A pilot observational study to identify reference values for the 6-minute walk test in Brazilian people with hypertension

Um estudo observacional piloto para identificar valores de referência para o teste de caminhada de 6 minutos em hipertensos brasileiros

Afonso Lima
João Paulo Prado
Tarcísio Nema de Aquino
Juliana Bassalobre Carvalho Borges
Fernanda de Carvalho Vidigal
Giovane Galdino*

Universidade Federal de Alfenas (UNIFAL-MG), Alfenas, MG, Brazil

Date of first submission: January 19, 2023
Last received: December 27, 2023
Accepted: January 19, 2024

***Correspondence:** giovanegsouza@yahoo.com.br

Abstract

Introduction: Systemic arterial hypertension (SAH) is responsible for 9.5 million deaths in the global population. Lifestyle factors, including physical inactivity, are important modifiable risk factors in the development of SAH. Thus, physical exercise has been shown to be effective to control SAH and before the prescription, the six-minute walk test (6-MWT) has been commonly used to assess the physical capacity. **Objective:** To propose reference values for the 6-MWT test in Brazilian people with SAH. **Methods:** A cross-sectional observational study was conducted with 302 hypertensive subjects (62.61 + 10.93 years) admitted to a cardiac rehabilitation program. Participants were divided into different age quartiles and submitted to 6-MWT. The walking distance data was compared between the quartiles and adjusted by multiple linear regression analysis. **Results:** The hypertensive subjects walked 388.07 + 115.03 m during the 6-MWT. No significant difference between the genders was found. However, when the age quartiles were compared, for the 46–59 age group, the women walked less than the men. Intra-group comparisons showed that the distance walked in the 6-MWT decreased with the increase in age, in both men and women. **Conclusion:** The present study provides reference values for the 6-MWT, both for Brazilian men and women of different age groups. This data may be an important parameter for future clinical studies, prevention strategies, and clinical intervention.

Keywords: Cardiovascular disease. Cardiac rehabilitation. Functional capacity. Hypertension. 6-minute walk test.

Resumo

Introdução: *A hipertensão arterial sistêmica (HAS) é responsável por 9,5 milhões de mortes na população mundial. Condições do estilo de vida, incluindo a inatividade física, são importantes fatores de risco modificáveis no desenvolvimento da HAS. Desse modo, o exercício físico tem se mostrado eficaz no controle da HAS e, antes da prescrição, o teste de caminhada de seis minutos (TC6) tem sido comumente utilizado para avaliar a capacidade física.* ***Objetivo:*** *Propor valores de referência para o teste de TC6 em brasileiros com HAS.* ***Métodos:*** *Realizou-se um estudo observacional transversal com 302 hipertensos (62,61 + 10,93 anos) admitidos em um programa de reabilitação cardíaca. Os participantes foram divididos em diferentes quartis de idade e submetidos ao TC6. Os dados de distância percorrida foram comparados entre os quartis e ajustados por análise de regressão linear múltipla.* ***Resultados:*** *Os hipertensos caminharam 388,07 + 115,03 m durante o TC6. Não encontrou-se diferença significativa entre os gêneros. No entanto, quando comparados os quartis de idade, para a faixa etária de 46 a 59 anos, as mulheres caminharam menos do que os homens. As comparações intragrupo mostraram que a distância percorrida no TC6 diminuiu com o aumento da idade, tanto em homens quanto em mulheres.* ***Conclusão:*** *O presente estudo fornece valores de referência para o TC6, tanto para homens quanto para mulheres brasileiras de diferentes faixas etárias. Esses dados podem ser um parâmetro importante para futuros estudos clínicos, estratégias de prevenção e intervenção clínica.*

Palavras-chave: *Doença cardiovascular. Reabilitação cardíaca. Capacidade funcional. Hipertensão. Teste de caminhada de 6 minutos.*

Introduction

Systemic arterial hypertension (SAH) is a chronic disease, with multifactorial causes associated with functional, structural, and metabolic changes.[1] One of the most common changes due to SAH is the reduction in capillary density,[2] which causes a modification in the perfusion dynamics of all organs and systems (e.g., muscles), thus leading to reduced availability of nutrients and oxygen, which can impact muscle contractility and efficiency and directly affect physical capacity.[3,4]

These changes indicate that SAH is a significant aggravating factor for public health, making it very important to elaborate and/or adapt risk-predictive parameters that can measure the physical capacity of patients and outline more individualized treatment approaches. Thus, besides drug treatment, physical exercise has been shown to be a highly effective strategy for controlling and reducing blood pressure[5] and is an important element in reducing the prevalence of SAH worldwide.

Among the instruments most used to assess functional capacity, the six-minute walk test (6-MWT) has stood out. It was proposed in 1982 as a shorter alternative to the 12-minute walk test,[6,7] and the results proved to be similar to those of the 12-minute test, thus facilitating applicability to individuals with physical deconditioning. The performance of the 6-MWT is relatively simple, because it does not depend on complex instruments. It is easy to administer, better tolerated, and more reflective of activities of daily living than the other walk tests, in addition to being performed at submaximal intensity.[8] Thus, the 6-MWT is safe and ideal for assessing functional capacity and post-intervention changes, and it is also considered to be a predictor of morbidity and mortality in patients with cardiovascular disease (CVD).[9]

Despite the easy application of the test, the standards recommended in the Guidelines of the American Thoracic Society must be followed in order to maintain its safety and reliability.[10] The results of the 6-MWT may also be influenced by gender, age and the subject's health condition, thus making it pertinent to conduct studies that seek to investigate reference values specific to each disease.[11,12]

Cross-sectional studies found preservation in the 6-MWT walking distance in the mild stage of hypertension, while found lower values in the more severe stage of hypertension or in the presence of comorbidities.[13] A study also found that hypertensive subjects presented 6-MWT walking distance values lower than healthy subjects. In addition, the distance walking was even lower in older hypertensive patients.[14] However, no study has used a reference value for the distance walked by hypertensive subjects in the 6-MWT.

Thus, this present study aimed to establish reference values of the 6-MWT in Brazilian people with hypertension of either gender and from different age groups.

Methods

This cross-sectional observational study was conducted at the Cardiovascular Rehabilitation Sector of the Federal University of Alfenas (UNIFAL), Brazil, and the study was reported in accordance with the STROBE guidelines.[15] A total of 302 hypertensive subjects were enrolled in the UNIFAL cardiovascular rehabilitation program from January 1st, 2013 to August 31st, 2019. This study was approved by the UNIFAL Ethics Committee (CAAE: 09381018.6.0000.5142; Protocol Number: 3.262.183). All participants signed an informed consent form.

Inclusion criteria were: adults, either sex; had not performed regular physical activity and/or cardiac rehabilitation in the last three months. Exclusion criteria were: patients with dysfunctions and impairments in the lower limbs; Parkinson's disease, sequelae of a stroke that affects walking, peripheral arterial obstructive disease, and vestibulopathies; with some type of pain that affected the 6-MWT; and uncontrolled blood pressure values. All participants were eligible for inclusion and analysis.

Firstly, we collected data on medical history and physical examination at the beginning of the cardiovascular rehabilitation program, including age, body mass index (BMI), comorbidities associated (chronic obstructive pulmonary disease, myocardial infarction, cardiac surgery, heart failure, and obstructive sleep apnea), and pharmacotherapy (angiotensin II receptor antagonists; β-blockers, angiotensin-converting enzyme inhibitors, calcium channel blockers, and thiazide diuretics). Height and body mass were then measured to calculate BMI. Height was measured using a portable stadiometer (Seca 217, CA, USA), in which the barefoot subjects were positioned upright, with upper limbs hanging at the sides of the body, and heels, back, and head touching the metal column. Body weight was measured in kilograms on a platform-type scale (Filizola, São Paulo, Brazil) - 200 kg capacity and accurate to 100 g - placed on a flat surface and calibrated for each weighing. The World Health Organization guidelines for classifying individuals by nutritional status according to BMI [weight (kg)/height (m^2)] were used.[16]

We also registered findings about waist circumference (WC), diastolic and systolic blood pressure (DBP and SBP), and resting heart rate (HR). WC was measured with a tape measure, at the midpoint between the last rib and the iliac crest. This measurement was taken with the subject standing erect, abdomen relaxed, arms hanging by the side, and feet together.[17] For DBP and SBP measurements, participants were seated at rest for 10 min, and the mid-upper arm circumference was evaluated using a calibrated aneroid sphygmomanometer coupled to an appropriate-sized brachial blood pressure cuff placed on the arm. All measurements were made on the left arm at the level of the heart. The average of two readings was recorded as the BP value for the individual. Standard recommended procedures were used for the selection of the position and size of cuffs used.[18] Using a wristwatch, the resting HR was measured for 60 seconds, by palpation at the radial artery. This measurement was preceded by at least five minutes of seated rest.

Finally, as the main focus of this present study, the 6-MWT was applied. The 6-MWT is widely used in physiotherapy practice to evaluate the physical capacity of an individual. This test was done on a 30-meter indoor walkway, whose length was marked every five meters with non-slip colored tape glued to the floor. After each minute, participants were informed of the time remaining and were encouraged and instructed to walk at their own pace, but to cover as much ground as possible in the 6 minutes. The HR, arterial BP, and rating of perceived exertion were measured at rest and after the test, in accordance with the guidelines of the American Thoracic Society.[10] The results for distance walked in the 6-MWT were compared with prediction equations.[11,12]

All measurements previously described were taken between 7:30 and 10:00 am, with the participants instructed to avoid coffee, alcohol, nicotine, and exercise for at least two hours before the assessment. All assessments were performed by blinded investigators.

The data show that in the descriptive statistics, the quantitative variables (age, WC, HR, and 6-MWT values) with normal distribution are expressed as mean and standard deviation values; whereas the nonparametric variables (SBP, DBP, and BMI) are expressed in terms of median values and interquartile range, in accordance with the Kolmogorov-Smirnov normality test. The Student's t-test and t-test were used for normally distributed data, while the Mann-Whitney test was used to compare continuous data with non-normal distribution. Descriptive measures were calculated, classifying both genders into quartiles according to age (30-45, 46-60, 61-75, and > 76 years). Pearson's Chi-Square test was used to compare the categorical variable use of antihypertensive drugs and comorbidities between men and women.

A multivariate linear regression model was constructed to analyze the factors associated with the 6-MWT walking distance. The independent variables (age, BMI, WC, SBP, DBP, HR) and chronic obstructive pulmonary disease (COPD) were previously selected by the researchers based on theoretical criteria and were included in the regression model. The final model with the independent variables significantly associated with 6-MWT was adjusted using the "backward" method. Linear relationship between the independent variables and the dependent variable, absence of multicollinearity, presence of homoscedasticity, independent distribution of errors and normality of the residuals were assumptions observed and respected in the final regression model.

The statistical significance was assessed using the 95% confidence interval for the differences between the variables with normal distribution. On the other hand, a significance level of 0.05 was used for comparisons of variables with non-normal distribution. Blind data analysis was performed by an independent researcher. The statistical analyses were done using the Statistical Package for Social Sciences (SPSS, version 16.0; Chicago, IL, USA). GPower 3.1 software was used to calculate the sam-ple size, for propose reference values of the distance walked in the 6-MWT between hypertensive men and women, considering an effect size f of 0.25 (medium), which resulted in a total sample size of 208 participants, providing a power of 80% and $\alpha = 0.05$.

Results

Three hundred and two hypertensive subjects, with an average age of 60 years, participated in the study. There was no difference between men (62.65 ± 10.65 years) and women (62.67 ± 11.20 years) (Table 1). Ninety-three participants (30.8%) were moderate alcohol consumers or ex-moderate alcohol consumers, and 146 (48.3%) were smokers or ex-smokers. Besides age, there was a sample homogeneity between men (48.7%) and women (51.3%). The genders were also homogeneous in terms of WC and HR (Table 1). However, the women's BMI, SBP, and DBP values were significantly higher than for the men (Table 1).

Table 1 - Clinical and anthropometrics characteristics of participants

Variables	Total sample (n = 302)	Men (n = 147)	Women (n = 155)	Significance
Age (years)	62.61 + 10.93	62.55 + 10.69	62.67 ± 11.19	0.12 (-2.30 to 2.60)
BMI (kg/m^2)	28.88 (17.19-59.14)	28.35 (20.48-59.14)	29.76 (17.19-56.64)	0.002*
WC (cm)	99.87 ± 12.89	100.74 + 11.90	99.05 ± 13.77	1.69 (-1.23 to 4.61)
SBP (mmHg)	130 (90-190)	120 (90-190)	130 (90-180)	0.040*
DBP (mmHg)	80 (50-140)	80 (60-120)	80 (50-140)	0.020*
HR (bpm)	72.97 + 12.52	72.02 + 13.26	73.88 + 11.74	1.86 (-0.97 to 4.69)

Note: BMI = body mass index; WC = waist circumference; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate. Data are presented as mean ± standard deviation (for parametric data, t-test) or median and interquartile range 25-75 (for non-parametric data, Mann-Whitney test). *$p < 0.05$ indicates statistical difference between men and women.

When evaluating the drugs used by the study's participants, it was found that the most used were angiotensin II receptor antagonists (ARA II, 41.06%) and β-adrenoceptor antagonists (β-blockers, 27.48%) (Table 2). There was no significant difference in relation to the use of medications between the genders, with the exception of thiazide diuretics which women used more, and calcium channel blockers which were more consumed by men.

Besides SAH, the study's participants had other associated diseases, confirmed by medical diagnosis, which the most prevalent being the chronic obstructive pulmonary disease (COPD, 23.51%) and myocardial infarction (MI, 8.94%), mainly in women and men, respectively (Table 2). Furthermore, 8.61% of participants had undergone cardiac surgery (valve replacement or myocardial revascularization or pacemaker placement) (Table 2).

Table 2 - Medication and comorbidities of participants

Anti-hypertensive drugs	Total sample (n = 302)	Men (n = 147)	Women (n = 155)	p-value
ARA II	124	58	66	>0.050
β-blockers	83	36	47	>0.050
Thiazide diuretics	65	19	46	0.001
ACE inhibitors	56	28	28	>0.050
CCB	36	31	5	0.001
Unmedicated	44	22	22	>0.050
Comorbidities				
COPD	71	24	47	0.001
MI	27	18	9	0.001
CS	26	13	13	>0.050
HF	15	7	8	0.001
OSA	9	2	7	0.001

Note: ARA II = angiotensin II receptor antagonists; β-blockers = β-adrenoceptor antagonists; ACE = inhibitors angiotensin converting enzyme inhibitors; CCB = calcium channel blockers; COPD = chronic obstructive pulmonary disease; MI = myocardial infarction; CS = cardiac surgery; HF = heart failure; OSA = obstructive sleep apnea. p = 0.001 indicates statistical difference between genders, t-test.

According to Table 3, the average distance walked in the 6-MWT by all participants was 388.07 + 115.03 m, with no statistical difference between men (394.63 + 117.49 m) and women (381.85 ± 112.83 m). Compared to the prediction equations by Enright and Sherrill[11] and Iwama et al.,[12] the distance walked by all participants of the present study was shorter [95% CI 93.3 (78.0 to 108.6)]. Similarly, a reduction in the distance walked by men [95% CI 110.1 (87.8 to 132.4)] and women [95% CI 77.2 (56.7 to 97.8)] was found when compared to the predicted values for each gender.

The intra-group comparisons between the age quartiles and the distance walked in the 6-MWT show that the average distance walked decreases in accordance with the increase in age for both men and women: 30-45 vs > 76 years [95% CI 103.9 (9.0 to 198.8)], and 46-59 vs 60-75 [95% CI 41.9 (1.14 to 82.7)] and > 76 years [95% CI 69.5 (20.4 to 118.5); and 30-45 vs 46-59 [95% CI 74.8 (3.8 to 145.8)] and > 76 years [95% CI 90.3 (25.3 to 155.3)], and 60-75 vs > 76 years [95% CI 48.7 (11.0 to 86.4)], respectively (Table 4). The intergroup comparison found that women had lower walking values than men (359.19 + 115.33 m vs 423.51 + 104.71 m) only in the 46-59 years-old quartile [95% CI 64.3 (20.9 to 107.7)].

Table 3 - Comparison of walking distance in the 6-MWT by the hypertensive subjects of the study with reference equations

Gender	6-MWT	Iwama et al.[12]	CI 95%	Enright and Sherrill[11]	CI 95%
Men (n = 147)	394.63 + 117.49[a]	568.45 + 19.73	173.8 (154.4 to 193.1)*	504.81 + 71.25	110.1 (87.8 to 132.4)*
Women (n = 155)	381.85 + 112.83	506.77 + 20.67	124.9 (106.7 to 143.0)*	459.11 + 64.67	77.2 (56.7 to 97.8)*
Total (n = 302)	388.07 + 115.03	536.81 + 36.91	148.7 (135.0 to 162.3)*	481.43 + 71.60	93.3 (78.0 to 108.6)*

Note: 6-MWT = six-minute walking test; CI 95% = 95% confidence interval. [a]No difference compared walking distance in the 6MWT between men and women = 12.7 (-13.3 to 38.8). *It indicates statistical difference compared to reference equations for each gender. Data are presented as mean ± standard deviation (for parametric data, t-test).

Table 4 - Comparison of distance walked in the 6-MWT according to gender and age quartile

Age (years)	6-MWT (m) Men (+SEM)	CI 95% Intra-men group comparison	6-MWT (m) Women (+SEM)	CI 95% Intra-women group comparison	CI 95% Between groups comparison
30-45	457.94 + 108.86 (n = 9)	34.4 (-41.9 to 110.7)[b]	434.06 + 135.94 (n = 16)	74.8 (3.8 to 145.8)[b*]	23.8 (-85.7 to 133.4)
		76.4 (-5.8 to 158.6)[c]		41.6 (-18.5 to 101.8)[c]	
		103.9 (9.0 to 198.8)[d*]		90.3 (25.3 to 155.3)[d*]	
46-59	423.51 + 104.71 (n = 50)	34.4 (-41.9 to 110.7)[a]	359.19+115.33 (n = 43)	74.8 (3.8 to 145.8)[a*]	64.3 (20.9 to 107.7)*
		41.9 (1.14 to 82.7)[c*]		33.2 (-7.7 to 74.1)[c]	
		69.5 (20.4 to 118.5)[d*]		15.5 (-29.9 to 61.0)[d]	
60-75	381.54 + 118.10 (n = 75)	76.4 (-5.8 to 158.6)[a]	392.41+104.26 (n = 76)	41.6 (-18.5 to 101.8)[a]	10.8 (-24.9 to 46.6)
		41.9 (1.14 to 82.7)[b*]		33.2 (-7.7 to 74.1)[b]	
		27.5 (-19.48 to 74.6)[d]		48.7 (11.0 to 86.4)[d*]	
≥ 76	353.97 + 132.09 (n = 13)	103.9 (9.0 to 198.8)[a*]	343.67+105.39 (n = 20)	90.3 (25.3 to 155.3)[a*]	10.3 (-38.8 to 59.4)
		69.5 (20.4 to 118.5)[b*]		15.5 (-29.9 to 61.0)[b]	
		27.5 (-19.48 to 74.6)[c]		48.7 (11.0 to 86.4)[c*]	

Note: 6-MWT = six-minute walking test; SEM = standard error of the mean; CI = confidence interval. [a]Age between 30-45 years; [b]Age between 46-59 years; [c]Age between 60-75 years; [d]Age > 76 years. Data are presented as mean ± standard deviation (for parametric data, t-test). *p < 0.05 indicates statistical difference.

These previous results are supported by regression analysis, which demonstrated that age and SBP are the strongest predictors of 6-MWT in both genders, as well as the BMI in women. Thus, Table 5 shows age was negatively associated with distance walked in the 6-MWT in males and women. In addition, in women, the 6-MWT was also negatively associated with BMI. Furthermore, SBP was positively associated with distance walking in the 6-MWT in both genders. Table 5 also shows that there is a significant influence of the factors age and SBP on the distance walked in the 6-MWT [F (5,17) = 3.650; p = 0,0020; R^2 adjusted = 0.092] in the men's group. In the group of women, the factors that influenced performance on the 6-MWT were age, SBP and BMI [F (3,149) = 5.726; p < 0.001; R^2 adjusted = 0.089)].

Table 5 - Predictors of six-minute walking test distance walked in hypertensive subjects

Multivariate linear regression for men (n = 147)					
Predictors	B (95%CI)	β	R^2	T	p-value
Age (years)	-3.070 (-4.785 to -1.356)	-0.279	0.067	-3.540	<0.01
Systolic blood pressure (mmHg)	1.239 (0.145 to 2.333)	0.177	0.025	2.238	<0.05
Multivariate linear regression for women (n = 153)					
Predictors	B (95%CI)	β	R^2	T	p-value
Body mass index (kg/m^2)	-5.295 (-8.140 to -2.450)	-0.305	0.039	-3.677	<0.01
Age (years)	-2.366 (-4.020 to -0.711)	-0.235	0.032	-2.825	<0.05
Systolic blood pressure (mmHg)	0.974 (0.091 to 2.039)	0.144	0.018	1.808	<0.05

Note: B = unstandardized coefficients; β = standardized coefficients that compared the strength of the effect of each individual independent variable to the dependent variable. The higher the absolute value of the beta coefficient, the stronger the effect; R^2 = adjusted coefficient of determination for by each factor; T = statistic t test. p < 0.05 indicates statistical significance of β in regression model and only significant predictors are shown. F statistic was used to assess the significance of means between groups in the multivariate linear regression analysis.

In addition, in the men's group, WC (p = 0.561), DBP (p = 0.140), COPD (p = 0.350), HR (p = 0.697) and BMI (p = 0.114) had no significant impact on the 6-MWT. Similarly, in the group of women WC (p = 0.870), DBP (p = 0.880), COPD (p = 0.617) and HR (p = 0.215) showed no significant association with the 6-MWT (Table 5).

Discussion

To the best of our knowledge, this study is the first to propose reference values for the distance walked in the 6-MWT for hypertensive subjects of both genders and from different age groups. Based on the 6-MWT, our study showed that with the increase in age there is a reduction in the distance walked in the test. Moreover, the values of the distance walked in the 6-MWT for the total sample and for each gender were lower than the values obtained in the reference equations described in the literature.

Few studies have documented in the literature the distance walked by hypertensive subjects in the 6-MWT, and most of them used a small number of patients, without comparing gender and age group. In this present study, the average distance walked by the participants in the 6-MWT was 388 m, with non-significant difference between men (394.63 + 117.44 m) and women (381.85 ± 112.73 m). Other studies reported that hypertensive patients walked a greater distance (> 400 m) than in this study; however, they were performed with only a small sample of women or men.[19-24] Additionally, a study conducted with 244 hypertensive older women (68.2 ± 5.8 years) found an average distance walked in the 6-MWT of 549.1 ± 115.6 m,[25] which is higher than what we found in the present study for this gender and age group (392.41 + 104.26 m). However, different to our study, the authors did not include hypertensive women with pulmonary disease, which has a direct influence on physical performance. We understand that the inclusion of patients with pulmonary diseases was important, as some of these diseases (e.g., COPD caused by smoking) are related to the development of SAH. Additionally, unlike other studies, which did not select participants by physical activity level in order to avoid an influence on the result of the 6-MWT, we only included individuals that not performed regular physical activity.

Besides the distance walked in the 6-MWT for the total study sample, we evaluated values for age group quartiles and found a reduction in walking distance with the increase in age, for both sexes. There are few studies in the literature that have evaluated the distances walked by hypertensive young adult subjects, or compared different age groups. Additionally, most of them have been performed on subjects older than 45, without differentiating gender and without assessing the participants' physical activity levels.

Regarding the 46-59 years-old age group, a study conducted on 38 hypertensive men with an average age of 56 years found that the average distance walked in the 6-MWT was 324 m.[26] Another study showed that 98 hypertensive men and women with an average age of 54.5 years walked an average of 540 m.[27] A similar distance was found for 200 hypertensive participants of both genders and an average age of 45.9, who walked an average of 513 m.[28] Despite the distance walked by participants from this age group being lower in the present study, we excluded a bias in relation to gender and physical activity level, which may interfere in the result.

A cohort study evaluating the mobility and function of 775 adults older than 30 also found that physical performance worsened in both genders in each subsequent 10-year age quartile.[29] In fact, it has already been well-defined that with the increase in age, there may be a reduction in muscle mass, with a consequent reduction in strength, motor coordination, and physical performance.[30] The reference values for each age group shown in the present study may assist in diagnosing these changes.

In addition, this study showed that from an inter-gender comparison for each age group, a difference in walking distance in the 6-MWT was found only in the 46 to 59-year-old quartile, in which women walked less than men. For women in this age group, important hormonal changes occur as a result of menopause, and these changes are physically reflected in several ways; for example, abdominal fat deposition and weight gain occur much more easily for women.[31] Moreover, the increase in adipose tissue is inversely proportional to the strength and the amount of muscle mass, which directly impacts functional capacity and exercise tolerance,[32] and loss of muscle mass and strength associated with aging starts at an earlier age in women than in men (around the time of menopause).[33] These data taken together may justify the lower physical performance of women aged 46 to 59 compared to men.

We also found that women had higher blood pressure than men. Recent studies have shown that blood pressure is higher in men than in women at similar ages.[34] The main factor associated with higher blood pressure in women is also likely to be the menopause or post-menopause period, which accounted for 139 women in that study. During and after menopause, the decline in estrogen levels is directly related to the development of SAH and is mainly due to factors such as increased androgen levels, activation of the renin-aldosterone system, increased plasma endothelin levels, greater sensitivity to salt, and increased sympathetic activity.[35]

The distance walked in the 6-MWT by the study's hypertensive subjects was lower than the values predicted by the reference equations. The demographic and anthropometric differences between individuals directly influence the prediction equation. Thus, this study used a universal reference equation and an equation applied to the Brazilian population. However, these equations were proposed for healthy subjects. The comparison of data from this present study with reference equations was important to show that the hypertensive subjects had reduced physical capacity, which can be justified by the pathophysiology of SAH, associated diseases, and the advanced age of some participants.

The anthropometric characteristics of the sample led to the BMI values, even with a variation in the interquartile range, and WC values indicating high cardiovascular risk.[16,17] Some studies have shown that higher BMI and WC values are associated with SAH,[36,37] and a population-based cohort study showed that overweight subjects have low physical activity and, consequently, a higher risk of cardiovascular disease.[38] In addition, the regression analysis showed that BMI is negatively associated with the 6-MWT walking distance. These evidence reinforces the importance of the applicability of the 6-MWT for hypertensive subjects, especially in assessing physical capacity and/or prescribing an exercise program to reduce CVD risk.

The resting HR values (72.97 + 12.52) found in this study may indicate a low risk for cardiovascular disease.[39] In a cohort study involving a population older than 65 and accompanied over a period of 6 years, it was observed that an HR > 79 bpm was associated with increased cardiovascular risk, as well as increased risk of cardiovascular and total mortality.[24] Low HR values are related to physical conditioning or, in the case of the present study, to the pharmacological treatment of SAH.

Additionally, although the blood pressure levels did not influence the distance walked in the 6-MWT, with an increase in age there is also an increase in arterial stiffening, which is one of the factors that contribute to the development of hypertension.[21] The blood pressure levels of the study's participants were controlled, which justifies the results presented by regression analysis influence, which demonstrated a positive association of SBP levels in the walking distance in 6-MWT in both genders. In our study, most participants had been using ARA II and β-blockers, followed by thiazide diuretics, angiotensin-converting enzyme inhibitors, and calcium channel blockers. This pharmacological treatment is in accordance with the recommendations of the guideline for the management of high blood pressure in hypertensive persons aged 60 years or older,[25] and kept participants at a reduced risk of CVD events.[17]

Among the pathologies associated with SAH in the present study, the main ones were COPD (23.51%) and AMI (8.94%). Additionally, 48.3% of the study's participants were smokers or ex-smokers, and smoking is recognized as the most significant causative factor for both of these pathologies.[26,27] Furthermore, 2.98% of participants had obstructive sleep apnea. In this disease, periods of obstructed breathing result in profound intermittent hypoxia with underlying bursts in sympathetic nerve activity, and dramatic increases in HR and blood pressure.[28]

Obstructive sleep apnea is also related to obesity.[28] Although the population of the present study was overweight and hypertensive, the percentage of subjects with obstructive sleep apnea was low. In addition, almost a quarter of the total sample of the present study had COPD, the multivariate linear regression showed that this pathology did not interfere with the distance walked in the 6-MWT in both women and men. Interestingly, a study conducted by Zeng et al.[40] did not find a significant correlation between the inspiratory capacity of elderly people (63 years) with COPD and the distance walked in the 6-MWT. Contrary to the distance walked, these authors demonstrated a significant correlation between alterations found in COPD and steps covered in the 6-MWT; that is, increased ventilation during exercise associated with fewer steps during this test.

Such mechanisms may also be responsible for the non-correlation between COPD and the distance walked in the present study, but further studies are still needed to confirm this hypothesis. The number of individuals who had AMI in the present study was very low and, due

to the differences not found between the groups, we believe that this alteration did not influence the results.

This is the first known study to investigate the distance walked by hypertensive subjects in the 6-MWT, and to correlate this with different age groups and blood pressure values. Despite the findings of the pre-sent study showing that the mean values for distances walked by hypertensive subjects in the 6-MWT were lower than predicted, studies involving other pathologies have shown that values less than 250 m are related to higher mortality.[32] Therefore, the values found in the present study may be similar to those for sedentary normotensive individuals, because none of our study's participants had a distance walked in the 6-MWT equal to or less than 250 m, which shows that when SAH is controlled, the risk of mortality may be reduced.

This study has some limitations, such as the investigated population being restricted to Brazil. In addition, some age group quartiles had a smaller number of participants, which may influence the values of the distance walked in the 6-MWT. Another limitation of the study was a significant number of heart disease patients with COPD may also interfere with the data, although the regression analysis did not find this influence.

Conclusion

The present study found that the average distance walked in Brazilian hypertensive people evaluated in the 6-MWT was 388.07 + 115.03 m. In addition, this is the first known study to propose reference values for the 6-MWT in accordance with different age groups of hypertensive subjects, from 30 years of age to the older than 75 quartile. Therefore, understanding the reference values of this test for a given population that includes different age groups composed of both sexes is of essential importance to making clinical decisions for the preparation of the physical exercise protocol for these patients.

Authors' contributions

All authors were responsible for the conception and design of the study, and for the acquisition, analysis and interpretation of the data. ASL and GG prepared the article and critically reviewed it for relevant intellectual content. All authors approved the final version.

References

1. Williams B, Mancia G, Spiering W, Rosei EA, Aziz M, Burnier M, et al. ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021-104. DOI

2. Yu BB, Zhi H, Zhang XY, Liang JW, He J, Su C, et al. Mitochondrial dysfunction-mediated decline in angiogenic capacity of endothelial progenitor cells is associated with capillary rarefaction in patients with hypertension via downregulation of CXCR4/JAK2/SIRT5 signaling. EBioMedicine. 2019;42:64-75. DOI

3. Acar S, Demİrbüken I, Algun C, Malkoç M, Tekİn N. Is hypertension a risk factor for poor balance control in elderly adults? J Phys Ther Sci. 2014;27(3):901-4. DOI

4. Hausdorff JM, Herman T, Baltadjieva R, Gurevich T, Giladi N. Balance and gait in older adults with systemic hypertension. Am J Cardiol. 2003;91(5):643-5. DOI

5. MacDonald HV, Johnson BT, Huedo-Medina TB, Livingston J, Forsyth KC, Kraemer WJ, et al. Dynamic resistance training as stand-alone antihypertensive lifestyle therapy: a meta-analysis. J Am Heart Assoc. 2016;5(10):e003231. DOI

6. Butland RJ, Pang J, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. Brit Med J (Clin Res Ed). 1982;284(6329):1607-8. DOI

7. McGavin CR, Gupta SP, McHardy GJ. Twelve-minute walking chronic bronchitis for assessing disability. Br Med J. 1976;1(6013):822-3. DOI

8. Solway S, Brooks D, Lacasse Y, Thomas S. A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. Chest. 2001;119(1):256-70. DOI

9. Ferreira PA, Ferreira PP, Batista AKMS, Rosa FW. Safety of the six-minute walk test in hospitalized cardiac patients. Int J Cardiovasc Sci. 2015;28(1):70-7. DOI

10. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-7. DOI

11. Enright PL, Sherrill DL. Reference equations for the six-minute walk in healthy adults. Am J Respir Crit Care Med. 1998;158(5 Pt 1):1384-7. DOI

12. Iwama AM, Andrade GN, Shima P, Tanni SE, Godoy I, Dourado VZ. The six-minute walk test and body weight-walk distance product in healthy Brazilian subjects. Braz J Med Biol Res. 2009;42(11):1080-5. DOI

13. Ramos RA, Ferreira AS. Functional capacity in adults with hypertension as assessed by the six-minute walk distance test: systematic review. Fisioter Pesqui. 2014;21(3):257-63. DOI

14. Ramos RA, Guimarães FS, Cordovil I, Ferreira AS. The six-minute walk distance is a marker of hemodynamic-related functional capacity in hypertension: a case-control study. Hypertens Res. 2014;37(8):746-52. DOI

15. Cuschieri S. The STROBE guidelines. Saudi J Anaesth. 2019;13(Suppl 1):S31-4. DOI

16. WHO World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser. 1995;854:1-452.

17. Lean ME, Han TS, Morrison CE. Waist circumference as a measure for indicating need for weight management. BMJ. 1995;311(6998):158-61. DOI

18. TRUE Consortium (inTernational consoRtium for qUality resEarch on dietary sodium/salt). Recommended standards for assessing blood pressure in human research where blood pressure or hypertension is a major focus. J Clin Hypertens (Greenwich). 2017;19(2):108-13. DOI

19. Ribeiro A, Younes C, Mayer D, Fréz AR, Riedi C. Teste de caminhada de seis minutos para avaliação de mulheres com fatores de risco cardiovascular. Fisioter Mov. 2011;24(4):713-9. DOI

20. Accyoli MF, Piotto RF. Efeito de um programa de reabilitação cardíaca - fase III realizado em piscina terapêutica e no solo, em mulheres hipertensas. Rev Inst Cienc Saude. 2007;25(2):141-6. Full text link

21. Lima MMO, Britto RR, Baião EA, Alves GS, Abreu CDG, Parreira VF. Exercício aeróbico no controle da hipertensão arterial na pós-menopausa. Fisioter Mov. 2011;24(1):23-31. DOI

22. Souza JF, Nogueira IDB, Lira MJL, Silva EC, Ferreira GMH, Nogueira PAMS. Correlação entre capacidade funcional e qualidade de vida em idosas hipertensas submetidas a treinamento resistido. ConScientiae Saude. 2011;10(2):312-8. DOI

23. Costa HS, Martins AMB, Quirino FC, Severino G, Novais LD, Lima MMO. Capacidade funcional em homens hipertensos pela distância caminhada e correlação com valores preditos. Fisioter Mov. 2009;22(4):557-64. Full text link

24. Pedrosa R, Holanda G. Correlation between the walk, 2-minute step and tug tests among hypertensive older women. Rev Bras Fisioter. 2009;13(3):252-6. DOI

25. Coelho Jr HJ, Rodrigues B, Aguiar SD, Gonçalves IO, Pires FO, Asano RY, et al. Hypertension and functional capacities in community-dwelling older women: a cross-sectional study. Blood Press. 2017;26(3):156-65. DOI

26. Ramos RA, Guimarães FS, Dionyssiotis Y, Tsekoura D, Papathanasiou J, Ferreira AS. Development of a multivariate model of the six-minute walked distance to predict functional exercise capacity in hypertension. J Bodyw Mov Ther. 2019; 23(1):32-8. DOI

27. Hall KS, Cohen HJ, Pieper CF, Fillenbaum GG, Kraus WE, Huffman KM, et al. Physical performance across the adult life span: correlates with age and physical activity. J Gerontol A Biol Sci Med Sci. 2017;72(4):572-8. DOI

28. Kurpaska M, Krzesiński P, Gielerak G, Uziębło-Życzkowska B, Banak M, Piotrowicz K, et al. Multiparameter assessment of exercise capacity in patients with arterial hypertension. Clin Exp Hypertens. 2019;41(7):599-606. DOI

29. Farag ESM, Al-Daydamony MM, Gad MM. What is the association between left ventricular diastolic dysfunction and 6-minute walk test in hypertensive patients? J Am Soc Hypertens. 2017;11(3):158-64. DOI

30. Tieland M, Trouwborst I, Clark BC. Skeletal muscle performance and ageing. J Cachexia Sarcopenia Muscle. 2018; 9(1):3-19. DOI

31. Davis SR, Castelo-Branco C, Chedraui P, Lumsden MA, Nappi RE, Shah D, et al. Understanding weight gain at menopause. Climacteric. 2012;15(5):419-29. DOI

32. Orsatti FL, Nunes PRP, Souza AP, Martins FM, Oliveira AA, Nomelini RS, et al. Predicting functional capacity from measures of muscle mass in postmenopausal women. PM R. 2017;9(6):596-602. DOI

33. El Khoudary SR, McClure CK, VoPham T, Karvonen-Gutierrez CA, Sternfeld B, Cauley JA, et al. Longitudinal assessment of the menopausal transition, endogenous sex hormones, and perception of physical functioning: the Study of Women's Health Across the Nation. J Gerontol A Biol Sci Med Sci. 2014; 69(8):1011-7. DOI

34. Brahmbhatt Y, Gupta M, Hamrahian S. Hypertension in premenopausal and postmenopausal women. Curr Hypertens Rep. 2019;21(10):74. DOI

35. Maas AHEM, Franke HR. Women's health in menopause with a focus on hypertension. Neth Heart J. 2009;17(2):68-72. DOI

36. Seo DC, Choe S, Torabi MR. Is waist circumference ≥102/88 cm better than body mass index ≥30 to predict hypertension and diabetes development regardless of gender, age group, and race/ethnicity? Meta-analysis. Prev Med. 2017;97:100-8. DOI

37. Lee CMY, Huxley RR, Wildman RP, Woodward M. Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. J Clin Epidemiol. 2008; 61(7):646-53. DOI

38. Koolhaas CM, Dhana K, Schoufour JD, Ikram MA, Kavousi M, Franco OH. Impact of physical activity on the association of overweight and obesity with cardiovascular disease: The Rotterdam Study. Eur J Prev Cardiol. 2017;24(9):934-41. DOI

39. Díaz BB, Sánchez JJA, León AC. Resting heart rate and cardiovascular disease. Med Clin (Barc). 2014;143(1):34-8. DOI

40. Zeng GS, Chen LC, Fan HZ, Wu LL, Wu XP, Fang ZK, et al. The relationship between steps of 6MWT and COPD severity: a cross-sectional study. Int J Chron Obstruct Pulmon Dis. 2018; 14:141-8. DOI