DOI: 10.7860/JCDR/2016/17643.7714

Original Article

Physiology Section

Reference Equation for Six Minute Walk Test in Healthy Western India Population

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ABSTRACT

Introduction: The Six Minute Walk Test (6MWT) is used to assess disease progression and survival in chronic cardiopulmonary disorders. However, variability is noted in the six minute walk test distance (6MWD) in different populations.

Aim: We aimed to develop a reference equation for 6MWD in healthy Western India population and compare the results with previously published Indian and Caucasian reference equations.

Materials and Methods: Total 174 healthy subjects between 25 to 75 years performed the 6MWT. Variables assessed were age, height, weight, body mass index and sex. Predicted equations were derived using multiple linear regression and compared with the equations for North Indian male, South Indian and Caucasian population using Bland – Altman method.

Results: The 6MWD mean (SD) was 512.38 (67.84) m for men and 457.27 (56.75) m for women with p=0.001. The 6MWD correlated with age (r=-0.44), height (r=0.43), weight (r=0.21) in univariate analysis. Stepwise multiple regression analysis showed age and sex to be independent predictors of 6MWD, R^2 =0.307. The reference equation for healthy Western India population is 553.289 + (-2.11 x age) + (45.323 x sex; men=1 and women =0). Bland Altman analysis showed that the mean bias was 50.87m (95% limits of agreement 134.77 to – 33.0) for North Indian male equation, 50.75m (95% limits of agreement 105.72 to - 4.22) for South Indian equation and 122.72m (95%limits of agreement 254.11 to – 8.67) for Enright and Sherrill's equation.

Conclusions: The North Indian male, South Indian and Caucasian equations significantly over-estimated the predicted walk distance for our healthy population. Hence, there is a need to develop subgroup population specific reference equations.

Keywords: Anthropometry, Exercise test, Physiology, Reference values, Six minute walk distance, Walking

INTRODUCTION

The six minute walk test (6MWT) was first developed by Balke in 1963 to evaluate the ability of an individual to engage in physically demanding activities of daily living [1]. It is a simple test done at submaximal effort and reflects the capacity of an individual to perform daily activities. This test is frequently used to assist clinicians on the severity of disease, prognosis and response to treatment [2,3]. The cycle ergometer or treadmill are more useful in assessing the exercise capacity but the 6MWT is easy to perform, less expensive and is well tolerated in patients with cardiopulmonary disease [4].

The 6MWD is variable in healthy population due to population related differences [5] and this is observed in various reported studies [6-9]. The American Thoracic Society encourages the scientific community to develop reference values for each population subgroups. There is no reference equation for six minute walk test distance (6MWD) in the population of Western India to interpret the level of fitness and intervention outcome.

AIM

Therefore, the aim of this study was: (i) to determine the 6MWD in a healthy population based sample in Goa, Western India and develop a reference equation for 6MWD; and, (ii) to compare it to the North Indian male and South Indian and Caucasian prediction equations.

MATERIALS AND METHODS

Study design and Study population

This was a prospective observational study conducted at the tertiary care teaching hospital from October 2014 - July 2015. The study was approved by Institutional Ethics Committee and all participants gave written informed consent. A total of 174 subjects were recruited from among patient's relatives and hospital employees; both males and females above the age of 25 years. Inclusion criteria included healthy subjects defined as absence of any diseases (history of stroke, arthritis, chronic diseases like old healed tuberculosis, chronic kidney disease, cardiac disease, musculoskeletal disorders, heart rate more than 100/min and BP more than 150 mmHg systolic and less than 90mmHg diastolic), and absence of any acute illness in the preceding six weeks. We excluded smokers and individuals with abnormal lung function on spirometry.

Pulmonary Function Tests

All participants underwent pre-bronchodilator spirometry according to the American Thoracic Society/European Respiratory Society guidelines [10]. Subject's standing height was measured to the nearest centimeter using a stadiometer and weight was measured with a calibrated weighing machine. Forced Expiratory Volume in one second (FEV1), forced vital capacity (FVC) and FEV1/FVC were recorded. Patients with normal spirometry values were included, FEV1>80% predicted, FVC>80% predicted and FEV1/FVC > 70% [10].

Six Minute Walk Test

6MWT was performed according to the standardized protocol of American Thoracic Society between 09:00 to 13.00 hours in order to avoid intra-day variability [4]. After an adequate rest of 15 minutes subjects were instructed to walk as far as possible at their own pace for six minutes undisturbed in a 30 meter straight corridor which was marked at every 3 meter interval. Standardized encouragement was provided e.g., "You are doing well", "Keep up the good work". They were informed that they could stop if they developed symptoms of dyspnea, dizziness, leg cramps or chest pain, but resume to walk as soon as they could. Prior to the 6MWT, the Heart Rate (HR), blood pressure and SpO_2 were measured and so also at the end of the test. To determine the effort made by subjects, the predicted HRmax (HRmax% pred) was derived from the formula 220-age. All subjects performed the test for the first time without any practice or warm up.

STATISTICAL ANALYSIS

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 20. Variables are described as mean and Standard Deviation (SD) for normally distributed continuous variables. Categorical variables are presented as percentages. Independent Student's t-test was used to study differences between two groups. The independent variables were checked for multicollinearity. Correlations were estimated using Pearson's correlation coefficient to evaluate the correlation between age, height, weight and gender as independent variable and six - minute walk distance as dependent variable. Stepwise multiple regression analysis was used to evaluate independent variables explaining the variance in 6MWD and generate the prediction equation for 6MWD. Agreement between two equations (North Indian male [11], South Indian [12], Enright and Sherrill [5], and present study) was assessed by Bland - Altman method [13]. The mean difference between values obtained by two equations was plotted against the average of the two values. Limits of agreement were calculated as mean difference between the two 6MWD±1.96 standard deviation. A p-value of <0.05 was considered as being statistically significant.

RESULTS

A total of 174 subjects were screened, one had obstructive lung disease and remaining 4 did not have reproducible and accepted spirometry efforts. Of the 169 subjects, 80 (47.3%) were males. The mean (SD) age was 43.4 (12.3), age range 25-75 years, weight was 62.55 (12.6) kg, height 158.49 (9.93) cm and BMI of 24.83 (4.0). The mean (SD) for 6MWD was 483.36 (67.91), men = 512.38 (67.84), women = 457.27 (56.75), p = 0.001. The subjects reached 53.29% (8.96) of their HR max. The baseline characteristics of study population are summarized in [Table/Fig-1] while [Table/Fig-2] shows 6MWT measures. There was significant correlation between 6MWD and age, height, weight, FVC%, systolic blood pressure, pre SpO_2 and gender (see [Table/Fig-3]). [Table/Fig-4a-c] shows the scatter plots of 6MWD and age, height and weight. All significant variables were considered for step-wise regression analysis and only age, sex, pre-test heart rate, post-test heart rate and pre SpO_2 were independent predictors of 6MWD. Equation derived with the common and easily available variables; age, height, weight and sex showed only age and sex to be the independent predictors of 6MWD with a coefficient of determination, R^2 = 0.307. The multiple regression equation derived from this study was 553.289 + (-2.11x age) + (45.323 x $sex_{male=1, female=0}$). SEE = 56.87, the lower limits of normal for 6MWD is the predicted – 93.55m. Residual statistics predicted value (SD) = 483.36(37.64), standardized predicted value (SD) = 0.000(1.0), standardized residual (SD) = 0.000(0.994) and residual standard deviation = 56.53. [Table/Fig-5] shows the plot of residuals relation between predicted and observed residual 6MWD equation. [Table/Fig-6] shows the relationship between predicted and observed 6MWD in male and female population.

Variable	Whole Group	Males	Females	p-value
Subjects n (%)	169	80 (47.3)	89 (52.7)	
Age yrs Mean (SD)	43.4 (12.3)	41.0 (10.9)	45.6 (13.1)	0.015*
Weight kg Mean (SD)	62.55 (12.60)	67.80 (12.30)	57.83 (10.9)	0.001*
Height cm Mean (SD)	158.49 (9.93)	165.73 (7.77)	151.98(6.60)	0.001*
BMI kg/m^2Mean (SD)	24.83 (4.09)	24.60 (3.64)	25.03 (4.47)	0.499
6MWD m Mean (SD)	483.36(67.91)	512.38(67.84)	457.27(56.75)	0.001*
FEV1% pred Mean (SD)	94.03 (10.31)	92.03 (9.39)	95.83(10.81)	0.016*
FVC% pred Mean (SD)	93.53 (12.05)	90.82 (11.07)	95.97 (12.36)	0.005*
FEV1/FVC Mean (SD)	83.04 (7.10)	82.59 (6.70)	83.44 (7.45)	0.44

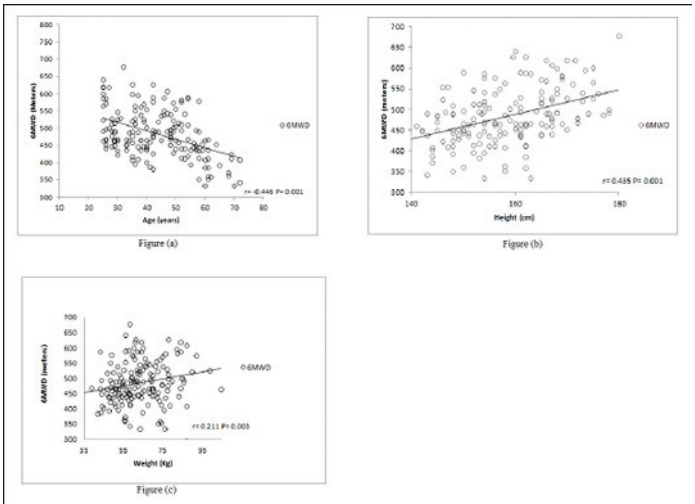
[Table/Fig-1]: Characteristics of study population.
BMI= body mass index, 6MWD= six minute walk distance, FEV1= forced expiratory volume, FVC= forced vital capacity. (* statistically significant)

Variables	Whole Group	Males	Females	p-value
Pre HR mean (SD)	76.95 (10.50)	75.64 (10.93)	78.13 (10.02)	0.123
Post HR mean (SD)	93.56 (13.64)	92.52 (13.8)	94.49 (13.5)	0.35
Pre SpO_2 mean (SD)	96.42 (1.45)	96.49 (1.24)	96.43 (1.63)	0.948
Post SpO_2 mean (SD)	97.62 (6.80)	97.58 (0.95)	97.73 (0.99)	0.303
HR max mean (SD)	176.52 (12.35)	178.99 (10.94)	174.39 (13.17)	0.015*
HR max pred% mean (SD)	53.29 (8.96)	51.94 (8.76)	54.51 (9.02)	0.062
Systolic BP mean (SD)	120.97 (8.4)	122.08 (7.2)	119.9 (9.3)	0.108
Diastolic BP mean (SD)	70.7 (7.1)	72.0 (7.0)	69.62 (7.2)	0.031*

[Table/Fig-2]: Six - Minute Walk Test measures.
HR= heart rate. (* statistically significant)

Variables	Correlation co-efficient	p-value
Age	-0.446	0.001*
Height	0.435	0.001*
Weight	0.211	0.003*
BMI	-0.061	0.214
FEV1%	-0.015	0.423
FVC%	-0.206	0.004*
FEV1/FVC	0.092	0.116
Systolic BP	-0.132	0.043*
Diastolic BP	-0.053	0.246
Pre HR	-0.015	0.423
Post HR	0.110	0.078
Pre $Sp0_2$	0.199	0.005*
Post SpO_2	0.025	0.375
Male	0.406	0.001*

[Table/Fig-3]: Univariate correlation coefficient for 6MWD.(* statistically significant)

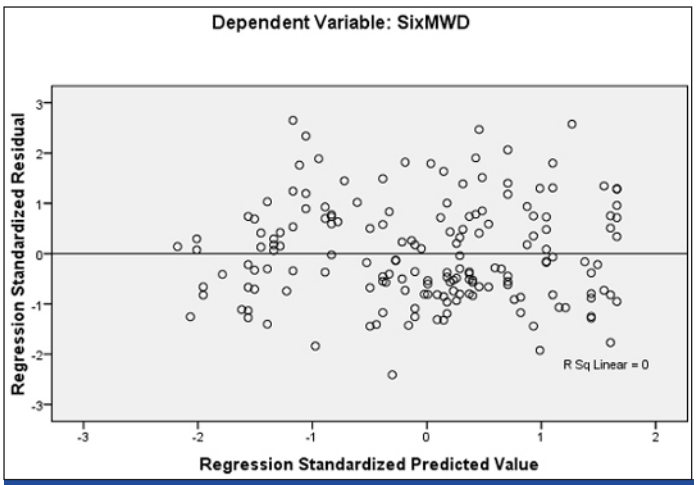


[Table/Fig-4]: (a-c) Scatter plot of age, height, weight and 6MWD showing a linear scatter. There is a good linear correlation in age and height plot while weight has a small correlation with 6MWD.

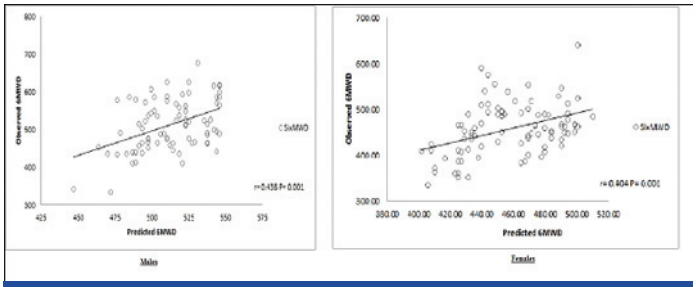
All equations significantly overestimated 6MWD for our population. The Bland Altman analysis for the predicted 6MWD showed that the mean bias was 50.87m (95% limits of agreement 134.77 to – 33.0) for North Indian males equation, 50.75m (95% limits of agreement 105.72 to - 4.22) for South Indian equation, and 122.72m (95% limits of agreement 254.11 to – 8.67) for Enright and Sherrill's equation. [Table/ Fig-7a-c] shows the Bland Altman plot demonstrating agreement between present study and other prediction equations for 6MWD.

DISCUSSION

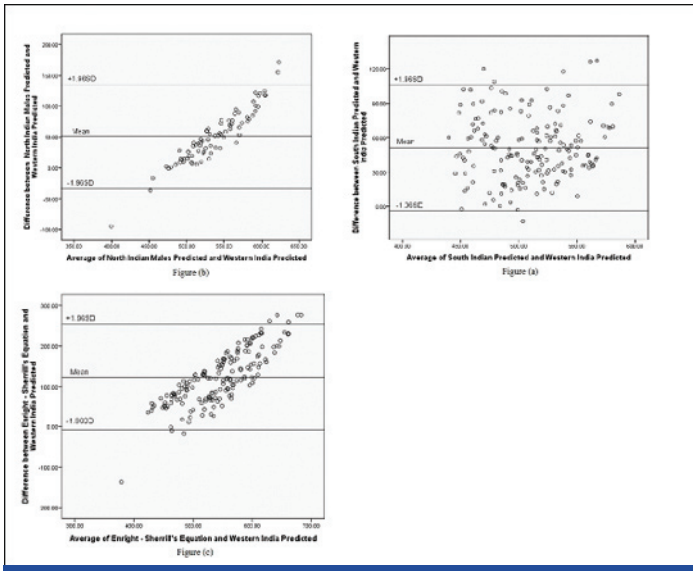
We determined for the first time, the 6MWD in the population of Western India and developed the prediction equation for 6MWD. This study also proved that population subgroups differ in their



[Table/Fig-5]: Scatter plot showing the relation between predicted and observed residual 6 min-walk distance equation.



[Table/Fig-6]: Scatter plot showing relation between predicted and observed Six minute walk distance in males and females.



[Table/Fig-7]: (a-c) is the Bland- Altman plot demonstrating agreement between study equation and the North Indian male, South Indian, Enright – Sherrill prediction equations.

6MWD. Our results apply to the first six minute walk performed by the subjects aged 25–75 years.

The stepwise regression found that age, sex, pre-test heart rate, post-test heart rate and pre-test SpO_2 were independent predictors of 6MWD. On selection of more easily measured characteristics like age, weight, height and sex, only age and sex were independent predictors explaining 30.7% of variance. Age and sex accounted for 40.0%, 30.0%, 41.0% and 49% variance in studies reported by Enright-Sherrill, Iwama et al., Gibbons et al., and Hill K respectively [5,14-16]. The smaller coefficient of determination of 30.7% informs of other possible factors influencing the 6MWD e.g. physical activity [4], psychological condition [14], and diet and lifestyle [17].

The Bland Altman analysis showed that the mean bias was clinically significant for the predicted 6MWD. The mean bias was 50.87m for North Indian males equation, 50.75m for South Indian equation and 122.72m for Enright and Sherrill's equation. When compared to the North Indian male equation as well as South Indian prediction equation, both these equations over-estimated the predicted walk distance significantly. The largest mean bias was for Enright and Sherrill equation confirming the observation that reference equations derived in different country are not applicable to their own country [7]. In the study by Vaish et al., although the North Indian males had similar height, weight and age (164.07(6.52), 67.65(10.91) and 46.02(6.52) respectively) as our study subjects, yet there was no agreement between the two equations [11]. They also performed the test for the first time without warm-up. The possibility of difference could be due to the effort exerted. Our male subjects had an average age predicted maximal HR (HRmax % predicted) of 51.94(8.76) while North Indian males reached average of 61.44(7.7). Such difference despite following standard techniques emphasizes the need for reference equations for specific population or ethnicities. This is in agreement with the geographical variations reported in previous studies [18]. It is also possible that 6MWD is diverse in different regions of India as was observed in Brazil [19].

LIMITATION

One limitation of our study was that we used convenience sample rather than a random sample. However, the subjects were from different parts of the state of Goa which is a part of Western India. Moreover most studies have used convenience samples [6,7,14,20-25]. Another limitation is that we considered Goa to be representative of Western India. This can be validated in future studies.

CONCLUSION

We developed a reference equation for 6MWT for Western India population. When compared to reference equation of North Indian male, South Indian and Caucasian, we found that equations developed in foreign or other regional populations are not adequate to our population. Our reference equation may be used to validate and evaluate exercise capacity in patients with chronic cardiopulmonary diseases in Western India population.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Nov 01, 2015**
Date of Peer Review: **Jan 19, 2016**
Date of Acceptance: **Jan 28, 2016**
Date of Publishing: **May 01, 2016**