Reference Equations for The Six-Minute Walk Distance in Obese Chinese Subjects Older Than 40 Years

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Research Article

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Abstract

Background

Some studies have showed that the reference equations for the walking distance derived mainly from healthy, normal-weight people are not suitable for obese subjects. The main purpose of this study is to establish reference equations for the 6MWD in Chinese obese subjects.

Methods

In the study, a total of 272 obese subjects underwent American Thoracic Society (ATS) protocolized six-minute walk testing (6MWT), and the longer walking distance was used for further analysis. The reference equations of the 6MWD were developed by stepwise multiple regression analysis. The established equations for the 6MWD were compared to existing prediction equations.

Results

The mean 6MWD for the cohort was 523±56 m. We found that the reliability of two 6MWTs was good. Age and BMI were identified as independent factors and explained 31% and 27% of the variance in the 6MWD for the male and female groups, respectively. These reference equations reported in previous studies cannot accurately predict the 6MWD in our subjects.

Conclusion

The study was the first to describe the 6MWD in Chinese obese subjects and to propose predictive equations. These established equations can contribute to improving the assessment of Chinese obese patients with diseases that affect their exercise capacity.

Introduction

With the progress of the times, people's living standards have also improved by leaps and bounds. People no longer have to worry about not having enough to eat; however, faced with the problem of obesity, people have begun exploring effective diagnostic tools to assess functional capacity and cardiovascular health. Relevant experiments, such as the walking test, have been carried out by professionals; these tests can be used to assess the functional status in a safe and reasonable way and can serve as a monitoring function(1). There is an easy-to-use, affordable tool called the six-minute walk test (6MWT) that can be used to measure cardiovascular fitness, and its results are very similar to those of the treadmill exercise test(2). At the same time, it can clearly show the patient's daily activity state. The 6MWT is a commonly used clinical assessment of exercise capacity in patients with cardiopulmonary disease(3-5). With the
increase in popularity of the 6MWT, it is now be used with a wide range of conditions, including stroke, obesity, Down syndrome, Alzheimer's disease, cerebral palsy and more(6-12).

The American Thoracic Association (ATS) has been concerned about the 6MWT since 2002. Comprehensive guidance that is potentially relevant was issued for this examination. These guidelines include the definition, concept and measurement standard of the inspection and attaches the relevant achievement record description and a specific explanation of the parameters(13). Although the test has been widely used, it has major problems. In particular, although the 6MWT has been used with obese Chinese people, there are no specific effective experimental data. In previous studies, we have established reference equations for the six-minute walk distance (6MWD) of healthy Chinese subjects(14, 15), but the equations were not applicable to subjects with BMI>30 kg/m². Some studies(16) have shown that reference equations for the 6MWD derived mainly from healthy, normal-weight populations are not suitable for obese subjects and that specific reference equations for the 6MWD in obese subjects should be established. Although the 6MWD prediction equations derived from obese subjects of other ethnicities have been established (9, 17), these equations are different, and the previously published equations may not be applicable to obese Chinese people. The lack of 6MWD reference equations for obese subjects will limit the use of the 6MWT for obese patients and will make it difficult for doctors who use the 6MWD.

The main purposes of this study are as follows: 1. standard measurement of anthropometric variables and walking distance for obese Chinese people older than 40 years according to the measurement standard stipulated by the ATS guidelines; 2. establishment of reference equations for the 6MWD in obese Chinese people; and 3. comparison of the 6MWD obtained in this study with previous equations for subjects in the same age range(17-20).

**Methods**

**Subjects**

We collected data over a 17-month period from May 2019 to December 2020, and obese subjects (BMI>30 kg/m²) older than 40 years were recruited from three local communities. The purpose of the whole study was presented prior to the recruitment of participants for this study to better complete the test. The subjects needed to complete a health questionnaire before participating in the 6MWT, and the researchers needed to verify the results of the questionnaires. We obtained the subjects' written informed consent before the study. This study was approved by the Ethics Committee of Wenzhou People's Hospital.

Subjects meeting the following criteria were excluded from the study:

- age >75 years;
- self-reported disease symptoms (including heart disease, lung disease and other organ or blood neurological diseases);
• baseline heart rate (HR) < 50 bpm or ≥100 bpm;
• baseline systolic blood pressure (SBP) ≥ 180 mmHg or diastolic blood pressure (DBP) ≥ 100 mmHg;
• trouble walking or need for a hearing aid.

Physical examination

The subjects underwent anthropometric measurement, which was performed by skilled operators following the procedures described in the anthropometric standardization reference manual. Age was verified by each subject's identity card. Height was measured to the nearest 0.1 cm with a height gauge; for this measurement, the subjects needed to take off their shoes and stand with their back straight. An electronic scale was used to measure body weight (kg) to the nearest 0.1 kg, and the BMI algorithm = weight/height\(^2\) (represented by kg/m\(^2\)) was used to calculate and obtain the BMI of each subject.

Six-minute walk test

Both 6MWTs were carried out in an enclosed space, a 30-metre-long corridor with a straight, flat surface. The space was marked by a distance marker every three meters, and orange traffic cones were placed at the turning points of the walk. The starting line represented both the starting point and the end of the sixty meters, with the colourful tape on the floor serving as a reminder. The room temperature for the test should be controlled between 20°C and 25°C, so the time was limited to between 9:00 AM and 1:00 PM. Participants had to follow strict rules such as no strenuous exercise or eating before the start of the test; they had to rest in a chair near the starting point for 10 minutes or more and then undergo measurement of resting blood pressure rates and heart rates prior to the test. The subjects were told before the test that the purpose of the test was to measure how far they could normally walk in six minutes. If the subjects experienced dizziness, chest pain or difficulty breathing or leg cramps during the test, they were allowed to stop and rest, but once they were well again, they were encouraged to continue walking quickly. To ensure the rigor with which participants conduct the experiment, two 6MWTs were finished by an operator to monitor and record data. The operator was also responsible for providing standard encouragement to the participants every 60 seconds ("you are doing well; you have five minutes left", "good job; there are four minutes left")(13). The distance recorded at six minutes was the 6MWD. At the beginning of the experiment and after the completion of the 6MWT, each subject was presented with the Borg dyspnoea scale(21). On a scale ranging from "0 = none" to "10 = very, very severe," the subjects used the scale to assess their current degree of shortness of breath. Two hours later, the subject's second test was completed by the same operator.

Statistical analysis

The Kolmogorov-Smirnov test was used to check and verify the normal distribution of the predicted data. The measured data are expressed as the mean ± standard deviation (SD) or as numbers and percentages, as appropriate. Descriptive analysis was used to analyse the characteristics of the subjects. Independent Student’s \( t \)-test was used to illustrate the relationship between the 6MWD and the
characteristics of categorical variables. In the study, we used paired-samples Student’s t-test to compare the measured 6MWD in our subjects and the predicted 6MWD based on the previously published reference equations derived from other studies(17-20). According to Bland-Altman analysis and calculation of the correlation coefficient (ICC), the repeatability of the two 6MWDs was calculated(22). First, the correlations between the 6MWD and variables (i.e., age, height, weight and BMI) were evaluated by Spearman's analysis of an individual variable. Second, the reference equations of the 6MWD were established by a forward stepwise multivariate regression analysis. In each procedure, the most significant categorical variable was added to the model, and then the same procedure was followed until no additional statistically significant variables remained. A p-value > 0.05 was used to detect whether the variable was entered or deleted. Data were analysed using SPSS for Windows statistical software (version 20.0; SPSS, Inc., Chicago, IL). A p-value < 0.05 was considered significant in all analyses.

Results

Demographic characteristics and 6MWT results

Two hundred ninety-five healthy subjects were recruited for this study. Eight-one subjects were excluded from the study (foot sprain: n = 2; cardiac disease: n = 26; abnormal basal heart rate: n = 10; unstable hypertension: n = 30; pulmonary disease: n = 6 and cerebral disease: n = 17). Finally, 214 subjects (102 men and 112 women) completed the 6MWTs, with no subjects prematurely requiring rest during the test or terminating the test. Table 1 shows the characteristics of these subjects and the 6MWT results. Males were significantly taller and heavier than females in our study, and there was a difference in BMI between the sexes. The mean 6MWD for all the subjects was 523±56 m. The mean distance was 540±57 m for males and 508±51 m for females, and the difference was significant (p < 0.001). Age- and sex-stratified values of the 6MWD are summarized in Table 2. The mean 6MWD of the first and second test sessions were 508 ± 53 m and 517 ± 55 m, respectively. The reliability of two 6MWTs was good (ICC = 0.89). We were able to see a difference in heart rate between the sexes. By the end of the test, subjects' heart rates had reached our predicted maximum of approximately 65%.
Table 1
Characteristics and 6MWT results of the study subjects.

| Characteristic | Males (n=102) | Females (n=112) | p-value* | Total (n=214) |
|----------------|---------------|-----------------|----------|---------------|
| Age, years     | 56.9±10.23    | 57.9±10.22      | NS       | 57.5±10.21    |
| Height, cm     | 166.9±6.29    | 154.4±5.40      | <0.001   | 160.4±8.57    |
| Weight, kg     | 87.4±7.26     | 76.0±6.87       | <0.001   | 81.4±9.04     |
| BMI, kg/m²     | 31.3±1.28     | 31.9±1.75       | <0.05    | 31.6±1.57     |
| HR1, bpm       | 74.3±8.99     | 71.8±8.53       | <0.05    | 73.0±8.82     |
| HR2, bpm       | 106.4±11.87   | 104.4±11.53     | NS       | 105.4±11.71   |
| Borg           | 2.1±0.70      | 2.2±0.37        | NS       | 2.1±0.57      |
| 6MWD, m        | 539.6±57.18   | 508.2±51.36     | <0.001   | 523.2±56.33   |

Values are expressed as the mean ± SD. *p-value between males and females.

Table 2
Age and gender stratified norms of the 6MWD

| Age, years (n) | Males (n=102) | Females (n=112) | p-value* | Total (n=214) |
|----------------|---------------|-----------------|----------|---------------|
| 40-49 (n=62)   | 557.5±57.31   | 528.1±55.32     | <0.05    | 543.3±57.83   |
| 50-59 (n=63)   | 549.4±54.90   | 520.9±45.07     | <0.05    | 534.9±51.76   |
| 60-69 (n=56)   | 538.6±49.54   | 510.0±44.71     | <0.05    | 523.3±48.74   |
| 70-75 (n=33)   | 474.5±26.16   | 455.0±22.15     | <0.05    | 462.7±25.32   |

Values are expressed as the mean (range).

*P-value between males and females.

6MWD: six-minute walking distance.

Associations with the 6MWD

Table 3 shows the summary of the relationships between the 6MWD and the variables between the males and females. According to the univariate linear regression analysis, the variables (age, height and BMI) in Table 3 were obviously correlated with the 6MWD. The variables (age, height and BMI) were included in the stepwise multivariate regression analysis. Age and BMI were identified as independent factors that influenced the 6MWD and explained 31% and 27% of the variance in distance for the male and female groups, respectively (Table 4).
Table 3
Pearson correlations between the variables and the 6MWD.

| Variable | Males (n=102) | | | Females (n=112) | | |
|----------|--------------|---|---|----------------|---|---|
|          | r value      | p-value | r value | p-value | r value | p-value | |
| Age      | -0.397       | <0.001  | -0.442  | <0.001  | |
| Height   | 0.167        | <0.05   | 0.164   | <0.05   | |
| Weight   | -0.030       | NS      | -0.030  | NS      | |
| BMI      | -0.359       | <0.001  | -0.263  | <0.05   | |

6MWD: six-minute walking distance; r value: Pearson's correlation coefficient; BMI: body mass index.

Table 4
Results of stepwise multiple linear regression analysis of the independent variables that explained the 6MWD.

|          | Males | | | Females | | |
|----------|-------|---|---|----------|---|---|
|          | B     | SE | p-value | B     | SE | p-value | |
| Constant | 1261.349 | 122.118 | <0.001 | 923.596 | 81.351 | <0.001 |
| Age      | -2.509 | 0.465 | <0.001 | -2.342 | 0.409 | <0.001 |
| BMI      | -18.484 | 3.701 | <0.001 | -8.783 | 2.382 | <0.001 |
| R²       | 0.327 | 0.285 | | | |
| Change in R² | 0.314 | 0.272 | | | |

Abbreviations: B, unstandardized coefficients.

The reference equations for the 6MWD were as follows:

Comparison with published regression equations

Table 5 shows a comparison between the measured 6MWD in our subjects and the predicted 6MWD by the previous reference equations (17-20) for the same age ranges. However, these reference equations reported in previous studies cannot accurately predict the 6MWD in our subjects, and there was a significant difference between the measured 6MWD and predicted 6MWD for the same age range (p<0.05). The 6MWD in our subjects was overestimated by the reference equations derived from previous studies.
Table 5
Measured 6MWD and predicted 6MWD for the same age range based on the equations reported in previous studies.

| Study                              | Measured (m) | Predicted (m) | Measured-predicted (m) |
|------------------------------------|--------------|---------------|------------------------|
| Ben Saad H et al[36]               | 523.2±56.33  | 559.9±101.93  | -72.7±90.03*           |
| Iwama AM et al.[38]                | 523.2±56.33  | 545.7±36.88   | -22.5±51.78*           |
| Capodaglio et al.[29]              | 539.7±54.77  | 601.2±30.20   | -61.5±51.75*           |
| Camarri B et al. [37]              | 508.1±49.37  | 615.8±42.54   | -143.7±48.52*          |

*p<0.05 according Student’s t-test.

Discussion
To the best of our knowledge, this is the first study to describe 6MWD in obese Chinese subjects older than 40 years. As shown in our study, there was a significant difference in the walking distance samples for men and women. Men tend to walk longer distances than women, probably due to their higher muscle mass and greater athletic ability.

There was a correlation between the 6MWD and independent variables in both men and women (Figure 1). We can see that age and BMI are negatively correlated with the 6MWD in our study. This probably is related to the loss of muscle mass as we age and the decrease in oxygen intake. Obese subjects have a certain complications with the increase in BMI, which is usually manifested as activity disorders caused by heart and breathing limitations(23, 24), and weakened skeletal muscle strength is also one of the main causes of disability(25, 26). Other possible reasons include skin friction caused by fat deposition in the thighs, increased plantar pressure, and physical discomfort caused by exercise for people with a BMI that is higher than normal(9, 27-29). We can see that height and walking distance are positively correlated in our study. This could be because, in general, taller individuals with larger strides cover more walking distance in the same amount of time than others. However, the target of our study was obese subjects, and BMI was more meaningful than height for the 6MWD, so height was not included in the final regression equation. From this study, we observed that the resting heart rate of male subjects was lower than that of female subjects. Previous studies have shown that the difference in heart rate is correlated with sex, and the resting heart rate of men is lower than that of women(30). This may be because men and women have different abilities to regulate the baroreflex heart rate, and oestrogen contributes to the ability to regulate the baroreflex heart rate in people(31).

Fig. 1. The relationship between the 6MWD and age, height and BMI for females and males.
In this study, categorical variables (age, height and BMI) were used for stepwise multiple regression analysis. Age and height were identified as independent factors that influenced the 6MWD, and they explained 31% and 27% of the variance in walking distance for the male and female groups, respectively.

After applying mathematical analysis, such as the theory proposed by Hulens et al(32), we found that other factors that correlate with walking distance in six minutes would certainly benefit the prediction equations. These factors (heart rate, blood pressure, muscle strength and lifestyle factors) also play an important role in predicting 6MWD, but they exist only in the equations and are impractical for clinical use.

By measuring the walking distance performance on 2 occasions, we can see that the mean 6MWD during the second test period was longer than the mean 6MWD during the first test period. This finding is the same as the previous findings for the 6MWT(5, 33). The reason why the distance can be increased is probably related to overcoming negative emotions, improving coordination and finding an appropriate stride distance. Although it was found that the performance of walking distance in the second 6MWT was higher than that of the first test in our study, the reliability of the two 6MWTs was good (ICC = 0.89). Previous studies have also proven that the two 6MWTs are reliable(33), which is consistent with our research results. The Bland-Altman chart shows the mean difference between the first and second 6MWD (Figure 2). Seventeen participants had error values outside the 95% confidence interval (CI), and seven participants showed an increase in the second 6MWD, which might be due to familiarity with the 6MWT. Ten participants showed shorter walking distances in the second 6MWT, which might be due to greater fatigue during the second test due to better performance in the first 6MWT.

**Fig. 2** Bland-Altman plot of the results for performance in the first and second 6MWTs.

These reference equations from previous studies (Ben et al. (18), Iwama et al.(19), Capodaglio et al(17). and Camarri et al.(20)) cannot accurately estimate the distance walked during the 6MWT when used with obese subjects. Judging from the results of our data, the walking distance of obese individuals in our sample is significantly different from the estimated distance of these reference equations mentioned above. These differences were often due to the test protocol, anthropometric factors, ethnic background and demographic differences among the participants. In the studies by Ben et al. (18), Iwama et al.(19) and Camarri et al.(20), healthy subjects were primarily recruited, while obese subjects accounted for only a small percentage of the study population. Even if the workload was small, the walking distance in these studies was higher than the walking distance in our sample. Although both study samples consisted of obese people, our results are not consistent with those provided by Capodaglio et al.(17). The difference may be due to the higher average age (20 years older) and the lower workload of the subjects in the study. In a sense, age represents a proxy of disability, which obviously affects the performance of subjects during the 6MWT. In our sample, 42% of subjects were over 60 years old, and 15% were 70 years old, whereas in the study by Capodaglio et al.(17), age ranged from 20 to 60 years. Even if age was taken into account as an explanatory variable(17), this equation has been verified in samples younger than 60
years old, thus reducing the predictive validity for elderly subjects. In addition to the daily physical activity of the participants, their mood and psychological factors may influence the 6MWD (34).

In our study, there are also some limitations. First, although the sample size of our study was relatively large, the sample was one of convenience, and relatively few subjects were over the age of 70 in the study. Second, we did not recruit obese subjects under 40 years of age. A large multicentre study is needed to address these limitations.

In summary, the study was the first to describe the 6MWD in Chinese obese subjects and to propose predictive equations. These established equations can contribute to improving the assessment of Chinese obese patients with diseases that affect their exercise capacity.

**What is already known on this subject?**

The 6MWT is a commonly used clinical assessment of exercise capacity in patients with cardiopulmonary disease. Although, the reference equations of the 6MWD for Chinese healthy subjects have been established, some studies have showed that the reference equations for the walking distance derived mainly from healthy, normal-weight people are not suitable for obese subjects. However, there is a lack of standard reference equations for the 6MWD in Chinese obese subjects.

**What this study adds?**

The study was the first to describe the 6MWD in Chinese obese subjects and to propose predictive equations. These established equations can contribute to improving the assessment of Chinese obese patients with diseases that affect their exercise capacity.

**Abbreviations**

6MWT, six-minute walk test; 6MWD, six-minute walk distance; BMI, body mass index; HR, heart rate; SpO₂, oxygen saturation; SBP, systolic blood pressure; DBP, diastolic blood pressure; ICC, intra-class correlation; SD, standard deviation; SPSS, Statistical Package for the Social Sciences.

**Declarations**

**Ethical approval** The study was approved by the ethics committee of Wenzhou People’s Hospital (approval number: 2013.10).

**Informed consent** All individuals were fully informed about the study and consented their participation by signing the consent forms.

**Competing interests**

The authors declare that they have no competing interests.
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Authors’ Contributions

HZ, JZ, YYZ, ZBW and XSC conceived and designed the experiments. HZ, JZ, YYZ, ZBW and XSC performed the experiments and wrote the paper. HZ, JZ, YYZ, ZBW, XSC, JYP, HZY and LC analyzed the data. All authors have read and approved the final manuscript.

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Figures

Figure 1

The relationship between the 6MWD and age, height and BMI for females and males.
Figure 2

Bland-Altman plot of the results for performance in the first and second 6MWTs.