






## Muscle health in Hispanic women. REDLINC VIII

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### ABSTRACT

**Objectives:** This study aimed to evaluate muscle strength and related factors in Hispanic women.

**Methods:** We studied 593 women between 40 and 89 years old. The women were asked about personal and clinical information. The following instruments were applied: dynamometer (strength), Short Physical Performance Battery (physical performance), SARC-F (sarcopenia), International Physical Activity Questionnaire (physical activity), Menopause Rating Scale (quality of life), 36-item Short Form (general health), and Frailty (Fried's criteria).

**Results:** Low muscle strength rises from 7.1% of women in their 40s to 79.4% in their 80s. Physical performance is low in 0.5% of the first group and rises to 60.5% in the second. The risk of sarcopenia increases significantly from 6.7% in younger women to 58.1% in older women. Frailty, which affects less than 1% of women under age 60 years, increases to 39.5% in their 80s. Sedentary lifestyle rises from 26% to 68.3%. Frailty impairs the quality of life and the perception of health ( $p < 0.0001$ ). The deterioration of different tests of muscle function is significantly associated with age  $>70$  years (OR 5–20) and with osteoarthritis (OR 4–9). Menopause before the age of 45 years increases the risk of sarcopenia (odds ratio 2.2; 95% confidence interval 1.2–4.0).

**Conclusion:** With aging there is a decrease in muscle strength and an increase in frailty. This entails a decrease in the quality of life.

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## Introduction

Sarcopenia is a syndrome characterized by progressive and generalized loss of muscle mass and strength. The European Working Group on Sarcopenia in Older People (EWGSOP2) focuses on low muscle strength as a key characteristic of sarcopenia, and uses the detection of low muscle quantity and quality to confirm the diagnosis of sarcopenia<sup>1</sup>. The Foundation for the National Institutes of Health (FNIH) Sarcopenia Project defines sarcopenia in women as having a grip strength  $<16$  kg and having a low lean mass, with appendicular lean mass adjusted for body mass index (BMI)  $<0.5122^2$ . These and other definitions have emphasized the importance of muscle function for the diagnosis of sarcopenia.

The term 'sarcopenia' was proposed by Rosenberg in 1989 to describe the loss of muscle mass related to aging<sup>3</sup>. The word sarcopenia comes from the Greek *sarkós*, which means meat (muscle), and *penia*, loss or reduction. The concept has evolved, being currently applied not only to the loss of muscle mass but also to a decrease in strength and muscular function<sup>1</sup>. Sarcopenia is associated with a tendency to fall, a risk of fracture, a decrease in the quality of life, and an increase in morbidity and mortality<sup>4</sup>.

In recent years, muscle function has acquired special relevance because muscle strength is associated with a functional decline in older people, regardless of muscle mass. There is evidence that mortality is not only influenced by muscle size, but is associated with the relationship between poor muscle strength and function<sup>5</sup>.

The updated concept of sarcopenia is strongly linked to that of frailty, a geriatric syndrome characterized by functional impairment in multiple physiological systems, such as neurodegeneration, sarcopenia, and cognitive changes. However, perhaps the most dramatic decreases in frailty, in terms of function and structure, are found in the musculoskeletal system, affecting balance, mobility, disability, and, ultimately, the ability to live independently. While sarcopenia is related to a specific organ, the muscle, the concept of frailty tends to be more easily applied in a clinical setting. However, the frequent prevalence of both conditions with aging makes it reasonable to evaluate both conditions together<sup>6,7</sup>.

Among the mechanisms that contribute to age-related loss of appendicular muscle mass and strength, we should mention the decrease in physical activity and poor nutritional intake, oxidative stress, inflammatory insults, and

hormonal changes<sup>8</sup>. Women have more pronounced muscle deterioration than men with aging. Baumgartner *et al.*, studying a random cohort of 833 subjects of both sexes, found a prevalence of sarcopenia of 13% and 24% for men and women, respectively, in individuals younger than 70 years; in those older than 80 years, the prevalence of sarcopenia is greater than 50%, mainly in women and Hispanic subjects<sup>9</sup>. Likewise, women have a higher prevalence of frailty; in a Chilean study in people over 60 years of age, they had twice the prevalence of men (16.4% vs. 8.7%)<sup>10</sup>. Estrogen deficiency could play a role in the prevalence of muscle deterioration in older women, since it has been observed that premenopausal women had greater muscle strength compared to postmenopausal women of a similar age<sup>11</sup>. This is not surprising given the high concentration of estrogen receptors in muscle tissue and their progressive decrease in postmenopausal women<sup>12</sup>.

Apart from classic chronic diseases, cognitive deterioration and muscle dysfunction are the main threats to a good quality of life in the elderly<sup>13</sup>. The progression of muscle deterioration with age, especially in women and a higher prevalence of these disorders in Hispanics, was an incentive for us to conduct a study in a population of Latin American women from 35 to 69 years old<sup>14</sup>, in which we found that 22.6% had low muscle mass defined as an appendicular lean mass index  $<5.45 \text{ kg/m}^2$ .

To complement that study, we designed a new project to analyze the prevalence of muscle strength disorders, and their relationship with menopause, physical activity, weight, and medical conditions, evaluating the impact on frailty and the influence of this condition on the perception of health and quality of life.

Our hypothesis is that not only age, but also menopausal hormonal changes, can affect muscle function, a result that could be modulated by different lifestyles such as physical inactivity or medical conditions.

## Methods

### Design

A cross-sectional study (survey) (REDLINC VIII) evaluated the muscular function in women and its association with their clinical history.

### Location

The study involved women's health centers in Latin American cities with more than 500,000 inhabitants.

### Subjects to study

Women between 40 and 89 years old who attended a preventive gynecological check-up were eligible for participation.

### Calculation of the sample size

If we estimate a prevalence of sarcopenia of 10% in this population and accept an error of 5% with a 95% confidence level, a sample of 138 women will be required. If we consider the

estimated population of women for 2015 and use the demographic profiles of Latin America in 2015 published by the United Nations Economic Commission for Latin America and the Caribbean (CEPAL)<sup>15</sup>, we will need a minimum of 50 (36.4%) women between 40 and 49 years old, 39 women (28.7%) between 50 and 59 years old, 26 women (18.6%) between 60 and 69 years old, 15 women (10.6%) between 70 and 79 years old, and eight women (5.7%) aged 80 years or older.

## Instruments

### Personal and clinical information

Personal information included age, years of schooling, most frequent occupation (work, manual, not manual, housewife, professional), weight, height, reproductive stage, number of children born alive, and sexual activity in the previous year. Clinical information included current use of medications for high blood pressure, diabetes mellitus, use of sedatives and antidepressants, joint diseases (osteoarthritis/arthritis), menopausal hormone therapy, hysterectomy, bilateral oophorectomy, and personal history of heart disease, chronic lung disease, and cancer.

### Hand grip strength

Using a manual dynamometer, the isometric strength is measured that not only allows us to identify muscle weakness of the upper limb, but also provides an indication of overall strength<sup>16</sup>. Hand grip strength is expressed in kilograms and measured using a hand dynamometer (Model EH 101; CAMRY). Measurements were obtained in standardized conditions, with the participants in a seated position, elbow bent at 90°, and after receiving an explanation regarding the procedures. Being previously familiarized with the instrument, they should apply their maximum grip strength for 3–5 s. The procedure was performed twice, using the dominant hand, with an interval of 1 min between each measurement. For the analyses of this study, the highest hand grip strength value of the two observations was considered; any value below the 25th percentile of women aged over 50 years is considered low grip strength<sup>17,18</sup>.

### Short Physical Performance Battery

The Short Physical Performance Battery (SPPB) includes three tests: balance, gait speed test, and stand up and sit on a chair five times<sup>19</sup>. In the balance test, the participant tries to maintain three positions: feet together, semi-tandem, and tandem for 10 s each. In the gait speed test, the participant walks 4 m at their usual pace. This test is performed twice, and the times are recorded with a stopwatch. In the sit-to-stand test, the participant gets up and sits down five times, as fast as they can, keeping their arms crossed over their chest. The total time needed is recorded. The test must stop if the participant starts using their arms or if the test is not completed after 1 min. Each test is scored from 0 (worst performance) to 4 (best performance). For the balance test, a score of 0–4 is assigned according to their performance in the three components. For the other two tests, a score of 0

is assigned for those who do not complete or try the task and scores of 1–4 as a function of the time needed to complete the task. In addition, we obtain a total score for the whole battery that is the sum of the three tests, which can range from 0 to 12. In the SPPB, low performance is defined as 0–6 points, intermediate performance is 7–9 points, and high performance is 10–12 points. This test was validated in Spanish by Gómez *et al.*<sup>20</sup>.

### **SARC-F questionnaire**

The SARC-F questionnaire has been developed as a possible rapid diagnostic test for sarcopenia. There are five SARC-F components: strength, assistance with walking, rise from a chair, climb stairs, and falls. The scores range from 0 to 10, with 0–2 points for each component; a score  $\geq 4$  is predictive of sarcopenia and poor outcomes<sup>21</sup>. SARC-F is an excellent test to exclude muscle function impairment and sarcopenia<sup>22</sup>.

### **International Physical Activity Questionnaire**

The International Physical Activity Questionnaire (IPAQ) records the last 7-day recall for four intensity levels of physical activity: vigorous-intensity activity, moderate-intensity activity, walking, and sitting. From the IPAQ-SF, data were converted to Metabolic Equivalent (MET)-minutes per week (MET walking,  $3.3 \times \text{minutes} \times \text{days a week}$  [e.g.  $3.3 \times 30 \text{ min} \times 5 \text{ days} = 495 \text{ MET-min/week}$ ]; MET moderate-intensity activity,  $4 \times \text{minutes} \times \text{days a week}$ ; and MET vigorous-intensity activity,  $8 \times \text{minutes} \times \text{days a week}$ ). Respondents who met the following criteria were defined as having moderate-intensity activity:  $\geq 3$  days of vigorous activity of at least 20 min per day, or  $\geq 5$  days of moderate-intensity activity and walking of at least 30 min per day, or  $\geq 5$  days of any combination of walking, moderate-intensity, and vigorous-intensity activities achieving a minimum of at least 600 MET-min/week. A person who performed vigorous-intensity activity on at least 3 days accumulating at least 1500 MET-min/week or  $\geq 7$  days of any combination of walking, moderate-intensity, and vigorous-intensity activities achieving a minimum of at least 3000 MET-min/week was considered active. Those respondents not meeting these criteria were categorized as inactive<sup>23</sup>.

### **Menopause Rating Scale**

The Menopause Rating Scale (MRS) questionnaire is composed of 11 symptoms and divided into three domains: somatic, including flushes, excessive sweating, heart discomfort, sleep disturbances, and muscle and joint discomfort (items 1–3 and 11, respectively); psychological, including depressive state, irritability, anxiety, physical, and mental tiredness (items 4–7, respectively); and urogenital, including sexual and vesical problems and vaginal dryness (items 8–10, respectively). For each item, the women assigned a score of 0–4 to the intensity of the symptom (0, absent; 1, mild; 2, moderate; 3, severe; and 4, very severe). For every woman, the score of a particular domain corresponds to the sum of the values obtained in each item of the subscale. The total MRS score will be the sum of the scores obtained in each

domain. An MRS score  $>16$  indicates severity of climacteric symptoms and the need for treatment<sup>24</sup>. The MRS has been validated in Spanish<sup>25</sup>.

### **36-Item Short Form health survey (general health)**

The 36-Item Short Form (SF-36) is one of the most widely used and evaluated generic health-related quality of life questionnaires. General health perception is one of the eight domains of the SF-36. Through five questions, it evaluates the personal perception of health that includes current health, future health prospects, and resistance to illness (five questions). Each answer is valued between 0 and 100. The average of the five questions gives the final score. The SF-36 has been validated in Spanish<sup>26</sup>.

### **Frailty**

Defining criteria were based on the presence or absence of the following measurable components: slowness, weakness, low weight, exhaustion, and low physical activity<sup>27</sup>. Briefly, slowness was defined by a score of 1–3 in the gait speed test according to the standards of the SPPB. To assess weakness, strength was measured with an electronic handgrip dynamometer according to a sex-specific cut-off point ( $<17.4 \text{ kg}$ ,  $<25$ th percentile). Low weight was defined as having BMI  $<18.5 \text{ kg/m}^2$  in women under 50 years old (World Health Organization) or  $\leq 20 \text{ kg/m}^2$  in women aged 50 years and over as has been applied in previous research in older adults<sup>28</sup>. Exhaustion was classified when participants provided a score of 3 (severe) or 4 (very severe) in Question 8 (physical and mental exhaustion) on the MRS scale. Finally, low physical activity was defined by an IPAQ score of  $<600 \text{ MET-min/week}$ .

### **Statistical analysis**

All data were analyzed using the statistical program EPI-INFO (versions 3.5.1 and 6.04; Center for Control and Prevention of Diseases, Atlanta, GA, USA and OMS, Basel Switzerland). Results are expressed as mean  $\pm$  standard deviation, percentage (confidence interval [95% CI]), and odds ratio (OR). The Kolmogorov–Smirnov test was used to evaluate normality of the data distribution and the Levene test to evaluate variance homogeneity. The comparison between groups was performed with the Student *t*-test (continuous parametric data) or the Mann–Whitney test (non-parametric data). The chi-squared test was used to compare percentages between groups. We also used Fisher's exact test when any cell contained fewer than five cases.

Logistic regression analysis was used to determine the factors related to strength (hand grip), physical performance (SPPB), risk of sarcopenia (SARC-F), and frailty. Inclusion of different variables in the model was done through a stepwise procedure, considering a level of 5% as significant. We also considered the different interactions between the variables found statistically significant in the univariate analysis. The Hosmer–Lemeshow test was used to determine the regression model adequacy. In all analysis,  $p < 0.05$  was considered statistically significant.

### Ethical considerations

The study was approved by the local ethics committee (Southern Metropolitan Health Service, Santiago de Chile, Chile) and complied with the Declaration of Helsinki. All patients provided written informed consent.

### Results

We studied 493 women from Mexico, Panama, and Peru, whose ages ranged from 40 to 89 years; their average age was  $57.4 \pm 12.3$  years. They had a mean  $13.4 \pm 4.7$  years of schooling, 68.1% had a partner and 57.2% had sexual

activity, their average number of children was  $2.9 \pm 2.2$ , and 71.5% were postmenopausal. The average weight was  $65.2 \pm 15.2$  kg with a height of  $1.55 \pm 0.09$  m and a BMI of  $27.2 \pm 6.4$  kg/m<sup>2</sup>. The percentage of women with low weight was between 16.0 and 18.4% in women under 70 years old, but from that age it rose to 26.2% and to 44.2%, respectively, in the following two decades. Other characteristics are presented in Table 1.

Table 2 presents the age-related changes through different tests that assess muscle function. The percentage of women with low muscle strength (hand grip strength) increases progressively from 7.1% in women between 40 and 49 years of age to 79.4% in those aged 80–89 years ( $p < 0.0001$ ). Physical performance (SPPB) is low in 0.5% of the first group and rises to 60.5% in the latter ( $p < 0.0001$ ). Likewise, the risk of sarcopenia (SARC-F) increases significantly from 6.7% in younger women to 58.1% in older women ( $p < 0.0001$ ). Frailty, which affects less than 1% in women under 60 years of age, progressively increases from that age, affecting 4.1%, 11.5%, and 39.5% of women in their 60s, 70s, and 80s, respectively ( $p < 0.0001$ ).

Physical activity decreases with age, as shown in Table 3; 26.0% of women aged 40–49 years are inactive (MET-min/week  $< 600$  points, IPAQ). This percentage increases significantly with age, reaching 68.3% of women older than 80 years ( $p < 0.0001$ ).

Table 4 shows that frailty, a geriatric disorder that comprises muscular deterioration due to aging, negatively impacts the quality of life and the perception of health that an older woman can have. Thus, the quality of life evaluated with the MRS shows that 58.1% of women with frailty have a poor quality of life, (score  $> 16$  points); in contrast, only 19.2% of the normal women have a poor quality of life ( $p < 0.0001$ ). Likewise, 45.2% of women without fragility have

**Table 1.** Characteristics of the women studied.

Characteristic	Mean $\pm$ standard deviation or percentage (95% confidence interval)
Age (years)	57.4 $\pm$ 12.3
Weight (kg)	65.2 $\pm$ 15.2
Height (m)	1.55 $\pm$ 0.09
Body mass index (kg/m <sup>2</sup> )	27.2 $\pm$ 6.4
Obesity (%)	19.2 (16.2–22.7)
Years of study	13.4 $\pm$ 4.7
House owners (%)	31.7 (28.0–35.6)
In a couple (%)	68.1 (64.2–71.8)
With sexual activity (%)	57.2 (53.1–61.2)
Number of children	2.9 $\pm$ 2.2
Postmenopausal (%)	71.5 (67.7–75.1)
Hysterectomy (%)	19.2 (16.2–22.7)
Bilateral oophorectomy (%)	10.5 (8.2–13.3)
Menopausal hormone therapy users (%)	11.1 (8.8–14.0)
Sedative users (%)	9.6 (7.4–12.3)
Antidepressants users (%)	6.4 (4.6–8.8)
Arterial hypertension (%)	21.9 (18.7–25.5)
Diabetes mellitus (%)	12.6 (10.1–15.7)
Joint diseases (%)	11.0 (8.6–13.8)
Bronchopulmonary disease (%)	5.6 (3.9–7.8)
Heart diseases (%)	4.4 (2.9–6.4)
Cancer (%)	2.9 (1.7–4.6)

**Table 2.** Prevalence of age-related muscular function deterioration in women.

Age (years)	Number of women	Low hand grip strength <sup>a,b</sup>	Low physical performance (SPPB) <sup>c,d</sup>	High risk of sarcopenia (SARC-F) <sup>e</sup>	Frailty <sup>d,f</sup>
40–49	194	7.1 (3.6–12.4)	0.5 (0.0–2.8)	6.7 (3.6–11.2)	0.5 (0.0–2.8)
50–59	174	6.3 (2.9–11.7)	2.9 (0.9–6.6)	11.5 (7.2–17.2)	0.6 (0.0–3.2)
60–69	121	20.2 (12.8–29.5)	5.8 (2.4–11.6)	19.8 (13.1–28.1)	4.1 (1.4–9.4)
70–79	61	49.0 (34.8–63.4)	29.5 (18.5–42.6)	36.1 (24.2–49.4)	11.5 (4.7–22.2)
80–89	43	79.4 (62.1–91.3)	60.5 (44.4–75.0)	58.1 (42.1–73.0)	39.5 (25.0–55.6)

Data presented as percentage (95% confidence interval).

<sup>a</sup>Hand grip  $< 17.4$  kg (25th percentile).

<sup>b</sup> $p < 0.0001$  (chi-square test).

<sup>c</sup>Short Physical Performance Battery (SPPB) score  $\leq 6$  points = low physical performance.

<sup>d</sup> $p < 0.0001$  (Fisher's exact test).

<sup>e</sup>SARC-F score  $\geq 4$  points = risk of sarcopenia.

<sup>f</sup>Three of five criteria present (slowness, weakness, weight, exhaustion, and low physical activity).

**Table 3.** Changes in physical activity with age (International Physical Activity Questionnaire).

Age (years)	Number of women	MET-min/week <sup>a</sup>	Inactive women <sup>b,c</sup> , % (95% confidence interval)
40–49	194	4.260 $\pm$ 6.143	26.0 (20.0–32.9)
50–59	174	3.172 $\pm$ 3.927	36.8 (29.6–44.5)
60–69	121	2.370 $\pm$ 3.775	34.7 (26.2–44.1)
70–79	61	1.561 $\pm$ 2.106	49.2 (35.9–62.5)
80–89	43	966 $\pm$ 1.800	68.3 (51.9–81.9)

<sup>a</sup> $p < 0.0001$  (Kruskal-Wallis test).

<sup>b</sup>Score  $< 600$  Metabolic Equivalent (MET)-min/week.

<sup>c</sup> $p < 0.0001$  (chi-square test).



**Table 4.** Quality of life (MRS and SF-36) according to fragility.

Frailty	Number of women	Low quality of life (MRS) <sup>a</sup>		Low general health perceptions (SF-36) <sup>b</sup>	
		% (95% confidence interval)	Odds ratio (95% confidence interval)	% (95% confidence interval)	Odds ratio (95% confidence interval)
No	562	19.2 (16.1–22.8)	1.00	45.2 (41.0–49.4)	1.00
Yes	31	58.1 <sup>c</sup> (39.1–75.5)	5.82 (2.77–2.24)	71.0 <sup>d</sup> (52.0–85.8)	2.96 (1.34–6.55)

<sup>a</sup>Menopause Rating Scale (MRS) score >16.

<sup>b</sup>36-item Short Form (SF-36) (general health perceptions) score <50 points (median).

<sup>c</sup> $p < 0.0001$  (chi-square test).

<sup>d</sup> $p < 0.0005$  (chi-square test).

**Table 5.** Risk factors (binary analysis) of disorders in muscle function in women.

Factor	Low hand grip	Low physical performance (SPPB)	Risk of sarcopenia (SARC-F)	Frailty
Age $\geq 70$ years	14.0 (8.1–24.1)	13.6 (6.8–27.0)	6.2 (3.9–10.0)	20.7 (8.6–49.5)
Joint diseases	4.1 (2.3–7.1)	8.8 (4.7–16.2)	4.5 (2.6–7.8)	6.1 (2.8–13.2)
Oophorectomy	2.7 (1.7–5.0)	1.2 (0.5–2.8)	3.0 (1.7–5.3)	1.7 (0.6–4.6)
Sedative use	2.4 (1.3–4.6)	2.5 (1.2–5.2)	2.2 (1.2–4.0)	4.4 (1.9–10.0)
Low physical activity <sup>a</sup>	2.4 (1.5–3.8)	1.1 (0.7–2.0)	2.9 (1.8–4.4)	8.1 (3.3–20.1)
Low weight (20th percentile) <sup>b</sup>	2.2 (1.3–3.7)	5.1 (2.9–9.0)	2.4 (1.5–3.9)	2.3 (1.1–5.0)
Antidepressant use	1.8 (0.7–4.1)	2.3 (1.0–5.4)	1.5 (0.7–3.3)	2.3 (0.8–7.0)
Diabetes mellitus	1.7 (0.9–3.1)	3.2 (1.7–6.0)	3.0 (1.8–5.1)	2.6 (1.1–6.0)
Menopause age <45 years	1.6 (0.9–2.7)	2.1 (1.1–3.9)	2.3 (1.4–3.7)	2.5 (1.1–5.5)
MHT users	0.5 (0.2–1.1)	0.1 (0.0–0.9)	0.0 (0.0–0.5)	0.9 (0.9–1.0)

Data presented as percentage (95% confidence interval). MHT, menopause hormone therapy; SPPB, Short Physical Performance Battery.

<sup>a</sup>Score <600 Metabolic Equivalent (MET)-min/week.

<sup>b</sup>Body mass index <23 kg/m<sup>2</sup>.

**Table 6.** Risks factors (logistic regression) for muscle function disorders in women.

Factor	Low hand grip strength	Low physical performance (SPPB)	High risk of sarcopenia (SARC-F)	Frailty
Age $\geq 70$ years	11.4 (6.4–20.3)	20.8 (10.1–42.5)	5.8 (3.4–9.6)	10.8 (4.3–17.0)
Joint diseases	2.5 (1.2–5.0)	3.3 (1.6–7.0)	4.9 (2.6–9.2)	6.1 (2.1–17.7)
Oophorectomy	ns	ns	ns	ns
Sedative users	ns	ns	ns	2.9 (1.1–8.0)
Low physical activity <sup>a</sup>	2.0 (1.1–3.5)	ns	ns	9.3 (3.0–28.4)
Low weight (20th percentile) <sup>b</sup>	ns	4.9 (2.2–11.1)	ns	ns
Antidepressant users	ns	ns	ns	ns
Diabetes	ns	ns	ns	ns
Menopause <45 years old	ns	ns	2.2 (1.2–4.0)	ns
MHT users	ns	ns	ns	ns

Data presented as percentage (95% confidence interval). MHT, menopause hormone therapy; ns, non-significant; SPPB, Short Physical Performance Battery.

<sup>a</sup>Score <600 Metabolic Equivalent (MET)-min/week.

<sup>b</sup>Body mass index < 23 kg/m<sup>2</sup>.

a poor health perception (SF-36), a percentage that rises to 71.0% in women with frailty ( $p < 0.005$ ).

Table 5 presents a binary analysis of the risk factors associated with the deterioration of muscle function with the different instruments used to evaluate it. Age older than 70 years is the main risk factor associated with the loss of strength (OR 14.0, 95% CI 8.1–24.1), low physical performance (OR 13.6, 95% CI 6.8–27.0), the risk of sarcopenia (OR 6.2, 95% CI 3.9–10.0), and frailty (OR 20.7, 95% CI 8.6–49.5). Following these is joint diseases, oophorectomy, the use of sedatives, low physical activity, underweight, the use of antidepressants, diabetes mellitus, and menopause. The use of menopausal hormone therapy seems to decrease the risk of low muscle function.

Using the categorical logistic regression model (Table 6) we evaluated the risk factors associated with muscle disorders, in a binary analysis, and confirmed that being over the age of 70 years and symptoms of joint disease are independent risk factors of muscle deterioration based on all of the instruments used to evaluate it. Other factors affecting muscle strength are physical inactivity, low physical

performance, low weight, the risk of sarcopenia from menopause before the age of 45 years, frailty, the use of sedatives, and a sedentary lifestyle.

## Discussion

Our study shows that the muscular function of women, evaluated with different instruments, decreases significantly with age. Low handgrip strength is a clinical marker of poor mobility and a better predictor of clinical outcomes than low muscle mass in older people<sup>29</sup>. In this study we observed a significant drop in hand grip strength in women older than 60 years. Along with this finding, we also found that the risk of sarcopenia (SARC-F) increases significantly with aging. Therefore, it is not surprising that, in women older than 60 years, we found a significant decrease in physical performance, evaluated with the SPPB. Thus, the measurement of isometric handgrip strength is a cost-effective clinical marker of sarcopenia, defining this disorder as a combination of low muscle mass and the deterioration of its function. Likewise, we observed that, in parallel with the decrease in muscle

strength, frailty increases with aging, and this observation is consistent with other studies, showing that low muscle strength is associated with a functional decline in older people regardless of muscle mass<sup>3</sup>.

In this study, physical activity decreases markedly with aging. The question which immediately arises is whether this decrease is a consequence of or a result of the decrease in muscular function. In a previous study, we found that the menopausal symptoms observed in women between 40 and 59 years of age are associated with a more sedentary lifestyle<sup>30</sup>. We could hypothesize that the decrease in muscular strength observed after 60 years of age could be influenced, in part, by the increase in a sedentary lifestyle that women have after 40 years of age. It is also clear that among the main causes of sarcopenia, defined by a decrease in muscle mass and function, are hormonal changes (reduced secretion of testosterone, estrogen, and growth hormone), nutritional deficiencies, and chronic inflammation<sup>31</sup>. The importance of physical activity, within this constellation of frequent changes of aging, is reflected in the fact that physical activity is a moderator in the relationship between sedentary time and frailty in older adults, offsetting the harmful effects of sedentary behavior with 27 min/day of moderate-to-vigorous activity<sup>32</sup>.

The reduction of muscle strength could be considered the core of frailty, a syndrome that strongly reflects the deterioration of muscular function, characteristic of aging. Our results show how frailty increases significantly with age, especially in women over 70 years old. This is associated with a deterioration in the quality of life (MRS) and a poor perception of health (SF-36). A meta-analysis also shows a consistent inverse association between frailty/prefrailty and the quality of life among community-dwelling older people<sup>33</sup>. Therefore, interventions targeted to reduce frailty may have the additional benefit of improving the quality of life.

In the logistic regression analysis, this study shows that old age, defined as an age equal to or greater than 70 years, is a risk factor according to all instruments used to assess muscle function. This increases the risk of poor performance by 5–20 times, when compared to younger women. Among the causes of muscle deterioration with aging, a meta-analysis did not find, in sarcopenic patients, a significant increase in inflammatory cytokines due to age, except for C-reactive protein<sup>34</sup>. It is also unclear whether there is a change in the oxidative capacity of muscles in elderly people<sup>35</sup>. It seems that the age-related changes in skeletal muscles can be attributed to the complex interaction of factors affecting neuromuscular transmission, muscle architecture, fiber composition, excitation–contraction coupling, and apoptosis<sup>36</sup>.

A second risk factor for muscle function deterioration in this study was the presence of joint diseases. A systematic review that evaluated the relationship of the muscle with osteoarthritis does not support the thesis of a direct effect of sarcopenia on osteoarthritis development or the inverse relation, because basic science studies on these topics are lacking<sup>37</sup>. However, we must consider that osteoarthritis and sarcopenia have a common factor, aging. In aging, one of

the paradigms that has emerged strongly, in recent years, is cellular senescence. This is a process by which cells enter a state of permanent cell cycle arrest, exerting detrimental effects on the tissue microenvironment by increasing the secretion of diverse proinflammatory cytokines, inducing dramatic changes in mitochondrial function, metabolism, and homeostasis<sup>38</sup>. Recent studies indicate that cellular senescence is a contributor to age-related loss of function in various organs including muscles and joints<sup>39</sup>.

We found that low physical activity was a risk factor for low hand grip strength and frailty. These results are concordant with a meta-analysis of 25 studies that observed a significantly lower rate of hand grip strength in electively admitted, older patients during a period of rest during hospitalization<sup>40</sup>. Likewise, a systematic review found that sedentary behaviors were associated with a higher prevalence and/or level of frailty<sup>41</sup>. The relationship of physical activity with the muscle seems to be based on changes in the patterns of DNA methylation that potentially allow an increased insulin sensitivity and a greater expression of genes involved in energy metabolism, myogenesis, contractile properties, and oxidative stress resistance in skeletal muscles of elderly individuals<sup>42</sup>.

We could not demonstrate that the hormonal changes of menopause and/or hormone therapy significantly modified a woman's muscle deterioration. However, menopause before age 45 years significantly increased the risk of sarcopenia assessed with SARC-F, suggesting some role of estrogen deficiency in muscle function. This should not be surprising, since there are both  $\alpha$  and  $\beta$  estrogenic receptors in the muscle and they decline progressively in postmenopause, causing a decrease in proteins, peroxisome proliferator-activated receptor gamma coactivator 1- $\alpha$  (PGC-1 $\alpha$ ), and 5' AMP-activated protein kinase (AMPK), which are related to the regulation of cellular energy homeostasis<sup>12</sup>. Estrogen deficiency is not the only hormonal disorder involved in the etio-pathogenesis of sarcopenia. The major endocrine causes of sarcopenia are diabetes mellitus, very low (25-OH) vitamin D levels, hyperthyroidism, decreased growth hormone, and insulin-like growth factor 1<sup>43</sup>. The measurement of hormone levels related to these disorders might be useful in trying to define potential early indicators of sarcopenia.

The evidence from nutritional epidemiology suggests a positive association between healthier diets, such as the Mediterranean diet, and muscle function<sup>44</sup>. Our study did not evaluate the quality of nutrition but, indirectly, caloric consumption through the BMI. A low BMI reflects a negative 'energy gap'<sup>45</sup>. The effect of a negative caloric balance with aging is reflected in our results by an increase in the percentage of women with low BMI among older women. In our logistic regression model, women with a low BMI had low physical performance.

It is not easy to compare our results with those of other ethnic groups because of the variability of the instruments used in the different investigations. However, considering only the hand grip test, there is a study that evaluates this by different ethnic groups and ages<sup>17</sup>. This study shows that European women between 60 and 70 years old have the

greatest grip strength (25 kg), followed by Chinese (23 kg) and Latin American (23 kg) women; in the last places are Malay (18 kg) and African (18 kg) women. Our result in that age group of women was 22 kg, quite consistent with what was published in the mentioned study.

We can summarize that there is an association between aging and declining muscle strength and an increase in frailty which is associated with a detriment in the quality of life. In addition to aging, osteoarthritis is another very important factor associated with the deterioration of muscle function, but we were not able to determine whether this disease is associated with a disorder or an etiological factor in the muscle failure of the elderly. On the other hand, menopause before the age of 45 years is associated with an increased risk of sarcopenia.

Finally, in light of these results and current knowledge, a program for the prevention of age-related muscle deterioration should be recommended to health authorities, based on greater physical activity, a recommendation to adhere to an appropriate diet with the right amount of energy and proteins, and avoiding superfluous or harmful polypharmacy<sup>46</sup>.

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