

Research article

Association between sarcopenia-related phenotypes and aerobic capacity indexes of older women

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Abstract

The purpose of the present study was to examine the association between fat-free mass (FFM), quadriceps strength and sarcopenia with aerobic fitness indexes of elderly women. A total of 189 volunteers (66.7 ± 5.46 years) underwent aerobic capacity measurement through a symptom-limited cardiopulmonary exercise test to determine their individual ventilatory thresholds (VT) and peak oxygen uptake (VO_2 peak). Quadriceps muscle strength was assessed using an isokinetic dynamometer. Also, dual energy X-ray absorptiometry was used to assess FFM and cutoff values were used to classify subjects as sarcopenic or nonsarcopenic. Correlations, student t-test and analysis of variance were used to examine the data. Both FFM and quadriceps strength variables were positively and significantly correlated with the measured aerobic capacity indexes. These results were observed for peak exercise as well as for ventilatory thresholds. Individuals classified as sarcopenic presented significantly lower muscle strength and (VO_2 peak) when compared to nonsarcopenic. It can be concluded that FFM and quadriceps strength are significantly related to aerobic capacity indexes in older women, and that besides presenting lower quadriceps strength, women classified as sarcopenic have lower peak oxygen consumption. Taken together, the present results indicate that both FFM and strength play a role in the age-related decline of aerobic capacity.

Key words: Sarcopenia, VO_2 peak, muscle strength, elderly, cardiorespiratory fitness, peak torque.

Introduction

The aging process is associated with a progressive decline in most physiological systems. Among the most important changes with regard to quality of life and functional independence are declines in muscle strength and aerobic capacity (Fleg et al., 2005). For example, maximal aerobic capacity, generally expressed as peak oxygen consumption (VO_2 peak), declines with advancing age even in older subjects that remain engaged in regular vigorous endurance training (Rogers et al., 1990). Holleberg et al. (2006), in a recent six year longitudinal study, reported that VO_2 peak declined at a rate of 18% and 24% per decade for women and men, respectively. This finding requires attention since individuals who maintain adequate aerobic fitness are less likely to die from all causes including cardiovascular diseases (Blair et al., 1995). Therefore, a better understanding of the pathways leading to the age-associated VO_2 peak decrease is of great importance.

Physiological aging contributes to the concomitant decline in aerobic capacity (Ades and Toth, 2005). VO_2 peak reflects the product between maximum cardiac output and maximum oxygen extraction capacity (i.e., oxygen arteriovenous difference). With aging, there is a decline in cardiovascular performance, that is, maximum cardiac output, stroke volume and heart rate decline (Ferrari et al., 2003; Landin et al., 1985). Cardiac responsiveness to Beta-adrenergic stimuli is decreased in older individuals; therefore, exercise-induced tachycardia and myocardial contractility are blunted (Fleg et al., 1995). Also, the decline in muscle mass and strength, a process broadly referred to as sarcopenia, may also contribute to the age-associated decline in aerobic fitness (Fleg and Lakatta, 1988), however, this observation has been questioned (Proctor and Joyner, 1997). Different methodological approaches have produced conflicting results and the role of sarcopenia in the decline of VO_2 peak with aging remains obscure.

Cardiopulmonary exercise testing using a ramp protocol enables exercise specialists to identify the ventilatory thresholds. The first ventilatory threshold (VT1), also referred to as anaerobic threshold (Wasserman, 1964), corresponds to an increase in the ratio of ventilation to oxygen uptake and is considered to be a reproducible measure of aerobic fitness (Yamamoto, 1991). With further increases in exercise intensity, the second ventilatory threshold (VT2), also referred to as the respiratory compensation point, can be observed. Both VT1 and VT2 have been extensively used for prescription of individualized exercise intensities, for both athletic performance and clinical rehabilitation (Meyer et al., 2005). Exercise intensities above VT2 promote a net contribution of energy associated with lactate accumulation and, if sustained, fatigue will rapidly occur (Svedahl and MacIntosh, 2003). For low fit older individuals, some activities of daily living might exceed this threshold intensity and thus will be performed under a high perceived effort. Unfortunately, the relationships between fat-free mass (FFM) and muscle strength with VT1 and VT2 have not been previously investigated in older individuals, and available studies are limited to associations with VO_2 peak only.

Determination of the consequences of sarcopenia in regards to cardiorespiratory function, among other issues, is important to establish its clinical relevance. Based on appendicular FFM (AFFM) values, Baumgartner et al. (1998) proposed cutoff points to define sarcopenia. However, comparisons of aerobic fitness

between sarcopenic and nonsarcopenic individuals remain to be performed. The purpose of the present study was to examine the association between FFM, muscle strength, and sarcopenia with aerobic fitness of older women.

Methods

Subjects

Volunteers resided in the university neighborhood and were invited to participate in the present investigation by telephone solicitation. Figure 1 illustrates the fluxogram of the sample recruitment process. Approximately 500 phone numbers were called with 300 acceptances. The main reasons for unsuccessful solicitations were phone number alteration, acute illness and lack of interest. Exclusion criteria were as follows: individuals with any metallic implant or artificial pacemaker, who had undergone hip surgery, who were unable to walk without assistance, those affected by metabolic or endocrine disorders that affect the muscular system, who were taking beta-blockers and those who presented ECG alterations during the cardiopulmonary exercise test. After exclusion criteria were applied, 225 volunteers completed the first visit to the laboratory, from which 17 were contraindicated to the exercise test after physician evaluation. In addition, 19 older women did not reach volitional exhaustion in the exercise test due to arrhythmias and other ECG abnormalities, breathless or angina pectoris. Therefore, a total of 189 volunteers (66.7 ± 5.46 years) participated in this study. The participant's characteristics are outlined in Table 1.

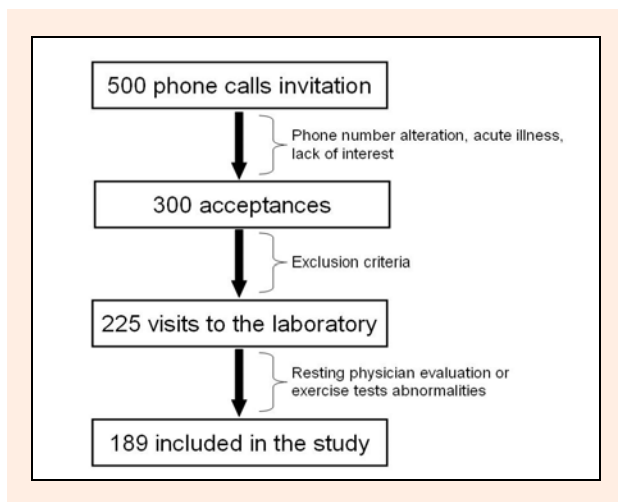


Figure 1. Fluxogram of the sample recruitment process.

All volunteers were fully informed of all possible risks and benefits associated with the procedures and freely signed consent forms prior to participation. The study protocol was conducted in accordance to the Declaration of Helsinki and was approved by the University Ethics Committee under protocol CEP/UCB 024/2007.

Cardiopulmonary exercise test

Participants underwent a treadmill (RT 300, Moviment, Brazil) symptom-limited cardiopulmonary exercise test using a ramp protocol. The same protocol, which was designed to elicit exhaustion in approximately 10 minutes,

was used for all participants. Before testing, subjects were instrumented with a thirteen-lead resting ECG (ECG Digital, Micromed, Brasil). There were also provided with basic instructions regarding the procedures and use of the Borg perceived exertion scale (Borg, 1982). Subjects were then asked to exercise until they felt unable to continue. Blood pressure was continuously measured using a mercury column sphygmomanometer at three-minute intervals, whereas perceived exertion was collected in two-minute intervals and at exhaustion. Throughout the test, expired gases were continuously measured "breath by breath" using the Cortex Metalyzer 3B apparatus (Cortex Biophysik, Germany). Volume and gas calibration were performed according to manufacturer's instructions. All procedures were conducted under physician supervision and volunteers were allowed to hold the frontal treadmill handrail. VO_2 peak was recorded as the mean of the last 30 seconds of exercise.

VT1 was determined as the point at which a loss of linearity occurred between oxygen uptake and carbon dioxide production, identified when the ventilatory equivalent for oxygen and end-tidal oxygen partial pressure curves reached their minimum values and began to systematically increase. VT2 was determined as the point at which the ventilatory equivalent for carbon dioxide began to systematically increase with a concomitant decrease in end-tidal carbon dioxide partial pressure. Both VT1 and VT2 were determined by two proficient physiologists.

Isokinetic muscle peak torque

Aerobic capacity and muscle strength measurements were separated by at least 48 hours, but no longer than 13 days. Thus, it is not expected that the measurements affected each other. Quadriceps isokinetic peak torque (PT) was measured on the dominant leg using the Biodex System 3 dynamometer (Biodex Medical System, Shirley, NY). After a five minute warm-up and full explanation of the procedures, participants were seated on the dynamometer which was then carefully adjusted. Velcro belts were used to stabilize the body and the rotational axis of the dynamometer arm was oriented with the lateral condyle of the participant's femur. The testing protocol consisted of three sets of four knee extensor contractions at $60^\circ \cdot \text{s}^{-1}$ with 30 seconds between sets (Bottaro et al., 2005). The recorded value was the highest PT achieved during the three sets, which was expressed both in absolute values (Nm) and relative to body weight (Nm/kg). Participants were instructed and verbally encouraged to perform the movement with their maximal strength.

Body composition

After standard procedures for determining body weight, height and body mass index (BMI), body composition measurements were performed using Dual Energy X-ray Absorptiometry (DXA) (DPX-L, Lunar Radiation Corporation, Madison, WI). Detailed procedures have been previously presented (Lima et al., 2007). After analyses, whole body and appendicular FFM were recorded in absolute values (kg) and relative to body heightsquared ($\text{kg} \cdot \text{m}^{-2}$), analogous to the use of BMI. Sarcopenic individuals were defined as having a relative AFFM below

Table 1. Mean and standard deviation (SD) of participant's characteristics (n=189).

Variable	Mean	± SD
Age (years)	66.7	5.46
Weight (kg)	64.65	10.36
Height (m)	1.52	0.06
BMI (kg·m ⁻²)	27.69	3.95
Percent body fat (%)	39.62	5.96
PT (Nm)	95.96	22.87
PT relative to body weight (Nm·kg ⁻¹)	147.55	30.51
Total FFM (kg)	37.17	4.19
Relative total FFM (kg)	15.91	1.36
AFFM (kg)	14.32	1.94
Relative AFFM (kg)	6.12	0.66
Resting heart rate (bpm)	74.26	11.1
Systolic blood pressure (mmHg)	126.11	16.23
Diastolic blood pressure (mmHg)	77.72	9.22
Time to exhaustion (s)	587	126
VO ₂ peak (L·min ⁻¹)	1.11	0.25
VO ₂ peak (ml·kg ⁻¹ ·min ⁻¹)	17.19	3.25

BMI = body mass index; PT = peak torque; FFM = fat-free mass; AFFM = appendicular fat-free mass.

5.45 kg·m⁻², as previously proposed by Baumgartner et al. (1998). Coefficients of variation for the system were 2.1% and 1.9% for fat mass and FFM, respectively. The equipment was calibrated daily and all examinations were done by the same trained technician.

Statistical analyses

The Kolmogorov–Smirnov test was used to verify data distribution normality. Descriptive statistics are expressed as the mean ± standard deviation. Linear regressions and Pearson correlation coefficients were used to examine the relationships between FFM and strength variables with aerobic fitness indexes. Independent sample student t-tests were used to compare variables between sarcopenic and nonsarcopenic individuals. Analyses were considered significant at $p < 0.05$ and all statistical procedures were performed using the SPSS12.0 software.

Results

All participants that were included in analyses underwent FFM, muscle strength and cardiorespiratory fitness evaluations with no injury related to the procedures. The Kolmogorov–Smirnov test showed that all variables were normally distributed; therefore, all evaluated subjects were included in subsequent analyses using parametric tests. Volunteers' characteristics are presented in table 1. Cardiopulmonary exercise tests lasted an average of 587 ± 126 seconds and elicited a mean relative VO₂peak of

17.19 ± 3.25 ml·kg⁻¹·min⁻¹, a value that is considered normal according to the American Heart Association (American Heart Association, 1972). Participants' average rating on the Borg perceived exertion scale at the end of the test was 17 (very hard).

Table 2 shows the correlations between isokinetic PT (both in absolute and relative values) and the cardiorespiratory fitness indexes obtained in the cardiopulmonary exercise test. When analyzed in absolute values, quadriceps PT presented positive and significant correlations with all the measured indexes. Similarly, quadriceps PT relative to body weight showed positive and significant correlations with all aerobic fitness variables except for oxygen uptake at the moment of VT₁. The correlations between FFM-related variables and cardiorespiratory fitness indexes are presented in Table 3. In most situations (i.e., 21 of the 36 analyzed relationships), the correlations were positive and significant.

Table 4 demonstrates age, PT and cardiorespiratory fitness variables according to sarcopenia classification. In the present study sample, 28 subjects were classified as sarcopenic, representing a prevalence of 15.9%. No age difference between groups was observed, however, sarcopenic individuals presented significantly lower absolute and relative quadriceps PT when compared to nonsarcopenic individuals. Also, sarcopenic individuals showed significantly lower values for some of the cardiorespiratory fitness indexes, specifically, absolute oxygen uptake at VT₁, VT₂ and maximal effort as well as

Table 2. Correlations between isokinetic peak torque and cardiorespiratory fitness indexes evaluated by a cardiopulmonary exercise test.

Variables	PT (Nm)	PT (Nm·kg ⁻¹)
VT ₁ T (s)	.29 *	.35 *
VT ₁ VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	.19 *	.21 *
VT ₁ VO ₂ (L·min ⁻¹)	.46 *	.09
VT ₂ T (s)	.31 *	.42 *
VT ₂ VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	.26 *	.30 *
VT ₂ VO ₂ (L·min ⁻¹)	.56 *	.16 *
Tmax (s)	.33 *	.42 *
VO ₂ Peak (ml·kg ⁻¹ ·min ⁻¹)	.33 *	.37 *
VO ₂ Peak (L·min ⁻¹)	.61 *	.21 *

* $p < 0.05$. PT = peak torque; VT₁ = ventilatory threshold 1; VT₂ = ventilatory threshold 2; T = time; Tmax = time to exhaustion

Table 3. Correlations between fat-free mass variables and cardiorespiratory fitness indexes evaluated by a cardiopulmonary exercise test.

Variables	Total FFM	Relative total FFM	AFFM	Relative AFFM
VT ₁ T (s)	.10	-.01	.18 *	.10
VT ₁ VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	.19 *	.01	.23 *	.09
VT ₁ VO ₂ (L·min ⁻¹)	.61 *	.35 *	.51 *	.28 *
VT ₂ T (s)	.06	-.04	.16 *	.10
VT ₂ VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	.16 *	-.03	.26 *	.13
VT ₂ VO ₂ (L·min ⁻¹)	.63 *	.34 *	.58 *	.34 *
T _{max} (s)	.04	-.05	.14	.10
VO ₂ Peak (ml·kg ⁻¹ ·min ⁻¹)	.19 *	-.01	.29 *	.16 *
VO ₂ Peak (L·min ⁻¹)	.65 *	.37 *	.60 *	.36 *

* $p < 0.05$. FFM = fat-free mass; AFFM = appendicular fat-free mass; VT₁ = ventilatory threshold 1; VT₂ = ventilatory threshold 2; T = time; T_{max} = time to exhaustion

relative oxygen uptake at maximal effort.

Discussion

The aging process is frequently accompanied by a progressive and involuntary decline in FFM and muscle strength. This observable fact has been referred to as sarcopenia and has been linked to a range of negative outcomes in older individuals. The well recognized consequences include disability (Baumgartner et al., 1998), increased risk of falls (Orr et al., 2006) and metabolic impairments (Bloesh et al., 1988), all leading to a loss of autonomy. Sarcopenia may also contribute to the age-associated reduction in cardiorespiratory fitness (Fleg and Lakatta, 1988). Analyzing the correlations between FFM and strength with cardiorespiratory fitness indexes, and comparing levels between sarcopenic and nonsarcopenic individuals, the present study provides evidence that the loss of muscle strength and mass with advancing age is associated with the decline in aerobic fitness in older women. This association was observed not only with VO₂peak, but also with other cardiorespiratory performance indexes such as oxygen consumption at the ventilatory thresholds. Since all participants underwent exercise testing under the same ramp protocol, we were able to examine associations between muscle-related phenotypes and time at the ventilatory thresholds and at peak exertion. The results were in agreement with those observed for oxygen uptake.

The role played by skeletal muscle mass loss in the age-associated decline in VO₂peak was previously demonstrated in a pioneer study conducted by Fleg and Lakata (1988). These authors measured urinary creatinine excre-

tion as an index of muscle mass, and observed a positive correlation ($r = 0.64$, $p < 0.001$) with maximal oxygen consumption in 184 healthy volunteers aged between 22 and 87 years. Consistent with these findings, Rosen et al. (1998) reported maximal aerobic capacity declines in athletic and sedentary men, and that 35% of this observation is explained by the loss of FFM. Conversely, Proctor and Joyner (1997) suggested that body fat accumulation, and not FFM loss, contributes to the decline in maximal whole body oxygen uptake observed with aging. The present study does corroborate previous findings of a positive relationship between FFM and cardiorespiratory fitness indexes in older individuals. Among the FFM indexes analyzed in this article, AFFM (sum of arms and legs FFM) was the one that significantly correlated with more aerobic fitness variables. This result was not surprising since most of the oxygen uptake during exercise testing is consumed by the active muscles (Knight et al., 1992).

Previous studies have evaluated the relationship between FFM and aerobic capacity markers, but we are not aware of prior investigations that compared aerobic indexes between sarcopenic and nonsarcopenic individuals. In fact, there are limited data to establish what constitutes deficient muscle mass. Based on height-adjusted AFFM values, Baumgartner et al. (1998) proposed a method for determining sarcopenia which was reported to be strongly associated with an increased risk of disability in older people. Using this cutoff point, the present study found that sarcopenic older women present not only significantly lower quadriceps strength but also lower absolute and relative VO₂peak.

Table 4. Cardiorespiratory fitness indexes according to sarcopenia classification.

Variables	Sarcopenic	Nonsarcopenic
N (%)	28 (15.9)	151 (84.1)
Age (years)	66.5 ± 5.3	68.3 ± 6.1
PT (Nm)	74.3 ± 15.6 *	100.0 ± 21.7
PT relative to body weight (Nm·kg ⁻¹)	130.0 ± 22.5 *	158.9 ± 30.8
VT ₁ T (s)	287.9 ± 87.3	292.8 ± 98.3
VT ₁ VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	12.2 ± 2.4	12.7 ± 2.5
VT ₁ VO ₂ (L·min ⁻¹)	.71 ± .21 *	.83 ± .19
VT ₂ T (s)	485.8 ± 95.2	503.4 ± 115.9
VT ₂ VO ₂ (ml·kg ⁻¹ ·min ⁻¹)	15.1 ± 2.9	15.9 ± 3.0
VT ₂ VO ₂ (L·min ⁻¹)	.87 ± .23 *	1.05 ± .22
T _{max} (s)	562.7 ± 119.4	591.9 ± 127.0
VO ₂ Peak (ml·kg ⁻¹ ·min ⁻¹)	16.1 ± 3.0 *	17.4 ± 3.3
VO ₂ Peak (L·min ⁻¹)	.93 ± .24 *	1.15 ± .24

* $p < 0.05$. PT = peak torque; VT₁ = ventilatory threshold 1; VT₂ = ventilatory threshold 2; T = time; T_{max} = time to exhaustion.

Besides FFM, it is also important to evaluate the relationship between muscle strength and aerobic capacity of older individuals. In this regard, quadriceps muscle is of particular importance because it has been associated with performance of activities of daily living in this population (Bassey et al., 1992; Slade et al., 2002). Isokinetic testing has become a popular method to assess dynamic muscle strength in both clinical and research settings (Drouin et al., 2004). In the present study, it was found that quadriceps isokinetic torque was positively and significantly correlated with all aerobic capacity indexes measured. These results are in agreement with Kostka et al. (2000) who reported that quadriceps performance and maximal oxygen uptake are interrelated in older women. A relevant finding of the present study was that muscle strength was related not only with peak exercise but also with the ventilatory thresholds. This observation suggests that low strength older women experience an early utilization of anaerobic metabolism and its related discomfort. In fact, Slade et al. (2002) demonstrated that older adults who practice strength training present higher anaerobic power and have higher physical function when compared to their non-trained peers.

In the present study, aerobic capacity was evaluated by a cardiopulmonary exercise treadmill test using a ramp protocol. The treadmill provides a mode of exercise that closely approximates an activity that older people are familiar with (i.e., walking). Although it represents a typical endurance exercise, it has been shown that in older adults there is a significant correlation between muscle strength and walking speed (Bassey et al., 1992; Marsh et al., 2006). Thus, it has been suggested that the aerobic capacity in older subjects may be limited due to skeletal muscle weakness (Vincent et al., 2002). Alternatively, since quadriceps function is related to activities of daily living, it can be argued that older women who have low muscle strength are more prone to reduced habitual physical activity, which is well documented to attenuate the age-related decline of aerobic capacity (Berthouze et al., 1995). Supporting this scenario, an intervention that attempted to increase muscle strength also increased free-living physical activity in older adults (Hunter et al., 2000).

Endurance exercise training is typically viewed as an effective mean to improve aerobic fitness in both young and older subjects (Poehlman et al., 2002; Malbut et al., 2002). Also, it is well accepted that resistance training (RT) is an effective intervention for preventing sarcopenia (Trappe et al., 2002). In contrast to endurance training, RT is not considered to favorably alter aerobic capacity. In fact, studies in young and middle-aged individuals have failed to detect RT-induced improvements in VO_2 peak (Marcinik et al., 1991). However, in older subjects where FFM and strength are possibly related to aerobic fitness, it can be conjectured that RT may increase aerobic fitness. In this regard, previous studies demonstrated that significant improvements in aerobic capacity can be achieved with a RT program (Frontera et al., 1990; Vincent et al., 2002). Therefore, the well recognized importance of including resistance exercises in a global training program for older adults is reinforced by the present re-

sults. It does not mean, however, that aerobic training should not be included in conjunction with RT. Besides being well known to increase aerobic capacity, endurance training has been shown to positively affect rates of protein turnover and synthesis (Short et al., 2004).

Conclusion

It can be concluded that FFM and quadriceps strength are significantly related to aerobic capacity indexes in older women. Muscle-related phenotypes were also associated with the ventilatory thresholds, suggesting that low FFM and/or strength in older women are prone to early utilization of anaerobic metabolism and experience its connected discomfort and fatigue. Besides presenting lower quadriceps strength, women classified as sarcopenic have lower peak oxygen consumption. The present results indicate that both FFM and strength, phenotypes that characterize sarcopenia, play a role in the age-related loss of aerobic capacity. Future studies should analyze whether interventions designed to increase muscle strength have a positive effect on exercise test performance.

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Key points

- Maximal aerobic capacity, generally expressed as peak oxygen consumption (VO_2 peak), declines with advancing age and this process is associated with an increased risk for cardiovascular diseases.
- Also, the aging process is associated with a progressive loss of muscle mass and strength and this phenomenon has been referred to as Sarcopenia. Sarcopenia has been described in both elderly men and women and has been linked to multiple negative clinical outcomes.
- The present study provide evidence that muscle-related phenotypes are associated with aerobic capacity of older individuals, thus suggesting that sarcopenia explains in part the decline in aerobic fitness observed with advancing age.

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