Rev Bras Cineantropom Hum

original article

DOI: http://dx.doi.org/10.5007/1980-0037.2018v20n5p412

Prevalence of exercise intolerance in obese adults undergoing cardiopulmonary exercise testing

Prevalência de intolerância ao exercício em adultos obesos submetidos ao teste de exercício cardiopulmonar

Agatha Caveda Matheus[1]
Evandro Fornias Sperandio[1]
Vinicius Tonon Lauria[1]
Rodrigo Pereira da Silva[1]
Antônio Ricardo de Toledo Gagliardi[2]
Marcello Romiti[2]
Rodolfo Leite Arantes[2]
Victor Zuniga Dourado[1]

Abstract – We hypothesized that the prevalence of exercise intolerance (EI, peak O_2 uptake < 83%pred.) is not significantly affected by body mass index (BMI) in adults undergoing cardiopulmonary exercise testing (CPET). We aimed to evaluate the prevalence of EI and the influence of BMI in asymptomatic adults. The results of 780 adults (age 41 ± 13 years) who underwent CPET were evaluated. Participants were stratified according to BMI: normal weight (n = 227), overweight (n = 198), and obese class 1 (n = 155), 2 (n = 131), and 3 (n = 69). After cardiovascular risk assessment, the participants underwent CPET on a treadmill ramp protocol. The prevalence of EI was 20, 16, 21, 25, and 21% in the stratified groups respectively, and no significant differences were found. Predictors of EI were physical inactivity, age, and smoking. The prevalence of EI in asymptomatic adults is considerable, regardless of BMI. The obesity-related reduction in cardiorespiratory fitness seems to be as clinically relevant as in non-obese counterparts.

Key words: Cardiorespiratory fitness; Obesity; Physical activity; Smoking.

Resumo – *Levantamos a hipótese de que a prevalência de intolerância ao exercício (IE, pico de consumo de O2 < 83%pred.) não é significativamente afetada pelo índice de massa corporal (IMC) em adultos submetidos ao teste de exercício cardiopulmonar (TECP). Nosso objetivo foi avaliar a prevalência de IE e a influência do IMC em adultos assintomáticos. Foram avaliados os resultados do TECP de 780 adultos (idade 41 ± 13 anos). Os participantes foram estratificados de acordo com o IMC: eutrófico (n = 227), sobrepeso (n = 198), e obesidade grau 1 (n = 155), 2 (n = 131), e 3 (n = 69). Após a avaliação do risco cardiovascular, os participantes foram submetidos ao TECP em uma esteira, sob o protocolo de rampa. A prevalência de IE foi 20, 16, 21, 25, e 21% respectivamente nos grupos estratificados, e nenhuma diferença significativa foi encontrada. Os preditores da IE foi inatividade física, idade e tabagismo. A prevalência de IE em adultos assintomáticos é considerável, independentemente do IMC. A redução da aptidão cardiorrespiratória relacionada a obesidade parece ser clinicamente relevante como em não obesos.*

Palavras-chave: *Aptidão cardiorrespiratória; Atividade física; Obesidade; Tabagismo.*

1 Federal University of São Paulo. Laboratory of Epidemiology and Human Movement. Santos, SP. Brazil.

2 Angiocorpore Institute of Cardiovascular Medicine. Santos, SP. Brazil.

Received: September 27, 2017
Accepted: May 10, 2018

INTRODUCTION

The maximum oxygen uptake (VO_2) obtained during cardiopulmonary exercise testing (CPET) is the most commonly used index of cardiorespiratory fitness[1]. The peak VO_2 is defined as the highest value of pulmonary O_2 uptake during maximal exercise. In addition to measuring cardiorespiratory fitness, the peak VO_2 is very useful for prescribing physical exercise as well as for accurately measuring the results of exercise training programs and other interventions[1].

In obese individuals, whose body mass index is greater than 30 kg/m^2, the most striking characteristic of cardiorespiratory fitness is the lower values of peak VO2 corrected for body mass (e.g., peak VO2/kg). However, when aerobic capacity is expressed in absolute terms or as a percentage of predicted adjusted for ideal body mass, several studies have shown that individuals with mild to moderate obesity have aerobic capacity within the normal range for a given age and gender. Thus, it may be advantageous to report aerobic capacity in absolute, relative and percentage values to obtain a more complete view of the cardiorespiratory fitness of obese individuals. Finally, there are data in the literature that suggest that the simple relationship between cardiorespiratory fitness and body mass penalizes individuals with greater body size, such as obese ones[2,3]. Accordingly, it would be more appropriate to correct peak VO2 by lean body mass to improve the prognostic utility of aerobic capacity in obese individuals.

The standard for the evaluation of exercise tolerance is the CPET, which is a non-invasive, valid and reproducible exam[4] and has been used for early diagnosis[5]. CPET provides information that enables the determination of the functional condition of the cardiovascular and respiratory systems. One of the most important indications of the CPET is the identification of the presence, etiology, and degree of exercise intolerance (EI). The test may be decisive in cases of dyspnea/fatigue of undetermined cause, as well as to discriminate the preponderant mechanisms intolerance (e.g., ventilatory, cardiovascular or gas exchange impairment). Objective determination of EI in patients with systemic diseases can be made by identifying peak VO2 values below the lower limit of normality, generally $< 83\%$ of predicted. In these situations, it is a consensus that the reduction of cardiorespiratory fitness is of a pathological nature[3].

Unfortunately, the studies that assess cardiorespiratory fitness of obese individuals submitted to CPET are scarce in the literature, especially considering severely obese subjects[6]. The available studies have been conducted with small numbers of participants[3]. Whether or not EI is more prevalent in obese compared to normal-weight and overweight counterparts needs further clarification in an enough number of participants. If this influence exists, the values that define EI should be differentiated in obese individuals. Otherwise, the same consensual index could be used. Therefore, to evaluate such correlation is crucial to increase the interpretative power of CPET in obese patients.

Based on scarce evidence in this field, we hypothesized that body mass index (BMI) exerts little or no influence on the prevalence of EI. Accordingly, we aimed to assess the prevalence of EI and the influence of BMI on cardiorespiratory fitness of obese adults.

METHODOLOGICAL PROCEDURES

Participants

We retrospectively analyzed 780 individuals (age 40 ± 13 years; 459 women and 321 men) who underwent CPET at the Angiocorpore Institute of Cardiovascular Medicine, Santos/SP, Brazil. Participants were stratified into five groups according to BMI: normal weight (BMI < 24.99 kg/m^2), overweight (BMI between 25 kg/m^2 to 29.99 kg/m^2), obesity class 1 (BMI between 30 kg/m^2 to 34.99 kg/m^2), obesity class 2 (BMI between 35 kg/m^2 and 39.99 kg/m^2) and obesity class 3 (BMI greater than 40 kg/m^2)[7]. Patients underwent CPET for a variety of medical indications and all of them consented to the exam. The Ethics Committee on Human Research of the Federal University of São Paulo No. 1,079,239 approved the project.

Anthropometrics

Body weight and height were measured (2096 PP, Toledo, São Bernardo do Campo, Brazil) and then the BMI was calculated (kg/m^2)[7].

Health screening

The patients were interviewed. Cardiovascular risk was stratified according to the recommendations of the American College of Sports Medicine[8]. Participants were asked about the presence of key risk factors such as age, family history, hypertension, diabetes, dyslipidemia, obesity, physical inactivity and smoking. Those who reported less than two factors were considered at low cardiovascular risk, those who reported two or more were rated at moderate risk. Those with a history of cardiovascular symptoms were considered at high cardiovascular risk and were not included in the analysis. Those who reported performing less than 150 minutes per week of moderate to vigorous physical activity were considered physically inactive[8].

Cardiopulmonary exercise testing

The CPET was performed on a treadmill (ATL, Inbrasport, Curitiba, Brazil) following a ramp protocol, which increases in speed and inclination and was individualized according to the estimated maximum VO_2[9]. Metabolic, cardiovascular, and ventilatory responses were measured breath by breath through a gas analyzer (Quark PFT, COSMED, Pavona Albano, Italy). The necessary calibrations with air, a standard gas mixture, and with a 3 L syringe were performed before each test in accordance with the manufacturer's recommendations. The tests were conducted under the same altitude, atmospheric pressure and temperature (22° C) and were supervised by a cardiologist.

Pulmonary oxygen uptake (VO_2), carbon dioxide production (VCO_2), and minute ventilation (VE) were measured breath by breath and subsequently filtered through their arithmetic means every 15 seconds. Heart rate (HR) was monitored throughout the test with a 12-lead electrocardiography (C12x, COSMED, Pavano of Albano, Italy).

The VO_2 at anaerobic threshold (AT) was obtained by the v-slope method. The respiratory compensation point (RCP) was identified by the ventilatory method using the ventilatory equivalents of VO_2 (VE/VO_2) and VCO_2 (VE/VCO_2)[2].

The maximum effort was considered if at least one of the following criteria was present: maximum HR > 85% of predicted for age (220 – age in years), rate of gas exchange (R) ≥ 1.05, or presence of a VO_2 plateau (10). The EI was defined as VO_2 < 83% of the predicted values[11].

Five evaluators conducted the TECP in the present study. All were previously trained by an experienced researcher in performing CPETs, as well as by a cardiologist to identify electrocardiographic changes and signs and symptoms requiring exercise interruption.

Statistical analysis

Initially, we performed a descriptive analysis. The variables with normal distribution are expressed as mean ± standard deviation or median (interquartile range) in the case of non-normal distribution. Categorical variables were described by calculating their frequency.

We used analysis of variance (ANOVA) for comparing mean values of the variables obtained during CPET among the five groups stratified by BMI. All the analyses were adjusted for the main confounding factors such as age, sex and cardiovascular risk factors. We developed two separate models by gender, one for the ratio standard and one for the allometrically corrected peak VO_2.

The prevalence of EI was calculated and its main predictors were evaluated in a multivariate logistic regression model. We considered the BMI groups as the main predictor and the model was adjusted for the main confounders. We used SPSS software version 23 for all the analysis and the probability of alpha error was set at 5%.

RESULTS

The 780 participants were predominantly women, middle-aged and obese. In general, women in the study had a higher prevalence of hypertension, diabetes mellitus, dyslipidemia, physical inactivity and obesity and made use of medicines more often. The proportion of smokers was similar among men and women in the sample (Table 1).

Table 1. General characteristics of the sample size

	Men	Women
N	321	459
Age (years)	38 ± 13	43 ± 14
Weight (kg)	90 ± 21	77 ± 20 †
Height (m)	1.73 ± 0.07	1.59 ± 0.07 †
Body mass index (kg/m^2)	28 (18 - 56)	30 ± 7
Waist (cm)	96 ± 16	89 ± 18
Hip (cm)	105 ± 12	106 (88 - 163)
Waist to hip ratio (cm)	0.91 ± 0.62	0.82 (0.41 – 1.55)
Arterial hypertension	33 (10.3%)	93 (20.3%) †
Diabetes	19 (5.9%)	52 (11.3%) †
Dyslipidemia	64 (19.9%)	129 (28.1%) †
Physical inactivity	157 (48.9%)	275 (59.9%) †
Smoking	35 (10.9%)	59 (12.9%)
Obesity	128 (39.9%)	227 (49.5%) †
Exercise intolerance	51 (15.9%)	109 (23.9%) †

Note. †p < 0.05: men vs. women. Continuous variables are presented as mean ± SD or median (interquartile range) and categorical data are presented as count (%).

We observed that the main variables obtained in the CPET were influenced by BMI. The peak VO_2/kg was inversely related to the BMI. Similar results were observed for the maximum HR and maximum systolic blood pressure (Table 2).

The prevalence of EI was not significantly different among the groups (Figure 1).

Table 2. Physiologic responses at peak of exercise and at the anaerobic threshold obtained in the cardiopulmonary exercise testing

	Normal weight	Overweight	Obesity 1	Obesity 2	Obesity 3
Age (years)	37 ±13	42 ± 14^{a}	46 ±14$^{a, d}$	42 ±13^{a}	42 ±13
Male [n (%)]	141 (62)	91 (46)	94 (60)	86 (65)	47 (68)
Female [n (%)]	86 (38)^{b}	107 (54)	61 (40)	45 (35)^{b}	22 (32)^{b}
VO_2 (mL/min)	2343 ± 898	2469 ± 907	2247 ± 849	2281 ± 640	2308 ± 658
VO_2 (ml/min/kg)	37 ± 10$^{b, c, d, e}$	32 ± 9$^{c, d, e}$	24 ± 7$^{d, e}$	21 ± 4	18 ± 3
VO_2 (% of pred)	101 ± 23$^{c, d, e}$	99 ± 16$^{d, e}$	95 ± 17	92 ± 14	90 ± 14
VO_2@AT (ml/min)	1598 ± 717	1650 ± 660	1511 ± 568	1532 ± 378	1619 ± 402
VO_2@AT (% of max)	67 ± 10	67 ± 14	68 ± 9	68 ± 10	71 ± 8
R (VCO_2/VO_2)	1.17 ± 0.12	1.16 ± 0.15	1.13 ± 0.15	1.11 ± 0.09	1.06 ± 0.15
HR (bpm)	172 ± 16$^{c, d, e}$	168 ± 19$^{c, d, e}$	160 ± 18	159 ± 17	155 ± 18
HR (% of pred)	94 ± 6$^{c, d, e}$	94 ± 7$^{d, e}$	92 ± 8$^{d, e}$	89 ± 7	87 ± 8
SBP (mm/Hg)	169 ± 22	181 ± 24^{a}	185 ± 24^{a}	188 ± 25^{a}	195 ± 28$^{a, b,c}$
Pulse O_2 (L/bpm)	13.1 ± 4.7	14.8 ± 5.7^{a}	13.9 ± 4.7	14.3 ± 3.6	14.9 ± 3.9
VE (L/min)	78.2 ± 30.6	80.6 ± 31.1$^{c, d, e}$	70.4 ± 28.3	70.6 ± 21.7	67.1 ± 21.1
Tidal volume (L)	1.909 ± 0.613	2.056 ± 0.656	1.846 ± 0.588	1.926 ± 0.587	1.862 ± 0.660
Resp. rate (ipm)	40 ± 8	38 ± 7	48 ± 13	37 ± 7	37 ± 6

Note. The symbols a, b, c, d and e, represent significant differences (p <0.05). a = normal weight; b = overweight; c = obesity 1; d = obesity 2; and e = obesity 3.
*Continuous variables are expressed as mean and standard deviation and sex is presented as count (%). M = male; F = female; PRED = predicted; AT = anaerobic threshold; MAX = maximum; R = rate of gas exchange; HR = heart rate; SBP = systolic blood pressure; VE = minute ventilation; RESP = respiratory

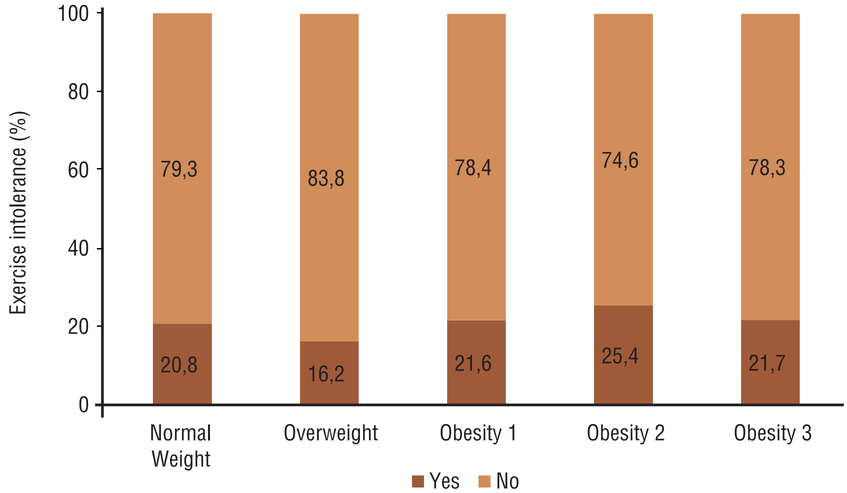

Figure 1. Prevalence of exercise intolerance according to body mass index (BMI) classification: normal weight (IMC < 25 kg/m2), overweight (IMC entre 25 e 29,9 kg/m2), obesity class 1 (BMI between 30 and 34.9 kg/m2), obesity class 2 (BMI between 35 e 39.9 kg/m2), and obesity class 3 (BMI ≥ 40 kg/m2). Exercise intolerance was defined as peak oxygen uptake during cardiopulmonary exercise testing below 83% of the predicted values. The difference among groups was not significant ($p \geq 0.05$).

After multivariate logistic regression analysis adjusted for the main confounding factors, BMI did not significantly influence the occurrence of EI. The EI was significantly predicted by age, sex, physical inactivity and smoking (Table 3).

Table 3. Results of the multivariate logistic regression model for identifying the main predictors of exercise intolerance

		95% confidence interval	
Predictors	Odds Ratio	Lower limit	Upper limit
Body mass index (kg/m2)			
< 25	1		
25 – 29.9	1.310	0.632	2.718
30 – 34.9	1.393	0.664	2.924
35 – 39.9	1.169	0.558	2.449
≥ 40	1.386	0.670	2.863
Age (years)			
≥ 60	1		
40 – 59	0.564	0.367	0.866†
< 40	0.451	0.230	0.884†
Sex (males)	0.606	0.409	0.896†
Family history of cardiovascular disease	1.112	0.645	1.915
Diabetes	1.419	0.740	2.722
Dyslipidemia	0.945	0.593	1.507
Physical inactivity	2.266	1.506	3.409†
Smoking	2.287	1.401	3.734†

Note. †$p < 0.05$

DISCUSSION

We evaluated the physiological responses to the CPET on a treadmill in adults with a wide range of BMI. Our hypothesis was largely confirmed. Despite the influence of BMI on peak VO_2, the BMI showed no significant association with EI.

We observed that obese adults have a similar prevalence of EI compared to normal and overweight subjects. Our results reinforce and highlight the inadequacy of the ratio standard of peak VO_2, e.g., peak VO_2/kg. The reference values commonly involve corrections related to age, sex and height, in addition to body mass[11,12]. The correlation between body mass and exercise capacity commonly presents nonlinear behavior inconsistent with linear correlation coefficients[2]. Accordingly, an overestimation of cardiorespiratory fitness would be unlikely in patients with BMI > 35 kg/m² involved in our study.

Dolfing et al.[13] evaluated 22 men and 34 women with morbid obesity without other comorbidities. After completion of CPET on a cycle ergometer, the authors found no physiological response indicating cardiovascular, ventilator, or metabolic limitation to maximal exercise. The average values of peak VO_2/kg of patients, between 92 and 119% of predicted, were similar to the average found in our study. Lorenzo et al.[14] compared 19 obese with 69 normal weight adults underwent CPET on a cycle ergometer. Patients with obesity had significantly reduced peak VO_2/kg. However, in relation to peak VO_2 in percentage of predicted values, there were no significant differences between the groups. We were unable to find a study with sufficient sample size describing the prevalence of EI in asymptomatic adults, particularly in obese individuals. Our results, with a wide range of BMI, reinforce previous findings[14], with the proportion of EI between 16 and 27%, and with no significant differences between obese and non-obese subjects.

We observed that about 15% of our participants presented cardiovascular limitation to exercise, with VO_2 below the lower limit of normal and with an early plateau in VO_2/HR[1]. Accordingly, our results suggest the need for special attention to individuals with EI, regardless of BMI.

After multivariate logistic regression analysis, we observed that BMI was not a significant predictor of EI. Our multivariate model was adjusted for the main confounders and we found that attributes such as age, sex, physical inactivity and smoking are more important than the severity of obesity in identifying adults with EI. The association between physical inactivity and poor cardiorespiratory fitness is well known. A recent study showed that individuals who meet the minimum recommendations of 150 minutes/week of moderate to vigorous physical activity present values of peak VO_2/kg 13% higher than the values of physically inactive individuals[15]. The negative impact of smoking on cardiorespiratory fitness is also well known[16]. Durakovic et al.[17] reported a significant reduction in peak VO2/kg even in smokers with smoking load < 5 pack-years. Borba et al.[18] found a similar statistically significant reduction in VO_2/kg in current and second-hand smokers compared to non-smokers. In another study found similar results and showed that in smokers, cardiorespiratory fitness is reduced regardless of the smoking load, thus is possible that the cessation of smoking can be used to prevent the reduction of cardiorespiratory fitness[19]. Additionally, in the same study the smoking was also related to other cardiovascular risk factors[19].

Age- and sex-related changes in peak VO_2/kg have already been widely reported in the literature[10]. A higher BMI is associated with higher cardiovascular risk[8]. Therefore, is necessary to investigate the influence of BMI on EI free of the confounding effect of variables such as age, sex and classics risk factors for cardiovascular diseases. Thus, the lower proportion of EI in younger individuals in the present study may be can be attributed to the smaller number of comorbidities in this age group. Additionally, cardiac output, heart rate, stroke volume, diastolic volume responses to exercise as well as left ventricular ejection fraction are all decreased with aging[20]. Thus, stroke volume and diastolic volume response are essential contributors to the increase in VO2 and cardiac output during upright exercise in healthy subjects and are altered by normal aging but not gender.

Our findings suggest that cardiorespiratory fitness of obese individuals has been underestimated in the literature. In fact, in a 16-year cohort study, Haapanen-Niemi et al.[6] found that physically inactive individuals or individuals who have reduced physical activity over time have increased BMI and higher cardiovascular risks. However, when adjusted for physical fitness, age, and smoking and socioeconomic status, BMI no longer appeared as an independent risk factor. Thus, the cardiovascular risk may be lowered by physical fitness independently of obesity.

This study has practical implications. Traditional methods for evaluating peak VO_2 adjusted by body mass, or even by lean body mass, are not suitable for obese individuals. The peak VO_2 in percentage of predicted values as well as the expression of cardiorespiratory fitness with allometric correction presents a more accurate representation of the subject's fitness and risk category. Our study adds to the evidence that the cardiorespiratory fitness of asymptomatic obese adults is significantly higher than has been commonly described in the literature, and that EI is not linked to the severity of obesity.

There are limitations to this study that should be considered. The most important of these is that we were unable to assess the body composition of all participants and therefore cannot calculate lean body mass. The assessment of body composition prior to a CPET is not routinely performed which can make the CPET less cost-effective. Instead, body weight has been a simpler correction strategy for the expression of peak VO_2. While our study was retrospective, it provided a large enough sample size to stratify patients into obesity classes 1, 2 and 3, and still maintain statistical power. To our knowledge, this has not previously been analyzed.

We conclude that the prevalence of EI in adults is substantial, regardless of BMI and is associated with cardiovascular risk factors other than obesity such as smoking and physical inactivity. In addition, despite the impact of obesity on cardiorespiratory fitness when using the ratio standard of peak VO_2/kg, obesity-related reduction on peak VO2 seems to be in a normal range compared to non-obese counterparts.

COMPLIANCE WITH ETHICAL STANDARDS

Funding

This study was supported by Angiocorpore Institute of Cardiovascular Medicine.

Ethical approval

Ethical approval was obtained from the local Human Research Ethics Committee – Federal University of São Paulo, and the protocol was written in accordance with the standards set by the Declaration of Helsinki.

Conflict of interest statement

The authors have no conflict of interests to declare.

Author Contributions

Conceived and designed the experiments: VZD. Performed the experiments: ACM; EVS; VTL; RPS. Analyzed the data: VZD. Contributed reagents/materials/analysis tools: ARTG; MR; RLA. Wrote the paper: ACM; VTL; RPS; EVS; VZD.

REFERENCES

1. Wasserman K, Hansen JE, Sue DY, Stringer WW, Sietsema K, Xing-Guo S, et al. Principles of exercise testing and interpretation. Philadelphia: Lippincott Williams & Wilkins; 2011.
2. Dourado VZ, McBurnie MA. Allometric scaling of 6-min walking distance by body mass as a standardized measure of exercise capacity in healthy adults. Eur J Appl Physiol 2012;112(7):2503-10
3. Neder JA, Andreoni S, Castelo-Filho A, Nery LE. Reference values for lung function tests. I. Static volumes. Braz J Med Biol Res 1999;32(6):703-17
4. Beaver WL, Wasserman K, Whipp BJ. On-line computer analysis and breath-by-breath graphical display of exercise function tests. J Appl Physiol 1973;34(1):128-32.
5. Belardinelli R, Lacalaprice F, Carle F, Minnucci A, Cianci G, Perna G, et al. Exercise-induced myocardial ischaemia detected by cardiopulmonary exercise testing. Eur Heart J 2003;24(14):1304-13.
6. Haapanen-Niemi N, Miilunpalo S, Pasanen M, Vuori I, Oja P, Malmberg J. Body mass index, physical inactivity and low level of physical fitness as determinants of all-cause and cardiovascular disease mortality--16 y follow-up of middle-aged and elderly men and women. Int J Obes Relat Metab Disord 2000;24(11):1465-74.
7. Lohman TG, Roche AF, Martorell R. Anthropometric standardization reference manual. Ilinois: Human Kinetics Books; 1988.
8. Thompson PD, Arena R, Riebe D, Pescatello LS. ACSM's new preparticipation health screening recommendations from ACSM's guidelines for exercise testing and prescription, ninth edition. Curr Sports Med Rep 2013;12(4):215-7.
9. American College of Sports Medicine. ACSM's guidelines of exercise testing and prescription. Philadelphia: Lippincott Wiliams & Wilkins; 2009.

10. Wasserman K, Hansen J, Sue DY, Whipp BJ, Casaburi R. Principles of exercise testing and interpretation. Philadelphia: Lippincott Wiliams & Wilkins; 2005.
11. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. Amer Rev Respir Dis 1984;129(2 Pt 2):S49-55.
12. Paap D, Takken T. Reference values for cardiopulmonary exercise testing in healthy adults: a systematic review. Expert Rev Cardiovasc Ther 2014;12(12):1439-53.
13. Dolfing JG, Dubois EF, Wolffenbuttel BH, ten Hoor-Aukema NM, Schweitzer DH. Different cycle ergometer outcomes in severely obese men and women without documented cardiopulmonary morbidities before bariatric surgery. Chest 2005;128(1):256-62.
14. Lorenzo S, Babb TG. Quantification of cardiorespiratory fitness in healthy non-obese and obese men and women. Chest 2012;141(4):1031-9.
15. Dyrstad SM, Anderssen SA, Edvardsen E, Hansen BH. Cardiorespiratory fitness in groups with different physical activity levels. Scand J Med Sci Sports 2015;26:291-8.
16. Laukkanen JA, Laaksonen D, Lakka TA, Savonen K, Rauramaa R, Makikallio T, et al. Determinants of cardiorespiratory fitness in men aged 42 to 60 years with and without cardiovascular disease. Am J Cardiol 2009;103(11):1598-604.
17. Misigoj-Durakovic M, Bok D, Soric M, Dizdar D, Durakovic Z, Jukic I. The effect of cigarette smoking history on muscular and cardiorespiratory endurance. J Addict Dis 2012;31(4):389-96.
18. Borba AT, Jost RT, Gass R, Nedel FB, Cardoso DM, Pohl HH, et al. The influence of active and passive smoking on the cardiorespiratory fitness of adults. Multidiscip Respir Med 2014;9(1):34.
19. Lauria VT, Sperandio EF, Sousa TL, Vieira W, Romiti M, Gagliardi AR, et al. Evaluation of dose-response relationship between smoking load and cardio-pulmonary fitness in adult smokers: A cross-sectional study. Rev Port Pneumol 2017;23(2):79-84.
20. James BS, Edward GL Aging-associated cardiovascular changes and their relationship to heart failure. Heart Fail Clin 2012; 8(1): 143–64.

CORRESPONDING AUTHOR

Victor Zuniga Dourado
Laboratory of Epidemiology and Human Movement (EPIMOV)
Federal University of São Paulo (UNIFESP)
Street Silva Jardim, 136, Room 338, Vila Mathias, Santos, SP, Brazil
Zip code: 11015-020.
E-mail: vzdourado@yahoo.com.br