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Original Article

Development of a reference equation for maximal exercise capacity in normal Indian subjects using cardiopulmonary exercise testing

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ABSTRACT

Objectives: Cardiopulmonary exercise testing (CPET) is an integrative assessment of multiple interdependent variables contributing to exercise response. CPET parameters such as maximum or peak oxygen uptake (VO2max/peak) are used to estimate this response. VO2max/peak varies with physiological predictors such as age, sex, body mass index (BMI), and activity level. The existing normative values for Indian subjects have, thus, far been adapted from Western populations who have a different body habitus in terms of these physiological predictors. We aimed to determine the relation and a prediction equation of these variables with VO_{2peak}.

Materials and Method: One hundred and twenty-one healthy subjects underwent CPET on a treadmill (Cortex Metalyzer) in a tertiary care hospital and VO_{2peak} was calculated through Metasoft software. Statistical analysis: Student's *t*-test and one-way analysis of variance (ANOVA) were used for calculating the between-group difference. Logistic regression with univariate and multivariate ANOVA was used for computing the reference equation.

Results: Mean VO_{2peak} (ml/min/kg) was 29.9 ± 7.7. It was higher for males (32.81 ± 7.9 vs. 26.79 ± 6.1 [$P < 0.001$]) and active individuals (32.8 ± 7 vs. 26.1 ± 6.9 [$P < 0.001$]). Higher values were observed in younger and non-obese population ($P < 0.001$). Regression coefficient (r2) was 0.44 and 0.36 for male and female, respectively. Reference equation was then calculated for males and females using the r2 value.

Conclusion: VO_{2peak} was higher in males and active individuals, it declined with increasing age and BMI. The values obtained were much lower than the Western population, therefore stressing the need for the development of our own set of reference equations.

Keywords: VO2max/peak, Cardiopulmonary exercise testing, Physiological variables

INTRODUCTION

The maximum level to which an individual can exert is dependent on multiple interdependent variables. Cardiopulmonary exercise testing (CPET) is an integrative assessment of these variables which result in an exercise response, involving the pulmonary, cardiac, haematopoietic, skeletal muscle and neurophysiological systems which are not adequately assessed when measured alone.[1] The response to incremental exercise on CPET can be estimated by various functional indices such as the maximum or peak oxygen uptake (VO2max/peak) and anaerobic threshold (VT). Other indices such as ventilatory efficiency expressed as minute ventilation (V'E), which changes as a function of pulmonary carbon dioxide output (V'E-V'CO2 slope).[2] The exercise tolerance as measured by these functional indices is dependent on various physical parameters such as age, gender, body mass index (BMI), and physical activity level. A strong correlation has been demonstrated between age and gender.[3] The reference values for these functional indices have been established with respect to the above-mentioned physical parameters.[1-3] However, it has several limitations with respect to sample size, the population selected and the protocol used, and all these studies have been performed in the Western population.[2-4] Majority of the exercise testing in these studies has been conducted on a cycle ergometer[5] in which the absolute values of VO2max or peak are 5–11% lower than that of treadmill exercise testing.[6] Thus, no study to date has evolved to overcome these limitations in Indian subjects and the search for optimal reference value is still ongoing. The association between the functional indices of exercise testing and the different baseline physical characteristics in an Indian population is still unexplored and there are very few studies to date that have tried to investigate the normal values for VO2max/peak and other indices in our population.[7,8] In this study, we aimed to correlate the demographic variables (age and gender), anthropometric parameters BMI and physical activity level with the values of VO2max/peak for healthy subjects using treadmill exercise testing. We, then, compared the values obtained for our normal population with the data available for the Western population and then attempted to derive our own set of reference equations.

MATERIALS AND METHODS

Healthy individuals >18 years with no complaints of dyspnoea, cough, chest pain, or leg cramps, who were working or visiting St. John's National Academy of Health Sciences, were recruited for the study. Informed consent was obtained from the participants before recruitment. They were excluded if they were smokers, had ongoing or had a prior history of chronic lung, liver, or heart disease if they had any history of peripheral vascular disease, neuromuscular disease, or malignancy. Pregnant females and patients with a psychiatric disorder in whom comprehension would be challenging were also excluded from the study. The data were, then, collected on a predefined clinical pro forma consisting of demographic profile, anthropometric measurements, history of smoking, presence of any current or past cardiorespiratory symptoms, and presence of any comorbidities. The level of physical activity was assessed with general practice physical activity index questionnaire.[9] The underlying respiratory function was assessed by performing spirometry before the CPET.

Subjects with normal values of lung function (80% and above of FEV_1) and no abnormality detected in the clinical pro forma were recruited to undergo CPET. Written informed consent was taken from all the subjects, they were, then, verbally explained about the exercise test and a leaflet containing all the information about CPET was given to them.

CPET was performed treadmill (on Cortex Metalyzer 3B-R3™, FW version 1.02.96 and MSS version 5.3.0 SR1) as follows:

The study subject was fitted with an ECG belt and an oronasal mask with sensors for monitoring the CO_2, O_2, and the total amount of expired gases. The mask fitting was checked for any air leak. He/she was, then, given a rest period of 3 min while standing on the treadmill, following which the test was started with speed and inclination increasing every 3 min as per Modified Bruce protocol. The individual was made to exert until they started complaining of any unbearable leg pain, leg cramps, breathlessness, chest pain, giddiness, and syncope, if they did not wish to continue anymore, if there were changes in the ECG recordings seen on the monitor or if SpO_2 decreases to <85%. At the end of the test, the subjects were, then, asked to continue walking at their own pace on the treadmill, if possible, for 3 min with the mask and belt on, with continuous monitoring of vital statistics. Thereafter, they were seated on a chair in a comfortable position and the mask and belt were removed. The VO_2 peak was, then, calculated with the Metasoft™ software and analysed with regression equations for determining the relationship with the physiological variables. The study protocol was approved by the ethics committee of the institution.

Statistical analysis

The sample size was calculated based on a previous study conducted for the generation of reference value[7] where the estimated mean of $VO_{2peak/max}$ was 31 ± 4 ml/kg/min.

The sample size was based on the mean estimation as described by Hozo *et al*.[10]

The between-group difference for VO_{2peak} and other functional indices with respect to gender and activity was computed by Student's *t*-test. The difference between different age bands and different BMI categories was estimated by one-way analysis of variance (ANOVA) with Bonferroni correction. A logistic regression analysis with univariate and multivariate ANOVA was done to compute the strength of association of the independent variables with respect to VO_{2peak} and also to compute the reference values for VO_{2peak}.

RESULTS

A total of 121 volunteers participated in the study. The descriptive characteristics are displayed in [Table 1].

The population was evenly distributed among different age groups. The percentage of males and active individuals was higher. Sixty-four individuals (52%) were in the overweight category.

The VO_{2peak} was, then, measured for the entire population. The results of VO_{2peak} are displayed in [Table 2].

The maximal oxygen uptake attained at maximal exercise capacity declined with increasing age. A significant decrease in VO_{2peak} was noted between 18 and 25 years (35.15 ± 7.7 ml/min/kg) and the age groups of >36 years (i.e., 36–45 years [28.58 ± 6.5 ml/min/kg] and >45 years [25.13 ± 6.8 ml/min/kg]). A significant decline was also seen between age groups of 26–35 years (31.97 ± 6.5 ml/min/kg) and >45 years (25.13 ± 6.8 ml/min/kg). A decreasing trend was also noted with increasing weight and a significant decline was noted in the obese population (BMI >25 kg/m^2) in comparison with the rest of the BMI categories. There was no significant difference among underweight, normal, or overweight groups.

Table 1: Descriptive characteristics of the study subjects.

Variables	Frequency (percentage)
Age group (years)	
18–25	26 (21.5)
26–35	31 (25.6)
36–45	33 (27.3)
>45	31 (25.6)
Gender	
Male	64 (52.9)
Female	57 (47.1)
BMI categories (kg/m^2)	
<18.5	11 (9.1)
18.5–22.9	46 (38.0)
23–24.9	32 (26.4)
>25	32 (26.4)
Physical activity level	
Active	70 (57.9)
Inactive	51 (42.1)

Table 2: Mean VO_{2peak} values for different age groups, gender, BMI and physical activity level.

Variables	VO_{2peak} (ml/min/kg)	p value
Overall population	29.9±7.7	
Age groups (years)		<0.001
18–25	35.15±7.7	
26–35	31.97±6.5	
36–45	28.58±6.5	
>45	25.13±6.8	
Gender		<0.001
Male	32.81±7.9	
Female	26.79±6.1	
BMI categories (kg/m^2)		<0.001
<18.5	31.45±7.6	
18.5–22.9	32.22±6.8	
23–24.9	31.06±7.5	
>25	25.16±7.3	
Physical activity level		<0.001
Active	32.8±7	
Inactive	26.1±6.9	

The regression coefficient (r^2 value) for the whole population was 0.46. When measured separately for the male and female population, the r^2 value calculated was 0.44 and 0.36, respectively. The overall difference ranged from 0 to 15% in males and 3–35% in females [Table 3].

The prediction equations [Table 4] for VO_{2peak} were, then, calculated through regression analysis for the male and female populations.

We compared the $VO2_{peak}$ of our study population with data from the FRIEND registry[11] and studies conducted in the Norwegian population,[4,12] which is the latest large data available for the estimation of VO_{2peak} in the healthy population [Table 5]. Due to the low sample size in each age band, we combined both genders for analysis. The VO_{2peak} of the whole population for a given age group in our study was lower than the VO_{2peak} of even the female population for that given age group of the other three studies.

DISCUSSION

Various direct and indirect methods are used to quantify the exercise capacity of an individual by measuring different functional indices of which $VO_{2max/peak}$ remains the main component. CPET is the gold standard for measuring this $VO_{2max/peak}$, using respiratory gas exchange analysis.[13]

It is known that the maximal exercise capacity of an individual is dependent on multiple demographic and anthropometric parameters, along with the training status.[1,13] Our study is one of the few in India to correlate these demographic and

Table 3: Comparison of regression coefficient for VO_{2peak} of various studies with the present study. r^2: Regression coefficient.

Studies	r^2	
	Male	Female
Current study	0.447	0.365
John *et al.*[8]	0.511	0.656
Jones *et al.*[5]	0.29	0.247
Wasserman *et al.*[17]	0.443	0.343
Fairbarn *et al.*[18]	0.453	0.351
Hansen *et al.*[4]	0.481	0.559

Table 4: Reference equation for $VO_{2peak/max}$ for healthy male and female population.

Gender	Reference equation for VO_{2peak} (ml/kg/min)
Male	[54.85–0.45 (age)–1.52 (BMI)–0.9 (physical activity level*)]×1000/weight
Female	[42.7–0.16 (age)–2.24 (BMI)–3.02 (physical activity level*)]×1000/weight
	[*physical activity level: Active=0 and Inactive=1]; weight in kilograms

Table 5: Comparison of $VO_{2peak/max}$ (ml/kg/min) of recent studies conducted on a treadmill**.**

Studies	20–39 years	30–39 years	40–49 years	50–59 years
Friend[10]				
Male	47.6±11.3	43.0±9.9	38.8±9.6	33.8±9.1
Female	37.6±10.2	30.9±8.0	27.9±7.7	24.2±6.1
Loe *et al.*[11]				
Male	54.4±8.4	49.1±7.5	47.2±7.7	42.6±7.4
Female	43±7.7	40.0±6.8	38.4±6.9	34.4±5.7
Evardsen *et al.*[12]				
Male	48.9±9.6	46.2±8.5	42.7±9.3	36.8±6.6
Female	40.3±7.1	37.6±7.5	33±6.4	30.4±5.1
Current study				
(M and F combined)	34.7±6.2	29.09±7.7	27.73±6.7	23.62±6.4

M: Male, F: Female

anthropometric variables with the maximal exercise capacity by direct measurement of $VO_{2max/peak}$.

For analysis, we stratified the participating individuals into four age bands. The last age band was open from 45 years and above. The maximum age of our population, 54 years, is lower than that of other studies determining the reference equations.[2,3,6,11] The VO_{2peak} decreased with advancing age with a mean difference of 3.34, which corresponded to a 9–11% decline per decade. These results concur with results obtained in the SHIP study[2] and data from the FRIEND registry, which have shown a decline in $VO2_{max}$ with increasing age and have also demonstrated a decline of 10% in VO_{2max} for every decade.[11,14] However, none of these studies determined the age difference at which the decrease in VO_{2max} becomes significant. Our study determined a statistically significant decline of VO_{2max} in subjects of >45 years as compared to the younger population (18–35 years).

The effect of gender on the maximal exercise capacity was similar to other studies with VO_{2peak} being significantly higher in males and active individuals.[6] These results reflect the previous studies that have documented the difference in maximal exercise capacity between sedentary and active individuals.[1,6] The previous studies focusing on the activity level have defined an active individual as those who exercise 3 times a week for 30 min and have not taken any scoring system to objectively assess the level of activity.[6] On the contrary, we have used general practice physical activity index questionnaire,[9] to objectively assess the level of physical activity.

The direct measurement of maximal exercise capacity in obese individuals has been conducted by only a few authors, due to the increased risk of complications and a higher motivation required to reach the maximum exhaustion.[15] The indirect assessment of maximal exercise capacity through the prediction equation for the obese population shows a discrepancy in the estimation of VO_{2peak} when measured directly.[15,16] The cutoff BMI from where the difference in VO_{2peak} starts to show a significant decline has not been explored to a large extent. In our study population, 64 individuals were overweight and 32 were categorised as obese. The mean VO_{2peak} decreased with increasing BMI and a significant difference was observed between the obese group and the non-obese group. This finding stresses the need for future studies to be conducted specifically on the obese population.

The overall regression coefficient (r^2) was 0.42, while r^2 for males and females was 0.44 and 0.36, respectively. These values are similar to those observed in the previous studies, which have attempted at deriving a reference equation for VO_{2peak} and other measured parameters such as workload and heart rate.[5,8,17-19] The values obtained in our study were lower than that observed in the study conducted by John *et al.* (r^2: male – 0.51 and female – 0.65)[8] who have attempted in deriving the reference value for the Indian population. One possible reason for this difference may lie in the selection of the study population. Although our study recruited hospital staff and caregivers of patients similar to the study by John *et al.*,[8] the total number of females (n = 57) was higher in our study as compared to the study by John *et al* (n = 19).

The ATS/ACCP statement on CPET specifically mentions the need to derive different reference equations for a different population.[1] Apart from knowing the absolute value of VO_{2peak} for an individual, it is also important to know how he or she fares with the rest of the healthy population. This helps in estimating the risk for cardiorespiratory mortality and formulating an objective exercise plan.[11] At present, the reference values used for comparison in our population are derived from data of the Western population. This can lead to over-or under-estimation of the exercise capacity of the population which we label as 'healthy.' There are only a few studies conducted in India that have shown a significant difference in the directly measured value of VO_{2peak} in comparison to the Western population.[7,8] John *et al.*[8] have attempted deriving a reference equation for healthy Indian subjects but their study has few limitations as discussed before. The reference equation derived in our study is different from that of the other studies,[1,5,8,17-19] as, unlike others, we found BMI to be better correlated with VO_{2peak} than weight and height alone. We, also, included physical activity level as a predictor for maximal exercise capacity in the equation which has been unexplored thus far.

In a systemic review by Paap and Takken,[13] the majority of the studies fulfilling the eligibility criteria were the ones conducted on a cycle ergometer. The VO_{2peak} attained is 10–15% higher when exercising on a treadmill.[1,6,11,14] Therefore, substituting the normal values obtained from a cycle ergometer for a treadmill protocol might underestimate the maximal exercise capacity. We have computed our data on a treadmill protocol, but unfortunately, there are no other data for comparison of absolute values of VO_{2peak} from the Indian subcontinent which has been conducted on the treadmill. The study by John *et al*., though, conducted on a treadmill had a lower number of females and had only compared the r^2 value.[8] Since individual numbers were low when grouped as male and female in our study, in comparison to the other studies (data from the FRIEND registry[14] and the studies conducted in the Norwegian population[4,12]), we compared the mean of our whole population in a particular age band with the age specified subgroups of the other three studies. When compared with their normative values, results obtained in our population were lower than the normal VO_{2peak} for both genders and across all age bands [Table 5]. The possible reason for it is the different ethnicity in comparison to the studies conducted in the west. These results, further, stress the importance of region-specific normative value.

There are certain limitations to this study. The in-hospital selection of participants makes the sample less representative of the community. The classification of physical activity level was based on a self-administered questionnaire in which there is a possibility of bias and misclassification and the results from our study cannot be applied to individuals more than 55 years of age as their number is very less in our sample. Similarly, our study does not have enough participants of both sexes to make male- and female-specific determinations. However, the strength lies in the fact that it is one of the few studies in India to analyse the relationship of the baseline physiological parameters with changes in VO_{2peak} and has attempted in deriving region-specific reference values. It is one of the few studies to be conducted on treadmill-based CPET equipment. Unlike the previous studies, where obese individuals were excluded while estimating the normal value for $VO_{2\ peak}$, our study has a fair number of obese and overweight individuals. The individuals recruited were mostly from the southern part of the country, who may have different body habitus and activity levels from the people in northern parts of India. Due to the vastly diversified population of our country, regional data from each region are required to cater to their local population. Larger studies compiling all these regional data will, then, be useful for the determination of reference equations for our population.

CONCLUSION

The maximal exercise capacity of an individual is dependent on various physiological characteristics such as age, gender, BMI, and physical activity level. The strongest predictor among them was gender and age. The mean value of the $VO_{2\ peak}$ of our healthy population is significantly lower than that of the Western population. Therefore, we need to develop reference equations for our population-based on studies involving a larger sample size.

Declaration of the patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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