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SARCOPENIA ACCORDING TO THE EUROPEAN WORKING GROUP ON SARCOPENIA IN OLDER PEOPLE (EWGSOP) VERSUS DYNAPENIA AS A RISK FACTOR FOR MORTALITY IN THE ELDERLY

T. DA SILVA ALEXANDRE[1], Y.A. DE OLIVEIRA DUARTE[2], J.L. FERREIRA SANTOS[3], R. WONG[4], M.L. LEBRAO[5]

1. Centro de Ciências Biológicas e da Saúde, Universidade Federal de São Carlos/UFSCar; 2. Department of Medical Surgical Nursing, Nursing School, University of São Paulo, Brazil; 3. Department of Social Medicine, University of São Paulo, Brazil; 4. Department of Preventive Medicine and Community Health, University of Texas Medical Branch, USA; 5. Department of Epidemiology, School of Public Health, University of São Paulo, Brazil. Corresponding author: Tiago da Silva Alexandre, Centro de Ciências Biológicas e da Saúde, Universidade Federal de São Carlos/UFSCar, Sala 16, Telefone 55 (16) 3306-6661, Brazil, tsfisioalex@gmail.com

Abstract: *Background:* Sarcopenia and dynapenia have been associated with poorer physical performance, disability and death. The aim of this study was to compare the association between sarcopenia and dynapenia with mortality. *Methods:* We studied 1,149 Brazilians aged 60 years or older residing in São Paulo. Sarcopenia was defined according to the consensus of the European Working Group on Sarcopenia in Older People (EWGSOP), which includes three components: low muscle mass (LMM) assessed by skeletal muscle mass index ≤ 8.90kg/m2 (men) and ≤ 6.37kg/m2 (women); low muscle strength (LMS) assessed by handgrip strength < 30kg (men) and < 20kg (women); and low physical performance (LPP) assessed by walking speed ≤ 0.8m/s. Diagnosis of sarcopenia required presence of LMM plus LMS or LPP. Dynapenia was defined as handgrip strength < 30kg (men) and < 20kg (women). Covariates included socio-demographic and behavioral variables, medical conditions, hospitalization, depressive symptoms, cognition, and disability in activities of daily living or instrumental activities of daily living. The outcome was all-cause mortality over five-year follow-up. *Results:* During the five-year follow-up, 187 subjects died. The mortality rate for those with or without sarcopenia were 65.9/1,000 person/years and 20.1/1,000 person/years and for dynapenia were 44.3/1,000 person/years and 14.9/1,000 person/years. The adjusted model showed that sarcopenia (HR=1.52, 95%CI: 1.06 – 2.19) and dynapenia (HR=2.04, 95%CI: 1.24 – 3.37) are independent risk factors for death. *Conclusions:* The EWGSOP definition of sarcopenia and dynapenia can help to determine risk for mortality and can be used as a screening instrument in public health.

Key words: Elderly, mortality, sarcopenia, dynapenia, SABE study.

Introduction

Sarcopenia, recognized as the age-related loss of muscle mass, has been described as a decline in muscle mass and muscle strength associated with aging (1, 2). Although there is no consensus on the definition, the European Working Group on Sarcopenia in Older People (EWGSOP) recognized sarcopenia as a syndrome and recommends diagnosis using the presence of low muscle mass (LMM) plus low muscle strength (LMS) or low physical performance (LPP) (strength measure by handgrip and performance measured by gait speed) in clinical practice in order to improve identification and treatment of the syndrome (3, 4).

Few studies have analyzed sarcopenia according EWGSOP as a risk factor for mortality. Landi et al. (5) used data from Italy to find that sarcopenia was associated with mortality in frail older adults aged 80 years and older. Arango-Lopera et al. (6), using data from Mexico, also found sarcopenia to be a risk factor for mortality in older adults 70 years and older. Landi et al. (7), in another Italian study, found that residents in nursing homes who had sarcopenia were more likely to die than those without sarcopenia.

The EWGSOP algorithm to determine sarcopenia has attracted interest because muscle mass alone has not been shown to be a risk factor for mortality in older adults while gait speed and dynapenia, defined as reduced muscle strength and/or decline in muscle strength over time, are important factors associated with this outcome (8-10).

The aim therefore of the present study was to compare the association of sarcopenia, defined according to EWGSOP, and dynapenia with mortality over five-year period among elderly residents in São Paulo, Brazil.

Methods

Study population

Data are from SABE Study (Saúde, Bem-Estar e Envelhecimento/Health, Wellbeing and Ageing), a study of three cohorts that began in 2000 with a probabilistic sample representative of the urban population aged 60 years and older in the city of São Paulo, Brazil, composed of 2,143 individuals.

In 2006, 1,115 individuals from the first cohort were interviewed in person, 11 were institutionalized, 51 had moved to another city, 178 refused to participate, 139 were lost to follow-up and 649 died. A new cohort of 298 individuals, representative of the urban population aged 60–64 years old in the same city, was added to the original cohort in 2006 for a total sample of 1,413. Detailed information about study design

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and sampling has been published previously (11, 12).

The present study used all data from the cohort interviewed in 2006. Of 1,413 participants interviewed in 2006, we excluded 264 due to missing data on handgrip strength, gait speed, weight and height, all variables needed to define sarcopenia, for a final sample of 1,149. These measurements were not taken in those unable to perform the handgrip strength test or the walk test of the Short Physical Performance Battery Assessing Lower Extremity Function, or in those confined to bed or unable to stand up to measure weight and height. All participants signed a statement of informed consent and the SABE study received approval from the Human Research Ethics Committee of the institution.

Mortality data were confirmed through state and municipal records in Brazil. For the present analyses, follow-up time was defined as the period from the first visit in 2006 until the day of death or the last contact date.

Covariates

Muscle mass was estimated by appendicular skeletal muscle mass (ASM) using the Lee equation (13):

ASM = 0.244*body weight + 7.8*height + 6.6*gender – 0.098*age + race – 3.3

The body weight must be in kilograms and height in meters. For gender, the value 0 must be used for women and 1 for men; for race, 0 is used for white people, 1.4 for black people and – 1.2 for Asian people (13).

This equation has been validated in the Brazilian population using dual-energy X-ray absorptiometry (DEXA) as the gold standard with high correlation between methods [r=0.86 for men and r=0.90 for women, respectively, ($p<0.05$)]. The agreement between DEXA and the predictive equation to determine sarcopenia prevalence is strong (k=0.74; $p<0.001$), with high specificity (89%) and sensitivity (86%) (14).

After estimating the values, the ASM was adjusted by height squared to create the skeletal muscle mass index (SMI). Following the studies of Delmonico et al. (15) and Newman et al. (16), the cutoff of SMI used in the present study was based on the 20% lowest percentile of the population distribution, representing 6.37 kg/m2 for women and 8.90 kg/m2 for men.

Physical performance was assessed by gait speed (in meter/seconds), determined by the walk test of the Short Physical Performance Battery Assessing Lower Extremity Function. The test was conducted on an 8-foot walking course, with no obstructions for an additional 2 feet at either end, denoted by the placement of a rigid 8-foot carpenter´s rule to the side of the course. Participants were instructed to "walk at your usual speed, just as if you were walking down the street to go to the store". Participants could use an assistive device if needed, and each was timed for two walks. The faster of the two was used for analyses (17). The cut-off point of ≤ 0.8 m/s was used to represent LPP (3, 18).

Muscle strength was tested in kg using a hand-held dynamometer (Takei Kiki Kogyio TK 1201). During the test, the participant rested in a sitting position, with elbow resting on the table with forearm and palm facing up; the participant was then was prompted to grip with as much strength as possible. Grip size was adjustable so that each participant felt comfortable while squeezing the grip. The test was performed twice in the dominant limb, with a 1-min rest between tests and the higher value of the two trials was used for scoring purposes. Cut-off values of < 30 kg for men and < 20 kg for women were considered to represent LMS (3,18).

Sarcopenia was defined using the EWGSOP criteria. Participants with LMM plus either LMS or LPP were considered positive for sarcopenia diagnosis (3).

Dynapenia was defined using the criteria of Laurentani et al.: < 30 kg for men and < 20 kg for women (3, 18, 19).

Socio-demographic characteristics included age, gender, marital status, income and schooling. Age was grouped in three 10-year categories, with individuals aged 80 years or older combined into a single group. Marital status was classified as married (married individuals or those in a stable relationship) and not married (divorced, separated or widowed individuals). Income, in terms of Brazilian monthly minimum salary (R$ 350.00 = US$ 161.74), was classified in three categories: up to two times the minimum salary (≤ US$ 323.50), two to five (US$ 323.51 - 808.70) and more than five times the minimum salary (> US$ 808.70). Schooling (in years) was analyzed as a continuous variable.

Smoking status was assessed by asking participants whether they were a non-smoker, former smoker or current smoker.

Alcohol intake was assessed by asking participants whether they were non-drinkers, drank once a week, drank two to six days a week or drank every day.

Physical activity was assessed using the Brazilian version of the International Physical Activity Questionnaire (IPAQ) (20). The calculation of caloric expenditure involved the metabolic equivalent, the activities performed by the participant, the number of days per week each activity was performed, the time spent performing the activity and the individual body weight (21). Men and women with a caloric expenditure ≤ 390.5 kcal and ≤ 478.15 kcal, respectively (smallest quintile), were classified as having a sedentary lifestyle.

Health status was assessed through number of diseases and self-report of arterial hypertension, diabetes, cancer, lung disease, heart disease, stroke, falls and hospitalizations in the previous 12 months. Cognitive status was assessed using the modified version of the Mini Mental State Exam (MMSE) due to the low level of schooling of the Brazilian elderly population (22). Participants with a cutoff score of ≤ 12 were considered to have cognitive impairment (23). Depressive symptoms were assessed using the Geriatric Depression Scale (24, 25). Participants with a score of ≥ 6 were considered to have depressive symptoms (25).

Disability was assessed with a modified version of the Katz Activity of Daily Living scale and the Lawton Instrumental Activities of Daily Living scale. Respondents were asked if

they had difficult in performing activities of daily living (ADLs) tasks (transferring, toileting, bathing, dressing, feeding and walking) (26). Despite its importance in terms of functionality among elderly individuals, incontinence was not included in ADLs because it does not necessarily imply physical limitation (27). For instrumental activities of daily living (IADLs) activities, respondents were asked whether they able to perform eight activities (using a telephone, shopping, preparing meals, performing light housework, taking medications, managing money, doing heavy housework and using transportation) (28). Disability in ADLs and IADLs were analyzed as a continuous variable.

Statistical Analyses

Differences in baseline characteristics between survivors or those who died and those lost to follow-up were assessed using Wald test and chi-square test with Rao and Scott correction. Descriptive data are expressed as mean ± standard deviation and proportions. For all analyses, $p<0.05$ was used to indicate statistical significance.

We examined all deaths which occurred during the 5-year follow-up. Survival curves were analyzed according to the Kaplan-Meier method to explore the impact of sarcopenia and dynapenia on survival. Differences between curves were evaluated using the log-rank test. The assumption of proportional hazards was verified graphically by means of a log-log plot of the response variable. Unadjusted and adjusted hazard ratios (HR) and 95% confidence intervals (CI) for mortality risk with sarcopenia and dynapenia were calculated using Cox proportional hazard models. The models were adjusted for sociodemographic characteristics, behavioral characteristics and medical conditions. The first model included only sarcopenia, the second one dynapenia and the third model included sarcopenia and dynapenia.

Because our data came from a multistage cluster sampling, sample weights were employed in all analysis. The Stata 10® program (StataCorp, College Station, TX) was used for all data analysis.

Results

From a total of 1,149 elderly at baseline, 187 died in a mean follow-up period of 4.19 ± 0.4 years. The mean age ± standard deviation of the participants was 69.6 ± 0.6 years; of these, 59.5% were female, 58.7% were married and the mean years of education was 4.6 ± 0.2 years. The most prevalent medical conditions were arterial hypertension (61%), heart disease (20.8%) and diabetes (19.3%). According EWGSOP, 14.4% of the elderly had sarcopenia while 41.4% dynapenia (Table 1). Baseline characteristics of those interviewed in 2010 or those who had died were compared to data of those lost to follow-up. We found that those lost to follow-up had lower income ($p<0.05$) (data not shown).

In the unadjusted model, there was a strong association between sarcopenia and mortality (HR = 3.31, 95%CI: 2.36 – 4.65). The mortality rate for those with or without sarcopenia were 65.9/1,000 person/years and 20.1/1,000 person/years, respectively.

Table 1
Baseline characteristics of 1,149 elderly residents in São Paulo, Brazil (2006)

Socio-demographic variables	
Age	69.6 ± 0.6
Gender (female)	59.5% (n = 712)
Marital status (married)	58.7% (n = 577)
Income	
>US$808.70	9.5% (n = 109)
< 323.5 US$ ≤808.70	20.0% (n = 260)
US$≤323.50	35.2% (n = 475)
Missing	35.3% (n = 305)
Schooling	4.6 ± 0.2
Behavioral variables	
Smoking	
Never smoked	53.1% (n = 634)
Ex-smoker	32.8% (n = 387)
Current smoker	14.1% (n = 128)
Weekly alcohol intake	
None	67.2% (n = 820)
Once a week	18.2% (n = 187)
Two to six days a week	9.1% (n = 85)
Every day	5.5% (n = 54)
Sedentary lifestyle	17.3% (n = 249)
Clinical Conditions	
Arterial hypertension	61.0% (n = 723)
Diabetes	19.3% (n = 216)
Lung disease	10.9% (n = 123)
Heart disease	20.8% (n = 263)
Stroke	7.3% (n = 85)
Cancer	5.8% (n = 56)
Number of diseases	1.7 ± 0.1
Falls	27.2% (n = 353)
Hospitalization	7.7% (n = 104)
Mini Mental State Exam (≤ 12 points)	10.0% (n = 157)
Geriatric Depression Scale (≥ 6 points)	13.4% (n = 154)
Anthropometric and Performance Measures	
Sarcopenia	15.4% (n = 266)
Dynapenia	41.4% (n = 582)
ADLs disability	0.4 ± 0.1
IADLs disability	0.6 ± 0.1

Data are given as mean ± SD or number and percentage. Means and proportions were calculated considering the weight of the sample.

The sarcopenia adjusted model by sociodemographic characteristics revealed a HR of 1.99 (95%CI: 1.34 – 2.94) while the model adjusted for sociodemographic and behavioral characteristics revealed a HR of 1.80 (95%CI: 1.24 – 2.62) (data not shown).

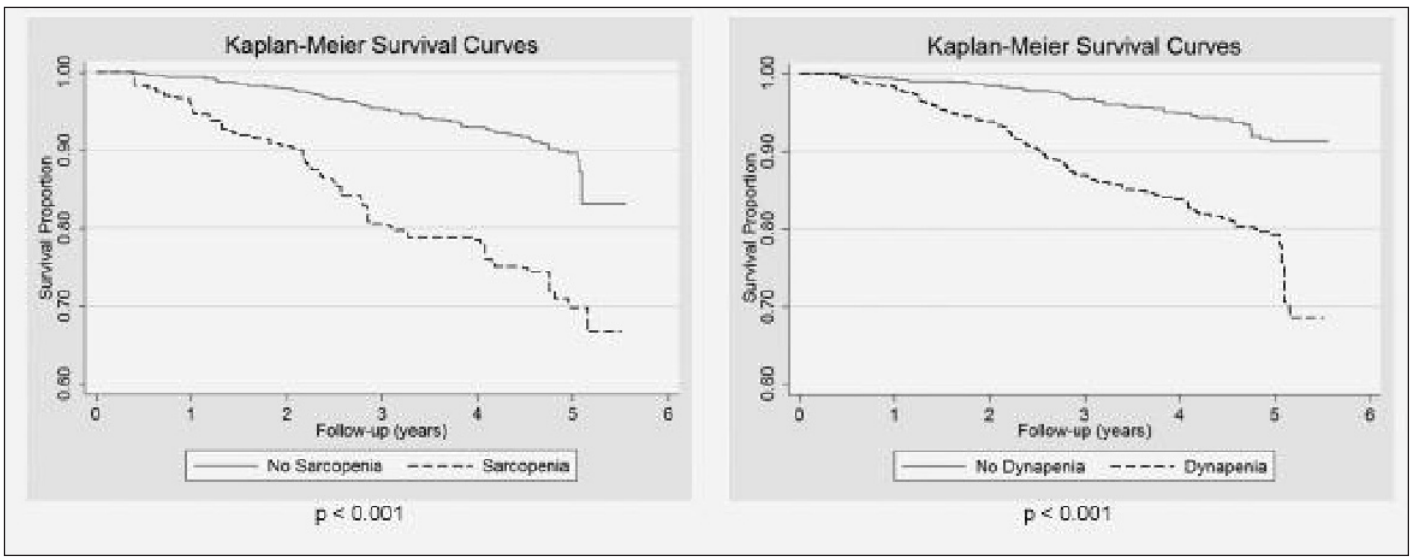
Table 2 gives the results of Cox proportional hazards models predicting the hazards for mortality. In the model adjusted for socio-demographic, behavioral and clinical characteristics

Table 2
Cox Proportional Hazards Models predicting mortality during 5 year follow-up period among 1,149* elderly resident in São Paulo, Brazil (2006-2011)

	Model 1 Sarcopenia n=1095*		Model 2 Dynapenia n=1095*		Model 3 Sarcopenia and Dynapenia n=1095*	
Variable	**Unadjusted Model HR (95%CI)**	**Adjusted Model HR (95%CI)**	**Unadjusted Model HR (95%CI)**	**Adjusted Model HR (95%CI)**	**Unadjusted Model HR (95%CI)**	**Adjusted Model HR (95%CI)**
Sarcopenia						
No	1.00	1.00			1.00	1.00
Yes	3.31 (2.36-4.65)	1.72 (1.20-2.47)			3.31 (2.36-4.65)	1.52 (1.06-2.19)
Dynapenia						
No			1.00	1.00	1.00	1.00
Yes			3.01 (2.08-4.36)	2.19 (1.32-3.62)	3.01 (2.08-4.36)	2.04 (1.24-3.37)

Adjusted model by age, sex, marital status, income, schooling, smoking, weekly alcohol intake, sedentary lifestyle, arterial hypertension, diabetes, lung disease, heart disease, stroke, cancer, number of diseases, falls, hospitalization, Mini Mental State Exam, Geriatric Depression Scale, Activities of Daily Living disability and Instrumental Activities of Daily Living disability, *The sample size decreased due to missing data on covariates.

Figure 1
Kaplan-Meier survival curves for mortality according to presence of sarcopenia and dynapenia



(Model 1), older adults with sarcopenia had a higher risk of death compared with those who did not have sarcopenia (HR = 1.72, 95%CI: 1.20 – 2.47).

There was a strong association between dynapenia and mortality in the unadjusted model (HR = 3.01, 95%CI: 2.08 – 4.36). The mortality rate for those with or without dynapenia were 44.3/1,000person/years and 14.9/1,000person/years, respectively.

The dynapenia model, adjusted for sociodemographic characteristics, revealed a HR of 2.57 (95%CI: 1.66 – 3.96); the model adjusted for sociodemographic and behavioral characteristics revealed a HR of 2.43 (95%CI: 1.57 – 3.76) (data not shown).

In the model adjusted for socio-demographic, behavioral and clinical characteristics (Model 2), older adults with dynapenia had a higher risk of death compared with those who did not have dynapenia (HR = 2.19, 95%CI: 1.32 – 3.62).

When we include sarcopenia and dynapenia in the same model (Model 3) we found a HR of 1.52 (95%CI: 1.06 – 2.19) for sarcopenia and a HR of 2.04 (95%CI: 1.24 – 3.37) for dynapenia.

The effect of sarcopenia and dynapenia on 5-year survival was also tested comparing Kaplan-Meyer survival curves for mortality. Survival curves differed significantly at the log-rank test (p<0.001) (Figure 1).

Discussion

The aim of the present study was to compare the association of sarcopenia and dynapenia with mortality over a five-year

period. We found that both sarcopenia and dynapenia were associated with mortality independent of socio-demographic, behavioral and clinical characteristics.

Our results are similar to those from previous studies. For example, Landi et al. (7), using data from nursing home residents older than 70 years in Italy, found that sarcopenia measured according EWGSOP is associated with mortality at six months´ follow-up (HR = 2.34, 95%CI: 1.04 – 5.24) independent of age, gender, stroke, chronic obstructive pulmonary disease, body mass index (BMI) and difficulty in ADLs. Arango-Lopera et al. (6) used data from community dwelling adults older than 70 years in Mexico to find that sarcopenia measured according EWGSOP was associated with mortality at three years´ follow-up (HR = 2.39, 95%CI: 1.05 – 5.43), independent of age (in those older than 80 years), ischemic heart disease and difficulty in ADLs.

Finally, Landi et al. (5), using data from community dwelling adults older than 80 years in Italy, found that sarcopenia according EWGSOP is associated with mortality over seven years´ follow-up (HR = 2.32, 95%CI: 1.01 – 5.43), independent of age, gender, education, ADL impairment, BMI, hypertension, congestive heart failure, chronic obstructive pulmonary disease, number of diseases and TNF-α levels.

Although all studies used the same concepts of muscle strength and gait speed, muscle mass was measured in different ways. Landi et al. (7) used bioelectrical impedance analysis, Arango-Lopera et al. (6) used calf circumference and Landi et al. (5) used mid-arm muscle circumference. Despite these differences, the similarity in HR values is a good indication of the validity of different measurement techniques of lean mass in clinical practice, independent of the gold standard of DEXA.

Singly, there is no consensus on how much low muscle mass can predict mortality, unlike low grip strength and low gait speed. Cesari et al. (8) using data from Italy, found that low gait speed but not muscle density or muscle and fat cross-sectional areas of the calf were associated with mortality.

Newman et al. (10) using data from the USA, found that strength, but not muscle mass, was associated with mortality. Moreover, they concluded that muscle strength as a marker of muscle quality, measured by handgrip, is more important than muscle quantity in estimating mortality risk.

Thus, using an algorithm that includes muscle mass, muscle strength and gait speed seems to be important in developing an instrument to diagnose sarcopenia in older people because such inclusion can measure the impact on physical performance of both quantity and quality of muscle.

This study has some limitations. First, the use of the regression equation to estimate muscle mass may under- or over-estimate the prevalence of sarcopenia. However, as the use of DEXA in community dwelling populations is limited, this equation was validated in a Brazilian and American population showing high correlation with DEXA and magnetic resonance imaging, respectively (10, 11). Second, the SABE Study is focused on the community-dwelling population of older adults and did not include residents of nursing homes. Thus, the estimates may have some degree of bias, as institutionalized older adults may have a greater prevalence of sarcopenia and dynapenia. However, the institutionalized population in Brazil is relatively small, minimizing such bias (29).

Third, the missing data could be considered an important limitation, but the differences at baseline in those interviewed or died and those lost at follow up were significant only for income. Thus, this loss may be considered random, reducing the bias.

This study also has three strengths. First, the study was conducted on a large sample of community-dwelling adults that represents the older adult population in the city of São Paulo. Second, to our best knowledge this study is the first to analyze sarcopenia using the EWGSOP criteria as a risk factor for mortality in adults older than 60 years in Latin America. Third, we used survival analysis in a large group of confounding variables associated with mortality.

The EWGSOP definition of sarcopenia and dynapenia are useful to determine risk for mortality and can be used as a screening instrument in public health. Moreover, the use of equations to measure muscle mass associated with handgrip and gait speed can be an important alternative to DEXA to improve the diagnosis of sarcopenia and reduce costs.

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