Original Article

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TANAFFOS

Predicted Values of Cardiopulmonary Exercise Testing in Healthy Individuals (A Pilot Study)

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Background: Cardiopulmonary exercise testing evaluates the ability of one's cardiovascular and respiratory system in maximal exercise. This was a descriptive cross-sectional pilot study conducted at Masih Daneshvari Hospital in order to determine predicted values of cardiopulmonary exercise testing in individuals with normal physical activity patterns.
Materials and Methods: Thirty four individuals (14 women, 20 men) between 18-57 years of age were chosen using simple sampling method and evaluated with an incremental progressive cycle-ergometer test to a symptom-limited maximal tolerable work load. Subjects with a history of ischemic heart disease, pulmonary disease or neuromuscular disease were excluded from the study. Smokers were included but we made sure that all subjects had normal FEV1 and FEV1/FVC.
This study aimed to compare measured values of VO_2, VCO_2, VO_2/Kg, RER, O_2pulse, HRR, HR, Load, Ant, BF, BR, VE, $EQCO_2$, and EQO_2 with previously published predicted values.
Results: We found that our obtained values for VO_2 max, HRR max and HR max were different from standard tables but such difference was not observed for other understudy variables. Multiple linear regression analysis was done for height, weight and age (due to the small number of samples, no difference was detected between males and females). VO_2 max and load max had reverse correlation with age and direct correlation with weight and height ($P<0.05$) but the greatest correlation was observed for height.
Conclusion: Due to the small number of samples and poor correlations it was not possible to do regression analysis for other variables. In the next study with a larger sample size predicted values for all variables will be calculated.
If the future study also indicates a significant difference between the predicted values and the reference values, we will need standard tables made specifically for our own country, Iran.

Key words: Cardiopulmonary exercise test, Ergospirometry, Maximal exercise capacity

INTRODUCTION

Oxygen transfer for supporting the energy needs of muscle cells (especially the heart muscles) and excretion of CO_2 as a by-product of metabolism have utmost importance during exercise.

Cardiopulmonary exercise testing (CPET) is used to generally evaluate the response of various organs and cardiovascular, pulmonary, circulatory, neural and musculoskeletal systems to maximal exercise. Assessment of the function of each of the mentioned systems alone cannot yield such result.

By using this dynamic and relatively non-invasive method we can evaluate one's physiologic and pathologic response to maximal exercise.

CPET can provide so much information while a simple cardiac exercise test can only determine the presence or absence of myocardial ischemia (1).

Indications of CPET include evaluation of the exercise capacity and reasons why exercise is not tolerated (2, 3), unexplained dyspnea (4-7), evaluation of patients with cardiovascular disease (8-10), assessment of patients with respiratory diseases (11), pre-operative evaluations (12), and pulmonary rehabilitation (13-16).

CPET has long been the subject of interest to many researchers. For example, in 1972 Bruce et al. evaluated the maximal oxygen intake among males and females and predicted the mean normal values for healthy individuals based on their age, sex and physical activity using regression equations (17).

In 1975 Drinkwater et al. designed a study to show how age and physical activity patterns affect women's response to maximal exercise (18).

Some other studies were conducted by Jones et al. in 1985 (19) and Blackie et al, in 1989 (20) and 1994 (21) and prediction equations were calculated for different variables using linear regression.

Considering the high applications of CPET and lack of a study determining reference values and also easy accessibility of CPET in Masih Daneshvari Hospital we decided to perform such a study in this center.

MATERIALS AND METHODS

Study design:

This was a descriptive cross-sectional study conducted as a pilot study for a larger one evaluating a larger population of healthy individuals.

A total of 34 subjects (14 women and 20 men) in the age range of 18 to 57 years were selected using simple sampling method.

The general goal of the study was to determine the predicted values for ergospirometry test in healthy individuals with normal physical activity patterns presenting to Masih Daneshvari Hospital. The specific goals were to determine the normal values of load, HR, HRR, O_2 pulse, VO_2, VO_2/kg, VCO_2, RER, BF, AT, EQO_2, $EQCO_2$, VE and BR in these cases during maximal exercise. The hypothesis to be proved was that the normal ergospirometry test values measured in normal healthy Iranians were in accord with international reference values.

Protocol:

Subjects were provided with instructions before the study through which they were informed about the necessary preparations required for exercise testing. For example, subjects should not have intense physical activity during the last 4 hours before testing and should not eat or drink caffeinated beverages or smoke in the last 2 hours. A history was taken from all subjects and a physical examination was done for them. Smokers underwent pulmonary function test (PFT) and EKG was performed for all subjects over the age of 55 yrs.

Data were recorded in the prepared questionnaires. Subjects were well informed about the test and a written consent was obtained from them.

Clinical and functional evaluations:

Upon admission, a history was taken from all subjects and presence of any risk factors for cardiac, respiratory or neuromuscular diseases was evaluated and noted in the questionnaire. All subjects underwent physical examination and height and weight measurement, cardiac, pulmonary, neuromuscular, skin and abdominal examinations were performed. EKG was performed for all subjects over the age of 55 yrs and PFT was conducted for smokers. Ergospirometry exercise testing was then performed for all subjects.

Those who had a normal history and physical examination and if smoking, had FEV1 over 80% and normal FEV1/FVC were included in the study (understudy subjects all had normal physical activity patterns like walking and did not have a sedentary life style).

Subjects who had a positive history, their physical examination showed any sign of cardiac, respiratory, or neuromuscular diseases, developed arrhythmia or hypotension or their EKG showed ischemic findings during exercise testing under the supervision of a physician and also those over 55 yrs with abnormal EKG were excluded from the study.

CPET was performed on a cycle ergometer with incremental exercise test method and included the following phases:

1) 2 minutes of resting
2) 3 minutes exercise below the actual level of work load and then reaching up to 60 cycles per minute
3) Incremental phase
4) 4 minutes of recovery phase

The exercise work load increases constantly (15-25 W/min in women and 25-30 W/min in men). Therefore, each test takes about 8 to 12 minutes to accomplish.

The criteria for reaching maximum capacity were one or more of the followings:

1) Reaching a plateau in VO_2
2) Maximum heart rate more than 90% of the predicted value for that age (age-220)
3) RER more than 1/15 (although RER values are not exactly indicative of maximum capacity)

Data were automatically processed using standard formula (based on the reference values) and were shown as descriptive figures.

The amount of variables including VO_2 (L/min), VCO_2(L/min), VO_2/kg (ml/min/kg), load (W/min), HR (b/min), HRR (b/min), O_2 pulse (ml/beat), RER and VCO_2 (L/min), EQO_2, $EQCO_2$, VE (L/min), BR (%), BF (L/min) and Ant were calculated.

RESULTS

Analysis of this study was conducted in 2 phases:

1) Descriptive phase: in this phase, mean and standard deviations for age, sex, height, weight, HR, BMI and BP (systolic and diastolic)(Tables 1 and 2) and variables obtained from CPET at maximal exercise were calculated (Table 3) and compared with reference values. Also, the obtained data were compared between males and females using t test (Tables 4, 5 and 6).

Table 1. Demographic and anthropometric characteristics of understudy subjects.

Variables	5th percentile	10th percentile	25th percentile	Median	75th percentile	90th percentile	95th percentile	Standard deviation
Age (yrs)	20	23	30	36	47	54	56	11.5
Height (cm)	152	157	165	171	178	184	185	9
Weight (kg)	56	60	66	75	84	101	105	15
BMI (kg/m²)	20	22	24	25	29	31	32	17

Table 2. Clinical characteristics of understudy subjects.

Variables	5th percentile	10th percentile	25th percentile	Median	75th percentile	90th percentile	95th percentile	Standard deviation
HR(b/min) At rest	69	70	73	78	80	85	85	5
SBP(mmHg)	110	110	119	120	130	130	130	6.7
DBP(mmHg)	55	58	60	60	65	70	85	6.5

Table 3. Amount of CPET variables for understudy subjects.

Variables	5th percentile	10th percentile	25th percentile	Median	75th percentile	90th percentile	95th percentile	Standard deviation
Load max(W/min)	95	108	140	180	211	250	258	46
HR max %(b/min)	75	78	83	91	95	98	102	7.5
HRR max (b/min)	0	3.5	9.25	16	30	41	46	14
O_2pulse max%(ml/b)	64	78.5	86	94	100	117	137	18.5
Vo_2max%(ml/min/kg)	59	67.5	76.5	90	99	110	123	17
VCo_2 max%(l/min)	66	72.5	80	96.5	109	120	138	20
RER .max	1.05	1.07	1.13	1.20	1.24	1.30	1.34	0.08
EQO_2.max	24	27	30.5	36	41	47	51	7
$EQCO_2$.max	23	25	27	30	33	36	40	4.5
VE.max (L/min)	43	49	59	79	95	114	123	23
Ant.max%	44	46	56	65	74	82.5	89	12.5
BR.max%	13	19	29	47	53.5	59.5	62	14.5
VO_2max% (l/min)	60	67.5	75	89.5	99	109	121.5	17
BF.max(l/min)	22	23	33	38	43	48.5	53	8.5

Table 4. Comparison of anthropometric and demographic characteristics of understudy men and women,

Variables	Women (n=14)	Men (n=20)
Age (yrs)	42±13	35±10
Height (cm)	164±7	176±6
Weight (kg)	65±7	85±14
BMI (kg/m²)	25±3.5	27±3

Table 5. Comparison of clinical characteristics between understudy males and females.

Variables	Women (n=14)	Men (n=20)
Resting HR (b/min)	77±5	76±6
SBP (mmHg)	121±7	122±7
DBP(mmHg)	63±9	62±5

Table 6. Comparison of the amount of CPET variables between males and females in our study.

Variables	Women (n=14)	Men (n=20)
Load max (w/min)	138 ± 33	205 ± 33
HR Max% (b/min)	89 ± 9	89±7
HRR Max (b/min)	18.5±16	20±13
O_2 pulse max% (ml/b)	100±24	92±13
VO_2/kg max%(ml/min/kg)	95±20	85±13
EQO_2.max	38±8.5	38±6
VCO_2 max% (L/min)	100±25	93±17
$EQCO_2$.max	32±5	29±3.5
RER.max	1.19±0.1	1.19±0.06
VE.max(L/min)	63.5±18	88±21
Ant.max%	67±15	63±11
BR.max%	40±15	44±14
Vo_2 max%(L.min)	95±20	84.5±13
BF.max (L/min)	39±8	36±9

2) Multiple linear regression was performed to determine normal values for each variable. The results in this regard are presented in Table 7 and Figures 1 to 6.

This study was conducted aiming at evaluation of cardiovascular and pulmonary system responses during an incremental progressive cycle ergometer test in healthy subjects with normal physical activity patterns and the following results were obtained:

The mean ±SD for VO2max% was 89.5%±17 L/min (95%±20 in women and 84.5%±13 in men). The standard reference for this variable is 84%.

The mean HR max was 91%±7.5 b/min (89%±9 b/min in women and 89%±7 b/min in men) which was significantly different than the suggested reference rate of over 90% as normal.

The mean HRR max was 16±14 b/min (18.5±16 b/min in women and 20±13 b/min in men) which was different that the standard reference value of below 15.

The mean pulse O2 max was 94%±18.5 ml/b (100%±24 in women and 92%±13 in men). The reference normal value is 80%.

Table 7. VO2max (L/min) and load (W/min) during cycle ergometry (linear prediction equations).

Variables	Age	Weight	Length	R^2
VO_2	-0.28 (p=0.052)	0.024 (p<0.001)	-	0.36
	-0.137 (p=0.36)	-	0.044 (P<0.001)	0.44
Load	-0.0157(P=0.281)	-	3.6 (p<0.001)	0.49
	-1.2 (p<0.05)	1.8(p<0.001)	-	0.53

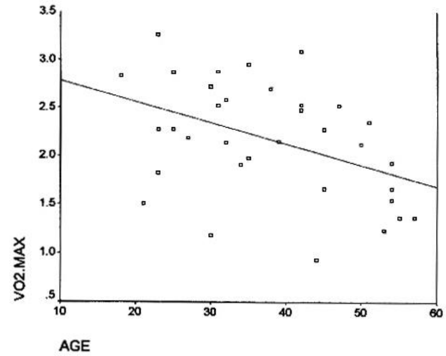

Figure 1. The correlation of VO2max and age

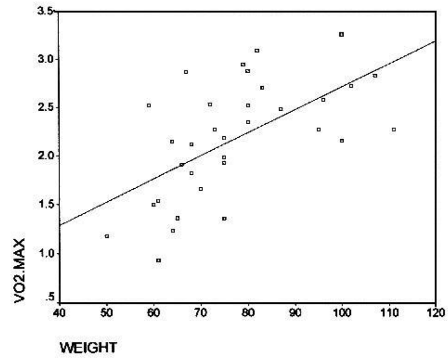

Figure 2. The correlation of VO2max and weight

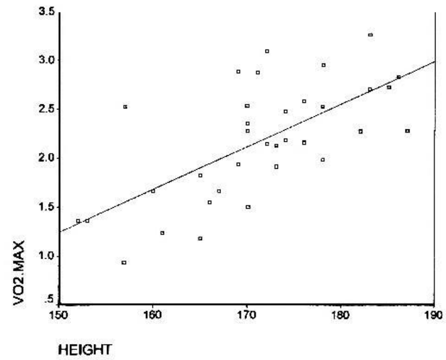

Figure 3. The correlation of VO2max and height

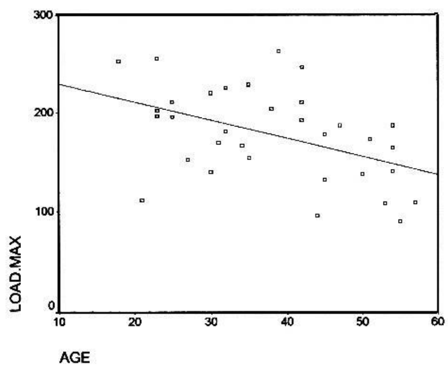

Figure 4. The correlation of load max and age

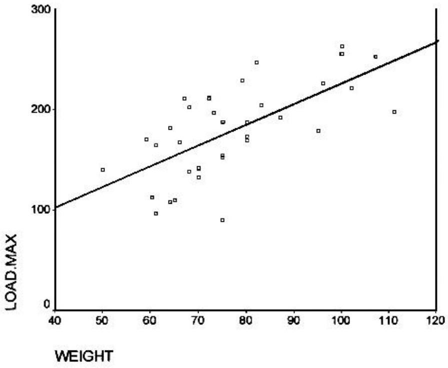

Figure 5. The correlation of load max and weight

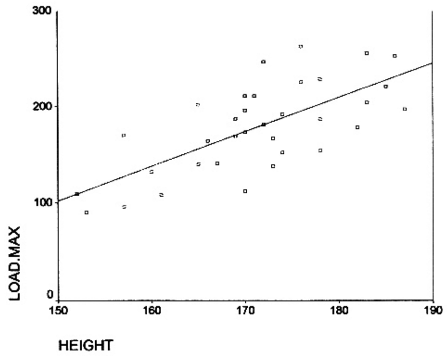

Figure 6. The correlation of load max and height

The mean VR or BR max was 47±14.5% (40%±15 in women and 44%±14 in men) which was in accord with the suggested reference value of below 85%.

The mean BF max was 38±8.5 L/min (39±8 L/min in women and 36±9 in men) which was within the standard normal range of below 60 b/min.

The mean EQCO2 max was 30±4.5 which was similar to the standard normal reference of below 34.

The mean rate of Ant max was 65%±12.5 of the predicted VO2 max which was within the standard range (more than 40% of the predicted VO2max).

The mean load max was 180±46 W/min (138±33 in women and 205±33 in men).

The mean VO2/kg max was 90%±17 ml/min/kg (95%±20 in women and 85±13 in men).

The mean VCO2max was 96.5%±20 L/min (100%±25 in women and 93%±17 in men).

The mean RER max in this study was 1.20±0.08 and most studies considered the rate over 1.15 as normal.

The mean EQO2 max was 36±7 (38±8.5 in women and 38±6 in men).

The mean VE max was 79±23 L/min (63.5%±18 L/min in women and 88±21 L/min in men).

Unfortunately no data was available regarding the standard normal values for load, VO2/kg, EQO2, VE and VCO2 and therefore, we could not make a comparison for these variables.

After calculating the mean ±SD for variables and comparison between males and females, linear regression analysis was performed for determination of normal values.

Since this was a pilot study, correlations based on gender were not significant due to the small number of under study subjects and therefore analyses were performed in both sexes together.

Regression analysis was performed for VO2max and load max. VO2max decreased by advanced age (P-value=0.012 and correlation coefficient=-0.425).

By increasing age, an elevation was observed in VO2 max (P-value=0.001 and correlation coefficient=0.601). By increased height, VO2max increased as well (P-value=0.001, correlation coefficient=0.666).

The greatest correlation however was observed between VO2max and height whereas, in some other studies like Neder et al. study in 1992, the greatest correlation was observed between VO2 max and age.

A prediction equation for VO2max was calculated using linear regression as follows:

VO2max=-5.3+0.044 (height)(R^2=0.44)

VO2max=-5.3-0.28(age)+0.024(weight)(R^2=0.36)

Load max also decreased by increased age (P-value=0.07, correlation coefficient=-0.45). By increased height, load max elevated as well (P-value=0.001 and correlation coefficient=0.701). In addition, an increase was observed in load max by increased weight (P-value=0.001 and correlation coefficient=0.6).

The greatest correlation was observed between load max and height.

The prediction equation for load max was calculated using linear regression as follows:

Load max=-436-1.2 (age)+1.8 (weight)(R^2=0.53)

Load max=-436+3.6 (height)(R^2=0.49)

When evaluating the correlation of other variables with age, height and weight, a direct correlation was found between O2 pulse and height (P-value=0.001, correlation coefficient=0.676).

A direct relationship was also observed between O2pulse and weight (P-value=0.001, correlation coefficient=0.722).

However, no correlation was detected between O2pulse and age (P-value greater than 0.05) and since height and weight were correlated with each other, conduction of regression analysis was not possible.

VE max had a direct relationship with height (P-value=0.001 and correlation coefficient=0.549) and weight (P-value=0.019 and correlation coefficient=0.401). However, no such correlation was observed with age (P-value>0.05) and therefore regression analysis could not be performed.

For other variables, due to the poor correlation with age, weight, height and gender, the R squared was very tiny and had low predictive value due to the small number of samples. In the next study which is going to be performed on a larger sample size regression analyses can be easily performed for all variables.

DISCUSSION

CPET in our country, Iran, is usually performed according to the standards of foreign countries and the results are interpreted mainly based on ATS reference values (22). Considering the ethnic, geographical and behavioral differences between Iranians and people of other nationalities, a new definition for normal values of CPET in Iran seems necessary. In spite of ethnical and climate differences, Iranians are less interested in physical activities and have unhealthy eating habits that separates our citizens from other nationalities. The mentioned facts enlighten the need for such study.

In this study, the ATS criteria and guidelines were considered for initiation and termination of the test. By performing this test, we can somehow differentiate the pulmonary causes of dyspnea from each other and from its cardiac etiologies.

In some centers during CPET, pulse oximetry is used instead of the measurement of arterial blood gases and ABG is done if the arterial oxygen saturation rate drops. Considering the limitations in our study, we only used pulse oximetry and since the understudy subjects were healthy and normal, no decrease was observed in their arterial oxygen saturation rate.

Regarding the observed differences between our obtained mean values and standard references especially in VO2max, HRR max and HR max three hypotheses are suggested:

1) Considering the small number of samples, these differences are not much acceptable and such differences may not exist or may be insignificant in the next study that is going to be conducted on a larger population.
2) If such differences were observed in the next study too, ethnic differences might be the cause and if so, the results of the exercise test of Iranians should be compared with our own standard normal values.
3) Although understudy subjects mentioned no history of cardiovascular or pulmonary diseases and were doing daily exercise, there was a possibility of presence of underlying conditions in them and further evaluations might be required in this respect.

In conclusion, in order to answer the above mentioned questions another study on a larger sample size is required to obtain normal values for different variables with greater confidence.

Also, obtaining normal values for the variables like VCO2, VE, VO2/kg, load, and EQO2 that were not adequately addressed in the suggested standard reference pattern would be possible in the next study.

Abbreviations

RGR: Respiratory equivalent ratio; **HRR**: Heart rate reserve; **Ant**: Anaerobic threshold; **BF**: Breathing Frequency; **BR**: Breath rate; **VE**: Minute Ventilation; **$EQCO_2$**: Ventilatory equivalent for CO_2; **EQO_2**: Ventilatory equivalent for O_2; **VO_2**: O_2 consumption; **VCO_2**: CO_2 production; **VO_2 max**: Maximal O_2 consumption

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