

## Six-minute walk test: reference values for healthy adults in Brazil\*

Teste de caminhada de seis minutos: valores de referência para adultos saudáveis no Brasil

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### Abstract

**Objective:** To develop regression equations for six-minute walk distance (6MWD) in healthy adults (20-80 years of age) in Brazil. **Methods:** We included 132 volunteers (66 males) without respiratory disease, cardiac disease, or comorbidities that affect ambulation. The volunteers completed three six-minute walk tests. Prior to and at the end of each test, we obtained SpO<sub>2</sub> and maximal HR, as well as the Borg scale scores for sensation of dyspnea and lower limb fatigue. The data included in the final analysis were derived from the test with the greatest 6MWD. **Results:** The mean 6MWD values were 566 ± 87 m and 538 ± 95 m in males and females, respectively (p = 0.08). The 6MWD was greater in taller individuals and decreased in parallel with increases in age or body index mass (BMI). The best adjusted model was the quadratic model. We derived the following equation (valid for both genders): 6MWD = 511 + stature<sup>2</sup> (cm) × 0.0066 – age<sup>2</sup> × 0.030 – BMI<sup>2</sup> × 0.068. This equation explained 55% of the variance in 6MWD. **Conclusions:** Reference values explaining a high proportion of the variance were derived by a quadratic regression model in healthy adults (of a wide range of ages) in Brazil.

**Keywords:** Reference values; Exercise test; Walking.

### Resumo

**Objetivo:** Desenvolver equações de regressão para a distância caminhada no teste de caminhada de seis minutos (DTC6) em adultos saudáveis (20-80 anos de idade) no Brasil. **Métodos:** Foram incluídos 132 voluntários (66 homens) sem doenças respiratórias ou cardíacas, assim como sem comorbidades que afetassem a deambulação. Os voluntários completaram três testes de caminhada de seis minutos. Foram obtidos antes e ao final de cada teste: SpO<sub>2</sub>, FC máxima e escores da escala de Borg para dispneia e fadiga de pernas. Os dados incluídos na análise final foram os derivados do teste com a maior DTC6. **Resultados:** Os valores médios de DTC6 foram de 566 ± 87 m e 538 ± 95 m em homens e mulheres, respectivamente (p = 0,08). A DTC6 aumentou com a estatura e diminuiu com a idade e com o índice de massa corpórea (IMC). O melhor modelo ajustado foi o quadrático. A equação derivada para ambos os sexos foi: DTC6 = 511 + altura<sup>2</sup> (cm) × 0,0066 – idade<sup>2</sup> × 0,030 – IMC<sup>2</sup> × 0,068. Esta equação explicou 55% da variação na DTC6. **Conclusões:** Valores de referência com uma elevada variância explicada foram derivados por um modelo quadrático de regressão em adultos saudáveis com ampla variação de idade no Brasil.

**Descritores:** Valores de referência; Teste de esforço; Caminhada.

### Introduction

Reference values for diagnostic tests are important in order to characterize a variety of diseases and determine their severity. The reference values for pulmonary function tests vary considerably from population to population.<sup>(1,2)</sup> Walk tests have been used in clinical practice since the 1960s.<sup>(3)</sup> The distance covered on the six-minute walk test (6MWT), commonly referred to as the six-minute walk distance (6MWD), adequately reflects the physical capacity of

patients to perform routine tasks.<sup>(4)</sup> The 6MWT is simple, well-tolerated, and reproducible. In addition, the equipment required to perform the test is affordable. The importance of the 6MWT for the evaluation of the functional status of patients for comparing the effects of therapeutic interventions, as well as for predicting the morbidity and mortality associated with various cardiopulmonary diseases, has been extensively described in the literature.<sup>(5-8)</sup>

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Financial support: None.

Submitted: 22 December 2010. Accepted, after review: 6 June 2011.

The primary objective of the 6MWT is to determine the greatest 6MWD on a level course. The results obtained should be compared with appropriate reference values. Since 1998, a number of equations have been devised in order to calculate predicted values. Various studies have employed a variety of methods and investigated small patient samples.<sup>(9-13)</sup> In other studies, the methods and sample size have been appropriate.<sup>(14-17)</sup> In a study recently conducted in Brazil and involving 134 individuals, the predicted 6MWD was determined considering only age and gender.<sup>(18)</sup> However, in most studies, stature is also considered a relevant variable for determining the predicted 6MWD.<sup>(9,10,12-17)</sup> Other authors have devised equations indicating that body weight or the body mass index (BMI) significantly influence the predicted 6MWD.<sup>(9,10,12,13,15,17)</sup> A multicenter study, involving 10 centers in seven countries, determined 6MWD reference values for individuals over 40 years of age.<sup>(19)</sup> In that study, the 6MWD reference values were found to vary in function of the geographic location; therefore, different countries require specific equations. The objective of the present study was to determine reference values for the 6MWD in healthy adults of a wide range of ages (20-80 years) in Brazil.

## Methods

We evaluated 132 individuals (66 males and 66 females) between 20 and 80 years of age. The individuals included in the present study were recruited from among those working at the São Paulo Hospital for State Civil Servants, located in the city of São Paulo, Brazil. All of the participants volunteered for the study, in response to a verbal invitation or to advertisements posted on the walls of the hospital (either on bulletin boards or near the clock-in points). Patients who were in the hospital for a medical appointment or for outpatient tests because of conditions other than those that constituted the exclusion criteria were also invited to participate in the study, as were their companions.

All of the participants were evaluated with a standardized respiratory epidemiology questionnaire,<sup>(20)</sup> as well as with a questionnaire developed by Baecke et al. in order to quantify habitual physical activity,<sup>(21)</sup> which translated to Portuguese and validated for use in Brazil.<sup>(22,23)</sup> The questionnaire developed by Baecke et al.

<sup>(21)</sup> is designed to be administered exclusively to individuals who are fully ambulatory.

The study was approved by the São Paulo Hospital for State Civil Servants Research Ethics Committee (Ruling no. 087/07). All of the participants gave written informed consent.

The exclusion criteria were as follows:

- having any difficulty in walking
- presenting with diseases that could affect ambulation, including stroke, neuromuscular diseases, peripheral vascular disease, musculoskeletal disorders, claudication, cognitive deficit, and arthritis
- having had respiratory symptoms, the flu, or any other lung disease in the last seven days
- having had any respiratory disease, with the exception of pneumonia, that could result in dysfunction, including tuberculosis and asthma (the latter characterized as a lifetime history of two or more wheezing attacks, which improved with the use of a bronchodilator)
- having undergone thoracic surgery
- having a history of physician-diagnosed heart disease
- presenting with uncontrolled hypertension
- presenting with a pre-test (at-rest) systolic blood pressure  $\geq 150$  mmHg or diastolic blood pressure  $\geq 100$  mmHg
- having worked, for one year or more, in environments in which the concentration of dust was high and there was a risk of developing respiratory disease
- having a history of smoking
- having a history of exposure to cigarette smoke in sleeping quarters
- Having a history of exposure to smoke from wood-burning stoves
- Being considered an athlete, as determined by a score  $\geq 8$  on the questionnaire employed<sup>(19)</sup>
- having diabetes
- being underweight (BMI  $< 18$  kg/m<sup>2</sup>) or presenting with class III obesity (BMI  $> 40$  kg/m<sup>2</sup>)
- presenting with self-reported blood diseases, metabolic diseases, or both
- being under treatment with drugs that can affect muscle function (e.g., statins)

Prior to the 6MWT, we determined the weight, height, and blood pressure of all of

the individuals under study. The 6MWT was performed three times on the same day, in accordance with the American Thoracic Society (ATS) guidelines.<sup>(5)</sup> The test was repeated after the HR had returned to baseline levels (to within  $\pm 10$  bpm of the at-rest HR before the initial test). Before and after each test, we measured SpO<sub>2</sub> (by pulse oximetry) and HR, as well as calculating the Borg scale scores<sup>(24)</sup> for sensation of dyspnea and leg fatigue. We measured SpO<sub>2</sub> at the beginning of and immediately after the 6MWT. The pulse oximeter (Fingertip Pulse Oximeter model CMS50DL; Contec Medical Systems Co., Ltd, Qinhuangdao, China) was previously tested by comparing SpO<sub>2</sub> values as measured by the equipment with those of SaO<sub>2</sub> obtained by ten arterial blood gas measurements taken at the emergency room of the hospital (SpO<sub>2</sub> – SaO<sub>2</sub> = 0.45  $\pm$  1%). Before administering the Borg scale to the individuals, the examiner explained the meaning of the score. The data included in the final analysis were derived from the test with the greatest 6MWD. The tests were performed in a 30-m outdoor corridor that was level and free of any other foot traffic. The corridor surface was marked at every 3 m. The course was delineated with traffic cones. Immediately before the beginning of the tests, the participants received instructions in accordance with the Brazilian Portuguese-language version of the ATS guidelines for the 6MWT.<sup>(5)</sup> The individuals were instructed to remain in place after the completion of the 6MWT until the abovementioned measurements had been taken. The measurements were taken immediately after the completion of the test. The examiner did not walk alongside the participants. At the end of every minute, the examiner informed the participants of how many minutes remained and provided standard phrases of encouragement (“You’re doing well!”, “Good job, keep it up!”, and “You’re doing well, keep it up!”). Fifteen seconds before the end of the test, the examiner informed the participants that the test was about to end, and, at the end of the sixth minute, the examiner clearly informed the participants that the test was over by saying “Stop!”

To calculate the minimum sample size needed in order to give the study sufficient statistical power, we used the following formula:

$$N > 50 + 8m$$

where *m* is the number of variables.<sup>(25)</sup> Given that there should be a separate equation for each gender and that stature and age were dependent variables, we included 50 + 16 males and 50 + 16 females (i.e., a total of 132 individuals). In order to analyze the results, we used the Statistical Package for the Social Sciences, version 17 (SPSS Inc., Chicago, IL, USA).

After data collection, the steps were as follows: We determined the distribution of functional and anthropometric variables, as well as determining discrepant values. We performed univariate regression analysis, in which the 6MWD correlation coefficients were tested with the anthropometric variables and their transformations. Variables with a value of *p* < 0.10 were selected for inclusion in the multivariate analysis. We calculated the regression equations and determined discrepant values, which were detected by standardized residuals above 3.3 standard deviations and by analyzing the Mahalanobis distance.<sup>(26)</sup> In order to evaluate the influence that the conflicting results had on the results of the regression models, we analyzed Cook’s distance<sup>(26)</sup> for the residuals. Cases with values above 1 were excluded. We determined the multiple regression equation, and, subsequently, we evaluated the residuals. Their adherence to the normal curve was confirmed graphically. The residuals were plotted against each of the independent variables, as well as against the expected values, as determined by the regression equation. The lower regression limit was calculated by the 5th percentile of the residuals. We determined the influence of habitual physical activity on the 6MWD by analysis of covariance, taking the gender into account. Finally, we identified the test with the greatest 6MWD. The level of significance was set at *p* < 0.05.

## Results

The tests were well tolerated by all of the participants, and none of the tests were interrupted before the 6-min mark. A total of 132 individuals (66 males and 66 females) were included in the final analysis. Of those 132, 113 were White, and 19 were Black. Table 1 shows the distribution of individuals by gender and anthropometric data.

The determination of discrepant values led to the exclusion of 3 individuals: 2 because

**Table 1** - Distribution of the reference population by gender, age bracket, stature, and body mass index.<sup>a</sup>

Variable	Males	Females
	n = 66	n = 66
Age, years		
20-29	9 (13.6)	11 (16.7)
30-39	10 (15.2)	7 (10.6)
40-49	10 (15.2)	17 (25.7)
50-59	12 (18.2)	12 (18.2)
60-69	12 (18.2)	6 (9.1)
≥ 70	13 (19.7)	13 (19.7)
Stature, cm		
135-144	0 (0.0)	2 (3.03)
145-154	2 (3.03)	23 (34.8)
155-164	16 (24.2)	29 (43.9)
165-174	31 (46.9)	9 (13.6)
175-184	17 (25.8)	3 (4.5)
≥ 185	0 (0.0)	0 (0.0)
BMI, kg/m <sup>2</sup>		
18-24	19 (28.7)	28 (42.4)
25-29	28 (42.4)	22 (33.3)
30-38	19 (27.2)	16 (24.2)

BMI: body mass index. <sup>a</sup>Values expressed in n (%).

their statures were at either end of the spectrum (1.95 m and 1.33 m, respectively); and 1 for walking only 240 m during the 6MWT. The latter individual was subsequently contacted by telephone and reported having been, during the week of the 6MWT, under clinical suspicion of angina (which was subsequently confirmed). The individual also reported having omitted that information because of a strong desire to participate in the study. Subsequently, the determination of discrepant values when calculating the regression equations led to the

exclusion of 3 additional individuals. Of those, 2 were excluded on the basis of the Mahalanobis distance, and 1 was excluded for not achieving a value that was within the accepted range for the residuals (3.3 standard deviations).

The anthropometric variables that significantly correlated with the 6MWD in the univariate analysis were age ( $r = -0.66$ ;  $p < 0.01$ ), stature ( $r = 0.42$ ;  $p < 0.01$ ), and BMI ( $r = -0.37$ ;  $p < 0.01$ ). Weight in isolation was not significantly correlated with the 6MWD. Although the 6MWD was greater in males than in females, the difference was not statistically significant ( $p = 0.08$ ; Table 2). Although habitual physical activity showed a borderline significant correlation with the 6MWD in the univariate analysis ( $r = 0.23$ ;  $p = 0.07$ ), that correlation did not remain significant in the multivariate analysis.

Various regression models were tested in order to determine the best adjustment of the anthropometric data to the 6MWD (Table 3). The quadratic model was the best adjusted model, showing the highest coefficient of determination and the lowest values for the 5th percentile for the residuals. The model explained 55% of the total variance in the 6MWD ( $r^2 = 0.55$ ). In order to predict the 6MWD, we derived the following equation (valid for both genders):

$$6MWD = 511 + stature^2 \times 0.0066 - age^2 \times 0.030 - BMI^2 \times 0.068$$

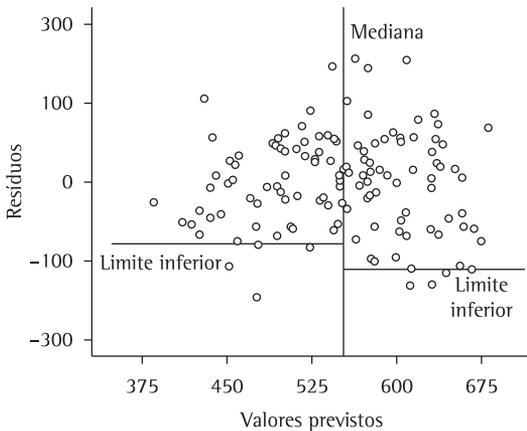
where stature is expressed in cm, age is expressed in years, and BMI is expressed in kg/m<sup>2</sup>. When the residuals were plotted against the 6MWD, we found that the dispersion decreased in parallel with decreases in the 6MWD (Figure 1). On the

**Table 2** - General data regarding the six-minute walk test, by gender.

Variable	Male gender		Female gender	
	n = 66		n = 66	
	Initial	Final	Initial	Final
HR, bpm <sup>a</sup>	77 ± 11	109 ± 18	80 ± 11	115 ± 16
Predicted HR <sub>max</sub> , bpm <sup>a,b</sup>	-	168 ± 17	-	171 ± 17
HR <sub>max</sub> , % <sup>a</sup>	-	65 ± 11	-	68 ± 10
SpO <sub>2</sub> , % <sup>a</sup>	97 ± 1	96 ± 1	97 ± 1	96 ± 1
ΔSpO <sub>2</sub> , % <sup>c</sup>	-1.0 (-2.0 to 1.0)		-0.5 (-2.0 to 1.0)	
Borg scale score for sensation of dyspnea <sup>c</sup>	0 (0-0)		0 (0-0)	
Borg scale score for leg fatigue <sup>c</sup>	0.0 (0.0-0.5)		0 (0-3)	
Greatest 6MWD, m <sup>a</sup>	-	566 ± 87	-	538 ± 95*
HPA questionnaire score <sup>a</sup>	7.38 ± 1.23		7.2 ± 1.26**	

HR<sub>max</sub>: maximal HR; 6MWD: six-minute walk distance; HPA: habitual physical activity. <sup>a</sup>Values expressed as mean ± SD.

<sup>b</sup>Predicted HR<sub>max</sub> = 220 - age. <sup>c</sup>Values expressed as median (range). \*t = 1.76; p = 0.08. \*\*t = 0.79; p = 0.43.



**Figure 1** - Calculation of the lower limit, expressed as percentage of predicted, of the regression equation derived for the six-minute walk distance in both genders. Note the difference between the cases with values above the median and those with values below the median regarding the mean dispersion of residuals.

basis of that finding, the 5th percentile for the 6MWD was calculated separately for values above and below the median. The lower limit, transformed into a proportion, was found to be 81% of the value predicted for both groups. Table 3 shows the equations for both genders.

Nine individuals were using beta blockers as antihypertensive agents. In those individuals, the maximal HR ( $HR_{max}$ ) was  $91 \pm 20$  bpm, compared with  $114 \pm 17$  bpm in the remaining 123 individuals, who were not using beta blockers ( $t = 3.97$ ;  $p < 0.001$ ).

The maximum drop in  $SpO_2$  was 2% (Table 2). The Borg scale score for sensation of dyspnea increased to a maximum of 4, and the Borg scale score for leg fatigue increased to a maximum of 5. Of the total of individuals under study, 104 (79%) were considered sedentary (total habitual physical activity questionnaire score  $< 8.0$ ) and

28 (21%) were considered physically active but not physically fit.

The mean 6MWD on the first, second, and third attempts was 525 m, 534 m, and 534 m, respectively (repeated measures ANOVA;  $F = 3.21$ ;  $p = 0.044$ ). Regarding the three sequential 6MWD measurements, 35 (27.7%) of the individuals achieved the greatest 6MWD on the first test, compared with 51 (40.4%) on the second test and 40 (31.7%) on the third test. For 6 individuals, the 6MWD was the same on all three tests.

### Discussion

In the present study, we derived an equation for the 6MWD in a sample composed of 20- to 80-year-olds in Brazil. The model that best fit the data was the quadratic model. In that model, stature, age, and BMI explained 55% of the total variance. Although there were no significant differences between the genders, the 6MWD was slightly greater in males. In addition to deriving an equation that is valid for both genders, we derived separate equations for each gender, because of the borderline significant difference ( $p = 0.08$ ). The establishment of 6MWD equations considers, a priori, that the 6MWD is greater in males, which is why equations are derived separately for each gender. However, not all studies have found differences between the genders when calculating the 6MWD on the basis of stature and weight. In one study, for instance, the findings were clearly similar for both genders.<sup>(14)</sup> In the present study, habitual physical activity showed a borderline significant correlation with the 6MWD only in the univariate analysis. However, it should be borne in mind that physically fit individuals were excluded. Habitual physical activity has been evaluated in seven studies of 6MWT reference values,<sup>(10-12,16-19)</sup>

**Table 3** - Models tested for the six-minute walk distance and the anthropometric variables selected.

Model	Constant	Stature cm	Age years	BMI kg/m <sup>2</sup>	r <sup>2</sup>	5th percentile
Quadratic, general	511	0.0066	-0.030	-0.068	0.55	107
Quadratic, males	504	0.0059	-0.025	-0.044	0.37	118
Quadratic, females	636	0.0025	-0.039	-0.074	0.74	84
Linear, general	417	2.31	-2.95	-3.49	0.52	114
Linear, males	390	2.14	-2.37	-2.34	0.33	121
Linear, females	683	0.91	-3.94	-3.57	0.71	97

BMI: body mass index; r<sup>2</sup>: coefficient of determination.

in which it was shown to correlate, albeit poorly, with the 6MWD.

Ideal samples are those that consist of people who are randomly chosen from among the general population. In the present study, we included volunteers (convenience sample), which might have introduced a selection bias. Although the individuals included were selected primarily by age, they had a variety of occupations and were in different socioeconomic strata. Various conditions that can affect ambulation and cardiorespiratory function constituted the exclusion criteria. Therefore, the volunteers that were included met the criteria for a sample to be used in the establishment of reference values.<sup>(2)</sup>

Because our sample comprised only individuals who had never smoked and who had no signs or symptoms of respiratory disease (as determined with a validated respiratory epidemiology questionnaire), spirometry was not performed. The exercise capacity of individuals without respiratory disease is limited by the cardiovascular and peripheral muscle systems rather than by pulmonary function.<sup>(27)</sup>

Because of the well-established role of the 6MWT in the follow-up of patients with diseases that affect various age groups, it is important to consider not only a significant sample but also a wide range of ages in order to derive reference values. Of the studies investigating reference values for the 6MWT, only seven have evaluated samples comprising more than 100 individuals.<sup>(13-19)</sup> Of those seven studies, four included only individuals over 40 years of age<sup>(14,15,17,19)</sup> and two included individuals between 18 and 50 years of age.<sup>(13,16)</sup> A study conducted by Iwama et al.<sup>(18)</sup> included 134 individuals between 13 and 84 years of age. However, only 5 of the volunteers were older than 65 years of age, and only 10 were younger than 20 years of age. In the present study, the 132 individuals included were well distributed by gender and age bracket.

The 6MWD is influenced by the learning effect. One group of authors<sup>(28)</sup> suggested that three tests were required in order to determine the greatest 6MWD more accurately. Studies of the 6MWD in normal individuals confirmed that at least three tests are required.<sup>(8-10,17)</sup> In studies in which only two tests were performed,<sup>(9,13,15,17,18)</sup> as well as in those in which only one test was performed,<sup>(14,16)</sup> it is likely that the 6MWD was underestimated. Although Iwama et al.<sup>(18)</sup>

performed only two tests, the authors used the 6MWD achieved on the second test, even if the 6MWD was greater on the first test.

Stature was a relevant anthropometric variable for the prediction of the 6MWD in the present study, as it was in all such studies involving significant samples.<sup>(13-17,19)</sup> In the study conducted by Iwama et al.,<sup>(18)</sup> only age and gender were taken into consideration when the regression equation was being derived. However, in the univariate analysis, the authors found that stature had the highest correlation coefficient, and its inclusion in the multivariate equation was therefore obligatory. In three studies,<sup>(14,15,19)</sup> weight was included in the prediction equation. This was not the case in the present study, in which, unlike BMI, weight in isolation had no significant influence on the 6MWD. In all studies investigating 6MWD reference values, age has been shown to be relevant.

The 6MWD coefficient of determination ( $r^2$ ) provided by anthropometric variables varies from 0.25 to 0.42 across most studies, with the exception of one study, in which a surprising value of 0.77 was found.<sup>(15)</sup> In the present study, the  $r^2$  was 0.55, a high value that can be explained, at least in part, by the evaluation of the best regression model, which was not performed in any other study. In other studies, the  $r^2$  was increased by the inclusion of  $HR_{max}$  in the prediction equation.<sup>(11,17)</sup>

In the present study,  $SpO_2$  at the end of the 6MWT dropped no more than 2 points, a result that is in agreement with those of other studies involving normal individuals.<sup>(13-16,18)</sup> Many consider oxygen desaturation during exercise to be significant when there is a drop  $\geq 4\%$  in baseline saturation. However, that cut-off value was derived from studies involving maximal cardiopulmonary exercise testing in athletes.<sup>(29)</sup>

In the present study, we found that the Borg scale scores for sensation of dyspnea and leg fatigue were no higher than 4 and 5, respectively. One group of authors<sup>(30)</sup> used the Borg scale scores for sensation of dyspnea and leg fatigue in order to evaluate 460 normal individuals who underwent incremental cycle ergometer exercise. At 60% of the maximum workload, a value that is similar to the workload estimated by the HR found in the present study, the highest scores for sensation of dyspnea and leg fatigue were 5 and 6, respectively, for both genders.

Reference values should be established in specific populations.<sup>(19)</sup> The values obtained in the present study are different from those derived from another sample of the Brazilian population,<sup>(18)</sup> which can be explained by the aforementioned factors. No comparisons were drawn with other equations, because the age range was limited in those studies.<sup>(14,19)</sup>

In the present study, reference values for the 6MWT were derived from a sample of male and female adults of a wide range of ages in Brazil. A quadratic equation was the model that best adjusted to the data, with a high  $r^2$ . The values found in the present study are different from the predicted values previously reported.

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