Reference Equations for the Six-Minute Walk Distance in Healthy North-East Indian Population Aged 18-60 Years

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ABSTRACT

BACKGROUND
Six-minute walk test is a simple and objective tool for functional assessment of patients with cardiopulmonary disease. Healthy population-based reference equations to predict 6MWD show wide variations from region to region. Our study derives reference equations for the north-eastern population of India.

METHODS
150 healthy, non-smoker subjects aged 18-60 years were enrolled. Spirometry and 6MWT was done for all subjects according to the American Thoracic Society prescribed protocol. Pearson correlation and subsequently stepwise multiple regression analysis was used to develop the reference equations.

RESULTS
The mean six-minute walk distance (6MWD) for males was 503.39 ± 31.95 meters which was significantly more than that for females which was 454.19 ± 36.46 meters (p= 0.001). The regression equation derived in our study shows age, height and weight as the most important predictors of the 6MWD. The predictive equations derived are- Males: 6MWD= 377.18-[1.235 x Age (yr.)] + [1.006 x Height (cm)]; r2= 0.427, p<0.001 Females: 6MWD= 129.75-[0.510 x Age (yr.)] + [2.186 x Height (cm)]; r2= 0.375, p= 0.028. Alternative equations derived- Males: 6MWD= 381.52 - [1.235 x Age (yr.)] + [0.963 x Height (cm)] + [0.062 x Weight (Kg)]; r^2=0.427, p<0.001; Females: 6MWD= 107.255 - [0.430 x Age (yr.)] + [2.451 x Height (cm)] - [0.421 x Weight (Kg)]; r^2=0.38, p= 0.064. Reference equations from other regions of the world over-predicted the 6MWD for our population probably due to anthropometric and demographic variations.

CONCLUSIONS
The 6MWD shows considerable variability according to anthropometric, cultural and social characteristics of the population studied. The regression equation derived in our study shows age and height as the most important predictors of the 6MWD. There is over prediction of 6MWD by equations from Western and other Asian studies. The gender specific equations derived in our study from this region may thus help in the assessment of patients with chronic cardiorespiratory diseases by providing correct reference values of normal.

KEYWORDS
Six-Minute Walk Test, Distance, Healthy, Reference Equation, Anthropometric, North-East India

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BACKGROUND

The six-minute walk test (6MWT) is a simple, safe and reproducible submaximal exercise test for functional capacity in a patient with cardiovascular and respiratory diseases. It is widely used as an objective tool for evaluation of functional state, monitoring response to therapy, prognosticating and planning pulmonary rehabilitation programmes.[1] Attempts to objectively measure functional capacity dates back to the 1960's when researchers developed methods to assess physical fitness by measuring the distance walked in a fixed interval of time.[2] Initially the 12-minute frame was used but with more research and refinement, the 6-minute test is now considered optimal.[3] The official statement of the American Thoracic Society (ATS) published for the first time in 2002 prescribes guidelines for the proper procedure and interpretation of results of the 6MWT.[1] Mean six-minute walk distance (6MWD) for the healthy population observed in many studies across different regions of the world show wide variability.[1] This is attributable to regional and racial differences in anthropometric measurements besides variability in the methods of conducting the test like corridor length used, proper understanding of the procedure and practice by the subject. Healthy population-based reference equations for 6MWD have not been derived for many populations. To the best of our knowledge, this is the first study to establish reference equations for the North eastern population of India.

In this study, we aim to measure the six-minute walk distance (6MWD) covered by a healthy adult north-east Indian population aged 18-60 years, construct reference equations to predict the 6MWD and compare the equations derived with previously established equations.

METHODS

The study sample was selected from healthy attendants of patients attending our centre and students and staff of our institute who were aged between 18 years to 60 years. Smokers and ex-smokers (anyone who has smoked more than 100 cigarettes in a lifetime), those with obesity (BMI ≥ 30 Kg/m^2) and those who had any other medical illness, acute or chronic were excluded from our study. Spirometry was done for all subjects. Only those with normal spirometry, that is, forced expiratory volume in 1st second (FEV1) and Forced vital capacity (FVC) more than 80% predicted for age and height and FEV1/FVC more than 0.7 were included. A total of 150 subjects, 100 males and 50 females were enrolled.

Six-minute walk test (6MWT) was conducted in a secluded hospital corridor as per guidelines prescribed by the American Thoracic Society (ATS).[1] The subjects were instructed to walk at their own pace for 6 minutes along a 30-metre long straight path with markings at every 3-metre interval. The course was marked by two traffic cones at each end. Patients were encouraged to cover as much distance as possible and were instructed to rest in case of any discomfort. Total distance walked in 6 minutes was calculated. Blood pressure, heart rate, % oxygen saturation and dyspnoea rating according to Borg Scale were noted before and after the test.

Statistical Methods

Descriptive and inferential statistical analysis were used. The Statistical Package for the Social Sciences (SPSS) version 22.0, and R environment version 3.2.2 were used for the analysis of the data. Student t-test (two tailed, independent) was used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven's test for homogeneity of variance was performed to assess the homogeneity of variance. Analysis of variance (ANOVA) was used to find the significance of study parameters between three or more groups of patients. Chi-square/ Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. Pearson correlation between study variables was performed to find the degree of relationship. Stepwise multiple regression analysis was used to develop the reference equations. P-value <0.05 was considered significant.

RESULTS

A total of 150 subjects, 100 males and 50 females, who fulfilled the inclusion criteria were enrolled. The mean age of the study population was 32.29±10.68 years. The age and sex-wise distribution of the subjects is shown in Table 1. The mean height, weight and Body mass Index (BMI) of the subjects are as shown in Table 2. 54% subjects were physically active, defined as those who performed at least 20 minutes per session of lower extremity exercise or equivalent for at least 3 days per week in the preceding month.[4,5] The rest had sedentary lifestyle. More males (63%) were active compared to females (36%). The mean FEV1 and FVC for males were 3.28±0.39 and 3.84±0.52 litres respectively, while that for females was 2.44±0.40 and 2.84±0.45 litres. The mean six-minute walk distance (6MWD) for males was 503.39±31.95 meters which was significantly more than that for females which was 454.19±36.46 meters (p=0.001). The distance walked by males was greater than females in all age groups which is graphically depicted in Figure 1. There were significant increases in heart rate, systolic and diastolic blood pressures after the test in both males and females. Change in SpO_2 and Borg dyspnoea scores after the test were not found to be significant. Changes in pre and post-test parameters are shown in Table 3. The mean 6MWD of physically active subjects (500.77±38.34 meters) was significantly more than that for sedentary subjects (471.81±37.54 meters) irrespective of age and sex (p<0.001).

Pearson correlation study showed significant correlation between 6MWD and Age, Weight and Height. Correlation with BMI was not found to be significant. There was positive correlation between 6MWD and height and weight but negative correlation with age. The correlation coefficients are as shown in Table 4. Figure 2 and 3 shows the scatter plot with correlation between 6MWD and Age, Height and BMI for males and females respectively. Multiple regression analysis was used to find the most significant predictors of the 6MWD, and the following prediction equations were derived which explained about 43% and 38% variance in 6MWD for males and females respectively.

Males: 6MWD=
377.18 - [1.235 x Age (yr.)] + [1.006 x Height (cm)]
r^2= 0.427, p<0.001
Females: 6MWD=
129.75 - [0.510 x Age (yr.)] + [2.186 x Height (cm)]
r^2= 0.375, p= 0.028

or

Males: 6MWD=
381.52 - [1.235 x Age (yr.)] + [0.963 x Height (cm)] + [0.062 x Weight (Kg)];
r^2= 0.427, p<0.001
Females: 6MWD=
107.255 - [0.430 x Age (yr.)] + [2.451 x Height (cm)] - [0.421 x Weight(Kg)]
r^2= 0.38, p= 0.064

Age in Years	Gender		Total
	Female	Male	
<20	9(18%)	6(6%)	15(10%)
20-30	20(40%)	43(43%)	63(42%)
31-40	8(16%)	28(28%)	36(24%)
41-50	8(16%)	17(17%)	25(16.7%)
51-60	5(10%)	6(6%)	11(7.3%)
Total	50(100%)	100(100%)	150(100%)
Mean ± SD	31.50±12.14	32.69±9.92	32.29±10.68

Table 1. Age and Sex-Wise Distribution of Study Population

Variables	Gender		Total	p Value
	Female	Male		
Weight (Kg)	50.99±6.48	60.72±7.86	57.48±8.72	<0.001**
Height (cm)	155.82±5.14	164.88±5.82	161.86±7.04	<0.001**
BMI* Kg/m^2)	20.97±2.51	24.03±17.33	23.01±14.28	0.216

Table 2. Comparison of Weight, Height and BMI According to Gender of Population Studied

*BMI-body mass index

Variables	Gender	
	Female	Male
Heart Rate (bpm*)		
• Pre	84.28±11.37	82.68±11.79
• Post	98.68±14.22	96.96±16.01
• p Value	<0.001	<0.001
SBP† (mmHg)		
• Pre	117.40±9.35	120.28±14.59
• Post	124.84±11.10	132.02±12.54
• p Value	<0.001	<0.001
DBP‡ (mmHg)		
• Pre	76.40±5.98	78.20±6.72
• Post	80.80±5.28	84.54±7.54
• p Value	<0.001	<0.001
Oxygen Saturation%		
• Pre	97.94±0.84	97.33±1.12
• Post	97.86±0.97	97.17±1.16
• p Value	0.552	0.162

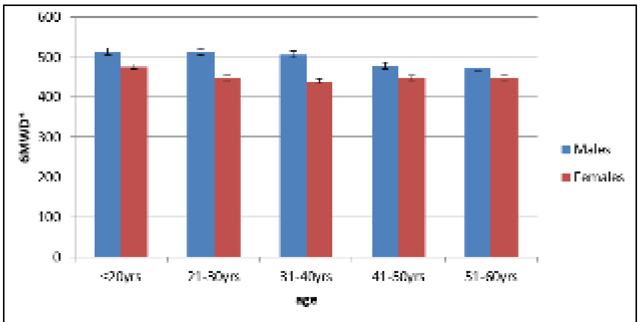
*beats per minute, †systolic blood pressure, ‡ diastolic blood pressure

Table 3. Comparison of Pre and Post-Test Heart Rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Percentage Oxygen Saturation (SpO_2)

Variables	r Value	p Value
6 MWD* (Meters) vs. Age in years	-0.230	0.005
6 MWD (Meters) vs. Weight (Kg)	0.324	<0.001
6 MWD (Meters) vs. Height (cm)	0.501	<0.001
6 MWD (Meters) vs. BMI (Kg/m^2)	0.054	0.511

* Six-minute walk distance

Table 4. Correlation of 6MWD with Age, Weight, Height and BMI



*6MWD-six-minute walk distance, p<0.001

Figure 1. Age and Sex Wise Difference in 6MWD

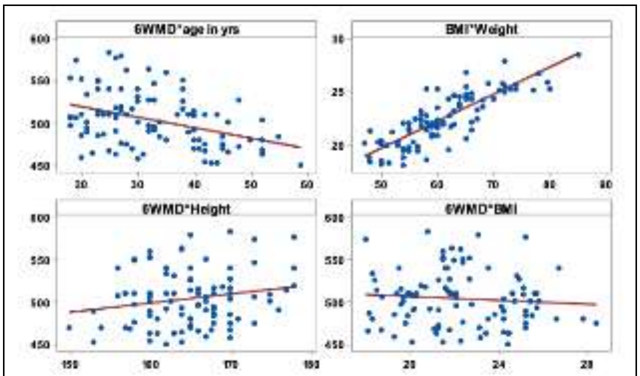


Figure 2. Scatter Plot for Males

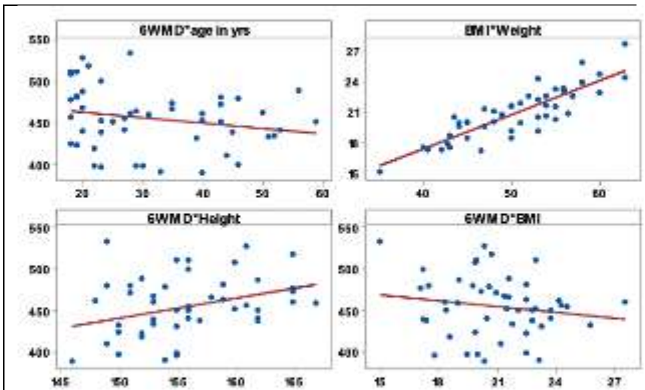


Figure 3. Scatter Plot for Females

Comparison with established equations from other regions- We used the first equation for comparison with equations derived for other populations for simplicity. The Enright and Sherrill[6] derived equation for American population over predicts 6MWD of males by about 165 meters and females by about 243 meters. Equation derived by Zou et al.[5] over predicts distance walked by 105 meters for males and 132 meters by females. Study from southern part of India by Ramanathan et al.[7] over predicts 6MWD by 58 meters for males and 105 meters for females. The North Indian study by Vaish H et al.[8] over predicts 6MWD of males by about 91 meters. The equation derived by Fernandes et al.[9] From a West Indian population also over-predicts 6MWD by about 26 meters for males and females by about 33 meters.

DISCUSSION

To the best of our knowledge this is the first such study from the North Eastern part of India. Because we intended to establish reference equations for the healthy population, we excluded children, elderly and obese subjects. The study was done to address the observation that predictive equations cannot be generalized to the whole population. Because of regional, social, anthropometric and other differences in different geographic areas, equation derived from a certain population cannot be applied to another population even in the same country.[10]

In our study, the mean distance walked was comparatively more for males than females. This conforms to all studies previously conducted.[2,5,6,7,8,9,10] Males are genetically taller and more muscular, which offers them the advantage of better physical efficiency and hence greater distance covered. Another reason is the relatively more number of physically active males compared to females in our study. It has been shown that physical activity is proportional to muscle strength.[11] This translates into greater distance walked by the more physically active males than females. Overall, we found clinically significant differences in distance walked by the physically active and sedentary population irrespective of age and sex. The study on Chinese population by Zou and colleagues[5] also found clinically significant increase in 6MWD with physical activity. We found clinically significant negative correlation between 6MWD and age, and positive correlation between 6MWD and height and weight. Multiple regression analysis showed that age and height were the most important predictive variables for the 6MWD and could explain 43% and 37% variability for males and females respectively. This correlation is consistent with the findings of other studies from different regions.[5,6,7,8,9,11,12] A greater height implies longer legs and hence lengthy steps and more distance covered. The positive correlation with weight in our study can be explained by the fact that only healthy non-obese subjects were taken. Age correlates negatively because aging leads to decreased muscle power and muscle mass and appearance of conditions like arthritis which hamper motility. Most of the studies conducted earlier over predicted the 6MWD when applied to our data. Study from western population by Enright et al.[6] over predicted the 6MWD by a big margin of 165 meters for males and 243 for females. A study on Chinese population[5] overestimated 6MWD of males by 105 meters and females by 132 meters. Indian studies showed lesser variation. The studies from Northern,[8] Southern[7] and Western[9] part of India also over predicted the 6MWD. No study under predicted the 6MWD when applied to our population. These findings can be explained by the anthropometric, demographic and cultural dissimilarity among different races in various geographic regions of the world. The lesser distance walked by our subjects compared to other Indian populations is also explained by the same factors. In general, people from North east India are shorter and of smaller built compared to the mainstream Indian population.[13]

CONCLUSIONS

The 6MWD shows considerable variability according to anthropometric, cultural and social characteristics of the population studied. The regression equation derived in our study shows age, weight as the most important predictors of the 6MWD. There is over prediction of 6MWD by equations from Western and other Asian studies. Studies from other regions of India also over predict the 6MWD of our subjects. This over prediction is best explained by the comparatively smaller built of the North East Indian population. The gender specific equations derived in our study from this region may thus help in the assessment of patients with chronic cardiorespiratory diseases by providing correct reference values of normal.

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