prevalence in aging stage III (70–80 years) and in aging stage I (60–65 years for males). The most prevalent MS-components for the overall sample were abdominal obesity (78.5%), low levels of HDL-c (57.3%), EABP (53.1%) and high levels of fasting blood triglycerides (45.5%). Female gender, a poor sarcopenia status, and be smoking were found to be significantly associated with probability of MS (after adjustment).

It should be noted that while the prevalence of MS in the present sample is high (54.9%), it is similar to other Latin American studies in older people, such as Ecuador 59.9% [24], Brazil with 51.5.% [16], Southern Cone of Latin America with 53% [25], in Ecuador elders (≥65 years) with 40% [26],Colombia with 52.2%, [27] and in the CARMELA study with 35.5% [28]. A reasonable explanation for the high prevalence of MS in the present study could be that most of the sample belonged to an urban area (83.3%), where people have a higher risk of MS [29,30]. This might be due to several lifestyle aspects, such as dietary patterns or low physical activity levels, as was found in our study where most of the sample (82.9%) was insufficiently active.

According to our results regarding sex, in the six Latin American studies previously mentioned [16,24–28], females also had a higher prevalence of MS than males in general, and particularly in the older adult groups (when it applied). As previously reported, MS is more common in females in an older North American population of Mexican origin [31]. Many of the typical aspects of MS, such as increased abdominal adiposity and dyslipidemia, hyperglycemia, and hyperinsulinism, are experienced in females along the menopausal transition [31]. The cessation of estrogen secretion at the beginning of menopause accentuates these aspects, decreasing the quality of life[32]. Additionally, it seems that the onset of menopause begins earlier in Latin American countries than in Europe and USA, what may be associated with higher altitude residency and lower educational-economical income [33,34]. In the present study, the overall sample belonged to social status 1-2 (72.7%), and with a residency at high altitude (Bogota, 2680 m), but without significant differences between genders.

Consequently, scientific investigations on Latin American postmenopausal women related to the MS prevalence and its associated factors have increased [35],

although little is known about older adult populations. In addition, males presented the highest MS prevalence (49.4%) in aging stage I (60–65 years), but not in the later ones. In agreement with our results, in a cross-sectional analysis of 4289 Taiwanese individuals [36], the male:female MS ratio reversed after the age of 60 (men 30.4% vs women 40.3%). Similarly, in a large population-based project enrolling 36 cohorts from 10 European countries [37], there was an increase in the prevalence of MS from age groups 19–39 years to 60–78 years was nearly two-fold in males, and five-fold in females, resulting in a higher prevalence of MS in women after the age of 50. Again, the typical changes in the hormonal status during and after menopause could explain the significant influence of sex in the age-related increase of MS [38,39]. Other explanation could be due to fluctuations in individual and social behavior, such as modifications in socio-economic status or adoption of an unhealthy lifestyle [40].

Overall, the most prevalent MS-components were abdominal obesity (78.5%), low levels of HDL-c (57.3%), EABP, and high levels of fasting blood triglycerides (45.5%). Likewise, in the study of Davila et al.[27], where 312 (34.7% of the whole sample) older adults (55–64 years) from Medellin (Colombia) were evaluated, the major MS-metabolic risk factor was abdominal obesity with a prevalence of 87.4%, followed by low levels of HDL-c (59.1%), HLFBTg (52.0%) and EABP (44.8%).

Concerning MS-components analyzed by sex in the whole sample, several statistical differences were observed. For instance, females presented a higher prevalence of HWC and LLHDL than males. Moreover, females displayed significantly higher HLFBTg than males, but males presented a higher prevalence of EABP. Accordingly, in a French study conducted in 3508 participants, females presented a higher prevalence of HWC, and low HDL-cholesterol, whereas EABP was the most commonly found metabolic disorder in males; however, the age range only covered 35–64 years [41]. Alike, a Taiwanese study found a high prevalence of BP and TG in males below 60 years, although without differences in MS-components between genders in the age group above 60 years [42]. Additionally, a large Korean study including 103,763 participants aged 66 years or older revealed that females had a significantly higher percentage of abdominal obesity (+12%) and lower HDL-c levels (−47%) than men, whereas men presented higher rates of EABP (+6%). However, contrary to our results, the Korean study indicated that men had usually high levels of triglycerides (+5%), compared with woman [43]. Unfortunately, gender-

related differences are sensitive to social and cultural conducts, dietary behaviors and psychosocial aspects [38].

Finally, the multivariate regression model indicated that the clinical characteristics that were associated with MS were male gender, to have a sarcopenia status, and smoking (after adjustment). In accordance with our results of univariate regression analysis, numerous studies have shown the high prevalence of MS and associated risk in people with a nutritional status of normal weight near the upper range or slightly overweight [44]. Moreover, sarcopenia has been linked to several metabolic disorders, and a recent meta-analysis revealed that it is positively associated with MS in middle-aged and older non-obese people [45]. In our study, sarcopenia status was high (14% for the overall sample) compared with a previous study carried out in the same region [46], where 6.96% of the participants (≥60 years old) presented sarcopenia. Also, our sarcopenia prevalence is higher than most of the studies conducted in older adults in other countries, going from Belgium with 12% to the United States with 5%, but not Japan (24.2%) [45]. However, stratification cut-off values for community-dwelling populations could vary between studies, as well as age range included.

Lastly, regarding the significant association between MS and smoking status, a previous Chinese study showed that active smoking in men was strongly associated with increased CVD risk [47], independent of the presence of MS. Moreover, tobacco smoke exposure (including active and passive smoking) increased the prevalence of coronary heart disease, stroke, and CVD in both genders with or without MS. In the same line, smoking habits could also explain in part the association between MS and male gender, since in the present sample, significantly more smokers were males than females for the whole sample (males = 12.6% vs females = 6.9) and for most of the age stages.

In conclusion, the prevalence of MS is 54.9% among Colombian older adults and females presented the highest prevalence of MS irrespective of the aging stage. High abdominal obesity was the main prevalent MS-components (78.5%). Male gender, sarcopenia status, and being a smoker were found to be significantly associated with the probability of MS. New health policies and prevention strategies focused on the elderly Latin American population should be implemented based on these findings.

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Figure Legend

Figure 1. A: Distribution of the prevalence of metabolic syndrome according to aging stage and sex. B: Prevalence of the MS-components according to sex. (HWC = High Waist Circumference; EABP =Elevated Arterial Blood Pressure; HLFG = High Levels of Fasting Glucose; HLFBTg= High Levels of Fasting Blood Triglycerides; LLHDL = Low Levels of High Density Lipoprotein; C: Prevalence of MS according to metabolic abnormalities. **p<0.001; *p=0.001.

Figure 2. Multiple logistic regression model of the influencing factors associated with MS among Colombian older adults. Multiple logistic regression adjusted for age, ethnicity, socioeconomic status, urbanicity, BMI, medication use, and medical conditions (presence or absence of hypertension, diabetes, respiratory diseases, cardiovascular diseases, stroke, osteoporosis or cancer).

Table 1. Characteristic of the sample study according to age group (stage) and sex.

	All (n=1637)	Males (n=642)						Females (n=995)						P value Males vs females
		Overall males	STAGE I (n=166)	STAGE II (n=150)	STAGE III (n=213)	STAGE IV (n=113)	P value (between stages)	Overall females	STAGE I (n=303)	STAGE II (n=245)	STAGE III (n=312)	STAGE IV (n=135)	P value (between stages	
Sociodemographic characteristics														
Age*	70.5 (7.9)	71.1 (8.1)	62.0 (1.38)	66.98 (1.5)	74.1 (2.8)	84.3 (3.6)		70.5 (7.9)	62.0 (1.42)	66.8 (1.4)	74.1 (2.8)	84.7 (4.1)		
Social Stratus														
Level 1	492 (30.1)	205 (31.9)	50 (30.1)	48 (32.0)	68 (31.9)	39 (34.5)		287 (28.8)	90 (29.7)	73 (29.8)	91 (29.2)	33 (24.4)		
Level 2	697 (42.6)	266 (41.4)	75 (45.2)	58 (38.7)	92 (43.2)	41 (36.3)		431 (43.3)	129 (42.6)	108 (44.1)	132 (42.3)	62 (45.9)		
Level 3	410 (25.0)	158 (24.6)	35 (21.1)	41 (27.3)	51 (23.9)	31 (27.4)	0.352	252 (25.3)	73 (24.1)	62 (25.3)	81 (26.0)	36 (26.7)	0.719	
Level 4	30 (1.8)	10 (1.6)	3 (1.8)	3 (2.0)	2 (0.9)	0 (0.0)		20 (2.0)	10 (3.3)	1 (0.4)	6 (1.9)	3 (2.2)		
Level >5	8 (0.5)	3 (0.5)	3 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)		5 (0.5)	1 (0.3)	1 (0.4)	2 (0.6)	1 (0.7)		
Urbanicity														
Urban	1363 (83.3)	514 (80.1)	138 (83.1)	119 (79.3)	169 (79.3)	88 (77.9)		849 (85.3)	258 (85.1)	212 (86.5)	263 (84.3)	116 (85.9		
Rural	274 (16.7)	128 (19.9)	28 (16.9)	31 (20.7)	44 (20.7)	25 (22.1)	0.697	146 (14.7)	45 (14.9)	33 (13.5)	49 (15.7)	19 (14.1)	0.897	
Ethnic group														
Indigenous	85 (6.1)	50 (9.2)	14 (8.8)	11 (8.0)	22 (12.2)	3 (4.6)		35 (4.1)	12 (4.2)	14 (6.1)	7 (2.7)	2 (2.7)		
Black "mulato" or Afro-Colombian	130 (9.4)	57 (10.5)	16 (10.1)	15 (10.9)	15 (8.3)	11 (16.9)		73 (8.6)	31 (11.0)	16 (7.0)	21 (8.1)	5 (6.7)		
White	422 (30.4)	154 (28.5)	52 (32.7)	39 (28.30)	48 (26.7)	15 (23.1)	0.404	268 (31.7)	87 (30.7)	70 (30.7)	83 (32.0)	28 (37.3)	0.535	<.001
Others*	750 (54.1)	281(51.8)	77 (48.4)	138 (52.9)	95 (52.8)	36 (55.4)		469 (55.5)	153 (54.1)	128 (56.1)	148 (57.1)	40 (53.3)		
Anthropometric Characteristics														
Waist Circumference*	92.5 (11.0)	93.4 (10.9)	93.3 (10.8)	92.1 (11.5)	93.87 (10.2)	93.5 (11.8) @	1.000	91.8 (11.0)	91.7 (11.1)	92.8 (9.8)	92.7 (11.7)	88.4 (10.9)$*@	<.030	<.001

Abdominal Obesity	1285 (78.6)	410 (64.0)	108 (65.1)	95 (63.3)	137 (64.6)	70 (61.9)	0.950	875 (88.0)	265 (87.5)	223 (91.0)	279 (89.7)	108 (80.0)	.010	<.001
Non-Abdominal Obesity	350 (21.4)	231 (36.0)	58 (34.9)	55 (36.7)	75 (35.4)	43 (38.1)		119 (12.0)	38 (12.5)	22 (9.0)	32 (10.3)	27 (20.0)		
BMI*	27.36 (4.6)	26.0 (3.9)	26.5 (3.7)@	25.8 (4.1)@	26.1 (3.6)@	25.2 (4.0)	>1.000	28.2 (4.9)	28.3 (4.7)@	28.8 (4.5)@	28.6 (5.2)@	25.7 (4.3)$*	<.001	<.001
Nutritional Status														
Underweight (<18.5 kg/m2)	22 (1.5)	12 (2.0)	3 (1.9)	6 (4.1)	1 (0.5)	2 (2.2)		10 (15.0)	1 (0.4)	1 (0.4)	4 (1.4)	4 (3.9)		
Normal weight (18.5-24.9 kg/m2)	463 (30.9)	237 (39.8)	44 (28.0)	62 (42.8)	85 (42.1)	46 (50.5)		226 (25.0)	67 (23.5)	52 (22.4)	61 (21.6)	46 (44.7)		
Overweight (25-29.9 kg/m2)	618 (41.3)	255 (42.9)	83 (52.9)	55 (37.9)	87 (43.1)	30 (33.0)	0.011	363 (40.2)	121 (42.5)	85 (36.6)	120 (42.4)	37 (35.9)	<.001	<.001
Obese (>30 kg/m2)	395 (26.4)	91 (15.3)	27 (17.2)	22 (15.2)	29 (14.4)	13 (14.3)		304 (33.7)	96 (33.7)	94 (40.6)	98 (34.6)	16 (15.5)		
Sarcopenia status														
No	1393 (86)	551 (87.0)	149 (90.9)	130 (87.2)	183 (87.1)	89 (80.9)	0.122	842 (85.4)	275 (91.1)	224 (92.2)	261 (84.7)	82 (61.7)	<.001	0.350
Yes	226 (14.0)	82 (13.0)	15 (9.1)	19 (12.8)	27 (12.9)	21 (19.1)		144 (14.6)	27 (8.9)	19 (7.8)	47 (15.3)	51 (38.3)		
Blood Parameters														
ASBP (mmHg)*	132.64 (23.5)	134.0 (23.8)	131.6 (22.0)$@	131.4 (24.1)	135.3 (24.3)	138.5 (24.4)	>1.000	131.7 (23.3)	126.51 (21.9)$@	130.8 (22.3)	135.4 (10.4)$	136.7 (26.2)$	<.001	.024
ADBP (mmHg)*	72.66 (11.7)	74.3 (12.3)	76.95 (12.6)$@	74.4 (11.8)	73.4 (12.0)$@	72.2 (12.8)$@	<0.020	71.6 (11.1)	72.3 (10.4)@	73.3 (11.7)	71.3 (10.3)@	67.4 (11.9)$*@	<.001	.045
Fasting Glycemia (mg/dL)*	98.34 (26.5)	97.25 (26.3)	95.6 (23.7)	95.1 (21.3)	100.5 (33.1)	96.3 (24.0)	1.000	99.1 (26.3)	99.6 (27.1)	100.2 (32.1)	99.1 (23.6)	95.5 (17.1)	>.050	>.050
Fasting Serum Triglycerides (mg/dL)*	160.94 (83.3)	153.7 (81.6)	175.4 (9.3)$	154.1 (16.6)	145.3 (75.5)$@	137.8 (69.8)$	<0.004	165.6 (84.1)	166.1 (85.9)	167.7 (89.3)	170.9 (83.3)@	148.6 (69.9)	>.050	.001
HDL-Cholesterol (mg/dL)*	45.63 (12.9)	41.8 (11.3)	41.3 (11.7)@	42.1 (11.6)@	41.9 (11.0)@	42.1 (10.9)@	1.000	48.1 (13.3)	47.8 (12.5)@	47.29 (12.6)@	47.46 (13.7)@	51.6 (14.5)$*	<.020	<.001
LDL-Cholesterol (mg/dL)*	126.85 (35.3)	120.1 (32.7)	122.7 (12.1)@	125.4 (33.3)$	117.8 (32.8)@	113.4 (31.5)$@	0.033	131.2 (36.2)	137.6 (33.2)$@	129.10 (37.1)	129.3 (38.6)$@	125.2 (33.6)$@	<.030	.010
Total-Cholesterol (mg/dL)*	195.32 (41.4)	183.9 (38.6)	189.8 (39.4)$@	189.8 (39.28)$@	180.3 (37.4)@	174.5 (36.4)$@	<0.015	202.6 (41.4)	209.0 (39.4)$@	200.8 (42.1)@	200.2 (43.6)$@	197.2 (38.1)$@	<.040	.010
Physical Fitness Parameters														
Handgrip strength (kg)	32.4 (12.3)	40.03 (12.6)	44.8 (12.1)@	43.3 (10.9)@	38.87 (11.7)@	30.3 (11.6)$*@	<0.001	27.2 (9.1)	29.1 (9.0)$@	27.9 (8.7)$@	25.8 (9.3)@	24.7 (8.6)$@	<.040	<.001
Low**	270 (17.5)	131 (21.2)	15 (9.3)	15 (10.1)	45 (22.3)	56 (52.8)		139 (15.0)	25 (8.7)	32 (13.7	53 (18.3)	29 (25.0)		
Moderate**	357 (23.1)	138 (22.3)	29 (18.0)	33 (22.1)	54 (26.7)	22 (20.8)	<0.001	219 (23.6)	66 (22.9)	52 (22.2)	73 (25.3)	28 (24.1)	<.001	.007
High**	918 (59.4)	349 (56.5)	117 (72.7)	101 (67.8)	103 (51.0)	28 (26.4)		569 (61.4)	197 (68.4)	150 (64.1)	163 (56.4)	59 (50.9)		

Data have been expressed as frequency and percentage for qualitative variables and *mean and standard deviation for quantitative variables. MS: metabolic syndrome

** Low: men, ≤30 (kg); women, ≤18 (kg). Moderate: men, >30 (kg) and ≤38 (kg); women, >18 (kg) and ≤24 (kg). High: men, >38 (kg); women, >24 (kg). ASP: Arterial Systolic Blood Pression; ADBP: Arterial Diastolic Blood Pression; HDL: High Density Lipoprotein; LDL: Low Density Lipoprotein; WHO: World Health Organization.

Missing DATA: Abdominal obesity = 2; Sarcopenia =18; Handgrip strength = 92; Smoking habits = 1; Fasting Glycemia = 15; Fasting Serum Triglycerides = 5; HDL-Cholesterol = 8;

Two-way ANOVA statistical significance symbols: (for pairs comparisons a highest p value was presented) $ statistical differences between aging stage groups

@ statistical differences between sex groups; $* statistical differences regarding the rest of the age subgroups; @* statistical differences regarding the rest of the age subgroups

Table 2. Clinical characteristics and distribution by stage aged group

Clinical characteristics	All (n=1637)	Males (n= 642) Overall males	STAGE I (n=166)	STAGE II (n=150)	STAGE III (n=213)	STAGE IV (n=113)	P value (between stages)	Females (n=995) Overall Females	STAGE I (n=303)	STAGE II (n=245)	STAGE III (n=312)	STAGE IV (n=135)	P value (between stages)	P value Males vs females
Smoking habits														
No smoke	1486 (90.8)	561 (87.4)	138 (83.1)	121 (74.7)	194 (91.1)	108 (95.6)	<0.001	925 (93.1)	276 (91.1)	231 (94.3)	293 (94.2)	125 (92.6)	0.380	**<0.001**
Smokes	150 (9.2)	81 (12.6)	28 (16.9)	38 (25.3)	19 (8.9)	5 (4.4)		69 (6.9)	27 (8.9)	14 (5.7)	18 (5.8)	10 (7.4)		
Alcohol consumption														
Non alcoholic	1438 (87.9)	505 (78.7)	109 (65.7)	112 (74.7)	182 (85.4)	102 (90.3)	<0.001	933 (93.9)	278 (91.7)	227 (93.0)	299 (95.8)	129 (95.6)	0.144	**<0.001**
Alcoholic	198 (12.1)	137 (21.3)	57 (34.3)	38 (25.4)	31 (14.6)	11 (9.7)		61 (6.1)	25 (8.3)	17 (7.0)	13 (4.2)	6 (4.4)		
Physical Activity "proxy"														
Physically active	280 (17.1)	144 (22.4)	53 (31.9)	45 (30.0)	37 (17.4)	9 (8.0)		136 (13.7)	45 (14.9)	40 (16.4)	41 (13.2)	10 (7.4)		
Non Physically active	1354 (82.9)	498 (77.6)	113 (68.1)	105 (70.0)	176 (82.6)	104 (92.0)	<0.001	856 (86.3)	258 (85.1)	244 (83.6)	269 (86.8)	125 (92.6)	0.093	**<0.001**
Comorbid chronic diseases														
Hypertension	911 (44.2)	307 (48.0)	63 (38.2)	59 (39.9)	116 (54.5)	69 (61.1)	<0.001	604 (60.8)	151 (50.0)	141 (57.6)	215 (69.1)	97 (71.9)	**<0.001**	<.001
Diabetes	268 (16.4)	86 (13.4)	25 (15.2)	24 (16.1)	30 (14.1)	7 (6.2)	0.090	182 (18.3)	45 (14.9)	47 (19.2)	62 (19.9)	28 (20.7)	0.314	0.009
Respiratory diseases	183 (11.2)	64 (10.0)	11 (6.6)	11 (7.3)	22 (10.3)	20 (17.7)	0.013	119 (12.0)	25 (8.3)	27 (11.0)	47 (15.1)	20 (14.8)	**0.043**	0.209
Cardiovascular diseases	233 (14.3)	80 (12.5)	12 (7.2)	18 (12)	30 (14.2)	20 (19.9)	0.052	153 (15.4)	37 (12.2)	33 (13.5)	55 (17.6)	28 (20.7)	0.065	0.104
Stroke	85 (5.2)	39 (6.1)	5 (3.0)	10 (6.7)	18 (8.5)	6 (5.3)	0.169	46 (4.6)	11 (3.6)	11 (4.5)	13 (4.2)	11 (8.1)	0.330	0.316
Osteoporosis	207 (12.7)	33 (5.1)	3 (1.8)	6 (4.0)	15 (7.1)	9 (8.0)	0.054	174 (17.5)	38 (12.6)	37 (15.2)	72 (23.3)	27 (20.0)	**0.004**	<0.001
Cancer	90 (5.5)	37 (5.8)	8 (4.8)	6 (4.0)	13 (6.1)	10 (8.8)	0.367	53 (5.3)	15 (5.0)	14 (5.7)	18 (5.8)	6 (4.5)	0.925	0.710

Data have been expressed as frequency and percentage. P in bold = significant differences

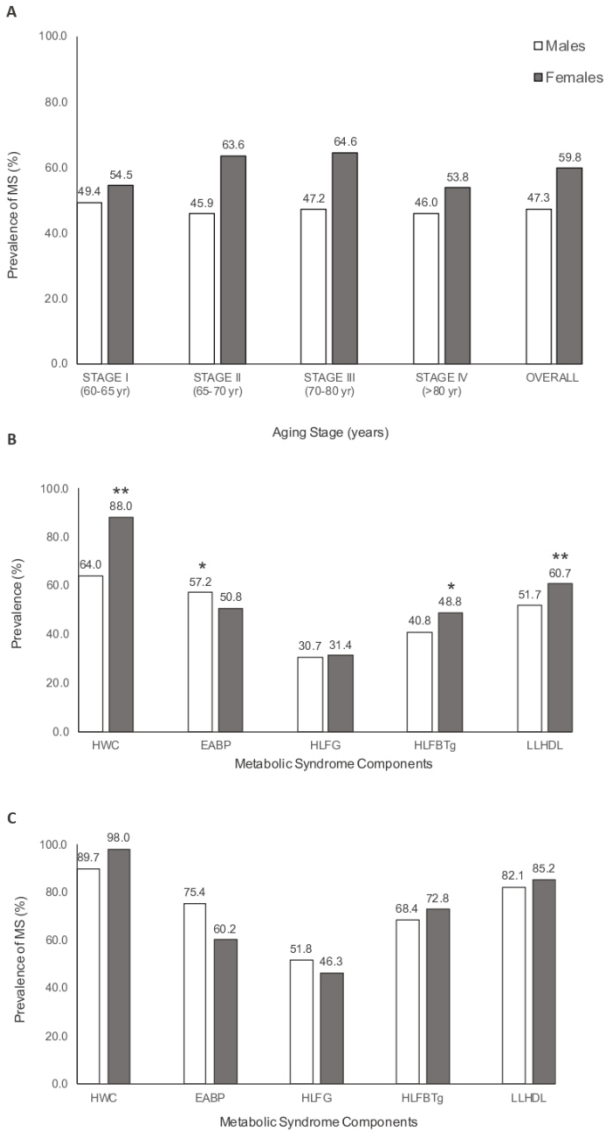
Table 3. Relationship between MS status and clinical characteristics

Clinical characteristics	Have MS	Not Have MS	Pearson Chi- square P value
Sex			
Men	336	301	**<0.001**
Women	395	588	
Sarcopenia status			
Yes	804	577	**<0.001**
No	78	143	
Handgrip strength			
Low	476	435	
Medium	201	151	**0.025**
High	163	104	
Smoking status			
Yes	76	72	0.108
No	654	817	
Alcohol intake			
Yes	789	633	0.212
No	100	97	
Physical Activity "proxy"			
Physically active	139	139	0.078
Non Physically active	747	592	

Table 4. Univariate association analysis between MS and clinical characteristics

Clinical characteristics	OR	95% CI		P value
Sex (reference males)	1.662	1.359	2.032	**<0.001**
Sarcopenia status				
Yes (reference No)	2.550	1.901	3.434	**<0.001**
Handgrip Strength (reference Hight)				
Low	1.432	1.084	1.892	**0.011**
Medium	1.216	0.949	1.559	0.121
Smoking status				
Yes (reference No)	1.319	0.940	1.850	0.109
Alcohol intake				
Yes (reference No)	1.209	0.897	1.629	0.212
Physical Activity "proxy"				
Non Physically active (reference active)	0.793	0.612	1.026	0.078

BMI: Body Mass Index; WHO= World Health Organization. p value in bold = significant association



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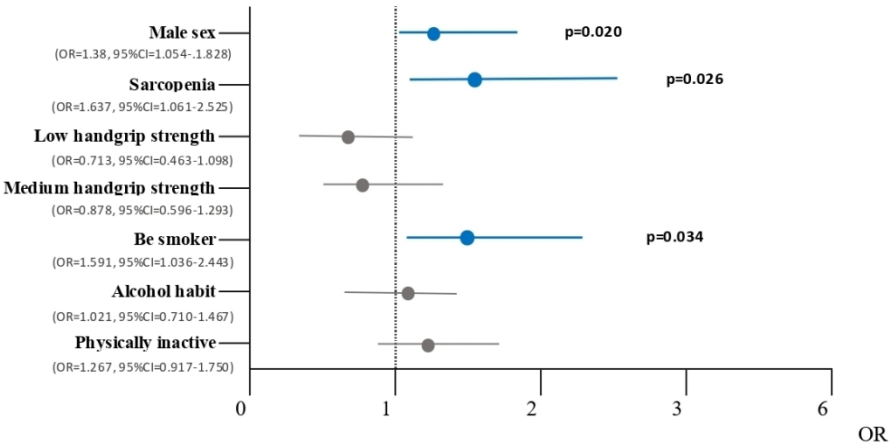

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Reference values for handgrip strength and their association with intrinsic capacity domains among older adults

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Abstract

Objective The purposes of this study were three-fold: (i) to describe handgrip strength in older individuals aged ≥60 years in Colombia; (ii) to identify sex-specific and age-specific muscle weakness cut-off points in older adults; and (iii) to determine the odds of adverse events for each of the intrinsic capacity domains for individuals with handgrip strength greater than the muscle weakness cut-off points, as compared with their weaker counterparts.

Methods A cross-sectional study was conducted in Colombia, among 5237 older adults aged ≥60 years old (58.5% women, 70.5 ± 7.8 years), according to 'SABE Survey 2015'. Handgrip strength data were obtained with a Takei dynamometer. Sociodemographic variables, five domains of intrinsic capacity (i.e. locomotion, vitality, cognition, psychological, and sensory), and medical conditions were assessed and analyzed. Adjustments variables were age, ethnicity, socio-economic status, urbanicity, body mass index, smoking status, alcohol intake, drug use, physical activity, and co-morbid chronic diseases. Sex-stratified analyses were conducted with logistic regression models.

Results Handgrip strength was greater among men than among women (26.7 ± 8.5 vs. 16.7 ± 5.7 kg, respectively, $P < 0.001$) at all ages. Weak handgrip strength cut-off points ranged from 17.4 to 8.6 and from 10.1 to 4.9 in men and women, respectively. Overall, participants with optimal handgrip strength had better intrinsic capacity [in men, odds ratio (OR) = 0.62, 95% confidence interval (CI) 0.53 to 0.71; $P < 0.001$; and in women, OR = 0.79, 95% CI 0.68 to 0.92; $P = 0.002$] than their weaker counterparts. Also, men with optimal handgrip strength had a lower risk of hospitalization (OR = 0.47, 95% CI 0.29 to 0.78; $P = 0.004$) than their weaker counterparts.

Conclusions This study is the first to describe handgrip strength values and cut-off points for muscle weakness among a nationally representative sample of Colombian older adults by age and sex. After categorizing older adults as weak or not weak based on the handgrip cut-off points, non-weakness was associated with a decreased odds of intrinsic capacity impairments. These cut-off points may be good candidates for clinical assessment of risks to physical and mental health in older Colombian adults.

Keywords Skeletal muscle; Handgrip; Older adults; Locomotion; Vitality; Cognition; Mental health

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Introduction

Colombia is a country with approximately 48 million inhabitants, with some 5.2 million inhabitants aged 60 years and older.[1] Currently, the life expectancy in Colombia is 72.3 years, and by 2025, life expectancy is expected to be 77.6 years for women and 69.8 years for men. In this context, the World Health Organization has published the World Report on Aging and Health,[2] which describes healthy ageing as the result of the interaction between the physical and mental capacity of an individual (the intrinsic capacity) and the context of each individual's life (the environment).[3] Accordingly, healthy ageing depends upon intrinsic capacity, socio-economic status, and physical environment, and the interactions between these factors.[4] In this vein, the World Health Organization has proposed five domains—locomotion, vitality, cognition, psychological, and sensory—that can be used to evaluate an individual's intrinsic capacity.

Muscular strength as evaluated by handgrip strength has predictive value for assessing declines in physical and mental capacities in older adults,[5] which are both components of the intrinsic capacity construct. Recent studies have shown that greater handgrip muscular strength is associated with lower all-cause[6] and cancer mortality.[7]

The world's population is rapidly getting older[8]; thus, the preservation of muscle strength and power with advancing age is of considerable clinical significance. Against this background, the development of clinically viable screening tools for detecting individuals at heightened risk for functional limitations is warranted.[7] Indeed, it has been reported that handgrip strength reference values and muscular weakness cut-off points for older adults are needed,[9] but no data have yet been described for the Colombian elderly population. Additionally, several cross-sectional studies have presented different handgrip strength cut-off points in Italian,[10] Finnish,[11] Chinese,[12] and American[13,14] older adults, thus suggesting that different ethnicities may have different muscle weakness cut-off points for identifying clinically relevant health outcomes.

The results of the Survey on Health, Well-Being, and Aging in Latin America and the Caribbean (SABE, from the initials in Spanish SAlud, Bienestar, and Envejecimiento) have increased our understanding of the ageing process and have helped to create public policies aimed at improving the well-being of the Latin American and Caribbean populations. They have also provided a framework for performing a second set of studies in the region.

The purposes of this study were three-fold: (i) to describe handgrip strength in older individuals aged ≥60 years in Colombia; (ii) to identify sex-specific and age-specific muscle weakness cut-off points in older adults; and (iii) to determine the odds of adverse events for each of the intrinsic capacity domains for individuals with handgrip strength greater than the muscle weakness cut-off points, as compared with their weaker counterparts.

Materials and methods

Study design

This study is part of the 2015 SABE study Survey on Health, Well-Being, and Aging in Latin America and the Caribbean. Of the initial 23 694 elderly Colombians who took part in SABE Colombia, a total of 5237 were included in the present analysis after excluding participants without handgrip strength results (n = 18 457). There were no differences in the study key characteristics (i.e. age groups, body mass, height, body mass index, and sex distribution) between the current study sample and the original SABE study sample (all $P > 0.05$). The 5237 elderly Colombians constituted the final analytical sample of the non-institutionalized population. 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). The study protocol to the secondary analysis was approved by The Human Subjects Committee at the Pontificia Universidad Javeriana (ACTA ID 20/2017-2017/180, FM-CIE-0459-17).

Details of background and design methods (i.e. characteristics of participants, sample calculation, outcomes, and analysis plan) of the SABE study have been previously published elsewhere[1]; nevertheless, the most relevant information is briefly described in the succeeding texts. All information collected was obtained through face-to-face interviews conducted at each site on mobile capture devices (e.g. tablets) or with printed versions of the questionnaire. During the personal interviews, direct physical measurements were taken, including handgrip strength [absolute and relative; i.e. handgrip strength (kg)/body mass (kg)], measured with a Takei dynanometer (Takei Scientific Instruments Co., Tokyo, Japan), height (standing and sitting), and weight. Five domains of the intrinsic capacity (locomotion, vitality, cognition, psychological, and sensory) were assessed as follows: (i) the cognition domain was assessed by the modified version of the mini-mental state examination[15,16]; (ii) the locomotion domain was defined according to five definitions—sarcopenia,[17] prevalence of falls, functional impairments assessed with an activities of daily living scale,[18] mobility/disability,[19] and physical performance assessed by the validated Spanish version of the short physical performance battery[20]; (iii) the psychological domain was assessed by the Yesavage Geriatric Depression Scale and mental problems; (iv) the sensory domain was assessed as hearing and vision problems[21]; and (v) the vitality domain was assessed as loss of appetite[22] and weight loss.

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The self-reported co-morbidities or medical conditions category was assessed by asking the participants if they had been diagnosed by a physician with hypertension, diabetes, respiratory diseases, cardiovascular diseases, cancer, or osteoporosis. Drug use was evaluated with the following question: 'Do you currently take or use any prescription medication'? For the lifestyle domain, personal habits regarding alcohol consumption and cigarette smoking were recorded. A 'proxy physical activity' was also evaluated. Finally, hospitalization >24 h in the last year was recorded. Details of the methods are available in the Supporting Information.

Data analysis

We used SPSS v24.0 software for Windows (SPSS, Chicago, IL, USA), except for the LMS method calculations (see the succeeding texts). The optimal power to obtain normality was calculated for each of a series of age groups and the trend summarized by a smooth (L) curve. Trends in the mean (M) and coefficient of variation (S) were similarly smoothed. The resulting L, M, and S curves contain the information to produce any centile curve and to convert measurements (even extreme values) into exact standard deviation (SD) scores.[23] Anthropometric and handgrip characteristics from the study sample are presented as the mean and SD. Normality for the selected variables was verified using histograms and Q–Q plots. Differences were analyzed by two-way analysis of variance or the χ^2 test to compare sex and age differences.

The LMS method assumes that the outcome variable has a normal distribution after a Box–Cox power transformation is applied, according to the LMS method implemented in the LMS Chart Maker Pro Version 2.54 (Medical Research Council, London, UK). Smoothed and specific curves for each age were obtained via a penalized maximum likelihood with the following abbreviations: M (median), L (Box–Cox transformation), and S (coefficient of variation).[24] The appropriate number of degrees of freedom was selected on the basis of the deviance, Q-tests, and worm plots, following the suggestions of Royston and Wright.[25] The P3, P10, P25, P50, P75, P90, and P97 smoothing centiles were chosen as age-specific and sex-specific reference values. Statistical significance was assessed with a two-tailed α level of 0.05.

Finally, logistic regression models were used to compare the prevalence of adverse events in the five domains of the intrinsic capacity according to the cut-off for handgrip strength. The analysis was adjusted for age, ethnicity, socio-economic status, urbanicity, body mass index, smoking status, alcohol intake, drug use, physical activity, and medical conditions (presence or absence of osteoporosis, cardiovascular diseases, hypertension, diabetes, cancer, or respiratory diseases).

Results

The characteristics of the sample are summarized in *Table* 1. Age ranged from 60 to 85 years, with a mean of 70.5 ± 7.8 years. Absolute and relative handgrip strength was higher among men than among women ($P < 0.001$). In the total sample, self-reported co-morbidities were presented in the following proportions of cases: cancer (4.9%), respiratory diseases (10.8%), osteoporosis (12.3%), cardiovascular diseases (14.3%), diabetes (16.6%), and hypertension (55.9%). According to the intrinsic capacity domains, overall, women had more problems with locomotion, sensory, and psychological parameters than men ($P < 0.01$), except in terms of hearing problems.

Table 2 and *Figure 1* show smoothed age-specific and sex-specific percentiles of handgrip strength in men (panel A) and women (panel B). The data showed that men performed better in the test at all ages than women. In men, the 50th centile of handgrip strength ranged from 17.6 to 30.5 kg and in women from 12.4 to 18.5 kg. There was a decrease in muscle strength across the age range in both sexes.

Weak handgrip cut-off values using <1 SD by sex and age group are shown in *Table* 3. These cut-off points ranged from 17.4 to 8.6 and from 10.1 to 4.9 in men and women, respectively.

Finally, *Figure 2* shows the association between optimal handgrip strength (kg) with the domains of intrinsic capacity. Overall, participants with optimal handgrip strength had better intrinsic capacity than weak older adults, including both men [odds ratio (OR) = 0.62, 95% confidence interval (CI) 0.53 to 0.71; $P < 0.001$] and women (OR = 0.79, 95% CI 0.68 to 0.92; $P = 0.002$). Regarding the intrinsic capacity domains, older men with optimal handgrip strength had lower odds of having cognition (OR = 0.50, 95% CI 0.29 to 0.85; $P = 0.010$), locomotion (OR = 0.47, 95% CI 0.37 to 0.59; $P < 0.001$), and vitality (OR = 0.68, 95% CI 0.47 to 0.98; $P = 0.040$) problems than their weaker counterparts. Older women with optimal handgrip strength also had lower odds of having cognition (OR = 0.44, 95% CI 0.24 to 0.80; $P = 0.007$), locomotion (OR = 0.66, 95% CI 0.51 to 0.85; $P = 0.001$), and psychological (OR = 0.57, 95% CI 0.40 to 0.82; $P = 0.002$) problems than their weaker counterparts (*Figure 2*). Additionally, older men with handgrip strength greater than the muscle weakness cut-off points had lower odds of hospitalization than their weaker counterparts (OR = 0.47, 95% CI 0.29 to 0.78; $P = 0.004$).

Discussion

Using a nationally representative sample of older Colombian adults, this study presents normative data for handgrip strength, identifies sex-specific and age-specific muscle weakness cut-off points, and determines the odds of adverse events for each intrinsic capacity domain for individuals with

Table 1 Characteristics of the study participants (n = 5237)

Characteristics	Men (n = 2172) Mean ± SD	Women (n = 3065) Mean ± SD	Overall (n = 5237) Mean ± SD	P for group
Anthropometric and handgrip strength				
Age (years)	70.8 ± 8.0	70.2 ± 7.7	70.5 ± 7.8	0.004
Height (cm)	162.9 ± 6.9	150.9 ± 6.3	156.0 ± 8.8	<0.001
Weight (kg)	67.8 ± 12.5	62.7 ± 13.2	64.8 ± 13.1	<0.001
BMI (kg/m^2)	25.6 ± 4.0	27.7 ± 5.3	26.8 ± 4.9	<0.001
Handgrip strength (kg)	26.7 ± 8.5	16.7 ± 5.7	20.9 ± 8.6	<0.001
Handgrip (kg)/weight (kg)	0.40 ± 0.12	0.27 ± 0.10	0.33 ± 0.12	<0.001
	n (%)	n (%)	n (%)	
Sociodemographic outcomes				
Socio-economic status				
Level I	807 (37.2)	986 (32.2)	1793 (34.2)	0.088
Level II	897 (41.3)	1295 (42.3)	2192 (41.9)	0.397
Level III	417 (19.2)	662 (21.6)	1079 (20.6)	0.709
Level IV	38 (1.7)	90 (2.9)	128 (2.4)	<0.001
Level V–VI	13 (0.6)	32 (1.0)	45 (0.9)	0.763
Urbanicity				
Urban	1602 (73.8)	2453 (80.0)	4055 (77.4)	0.589
Rural	570 (26.2)	612 (20.0)	1182 (22.6)	0.016
Ethnic group				
Indigenous	171 (7.9)	142 (4.6)	313 (6.0)	<0.001
Black 'mulato' or Afro-Colombian	202 (9.3)	226 (7.4)	428 (8.2)	0.016
White	540 (24.9)	848 (27.7)	1388 (26.5)	0.671
Others[a]	955 (44.0)	1351 (44.1)	2306 (44.0)	0.342
Cognition outcome				
Cognitive impairment	304 (14.0)	498 (16.2)	802 (15.3)	0.014
Locomotion outcomes				
Sarcopenia	445 (20.5)	796 (26.0)	1241 (23.7)	<0.001
Falls	324 (14.9)	560 (18.3)	884 (16.9)	<0.001
Functional impairment < 90 points	126 (5.8)	229 (7.4)	335 (6.3)	<0.001
Difficulty walking 400 m	274 (12.6)	423 (13.8)	697 (13.3)	<0.001
SPPB < 6 points	455 (20.9)	1015 (33.1)	1470 (28.1)	<0.001
Psychological outcomes				
Depression	1073 (49.4)	1605 (52.4)	2678 (51.1)	<0.001
Mental problems	123 (5.7)	342 (11.2)	465 (8.9)	<0.001
Sensory outcomes				
Visual problems	1187 (54.7)	1715 (56.0)	2902 (55.4)	<0.001
Hearing problems	618 (28.5)	682 (22.3)	1300 (24.8)	<0.001
Vitality				
Weight loss	335 (15.4)	582 (19.0)	582 (11.1)	<0.001
Appetite loss	403 (18.6)	868 (28.3)	1271 (24.3)	<0.001
Co-morbid chronic diseases				
Hypertension	1040 (47.9)	1889 (61.6)	2929 (55.9)	<0.001
Diabetes	306 (14.1)	562 (18.3)	868 (16.6)	<0.001
Respiratory diseases	217 (10.0)	351 (11.5)	568 (10.8)	0.050
Cardiovascular disease	297 (13.7)	452 (14.7)	749 (14.3)	0.145
Osteoporosis	101 (4.7)	543 (17.7)	644 (12.3)	<0.001
Cancer	98 (4.5)	161 (5.3)	259 (4.9)	0.122
Clinical outcomes				
Hospitalized >24 h last year	249 (11.5)	378 (12.3)	627 (12.0)	0.187
Drug use	1360 (62.6)	2424 (79.1)	3784 (72.3)	<0.001
Lifestyle outcomes				
Alcohol	494 (22.7)	151 (4.9)	645 (12.3)	<0.001
Smoking	329 (15.1)	219 (7.1)	548 (10.5)	<0.001
Meeting PA recommendations	1683 (77.5)	2630 (85.8)	4313 (82.4)	<0.001

Data are presented as mean ± SD or no. (percentage) of participants. Significant differences between men and women group were analyzed by Student's t-test or χ^2 test.
BMI, body mass index; PA, physical activity; SD, standard deviation; SPPB, short physical performance battery.
[a]Others (mestizo, gitano and gypsy, etc.).

handgrip strength greater than the muscle weakness cut-off points. Overall, older adults with handgrip strength greater than the muscle weakness cut-off points had lower odds of adverse events in most of the intrinsic capacity domains (especially in cognition and locomotion domains) and hospitalization (only in men) than their weaker peers. Our results may inform intervention strategies aiming to increase muscle strength and promote healthy ageing.

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Table 2 Smoothed age-specific and sex-specific percentile of handgrip strength (kg) in men and women

Sex/age group	*n*	L	S	P3	P10	P25	P50 (M)	P75	P90	P97
Men (n = 2172)										
60–64	562	1.07	0.26	14.0	19.6	25.1	30.5	35.9	41.2	46.4
65–69	535	1.04	0.28	12.6	18.0	23.3	28.6	33.9	39.1	44.3
70–74	423	0.95	0.30	11.0	16.0	21.2	26.3	31.6	36.8	42.1
75–79	304	0.81	0.33	9.4	13.9	18.7	23.8	29.1	34.6	40.3
80–84	201	0.69	0.36	7.5	11.4	15.7	20.4	25.5	30.9	36.6
85+	147	0.60	0.40	6.0	9.3	13.2	17.6	22.5	27.8	33.6
Women (n = 3065)										
60–64	873	1.00	0.32	6.8	10.7	14.6	18.5	22.4	26.3	30.1
65–69	774	1.10	0.32	6.1	9.8	13.6	17.3	21.1	24.8	28.6
70–74	563	1.02	0.35	5.0	8.7	12.4	16.1	19.8	23.5	27.2
75–79	427	0.99	0.36	4.0	7.6	11.1	14.7	18.3	21.8	25.4
80–84	271	1.14	0.43	1.9	5.8	9.6	13.4	17.2	21.0	24.8
85+	157	0.98	0.44	1.4	5.1	8.8	12.4	16.1	19.8	23.5

L, power in the Box–Cox transformation for 'correcting' the skewness; M, median; P, percentile; S, coefficient of variation.

Figure 1 Absolute strength smoothed centile curves for men (A) and women (B) for Colombian aged 60+ years.

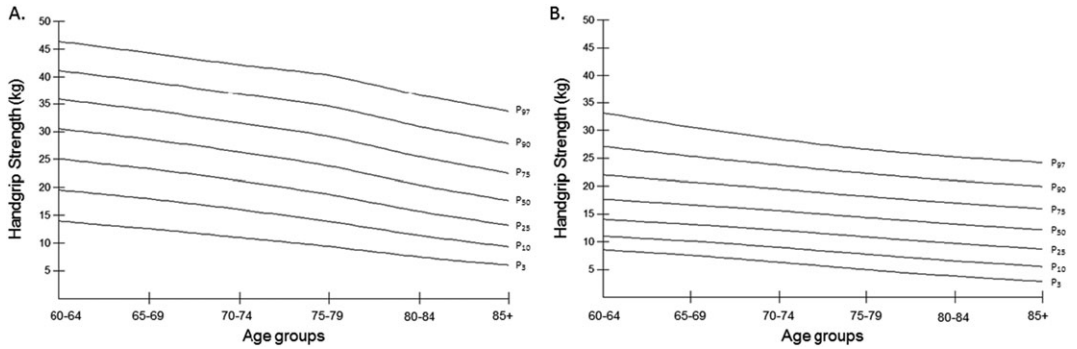

Table 3 Weak handgrip cut point values using <1 SD by sex and age group

Sex/age group	Cut point (kg)
Men	Mean
60–64	17.4
65–69	15.7
70–74	14.3
75–79	12.3
80–84	10.1
85+	8.6
Women	
60–64	10.1
65–69	8.9
70–74	8.2
75–79	6.7
80–84	5.3
85+	4.9

SD, standard deviation.

Several handgrip strength normative ranges for older adults from populations with different nationalities and ethnicities have been published in the last several years[26–30]; however, to our knowledge, normal handgrip strength values have never been described for the Colombian population. We found that, overall, older Colombian adults have lower handgrip strength values than their peers in other populations.[26–29] Our results showing that gender and age affect handgrip strength are in accordance with the findings of previous studies.[26–29] Thus, the results of this study contribute to the current body of literature by presenting sex-specific and age-specific weakness cut-off points among the Colombian elderly.

Different handgrip strength mean values have been observed in different countries, as reported previously,[20] but the nature of these differences is not known. Differences in handgrip strength mean values between Colombian older individuals from a less-developed country (this study) and individuals in developed countries may be due to a number of factors, although it is uncertain which of the three factors, genetic, environment, or biological, are more decisive for handgrip strength results.[31] For instance, biological or environment factors such as health status, lifestyle, and demographic and socio-economic characteristics vary greatly between countries with different handgrip strength levels. Along this line, education and socio-economic status are factors that might explain differences in handgrip strength

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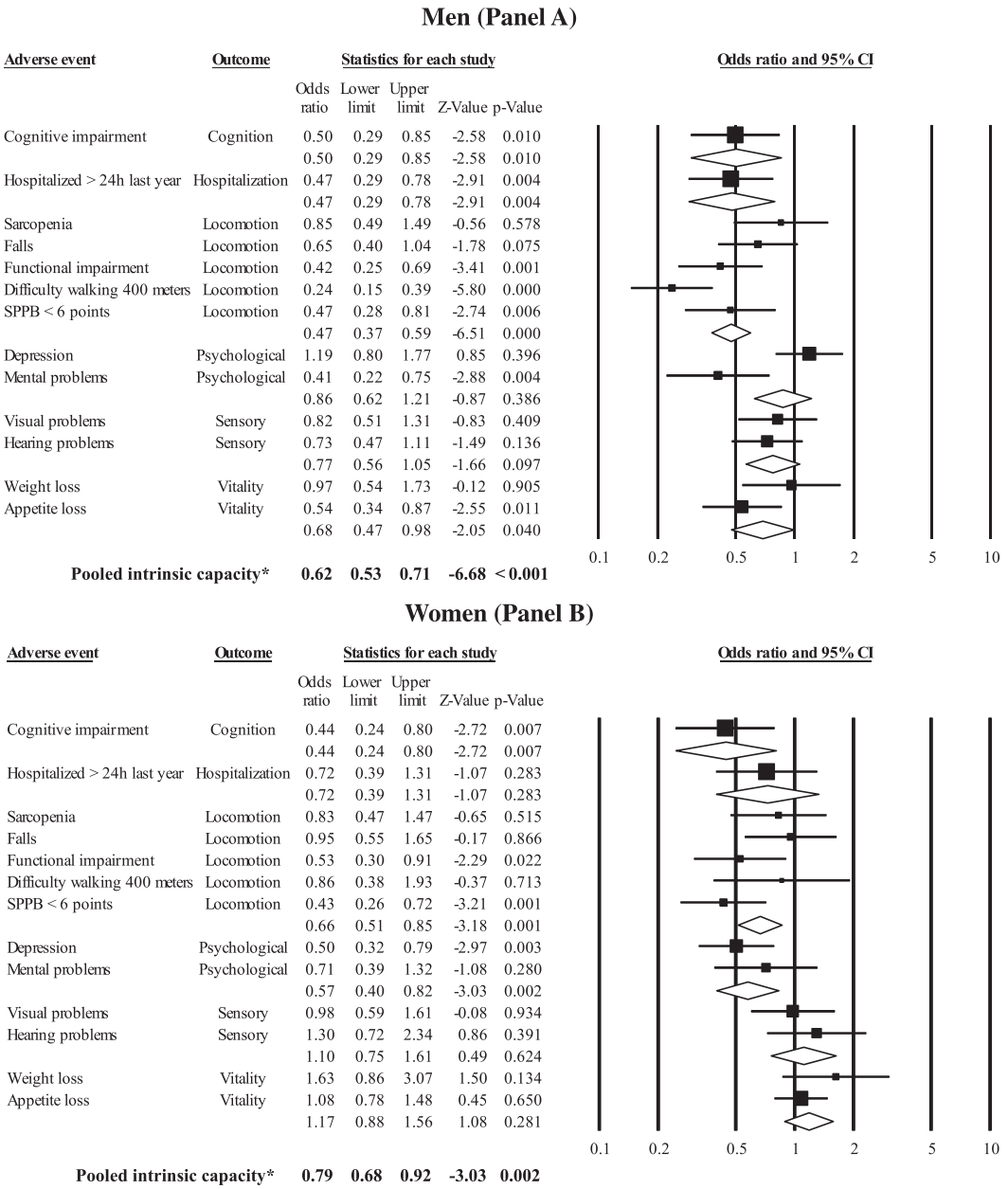
Figure 2 Association between healthy handgrip strength (kg) with the components of the intrinsic capacity and hospitalization. The analysis was adjusted for age, ethnicity, socio-economic status, urbanicity, body mass index, smoking status, alcohol intake, drug use, physical activity, and medical conditions (presence or absence of osteoporosis, cardiovascular diseases, hypertension, diabetes, cancer, or respiratory diseases). *Pooled intrinsic capacity was calculated without hospitalization outcome values. CI, confidence interval; SPPB, short physical performance battery.



ranges among countries.[32] Also, beyond ethnic differences in height and in skeletal muscle mass and function,[33] there are well-recognized differences in dietary protein intake between different countries, and this variation might also explain differences in muscle strength.[34] Absolute strength has also been related to nutrition status and is reported to have positive influence on individuals' grip strength. Another possible reason for the divergence between studies might be methodological differences (i.e. variability in the equipment used and the protocol for measuring handgrip strength).[35]

Several studies have determined absolute[10,11,14] and relative handgrip strength cut-off points[12,13] that are overall higher than our cut-off points. For example, Duchowny *et al.*[14] determined cut-off points for weakness associated with gait speed (<0.8 m/s) in older American adults, with

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values of <40 and <31 kg in men and women, respectively. Similarly, Cruz-Jentoft *et al*.[10] found that among community-dwelling older adults in Italy, a handgrip strength <30 kg in men and <20 kg in women was associated with slow gait speed and an inability to walk 1 km without difficulty. Therefore, different cut-off points are observed in different countries; however, while the nature of these differences is unclear,[31] as mentioned, heterogeneous designs, genetic, and environmental factors may explain some of the differences among the studies.

The handgrip strength cut-off points reported in the present study are useful for determining who among older adults may benefit from lifestyle modifications to preserve muscle strength and reduce the odds of physical and mental limitations. In this context, our results reveal that older men with handgrip strength greater than the muscle weakness cut-off points had a lower odds of hospitalization for >24 h than their weaker counterparts. However, the cross-sectional design of the present study did not allow us to determine whether the measured handgrip strength differed from habitual strength or if the handgrip was impaired as a result of the presenting condition (see limitations in the succeeding texts). Our results partially confirm those of previous studies that analyzed the prospective association between customary handgrip strength and hospital admission, which showed varying results[9,36] The Hertfordshire Cohort Study[9] provided evidence that handgrip strength among community-dwelling men and women in the UK was associated with risk of hospital admission over the following decade. In contrast, a prospective study of 279 older adults aged ≥70 years from Germany who were followed up for 18 months found no association between handgrip strength and the risk of hospital admission.[36] The differences between these studies may be explained by the thresholds for admission, which likely differ between healthcare systems and their cross-sectional design.

A recent narrative review reported that weak handgrip strength was associated with reduced cognitive performance over time; therefore, greater handgrip strength may be protective against cognitive decline in older adults.[37] Indeed, recent evidence has shown that weak handgrip strength is associated with an increased risk of psychological problems such as depression.[38,39] These findings were confirmed by the results of our analysis, which suggested that older adults with handgrip strength greater than the muscle weakness cut-off points had lower odds of cognitive impairment and depression than their weaker peers. Overall, weak handgrip strength, cognition, and depression share some risk and pathogenic factors (particularly an increased rate of oxidative stress[40] and inflammation,[41] decreased sex hormone levels,[42] and maximal voluntary contraction[43]) that may influence the onset of depression and cognitive impairment.[44] Given the strength of the evidence in this area, handgrip strength and our cut-off points are easy to utilize and are clinically useful biomarkers of cognitive decline and mental health across the lifespan of individuals from the Colombian population.

Physical decline, in terms of decreasing muscle weakness and poor mobility, has been repeatedly included as an additional vital sign[45] and a key instrument for the functional assessment of older patients.[46] The present results are also in agreement with those of previous research and suggest that handgrip weakness is associated with measures of functional limitations in older adults.[47] For example, Ishizaki *et al*.[48] determined that older adults with weak handgrip strength had difficulty performing many tasks, such as shopping for groceries, preparing meals, and performing housework. Our lower cut-off points appear to have the ability to identify older adults of both sexes with locomotion problems. Therefore, it seems that it is especially important for older adults to preserve muscle strength to avoid functional limitations, such as by participating in muscle strengthening activities to preserve function. Additionally, our results suggest that optimal handgrip strength is associated with a lower odds of experiencing weight loss in older men, and so muscle strength could favour the maintenance of optimal homeostasis.[7]

Finally, the only intrinsic capacity domain that did not appear to be related to handgrip strength was hearing impairment. Hearing loss in the elderly is of increasing importance as the global population ages. Disabling hearing negatively affects communication and social engagement and can lead to reduced quality of life in adults[49] and may also underlie cardiovascular risk and diseases (i.e. diabetes, hypertension, and history of cerebrovascular accident).[50] These associations are mainly related to the compromised blood supply to the cochlea under vascular disease conditions,[51] as well as other sensor neural, nutritional status, and medical co-morbidity factors that may accumulate with age and are not a result of normal ageing.[51] Peripheral age-related hearing loss is also a possible biomarker and modifiable risk factor for cognitive decline, cognitive impairment, and dementia.[50–52] Our results, however, revealed that an individual with low levels of handgrip strength might not necessarily have a worse hearing status and suggest that different age-related mechanisms could be underlying this.

The strengths of this study include the large sample size of older adults with a nationally representative proportion of persons aged ≥60 and the objective assessment of muscle strength. This study does, however, have some limitations. First, the cross-sectional design did not allow a definitive conclusion that weak muscle strength precedes adverse events. Second, several measures, such as falls, history of chronic disease, and drug use, were self-reported by participants; therefore, different types of response biases may have been introduced.

Conclusions

This study provides reference values for handgrip strength in Colombian individuals 60 years and older. After categorizing participants as weak or not weak based on the handgrip cut-off points, non-weakness was associated with a decreased odds of intrinsic capacity impairments, especially in the cognition and locomotion domains, and of hospitalization (only in men). Therefore, a simple handgrip strength test with the appropriate cut-off points may be a good candidate for clinical assessment of risks to physical and mental health in older Colombian adults.

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Online supplementary material

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Electronic Supplementary Material

Conflict of interest

None declared.

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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.

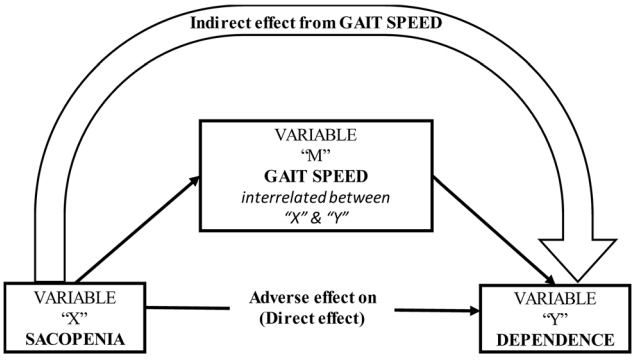
Method

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.



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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

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)	

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.

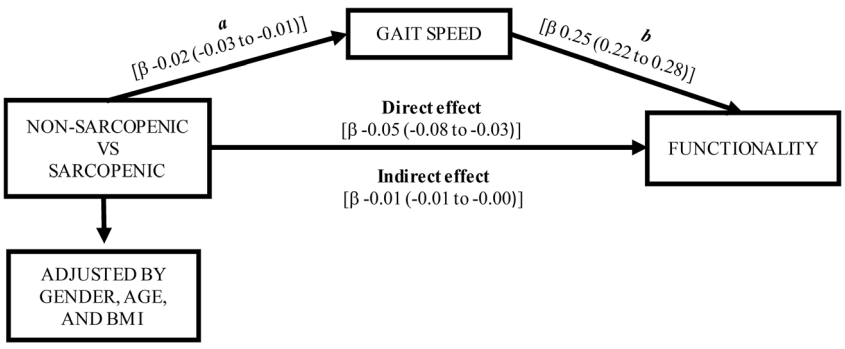
Discussion

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.

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Conflict of Interest

None declared.

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