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Spiroergometric assessment of cardiorespiratory fitness in subjects with severe obesity: A challenge of reference

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Abstract *Background and aims:* Severe obesity is associated with poor physical performance but objective data are scarce.
Methods and results: Bicycle spiroergometry data with focus on peak oxygen uptake ($\dot{V}O_{2,peak}$) and workload (W_{peak}) from 476 subjects with severe obesity (BMI $\geq$ 35.0 kg/m^2; 70% women) were analysed. In a first step, $\dot{V}O_{2,peak}$ values were compared with reference values calculated upon different formulas (Wassermann; Riddle). Thereafter, multivariate regression analyses were performed to identify determinants of cardiorespiratory fitness. Cardiorespiratory fitness reference classes for $\dot{V}O_{2,peak}$ and W_{peak} were established by stratifying the sample upon identified determinants.

Absolute $\dot{V}O_{2,peak}$ (1.87 $\pm$ 0.47 vs. 2.40 $\pm$ 0.59 l/min) and W_{peak} (131 $\pm$ 26 vs. 168 $\pm$ 44 W) were lower in women than men (both $p<0.001$). Same pattern was found for relative $\dot{V}O_{2,peak}$ and W_{peak}, respectively (both $p < 0.05$). In women, measured $\dot{V}O_{2,peak}$ was lower than predicted by Wasserman ($p < 0.001$) but not by Riddle ($p = 0.961$). In men, $\dot{V}O_{2,peak}$ was lower than calculated by both Wasserman and Riddle formulas (both $p \leq 0.003$). Multivariate analyses revealed height and age to be the main determinants of cardiorespiratory fitness in both sexes. Subsequent statistical analyses of calculated reference fitness classes revealed that $\dot{V}O_{2,peak}$ and W_{peak} differed between the age- and height-defined groups in both sexes (all $p < 0.001$).
Conclusion: Data indicate that the evaluation of cardiorespiratory fitness in subjects with severe obesity is largely biased by selected references values for comparison. Our newly established reference fitness classes upon height and age might be helpful in the clinical context when dealing with obese patients.

Introduction

Severe obesity is commonly assumed to be associated with poor physical performance but overall objective data on this issue are scarce. Indeed, studies with only a low number of subjects with severe obesity suggested markedly impaired cardiorespiratory fitness indicated by established fitness markers as peak oxygen uptake or

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workload in relation to body weight [1,2]. Of note, these values in extreme obesity are comparable to patients with systolic heart failure [3]. Marked weight loss induced by bariatric surgery improves cardiorespiratory fitness in subjects with severe obesity [4–7] but fitness levels appear to remain impaired when related to body weight or compared to non-obese subjects [8]. Furthermore, a low fitness level defined by a relative peak oxygen uptake below 15.8 ml min^{-1} kg^{-1} predicts the risk of perioperative complications associated with bariatric surgery in subjects with severe obesity [9]. Hence, the American Heart Association recommends the assessment of cardiorespiratory fitness for preoperative risk evaluation in subjects with severe obesity [10]. In this context, the role of physical fitness as a protective factor should be emphasized. There is strong evidence that a better cardiorespiratory fitness is associated with lower risk of cardiovascular disease as well as overall morbidity and mortality [11–13]. These data underpin the necessity for objective data on cardiorespiratory fitness in severe obesity. However, the commonly used adjustment for body weight and the lack of large scale reference values make an objective judgment on an individual's fitness, e.g. in the preoperative setting, very difficult.

Interestingly, some authors suggest that an adjustment of peak oxygen consumption to lean body mass is preferable in patients with high body fat since fat mass does not have high perfusion or metabolism. In this context, it has been shown that lean body mass adjusted O_2pulse is a significant predictor of prognosis in chronic heart failure [14,15].

Standardized exercise testing for the assessment of cardiorespiratory fitness has been performed in many different cohorts ranging from athletes to patients with coronary heart diseases, heart failure, or pulmonary disease [16]. Reference values for respective standardized exercise tests are necessary to judge on an individual's fitness as compared to a healthy reference population. However, in the clinical setting it is also of interest to compare an individual's physical performance with that of a reference population displaying the same disease such as severe obesity. For normal-weight to mildly obese subjects many reference values or reference ranges have been published [8,17,18]. Of note, respective reference values are often given in relation to body weight or lean body mass. This approach may be associated with an inherent bias since with increasing degree of obesity there is a disproportional rise in body fat mass, which is metabolically less active than other tissues such as skeletal muscle [19]. Putting this forward, it appears questionable whether such reference values can be extrapolated to subjects with severe obesity. It has been suggested that using reference values calculated upon ideal or predicted normal weight (PNW) might be more appropriate in obese subjects than relating performance to actual body weight [2,16] but whether this also pertains to subjects displaying a severe degree of obesity, i.e. BMI of at least 35.0 kg m^{-2} remains unclear.

The aim of the present study was therefore to provide a large data set on spiroergometric assessment in obesity so that a judgement of cardiorespiratory fitness in this specific group will be feasible.

Methods

Study population

For this retrospective study 476 subjects with severe obesity were selected from the database of the Interdisciplinary Obesity Center (IOC) St. Gallen, Switzerland, according to the following inclusion and exclusion criteria: All included subjects had a BMI of at least 35.0 kg m^{-2}, i.e. obesity WHO II° or higher, an age between 18 and 59 years, and underwent bicycle spiroergometric exercise testing. Subjects with overt cardiac and pulmonary diseases were excluded from the study. Data were collected between May 2006 and May 2012. Clinical data such as patients' history, diagnosis, medication, and smoking status were assessed by a standardized clinical assessment protocol. The performed exercise test was part of a preoperative evaluation protocol before bariatric surgery. All subjects gave written informed consent for scientific use of their clinical data and the retrospective data analysis was approved by the local ethical committee of the canton St. Gallen.

Assessment and analysed parameters

Body weight and height were measured with subjects wearing light clothes but no shoes and BMI was calculated from body weight and height.

Body composition was assessed by bioelectrical impedance analysis (BIA; up to May 2009: Akern RJL 101S, Akern, Pontassieve, Italy; since June 2009: Nutriguard-M, Data Input GmbH, Frankfurt, Germany). Fat mass (FM) and fat free mass (FFM) were calculated by using respective software tools provided by the manufacturers.

Pulmonary function parameters (forced expiratory volume within 1 s, FEV1; inspiratory vital capacity, VC) were assessed by standard spirometry (CARDIO-VIT CS-200, Schiller AG, Baar, Switzerland) and individual reference FEV1 and VC values were calculated [20].

Cardiorespiratory fitness was assessed by spiroergometry during a symptom-limited graded bicycle exercise test. Gas exchange was measured breath-by-breath using a computer-based system (CARDIO-VIT CS-200, Schiller AG, Baar, Switzerland) and average of 10 s breath-by-breath intervals were used for data analyses. The system was calibrated before each test using standard gas of known oxygen and carbon dioxide concentration and a 3 l syringe according to manufacturer's instructions. The step-by-step test protocol was characterized by starting at a workload (W) of 25–75 W depending on the presumed patient's fitness and increased by 25 W every two min until volitional exhaustion. Preceding the step-by-step test there was a phase of unloaded cycling of 2 min for warming-up purposes. A 12-lead ECG was recorded continuously during the test and recovery. Maximum achieved O_2 uptake ($\dot{V}O_{2,peak}$) along with corresponding heart rate (HR_{peak}), workload (W_{peak}), and respiratory exchange ratio (RER_{peak}) were recorded at the end of the exercise. The RER represents the ratio between exhaled carbon dioxide ($\dot{V}CO_2$) and simultaneously measured O_2 uptake ($\dot{V}O_2$). RER_{peak} as well as percentage of predicted maximal heart rate (%HR_{max}; HR_{max} = 220-age) were used to characterize the metabolic and cardiac states at the end of the exercise. Patients with a RER_{peak} of less than 1.0 were excluded from analysis. All tests were performed by trained medical staff and physicians.

Statistical analysis

Statistical analyses were performed by using SPSS for Windows (Version 20, SPSS, Inc., Chicago, IL, USA). All data are presented as mean ± standard deviation (SD) unless otherwise indicated. Stepwise multiple regression analysis was performed to identify independent predictors of cardiorespiratory fitness markers, including age, anthropometric parameters, smoking habits (never smoker = 0; smoker = 1; formerly smoker = 2; unknown smoking status = 3), diagnosis of diabetes mellitus (DM; yes = 1; no = 0; defined by a fasting plasma glucose level >/<7 mmol l^{-1}, respectively, or intake of anti-hyperglycemic drugs), and beta-blocker intake (yes = 1; no = 0) as independent variables in respective regression models. When analysing heart rate and related variables subjects on beta-blocker therapy were excluded. They were not excluded when data on oxygen uptake as well as workload parameters were analysed since a forgoing study did not show an effect of beta-blocker therapy on these variables [21].

Independent Student's t-Test was used to test for sex differences. To assess the differences between more than two groups one-way analysis of variance (ANOVA) was conducted. For all tests a p-value <0.05 was considered significant.

$\dot{V}O_{2,peak}$ values of the study population (separately for women and men) were compared with PNW-related reference values calculated upon the formulas provided by Wasserman [16] which correct for excess body weight in overweight subjects as well as with PNW-related reference values calculated upon formulas provided by Riddle et al. [22].

In order to establish reference cardiorespiratory fitness classes upon our study of severely obese women and men, we firstly divided the study sample by the medians of age and height, i.e. the variables that explained most of the variance in physical fitness. Accordingly, the following four sex-specific groups were established: Group I: age < median and height < median (women: <39 years and <163 cm; men: <44 years and <177 cm); Group II: age < median and height ≥ median (women <39 years and ≥163 cm; men: <44 years and ≥177 cm); Group III: age ≥ median and height < median (women: ≥39 years and <163 cm; men: ≥44 years and <177 cm); Group IV: age ≥ median and height ≥ median (women: ≥39 years and ≥163 cm; men: ≥44 years and ≥177 cm). In a second step, six classes of cardiorespiratory fitness ranges were defined upon mean and SD of $\dot{V}O_{2,peak}$ and W_{peak} values separately for each of the age- and height-specific groups. Performance within mean + 1 SD was classified as "slightly above average", between +1 SD and +2 SD as "moderately above average", and above mean + 2 SD as "markedly above average". Performance within mean −1 SD was classified as "slightly below average", between −1 SD and −2 SD as "moderately below average", and below −2 SD as "markedly below average" fitness.

Results

Patients' characteristics

Anthropometric and clinical characteristics of the subjects are presented in Table 1. The study population displayed an age range from 18 to 59 years and a BMI range from 35.0 to 71.3 kg m^{-2}. The majority of the subjects were women (70%). Men were on average older, taller, heavier, and had higher BMI values than women (all $p < 0.05$). Also, men displayed higher absolute FFM values than women ($p < 0.001$), while absolute and relative FM were higher in women (both $p \leq 0.001$). The prevalence of DM ($p < 0.001$) and beta blocker use ($p = 0.046$) was higher in men than in women, while smoking status showed no

Table 1 Anthropometric and clinical characteristics of the 476 subjects with severe obesity (all BMI ≥ 35 kg m^{-2}).

	Women (n = 333)	Men (n = 143)
Age [years]	39.0 ± 10.3	42.4 ± 10.3**
Body weight [kg]	118.8 ± 18.8	142.2 ± 21.8**
Body height [cm]	163.4 ± 6.9	176.4 ± 7.0
BMI [kg·m^{-2}]	44.4 ± 6.0	45.7 ± 6.4*
Fat mass [kg][a]	56.8 ± 13.3	51.7 ± 13.7*
Fat mass [%][a]	47.9 ± 5.4	36.4 ± 6.4**
Fat free mass [kg][a]	60.9 ± 8.1	89.5 ± 14.0**
BMI ranges [kg·m^{-2}]		
35.0–39.9 [n; %]	82; 24.6	29; 20.3
40.0–44.9 [n; %]	122; 36.6	44; 30.8
45.0–49.9 [n; %]	83; 24.9	39; 27.3
50.0–54.9 [n; %]	27; 8.1	23; 16.1
55.0–59.9 [n; %]	15; 4.5	4; 2.8
≥ 60.0 [n; %]	4; 1.2	4; 2.8
DM [n; %]	49; 12.6	49; 30.1**
Beta-blocker use [n; %]	26; 6.7	22; 13.5*
Smoking status		
Nonsmokers [n; %]	170; 43.6	70; 43.0
Smokers [n; %]	103; 26.4	39; 23.9
Formerly smokers [n; %]	47; 12.1	32; 19.6
Unknown smoking status [n; %]	70; 17.9	22; 13.5

Data are given as mean; SD or frequencies (%) values. P-values derived by unpaired t-Test.
BMI = body-mass-index; DM = diabetes mellitus.
*$p < 0.05$; **$p < 0.001$.
[a] Assessed in 261 women and 112 men.

differences between sexes ($p = 0.139$). Women had higher FEV1 and CV than men (both $p<0.001$; FEV1: 95.3 ± 13.7% vs. 88.2 ± 12.2%; VC: 102 ± 12.8% vs. 88.2 ± 12.2%).

Cardiorespiratory fitness

Relative, i.e. related to body weight, as well as absolute $\dot{V}O_{2,peak}$ and W_{peak} values were higher in man than women (all $p < 0.05$; Table 2), while, in turn, women displayed higher $\dot{V}O_{2,peak}$ and W_{peak} values when related to FFM (both $p < 0.001$). The metabolic and cardiac states at the end of the exercise as indicated by RER_{peak} and $\%HR_{max}$ values were well comparable between women and men (both $p \geq 0.251$). Of note, 48.0% of the tested women and 42.7% of the tested men displayed a RER_{peak} that was quite low, i.e. between 1.00 and 1.09, indicating a rather weak exercise tolerance. Also, only 27.9% of the women and 21.2% of the men reached a peak HR of 90% of the predicted HR_{max}. Men displaying a RER_{peak} between 1.00 and 1.09 showed an on average 0.2 l min^{-1} lower $\dot{V}O_{2,peak}$ than those with $RER_{peak} \geq 1.10$ ($p = 0.033$). In women, the difference in $\dot{V}O_{2,peak}$ between respective RER_{peak} group was smaller (0.1 l min^{-1}) but still significant ($p = 0.047$).

Comparison with predicted normal-weight reference values

When $\dot{V}O_{2,peak}$ values were compared with PNW reference values deriving from Wasserman formulas [16] women showed on average 8.5 ± 20.2% ($p < 0.001$) lower and men on average 23.2 ± 16.3% ($p < 0.001$) lower than predicted values. However, when PNW-related reference values deriving from Riddle formulas [22] were used for comparison women did not show any significant deviation from the predicted $\dot{V}O_{2,peak}$ values (0.3 ± 22.4%; $p = 0.961$) and men showed only slightly lower than predicted values (4.6 ± 20.7%, $p = 0.003$).

Multivariate regression analyses were then performed to detect determinants explaining part of the percentage deviation of $\dot{V}O_{2,peak}$ values from the PNW reference values (dependent variable %PNW-$\dot{V}O_{2,peak}$). In women, $\%HR_{max}$ and %VC explained 13.7% and 3.0%, respectively, of the variance in %PNW-$\dot{V}O_{2,peak}$ upon Wasserman (both beta < -0.180; both $p < 0.001$) and 14.7% and 2.7%, respectively, of the variance in %PNW-$\dot{V}O_{2,peak}$ upon Riddle (both beta ≤ -0.172; both $p \leq 0.001$). For both regression models (on Wasserman and Riddle PNW-$\dot{V}O_{2,peak}$) smoking habits, beta-blocker intake, diagnosis of DM, %FEV1, and RER_{peak} failed to reach significance (all $p \geq 0.134$).

In men, $\%HF_{max}$ and %FEV1 explained 6.7% and 5.0%, respectively, of the variance in %PNW-$\dot{V}O_{2,peak}$ upon Wasserman (both beta < -0.180; both $p < 0.03$) and 3.1% and 2.6%, respectively, of the variance in %PNW-$\dot{V}O_{2,peak}$ upon Riddle (all beta ≤ -0.180; both $p \leq 0.032$) while smoking habits, beta-blocker intake, diagnosis of DM, %VC, and RER_{peak} failed to reach significance (all $p \geq 0.173$).

Multivariate regression analysis on absolute $\dot{V}O_{2,peak}$ and W_{peak} values

In women, height alone explained 15.9% of the variance in $\dot{V}O_{2,peak}$ (beta = 0.268; $p < 0.001$). Age, body weight, and beta-blocker explained another 8.8%, 0.8%, and 0.8% (beta = −0.280, 0.127, and −0.102; all $p \leq 0.035$; total explained variance, $R^2 = 27.2\%$). Prevalence of DM and smoking status were not associated with $\dot{V}O_{2,peak}$ (all $p > 0.145$). When FFM and FM instead of body weight were included in respective regression models, FFM - along with height, age and beta-blocker use - turned out to be a significant predictor of $\dot{V}O_{2,peak}$ (explained variance 0.9%, beta = 0.122; $p = 0.044$) but the overall explained variance of the model ($R^2 = 24.2\%$) was not superior compared to the model including body weight.

Regarding W_{peak}, age turned out to be the strongest predictor accounting for 20.7% (beta = −0.419; $p < 0.001$) of its variance. Height and body weight explained 6.2% and 0.8%, respectively, of the residual variance (beta = 0.315 and −0.119, respectively; all $p \leq 0.029$; total $R^2 = 27.7\%$), while smoking habits, beta-blocker intake and diagnosis of DM showed no association (all $p \geq 0.168$). In the model including body composition variables, FM (explained variance 2.9%; beta = −0.197; $p < 0.001$) but not FFM ($p = 0.500$) turned out - along with age and height - to be significant predictors of W_{peak} but again the model was not better than when including body weight ($R^2 = 27.2\%$).

In men, age turned out to be the strongest predictor of $\dot{V}O_{2,peak}$ explaining 15.7% of its variance (beta = −0.315; $p < 0.001$) and height (beta = 0.350; $p < 0.001$) and beta blocker intake (beta = −0.160; $p = 0.031$) explained further 11.5% and 1.9%, respectively (total $R^2 = 29.1\%$). Body weight, smoking habits, and diagnosis of DM were not significantly associated with $\dot{V}O_{2,peak}$ (all $p \geq 0.277$). In the model including body composition variables instead of

Table 2 Cardiorespiratory fitness markers at peak performance during a bicycle exercise test assessed by spiroergometry in the 476 subjects with severe obesity (BMI ≥ 35 kg m^{-2}).

	Women (n = 333)	Men (n = 143)
Cardiorespiratory fitness		
HR_{peak} [beats·min^{-1}][a]	153 ± 19	149 ± 19
$\%HR_{max}$ [%][a]	84.4 ± 9.5	83.2 ± 9.8
W_{peak} [W]	131 ± 26	168 ± 44**
W_{peak}·BW^{-1} [W·kg^{-1}]	1.13 ± 0.26	1.22 ± 0.34*
W_{peak}·FFM^{-1} [W·kg^{-1}][b]	2.20 ± 0.47	1.93 ± 0.56**
$\dot{V}O_{2,peak}$ [l·min^{-1}]	1.87 ± 0.47	2.40 ± 0.59**
$\dot{V}O_{2,peak}$·BW^{-1} [ml·kg^{-1}·min^{-1}]	16.0 ± 4.0	17.2 ± 4.4*
$\dot{V}O_{2,peak}$·FFM^{-1} [ml·kg^{-1}·min^{-1}][b]	31.5 ± 7.5	27.5 ± 7.0**
%$\dot{V}O_{2,peak}$Wasserman [%]	91.5 ± 20.2	76.7 ± 16.3**
%$\dot{V}O_{2,peak}$Riddle [%]	100.3 ± 22.0	95.4 ± 20.7
RER_{peak}	1.11 ± 0.07	1.12 ± 0.07

Data are given as mean; SD; P-values derived by unpaired t-Test. HR_{peak} = heart rate at peak exercise; W_{peak} = workload at peak exercise; $\dot{V}O_{2,peak}$ = oxygen uptake at peak exercise; BW = body weight; FFM = Fat free mass; %$\dot{V}O_{2,peak}$=percentage of predicted $\dot{V}O_{2,peak}$; RER_{peak} = respiratory exchange ratio at peak exercise.
*$p < 0.05$; **$p < 0.001$.
[a] Subjects taking beta-blockers were excluded here.
[b] Assessed in 261 women and 112 men, respectively.

body weight neither FFM nor FM were significantly related to $\dot{V}O_{2peak}$ (both $p \geq 0.164$).

Regarding W_{peak}, age alone explained 16.4% (beta = −0.305; $p < 0.001$) of its variance, and height, beta-blocker intake, body weight, and diagnosis of DM explained another 10.6%, 3.0%, 1.6%, 2.0%, respectively (beta = 0.428; −0.151; −0.190; and −0.161, respectively; all $p \leq 0.038$; total R^2 = 33.6%). Again, smoking habits did not show a significant association ($p = 0.193$). In the model including body composition variables instead of body weight neither FFM nor FM was independently related to W_{peak} (both $p \geq 0.095$).

The revealed regression formulas including anthropometric variables were as follows:

For women:

$$\dot{V}O_{2,peak}\,[l \cdot min^{-1}] = -0.925 + 0.018\,H - 0.013\,A + 0.003\,W - 0.180\,B$$

$$W_{peak}\,[W] = 0.848 - 1.108\,A + 1.188\,H - 0.173\,W$$

For men:

$$\dot{V}O_{2,peak}\,[l \cdot min^{-1}] = -1.956 - 0.018\,A + 0.029\,H - 0.278\,B$$

$$W_{peak}\,[W] = -182.417 - 1.317\,A + 2.651\,H\,19.423\,B - 0.385\,W - 15.720\,DM$$

with A = Age in years; H = Body height in cm; W = Body weight in kg; DM = diagnosis of diabetes mellitus (yes = 1; no = 0); B = beta-blocker intake (yes = 1; no = 0).

Cardiorespiratory fitness classes

Statistical analyses on $\dot{V}O_{2,peak}$ and W_{peak} values revealed significant differences between the four the age- and height-defined groups in both sexes (all $p < 0.001$) confirming a major influence of age and height on respective cardiorespiratory fitness markers (Table 3 and Table 4). Of note, the metabolic and cardiac state at the end of the exercise test, as indicated by RER_{peak} and $\%HR_{max}$ was well comparable between the age- and height-defined groups (all $p > 0.096$; except for RER_{peak} in women, $p = 0.043$).

Discussion

We report on the largest published dataset on spiroergometric cardiorespiratory fitness markers, i.e. $\dot{V}O_{2,peak}$ and W_{peak}, in subjects with severe obesity. Comparison of measured $\dot{V}O_{2,peak}$ values with PNW reference values indicated that the extent of cardiorespiratory fitness impairment, if any, in our subjects with severe obesity largely depends on the formula for reference values calculation. Furthermore, our results indicate that height and age are the most important determinants of exercise performance in this subject group. Based on this finding we establish, in addition to distinct regression formulas, fitness classes for age- and height-defined groups of subjects with severe obesity that may allow for a better judgment on cardiorespiratory fitness in severely obese women and men who undergo bicycle spiroergometry.

The question whether and to what extent cardiorespiratory fitness is generally impaired in severely subjects is difficult to answer even upon our large dataset. When related to actual body weight, cardiorespiratory fitness of our severely obese study population, albeit showing a relatively wide variability, appeared to be very low. For instance, only 21.9% of our tested women and 8.4% of the men displayed $\dot{V}O_{2,peak}$ levels above the lowest 5% of body weight-related reference values deriving from non-obese healthy subjects [8]. However, when compared with PNW-related reference values cardiorespiratory fitness appeared much less impaired in men and even normal in the severely obese women when Riddle PNW references values were used for comparison. Based on these findings, one may conclude that the cardiorespiratory fitness markers $\dot{V}O_{2,peak}$ and W_{peak} should generally not be related to body weight in subjects with severe obesity. Our present finding that body weight explained only 1.1% of the $\dot{V}O_{2,peak}$ variance in women and nothing of the variance $\dot{V}O_{2,peak}$ in men as well as only 0.8% and 1.6% of the variance in W_{peak} in women and men, respectively, may further support this notion.

While it appears clear that a relation to actual body weight will not allow for a proper judgment on cardiorespiratory fitness upon $\dot{V}O_{2,peak}$ and W_{peak} data in severely obese individuals, it may still provide some useful information in the clinical context. For instance, even a regular

Table 3 Cardiorespiratory fitness classes relying on peak oxygen uptake ($\dot{V}O_{2,peak}$) during a bicycle exercise test as a marker of cardiorespiratory fitness in subjects with severe obesity (BMI ≥ 35 kg m^{-2}).

Group	Women				Men			
	I	II	III	IV	I	II	III	IV
Age- and Height range	<39 years <163 cm	<39 years ≥163 cm	≥39 years <163 cm	≥39 years ≥163 cm	<44 years <177 cm	<44 years ≥177 cm	≥44 years <177 cm	≥44 years ≥177 cm
n	70	94	84	85	26	45	38	34
Fitness Classes	Upper and lower limits for $\dot{V}O_{2,peak}$ ($l \cdot min^{-1}$)							
Markedly above average	≥2.68	≥3.07	≥2.47	≥2.61	≥3.30	≥3.92	≥3.11	≥3.35
Moderately above average	2.25–2.67	2.60–3.06	2.05–2.46	2.23–2.60	2.84–3.29	3.35–3.91	2.58–3.10	2.83–3.34
Slightly above average	1.82–2.24	2.14–2.59	1.63–2.04	1.85–2.22	2.38–2.83	2.76–3.34	2.06–2.57	2.31–2.82
Slightly below average	1.39–1.81	1.67–2.13	1.21–1.62	1.47–1.84	1.92–2.37	2.18–2.75	1.53–2.05	1.80–2.30
Moderately below average	0.95–1.38	1.21–1.66	0.79–1.20	1.09–1.46	1.46–1.91	1.60–2.17	1.00–1.52	1.28–1.79
Markedly below average	<0.95	<1.21	<0.79	<1.09	<1.46	<1.60	<1.00	<1.28

Table 4 Cardiorespiratory fitness classes relying on peak workload (W_{peak}) during a bicycle exercise test as a marker of cardiorespiratory fitness in subjects with severe obesity (BMI $\geq$ 35 kg m^{-2}).

Group	Women				Men			
	I	II	III	IV	I	II	III	IV
Age- and Height range	<39 years <163 cm	<39 years ≥163 cm	≥39 years <163 cm	≥39 years ≥163 cm	<44 years <177 cm	<44 years ≥177 cm	≥44 years <177 cm	≥44 years ≥177 cm
n	70	94	84	85	26	45	38	34
Fitness Classes	Upper and lower limits for W_{peak} (W)							
Markedly above average	≥181.9	≥193.3	≥164.0	≥171.3	≥227.5	≥277.6	≥225.7	≥233.8
Moderately above average	157.9–181.8	170.8–193.2	140.8–163.9	148.1–171.2	197.9–227.4	236.0–277.5	184.2–225.6	192.7–233.7
Slightly above average	132.9–157.8	148.1–170.7	117.6–140.7	125.0–148.0	168.3–197.8	194.4–235.9	142.8–184.1	151.6–192.6
Slightly below average	107.8–132.8	125.5–148.0	94.3–117.5	101.9–124.9	138.6–168.2	152.9–194.3	101.3–142.7	110.5–151.5
Moderately below average	82.8–107.7	102.8–125.4	71.1–94.2	78.7–101.8	109.0–138.5	111.2–152.8	59.8–101.2	69.4–110.4
Markedly below average	<82.8	<102.8	<71.1	<78.7	<109.0	<111.2	<59.8	<69.4

cardiorespiratory system may not have the capacity to sufficiently fuel a massively increased body mass with enough oxygen under stressful situations such as surgical operations. The previous observation that a $\dot{V}O_{2,peak}$ value below 15.8 ml min^{-1} kg^{-1} indicates an increased perioperative risk in subjects with severe obesity undergoing bariatric surgery [9] may support this notion. Also, a low – in relation to body weight – cardiorespiratory fitness will likely compromise a severely obese subject during his/her everyday activities, e.g. limiting walking speed. Putting this forward, we believe that it can be still useful to relate cardiorespiratory fitness indices to body weight in order to answer specific clinical questions.

It has been clearly shown that a good cardiorespiratory fitness largely neutralizes the adverse effects of increased body fat mass, obesity, and further metabolic risk factors, respectively (for review: [11]). This phenomenon is also known as the fat but fit phenomenon [23]. From this perspective, it seems even more urgent to establish reliable reference values in order to judge on cardiorespiratory fitness of subjects with severe obesity.

To assess and quantify cardiorespiratory fitness in obese subjects a relation of $\dot{V}O_{2,peak}$ value to PNW-related reference values has been recommended by several authors [2,16]. However, by using this approach we obtained quite variable results ranging from an average reduction in performance by 23.2% to 4.6% in men and from a reduction by 8.5% to no reduction in women depending of the used formula. A similar observation has recently been made in a study with a smaller sample ($n = 66$) of obese subjects [2]. Based on their results the authors recommended the use of the Wasserman formula [16] for the quantification of cardiorespiratory fitness in obese men and the Riddle formula [22] in obese women. In our study, however, measured performance was much closer to normal in both sexes when Riddle instead of Wasserman PNW-related reference values were used. This difference in findings may be due to the fact that the average degree of obesity in the previous study [22] was much lower than in our study, i.e. BMI 36 kg m^{-2} vs. 45 kg m^{-2}, respectively. We assume that for our more severe obese sample the Riddle formulas fit better than the Wasserman formulas in both sexes since the Wasserman formulas add 6 ml min^{-1} $\dot{V}O_2$ for each kg excess body weight to the $\dot{V}O_{2,peak}$ value calculated upon PNW. Considering the large number of excess kg in our subjects with severe obesity this adaption will likely lead to an overestimation of $\dot{V}O_{2,peak}$. In our study height, apart from age, was identified as a most important determinant of physical fitness. This finding is in accordance with guidelines of the American Thoracic Society and American College of Chest Physicians [24], which recommend that cardiorespiratory fitness – just like pulmonary function - indices should be related to body height. While this recommendation is frequently neglected in clinical practice and also in research studies our results indicate that the relation to height is of particular importance in subjects with severe obesity. Of note, the calculation of predicted normal weight (PNW) basically relies on body height which likely explains why the calculated PNW-related reference values met our measured $\dot{V}O_{2,peak}$ value quite well.

The deviation of measured $\dot{V}O_{2,peak}$ from PNW-related $\dot{V}O_{2,peak}$ values was partly explained by a reduced pulmonary function as well as by an reduced $\%HF_{max}$. While a reduced pulmonary function in subjects with severe obesity is likely explained by increased intra-abdominal pressure [7], the low $\%HF_{max}$ might point to an impaired exercise tolerance in this subject group. Of note in this context, only 27.9% of the women and 21.2% of the men reached to a peak HR of at least $90\%HR_{max,}$ and 48.0% of the tested women and 42.7% of the tested men displayed a RER_{peak} below 1.1. The reason for this early termination of the exercise test in a large number of subjects with severe obesity without any evidence for a cardiac or metabolic exhaustion remains to be explored. For the clinical setting our observation appears to be of great relevance since it indicates that classical criteria for a proper cardiorespiratory exercise testing might not be valid in subjects with severe obesity.

At a first glance, it may appear surprising that the inclusion of body composition variables in respective regression models on $\dot{V}O_{2,peak}$ and W_{peak} values did not improve the prediction of exercise performance in our subjects. However, it should be noted that the methodology of body composition assessment, i.e. bioelectrical impedance analysis, clearly has its limitations in particular in subjects with severe obesity [25]. Therefore, it would be interesting to see whether more accurate methods such as dual x-ray absorptiometry or air displacement plethysmography perform better in this context.

Our newly established fitness classes for subjects with severe obesity might be helpful in the clinical setting, since they will allow for easily giving feedback to respective subjects on how he/she performs in comparison to severely obese counterparts. Also, they will help to stratify subjects with severe obesity into different fitness classes. However, further studies will be needed to see whether a classification upon these reference values will also have a predictive value for clinical outcomes. It needs to be pointed out that our data set did not represent an assessment of maximal exhaustion according to general criteria [24], e.g. VO_{2peak} plateau phenomenon. However, different criteria for the detection of the plateau phenomenon are published which makes the analysis more difficult [26].

Several *further* limitations of our study need be pointed out. Since data were obtained in a Caucasian population, fitness classes might not be transferable to other ethnic groups. Secondly, it should be noted that we performed bicycle exercise tests, which represent a non-weight-bearing activity. Therefore, our cardiorespiratory fitness classes should not be extrapolated to other, e.g. treadmill, exercise testing protocols. Considering body weight-related VO_{2peak}, the selected population of the present study seems to be unfit. This implies at first glance that an establishment of reference values is not possible since it does not include fitness levels from low to high. Taking a closer look at the range of absolute VO_{2peak} values makes it obviously that the data set comprises a wide span of fitness, e.g. VO_{2peak} in women younger than 39 years and taller than 163 cm ranges from less than 1.21 L/min (group ‘markedly below average’) to higher than 3.0 L/min (group ‘markedly above average’; Table 3). Furthermore, our study sample did not exclusively include healthy subjects but also subjects suffering from metabolic diseases such as DM, which is obviously associated with a lower cardiorespiratory exercise performance [27–30]. In this context, it should be mentioned that there is evidence that beta blockade has a negative impact on cardiorespiratory performance whereas extent of reduction relies on type of used betablockers [31] and also on used test (i.e. six-minute walking test vs. submaximal cycling test [32]). In order to present a “most representative” dataset for subjects with obesity, subject taken betablocker (approx. 10%) were included in respective analyses. This data set was selected with regard to the underlying study design focusing on cardiorespiratory fitness parameters, correcting for diabetes status and beta blocker intake. The reason for this statistical approach was to cover a most representative sample of subjects with severe obesity but under a practical point of view. Since beta blocker use as well as diabetic status [27–31] - both known to influence cardiorespiratory fitness - are easily to assess in clinical routine, these parameters were integrated in the present model. Therefore, we believe that excluding such metabolically affected subjects from our analysis would have greatly limited the significance of our study since it would have excluded a large number of subjects health care providers are frequently confronted with.

Conclusion

Our study highlights the difficulties in quantifying and interpreting cardiorespiratory fitness markers in subjects with severe obesity. While relating respective markers to body weight may yield clinically relevant information this approach is obviously not useful for quantifying cardiorespiratory fitness. Our cardiorespiratory fitness classes might be helpful in the clinical setting when subjects with severe obesity undergo a bicycle exercise test.

Conflicts of interest

The authors declared no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.numecd.2019.07.014.

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