Ventilatory and perceptual responses to cycle exercise in obese women

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Ofir D, Laveneziana P, Webb KA, O’Donnell DE. Ventilatory and perceptual responses to cycle exercise in obese women. J Appl Physiol 102: 2217–2226, 2007. First published January 18, 2007; doi:10.1152/japplphysiol.00898.2006.—The main purpose of this study was to examine the relative contribution of respiratory mechanical factors and the increased metabolic cost of locomotion to exertional breathlessness in obese women. We examined the relationship of intensity of breathlessness to ventilation (Ve) when exertional oxygen uptake (VO2) of obesity was minimized by cycle exercise. Eighteen middle-aged (54 ± 8 yr, mean ± SD) obese [body mass index (BMI) 40.2 ± 7.8 kg/m2] and 13 age-matched normal-weight [BMI 23.3 ± 1.7 kg/m2] women were studied. Breathlessness at higher submaximal cycle work rates was significantly increased (by ≥1 Borg unit) in obese compared with normal-weight women, in association with a 35–45% increase in Ve and a higher metabolic cost of exercise. Obese women demonstrated greater resting expiratory flow limitation, reduced resting end-expiratory lung volume (EELV)(by 20%), and progressive increases in dynamic EELV during exercise: peak inspiratory capacity (IC) decreased by 16% (0.39 liter) of the resting value. Ve/VO2 slopes were unchanged in obesity. Breathlessness ratings at any given Ve or VO2 were not increased in obesity, suggesting that respiratory mechanical factors were not contributory. Our results indicate that in obese women, recruitment of resting IC and dynamic increases in EELV with exercise served to optimize operating lung volumes and to attenuate expiratory flow limitation so as to accommodate the increased ventilatory demand without increased breathlessness.

Activity-related breathlessness is a common symptom in obesity and the question arises whether this is due to 1) abnormal respiratory mechanical factors related to chest wall loading, 2) the increased metabolic demand of locomotion in obesity, or 3) both of these together. Babb et al. (6) showed that in younger women (mean age 35 yr) with mild obesity [mean body mass index (BMI) 34 kg/m2] measurements of work of breathing and ratings of breathlessness during incremental cycle exercise were similar to those of normal-weight controls. However, an explanation for these findings was not pursued in that study. The present study was undertaken to extend our knowledge of the physiological derangements of obesity and specifically to determine whether abnormalities of dynamic ventilatory mechanics peculiar to obesity (chest wall elastic loading combined with expiratory flow limitation) contributed to the quality and intensity of exertional breathlessness in female participants. In this study, the increased metabolic cost of locomotion in obesity was minimized by using weight-supported cycle exercise. We postulated that if the intensity of breathlessness at any given minute ventilation (Ve) and oxygen uptake (VO2) did not increase in obesity compared with normal-weight control subjects, then respiratory mechanical factors were unlikely to be contributory. Alternatively, an increase in breathlessness/Ve and breathlessness/VO2 slopes during weight-supported cycle exercise in obese compared with normal-weight participants would indicate that restrictive ventilatory mechanics as a result of obesity contributed to increased breathing discomfort. We therefore compared ventilatory (operating lung volumes, airway function, gas exchange, and breathing pattern) and perceptual responses (quality and intensity of breathlessness and leg discomfort) to incremental cycle exercise in 18 middle-aged, obese women (OB) and 13 age-matched women with normal BMI (NW).

METHODS

Subjects

Eighteen middle-aged (40–80 yr) obese women with a BMI >30 kg/m2 completed the study. In accordance with criteria established by the American Thoracic Society (2), there was no evidence that any subjects suffered from chronic obstructive pulmonary disease (COPD) or bronchial asthma. Obese subjects were also excluded if they had 1) other medical conditions that could cause or contribute to breathlessness, i.e., metabolic, cardiovascular or other respiratory diseases; or 2) other disorders that could interfere with exercise testing, i.e., neuromuscular diseases, musculoskeletal problems, etc.

As control subjects, we also included 13 older women showing 1) normal body weight (BMI = 20–25 kg/m2); 2) normal baseline spirometry [forced expiratory volume in 1 s (FEV1) ≥80% predicted, ratio of FEV1 to forced vital capacity (FVC) ≥80%]; and 3) absence of any health problems, including cardiovascular, neuromuscular,
musculoskeletal, or respiratory diseases which may contribute to breathlessness or exercise limitation. Healthy subjects were recruited from the local community using word-of-mouth, notices posted in community health care facilities and newspaper advertisements.

**Study Design**

This was a controlled, cross-sectional study in which informed consent was obtained from all subjects, and ethical approval was received from the University and Hospital Health Sciences Human Research Ethics Board. The subjects were tested on 2 separate days over the course of ~1 wk. On the first day, after informed consent and appropriate screening of medical history, all subjects (OB and NW) underwent anthropometric and dual-energy X-ray absorptiometry (DEXA) measurements, and they were familiarized with the various questionnaires and scales for rating the intensity and quality of breathlessness. On the second day, all subjects completed pulmonary function testing and cardiopulmonary exercise testing. Before testing at each visit, subjects were asked to avoid the ingestion of alcohol, caffeine-containing products, and a heavy meal for at least 4 h and to refrain from strenuous activity (e.g., cycling, running) for at least 12 h. Subjects were also required to eat a normal mixed diet before laboratory visits to provide valid metabolic results during exercise. Experimental visits were conducted at the same time of day for each subject.

**Anthropometric and DEXA Measurements**

Standard girth (including waist and hip circumference measurements) and skinfold measurements (triceps, biceps, subscapular, iliac crest, and medial calf) were assessed. A full-body DEXA scan was performed to measure fat, bone, and lean muscle mass.

**Evaluation of Dyspnea**

Assessments of chronic activity-related dyspnea were made on the first visit using the Baseline Dyspnea Index (BDI) (33) and the Oxygen Cost Diagram (OCD) (35). Exertional breathlessness was evaluated using the 10-point Borg scale (9) during exercise testing (see **Symptom evaluation**).

**Pulmonary Function Testing**

Lung function testing was conducted in accordance with recommended techniques (4, 31, 36, 37, 55). Routine spirometry, constant-volume body plethysmography, single-breath diffusing capacity for carbon monoxide (DLCO), and maximum inspiratory and expiratory mouth pressures [PImax and PEmax; measured at functional residual capacity (FRC) and total lung capacity (TLC), respectively] were performed while sitting at rest using an automated pulmonary function testing system (6200 Autobox DL or Vmax229d, SensorMedics, Yorba Linda, CA). Predicted normal values for spirometry, lung volumes, DLCO, airway resistance, PEmax, and PImax were those of Morris and associates (39), Crapo and associates (15), Burrows and associates (11), Briscoe and Dubois (10), Black and Hyatt (8), and Hamilton et al. (22), respectively; predicted normal inspiratory capacity (IC) was calculated as predicted TLC minus predicted FRC.

**Cardiopulmonary Exercise Testing**

Incremental exercise testing was conducted on an electronically braked cycle ergometer (Ergometrics 800S; SensorMedics, Yorba Linda, CA) using the Vmax229d Cardiopulmonary Exercise Testing System (SensorMedics) according to recommended guidelines (3). Equipment was calibrated immediately before each test. All exercise tests consisted of a steady-state resting period (at least 6 min of quiet breathing through a mouthpiece) and a 1-min warm-up of 10-W load pedaling followed by an incremental test in which the work rate was increased in 2-min intervals by increments of 20 W. Pedaling rate was maintained between 50 and 70 revolutions/min. All exercise tests were terminated at the point of symptom limitation (peak exercise).

Breath-by-breath data were collected at baseline and throughout exercise while subjects breathed through a mouthpiece with nasal passages occluded by a nose clip. Oxygen saturation by pulse oximetry (SpO2); electrocardiographic monitoring of heart rate, rhythm, and ST segment changes; and blood pressure by indirect sphygmomanometry were carried out at rest and throughout exercise testing.

**Gas exchange measurements.** VE, VO2, carbon dioxide production (VCO2), and end-tidal carbon dioxide partial pressure (PETCO2) were calculated using standard formulae (29). Exercise variables were measured and averaged over the last 30 s of each minute and at peak exercise. Peak VO2 was defined as the highest VO2 that could be sustained for at least 30 s during the last stage of exercise. VO2 was reported in absolute units (l/min), after correction of body weight (ml·kg⁻¹·min⁻¹) and fat-free mass (FFM) (ml·kg FFM⁻¹·min⁻¹), and as a percentage of predicted normal values accounting for gender, age, height, and ideal body weight (55). Exercise parameters were compared with the predicted normal values of Jones (29).

The ventilatory threshold (VTh) was detected individually using the V-slope method (55) and verified against other points, i.e., the VO2 at which the ventilatory equivalent for oxygen (Ve/Vo2) begins to increase systematically without an increase in the ventilatory equivalent for carbon dioxide (Ve/VCO2) and where end-tidal oxygen partial pressure (PetO2) begins to increase without a decrease in PetCO2 (55).

**Symptom evaluation.** Exertional dyspnea was defined as “the sensation of labored or difficult breathing” and leg discomfort as “the level of leg discomfort experienced during exercise.” Before exercise testing, subjects were familiarized with the Borg scale (9), and its end points were anchored such that zero represented “no breathing (leg) discomfort” and 10 was “the most severe breathing (leg) discomfort that they ever experienced or could imagine experiencing.” By pointing to the Borg scale, subjects rated the magnitude of their perceived breathing and leg discomfort at rest, every minute, and at peak exercise. On exercise cessation, subjects were also asked to verbalize their main reason for stopping exercise (i.e., breathing discomfort, leg discomfort, both, or others), and this reason was documented. Qualitative aspects of perceived breathing discomfort at peak exercise were described by completion of a questionnaire of descriptors of breathlessness modified (43) from Simon and co-workers (52).

**Operating lung volumes.** Changes in end-expiratory lung volume (EELV) were estimated from IC measurements at rest, at the end of each 2-min increment of exercise, and at peak exercise. Because TLC does not change during activity (53), the change (reduction) in IC reflects the inverse change (increase) in dynamic EELV (EELV = TLC – IC), whereas changes in inspiratory reserve volume (IRV) reflect changes in end-inspiratory lung volume (EILV = EELV – IRV). This has been found to be a reliable method of tracking acute changes in lung volume (44, 57). Techniques for performing and accepting IC measurements have been previously described (45). Confirmation of satisfactory technique and reproducibility of IC maneuvers for each subject was established during an initial practice session at rest.

**Tidal flow-volume loops.** Flow and integrated volume were recorded continuously during exercise testing. Tidal flow-volume curves at rest, every 2 min during exercise, and at peak exercise were constructed for each patient and placed within their respective maximal flow-volume envelopes according to coinciding IC measurements. The presence or absence of expiratory flow limitation was estimated by calculating the percentage of tidal volume (Vt) that encroaches on the maximal flow envelope, as well as the extent of encroachment of flow at the midrange of Vt on the maximal flow-volume envelope at isovolume (26, 28).
**Statistical Analysis**

A sample size of 16 provides the power (80%) to detect a significant difference in dyspnea intensity (Borg scale) measured at a standardized work rate during incremental cycle exercise based on a relevant difference in Borg ratings of ±1, a SD of 1 for standardized Borg ratings found at our laboratory in a healthy older population (45), \( \alpha = 0.05 \), and a two-tailed test of significance. Results are expressed as means ± SD. A \( P < 0.05 \) level of statistical significance was used for all analyses. Between-group comparisons were made using unpaired \( t \)-tests with Bonferroni correction for multiple comparisons; i.e., measurements at rest, at peak exercise, at the ventilatory threshold, and at a standardized work rate were compared in addition to baseline comparisons of anthropometric measurements and pulmonary function. Qualitative dyspnea descriptors were analyzed as frequency statistics and compared using the Fisher’s exact test.

**RESULTS**

Subjects’ characteristics are shown in Table 1. Eighteen older women with mild-to-severe obesity (OB) and 13 age-matched normal-weight women (NW) successfully completed the study protocol. The OB group included five obese class I (BMI 30–34.9 kg/m\(^2\)), four obese class II (BMI 35–39.9 kg/m\(^2\)), and nine obese class III (BMI >40 kg/m\(^2\)). Body weight, body surface area, sum of five skinfolds, waist circumference, trunk fat, body percent fat, as well as total lean body mass were all significantly (\( P < 0.05 \)) greater in OB compared with NW. In all women of the OB group, the primary distribution of fat was central: waist circumference was >88 cm in all obese subjects (18); waist-to-hip ratios were >0.8 in all but two subjects, one with class III obesity (BMI 59 kg/m\(^2\)) and the other with class I obesity (BMI 33 kg/m\(^2\)) but a high percentage (45%) of trunk fat.

The BDI and OCD revealed an important decrease in the ability to perform daily physical activities due to increased breathlessness (Table 1). OB scored ~3 units lower in the BDI questionnaire than NW (\( P < 0.05 \)), and they perceived shortness of breath at a lower relative intensity of daily activities in the OCD (\( P < 0.05 \)).

In the NW group, four subjects had a smoking history (13 ± 8 pack-yr). Of these four subjects, three had stopped smoking >20 yr before study, and the one current smoker had a smoking history longer than 20 pack-yr but no evidence of COPD or small-airway disease as assessed by pulmonary function tests or previous thoracic computed tomography scan results performed as part of another study comparing potential prognostic indicators in COPD and age-matched healthy subjects. In the OB group, 10 subjects had a smoking history (14 ± 9 pack-yr): 8 of the subjects had stopped smoking between 12 and 29 yr previously, and 2 were current smokers (20 and 29 pack-yr) with no evidence of changes in pulmonary function.

Habitual physical activity records were collected for 13 NW and 12 OB subjects. All 13 NW subjects reported that they performed between 3 and 5 aerobic activities (i.e., walking, cycling, etc) per week for at least 30 min, while 7 OB subjects performed aerobic activity between one and five times per week.

**Pulmonary Function**

Pulmonary function test results are summarized in Table 2. All subjects had normal FEV\(_1\), FVC, and FEV\(_1\)/FVC (47), as well as normal DL\(_{CO}\) normalized to alveolar volume. In absolute and relative terms, OB had significantly (\( P < 0.05 \)) lower expiratory reserve volume (ERV) (0.62 ± 0.22 vs. 1.29 ± 0.09 liters) and greater IC (2.98 ± 0.41 vs. 2.44 ± 0.17 liters) compared with NW, respectively. Similarly, FRC described in relative terms (Table 2), as a percentage of predicted TLC (46 ± 7 vs. 66 ± 8% predicted TLC) and in absolute terms (2.30 ± 0.45 vs. 3.42 ± 0.41 liters) was significantly (\( P < 0.05 \)) lower in OB. Interestingly, plethysmographic FRC (or resting EELV) correlated with the percentage of trunk fat (\( r^2 = 0.62 \), \( P < 0.05 \)). However, the decrease in FRC had no effect on \( P_{\text{max}} \) in the OB group, and both \( P_{\text{max}} \) and \( P_{\text{emax}} \) were similar to the NW group (Table 2).

**Cardiorespiratory Responses to Symptom-Limited Cycle Exercise**

Respiratory responses (\( \dot{V}_{\text{O2}}, \dot{V}_{\text{E}}, \dot{V}_{\text{E}}/\dot{V}_{\text{CO2}}, \) and \( \text{SpO}_2 \)) shown against work rate are provided in Fig. 1. Breathing pattern and operating lung volume responses to exercise are shown in Figs. 2 and 3, respectively. Compared with NW, OB had reduced \( V_t \) and an increased breathing frequency [associated with decreases in both inspiratory and expiratory time (\( T_i \) and \( T_e \), respectively)] with no difference in the duty cycle (\( T_d/T_t \)) for a given \( V_e \) during exercise (Fig. 2). Results at VTh and at peak exercise are summarized in Table 3.

**Steady-state rest.** At rest, OB had a higher \( \dot{V}_{\text{O2}} \) (0.26 ± 0.06 vs. 0.18 ± 0.05 l/min; \( P < 0.05 \)) than NW. There was no difference between groups when \( \dot{V}_{\text{O2}} \) was normalized for lean body mass. These results suggest that the higher metabolic rate measured in obese women at rest is a consequence of larger muscle mass.

VTh. The OB group, compared with NW group, reached their VTh at a lower (\( P < 0.05 \)) cycle work rate and at \( \dot{V}_{\text{O2}} \) indexed to FFM, indexed to actual body weight, and as a percentage of predicted maximum; however, the groups

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**Table 1. Subjects characteristics**

<table>
<thead>
<tr>
<th>Age, yr</th>
<th>Normal Weight (n = 13)</th>
<th>Obese (n = 18)</th>
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</thead>
<tbody>
<tr>
<td>54.6±2.0</td>
<td>54.2±2.0</td>
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</tbody>
</table>

| Height, cm | 164.8±1.1 | 161.5±1.1† |
| Weight, kg | 63.0±12 | 104.4±4.3† |
| Weight, %ideal body weight* | 98±2 | 168±8† |
| Weight/height, kg/cm | 0.38±0.03 | 0.65±0.12† |
| Body mass index, kg/m² | 23.3±0.5 (20–25) | 40.2±1.8† (30–59) |
| Body surface area, m² | 1.69±0.02 | 2.17±0.13† |
| Waist circumference, cm | 75.6±1.5 (65–82) | 112.1±3.7† (94–136) |
| Waist-to-hip ratio | 0.78±0.03 | 0.85±0.01† |
| DEXA measurements | |
| Body fat, % | 31.7±1.8 | 45.2±1.1† |
| Lean body weight, kg | 41.4±0.7 | 52.6±1.3† |
| Trunk fat, %total body weight | 26.8±2.2 | 45.1±1.4† |
| Chronic dyspnea questionnaires | |
| Baseline Dyspnea Index, 1–12 | 11.5±0.2 (10–12) | 8.9±0.5 (5–12)† |
| Oxygen Cost Diagram, 0–100 mm | 86±4 (69–100) | 71±4 (47–96)† |

Values are means ± SE with range in parentheses; n, no. of subjects. DEXA, dual-energy X-ray absorptiometry. *Ideal body weight was calculated from equation in Wasserman (55). †\( P < 0.05 \) obese group vs. normal-weight group.
reached their VTh at a similar \( \dot{V}O_2 \) if expressed as milliliters per minute, as well as at a similar \( \dot{V}E \) (Table 3). During exercise from rest to VTh, IC changed by 0.06 ± 0.29 and 0.27 liter in NW and OB, respectively (\( P < 0.05 \)). Acute changes in IC from rest to VTh correlated with BMI (\( r = 0.65, P < 0.01 \)) and with percent trunk fat (\( r = 0.60, P < 0.02 \)).

**Peak exercise.** Metabolic and ventilatory parameters measured during the last 30 s of exercise (peak) are shown in Table 3. Compared with NW, OB women stopped exercise at a lower \( \dot{V}O_2 \) normalized to body mass (\( P < 0.05 \)), and at a lower \( \dot{V}O_2 \) indexed to FFM (\( P < 0.05 \)), but at a similar absolute \( \dot{V}O_2 \) and \( \dot{V}E \). OB achieved lower maximal heart rate and a similar oxygen pulse compared with NW. IRV at peak exercise was similar in both groups (Fig. 3). At end exercise, OB experienced significantly greater dynamic increases in EELV than NW: IC decreased by 0.38 ± 0.01 vs. 0.01 ± 0.25 liter, respectively (\( P < 0.001 \)).

**Breathing and Leg Discomfort During Cycle Exercise**

At the end of exercise in the NW group, six women stopped primarily due to breathing discomfort, six due to leg discomfort, and one stopped due to the combination of leg and breathing discomfort. In the OB group, five women stopped due to breathing discomfort, eight due to leg discomfort, three due to the combination of breathing and leg discomfort, and two stopped exercise due to factors other than breathing or

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**Table 2. Pulmonary function**

<table>
<thead>
<tr>
<th></th>
<th>Normal Weight (n = 13)</th>
<th>Obese (n = 18)</th>
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<tbody>
<tr>
<td>FVC, %predicted</td>
<td>110 ± 3</td>
<td>107 ± 3</td>
</tr>
<tr>
<td>FEV1, %predicted</td>
<td>114 ± 3</td>
<td>108 ± 4</td>
</tr>
<tr>
<td>FEV1/FVC, %predicted</td>
<td>103 ± 2</td>
<td>101 ± 2</td>
</tr>
<tr>
<td>TLC, %predicted</td>
<td>112 ± 3</td>
<td>107 ± 2</td>
</tr>
<tr>
<td>IC, %predicted</td>
<td>108 ± 2</td>
<td>136 ± 4*</td>
</tr>
<tr>
<td>FRC, %predicted</td>
<td>115 ± 6</td>
<td>83 ± 3*</td>
</tr>
<tr>
<td>ERV, %predicted</td>
<td>132 ± 10</td>
<td>52 ± 8*</td>
</tr>
<tr>
<td>RV, %predicted</td>
<td>107 ± 5</td>
<td>89 ± 3*</td>
</tr>
<tr>
<td>DlCO/VA, %predicted</td>
<td>111 ± 5</td>
<td>111 ± 4</td>
</tr>
<tr>
<td>sRaw, %predicted</td>
<td>166 ± 81</td>
<td>178 ± 75</td>
</tr>
<tr>
<td>PImax, %predicted</td>
<td>114 ± 12</td>
<td>121 ± 10</td>
</tr>
<tr>
<td>PeMax, %predicted</td>
<td>80 ± 6</td>
<td>92 ± 6</td>
</tr>
</tbody>
</table>

Values are means ± SE; \( n \), no. of subjects. DLCO, diffusing capacity of the lung for carbon monoxide; ERV, expiratory reserve volume; FEV1, forced expired volume in 1 s; FRC, functional residual capacity; FVC, forced vital capacity; IC, inspiratory capacity; PImax, maximal inspiratory pressure measured at FRC; PeMax, maximal expiratory pressure measured at total lung capacity (TLC); RV, residual volume; sRaw, specific airways resistance; VA, alveolar volume. *Statistically different from normal weight control group, \( P < 0.05 \).

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Fig. 1. Oxygen consumption (\( \dot{V}O_2 \)), minute ventilation (\( \dot{V}E \)), \( O_2 \) saturation by pulse oximetry (\( S_pO_2 \)), and the ventilation equivalent for carbon dioxide production (\( \dot{V}E/\dot{V}CO_2 \)) responses to symptom-limited incremental cycle exercise in obese (OB) women (●) and in normal-weight (NW) women (○). Higher \( \dot{V}O_2 \) and \( \dot{V}E \) were found between rest and 80 W but not at peak exercise in OB compared with NW women. \( S_pO_2 \) was lower in OB compared with NW women at rest but not during exercise. Similar relationships in both OB and NW women were found between \( \dot{V}E/\dot{V}CO_2 \) and work rate. Values are means ± SE. *\( P < 0.05 \) OB vs. NW.
legs. No difference in the distribution of the reasons for stopping exercise was found between the two groups.

Ratings of intensity of breathing and leg discomfort relative to work rate are shown in Fig. 4. No differences were found for breathing or leg discomfort between NW and OB at the end of the symptom-limited cycle test. However, in the OB group, leg discomfort was rated higher than breathing discomfort (5.0 ± 2.7 vs. 4.1 ± 2.4 Borg units; \( P < 0.05 \)) (Table 3). OB started perceiving significantly greater breathing discomfort from a workload of 60 W (~55% predicted), which corresponded with VTh. Significantly (\( P < 0.05 \)) higher ratings of dyspnea intensity were found in OB compared with NW at 60 W (0.7 Borg units) and at 80 W (1.2 Borg units). Leg discomfort was greater in OB from exercise onset (20 W) and throughout exercise: differences for leg discomfort ranged from 0.4 unit of Borg (\( P < 0.05 \)) at 20 W to 1.6 units of Borg at 80 W (\( P < 0.05 \)).

**Dyspnea/VdotE and dyspnea/VdotO2 curves were superimposed for OB and NW (Fig. 4). At a standardized work rate (80 W) in OB, ratings of dyspnea intensity correlated significantly with VdotE/VdotO2 (\( r = 0.77, P < 0.0005 \)), VdotT/VdotE (\( r = 0.71, P = 0.001 \)), VdotT/VdotI (\( r = 0.67, P = 0.002 \)), VdotE expressed as a fraction of maximal breathing capacity (\( r = 0.60, P = 0.008 \)), and VdotE/VdotCO2 (\( r = 0.54, P = 0.021 \)).**

In comparison with NW, OB described their breathing discomfort at the end of exercise as more “shallow” and related to “expiratory difficulty” (\( P < 0.05 \)) (Fig. 5). NW reported that breathing discomfort could be described as “increased work” (\( P < 0.05 \)).

**Expiratory Flow Limitation at Rest and During Exercise**

Expiratory flow limitation relative to VdotE is presented in Fig. 2. Compared with NW, we found a significantly (\( P < 0.05 \)) greater extent of expiratory flow limitation in OB at rest and during submaximal exercise. In 10 of the 18 OB, resting VT was under some degree of expiratory flow limitation; i.e., 36–100% of VT overlapped the maximal flow-volume envelope. In contrast, none of the NW women were flow limited at rest. During exercise, the average extent of estimated expiratory flow limitation in obese was maintained, but it increased in NW. During exercise, OB were significantly more expiratory flow-limited than NW by an average of 42% at the 20-W load and by 27% at the 80-W load. Examples of tidal vs. maximal flow-volume loops in an OB and an age-matched NW woman are shown in Fig. 6; these flow-volume loops are representative of the EELV behavior in each group. While the majority (13 of 18) of the OB group increased EELV during exercise, the NW group had small inconsistent changes in EELV during exercise.
Dynamic changes in EELV during exercise were similar in the four NW participants with a smoking history to those of the nonsmokers. There was no significant difference between the OB smoking subgroups in resting pulmonary function (i.e., spirometry, plethysmographic lung volumes, and $\text{DL}_{\text{CO}}$) or in EELV changes during exercise: EELV increased similarly by 0.41 ± 0.36 and 0.36 ± 0.32 liter from rest to peak exercise in subjects with and without a smoking history, respectively.

**DISCUSSION**

The main findings of this study are the following. 1) Symptom-limited peak VO$_2$ when expressed as a percentage of predicted for ideal body weight was normal in OB. 2) Breathlessness intensity was significantly higher at any given submaximal cycle work rate in OB, reflecting the higher ventilatory demand as a result of a higher metabolic cost of performing this task. 3) Quantitative flow-volume loop analysis demonstrated significant mechanical ventilatory constraints in OB compared with NW. Despite this, breathlessness ratings were not increased at any given $V_E$ or VO$_2$ throughout exercise in OB compared with NW.

It is well established that when peak VO$_2$ is expressed as a fraction of actual body weight, peak aerobic capacity can be significantly underestimated in obesity, as was the case in this study. When peak VO$_2$ was indexed to ideal body weight utilizing the formula of Wasserman (55), we determined that values were well within the normal range in the OB group. Peak VO$_2$ corrected for the increased lean body mass was diminished by an average of 22% in OB compared with NW. In the absence of predicted values for VO$_2$ corrected for FFM, this finding is difficult to interpret. Compromised cardiovascular function, which has previously been described in morbid obesity (49), may have been contributory in some of our participants, but this remains conjectural.

Exercise limitation was multifactorial in OB, and it was impossible to identify the proximate physiological limit in this group. Peak heart rates were significantly lower in OB vs. NW, but this may simply reflect the lower peak VO$_2$ achieved in the former. Both groups reached a similar peak $V_E$ and reserves for $V_T$ expansion, as reflected by a high peak EELV/TLC ratio, were similarly reduced in both groups. Overt ventilatory insufficiency (CO$_2$ retention) at the peak of exercise was not evident in any participant, even in those with morbid obesity. The distribution pattern of exercise-limiting symptoms was similar in both groups. However, intensity ratings for leg discomfort were significantly higher than those for breathing discomfort at peak exercise within the OB group.

Obese women were, on average, almost twice the ideal body weight and reported mild-to-moderate activity-related breathlessness as measured by the BDI and the OCD. Ratings of breathlessness in OB were statistically higher at any given submaximal cycle work rate throughout cycle exercise compared with NW (Fig. 4). However, the OB group was able to exercise to 80% of their predicted maximum work rate while reporting only slight (Borg = 2 units) breathing discomfort. Thereafter, Borg ratings of breathlessness in OB rose more steeply by an average of ~2 units in the final phase of exercise as $V_E$ increased from 44 l/min to a peak of 59 l/min. The rate of rise in breathlessness in the final minutes of exercise was similar in both groups (Borg units increased by an average of 1 unit per 8.2 l/min increase in $V_E$).

### Table 3. Cardiorespiratory and perceived discomfort at the ventilatory threshold and at the peak of symptom-limited cycle exercise

<table>
<thead>
<tr>
<th></th>
<th>Normal-weight group</th>
<th>Obese group</th>
<th>Normal-weight group</th>
<th>Obese group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ventilatory Threshold</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Work rate, W (%predicted max)</td>
<td>85±5 (79±6)</td>
<td>59±4† (56±4)†</td>
<td>132±8 (121±7)</td>
<td>110±6† (102±5)†</td>
</tr>
<tr>
<td>VO$_2$, l/min (%predicted max)*</td>
<td>1.22±0.06 (66±3)</td>
<td>1.16±0.05 (69±3)</td>
<td>1.82±0.07 (99±5)</td>
<td>1.76±0.07 (105±5)</td>
</tr>
<tr>
<td>Vco$_2$, ml·kg FFM$^{-1}$·min$^{-1}$</td>
<td>29.0±1.3</td>
<td>21.7±0.9*</td>
<td>43.3±1.6</td>
<td>33.6±1.3†</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>130±4†</td>
<td>117±4†</td>
<td>162±5</td>
<td>144±4†</td>
</tr>
<tr>
<td>O$_2$ pulse, ml·O$_2$/beat</td>
<td>9.4±0.4</td>
<td>10.3±0.6</td>
<td>11.2±0.3</td>
<td>12.4±0.6</td>
</tr>
<tr>
<td>VE, l/min (%predicted)</td>
<td>32.2±1.4 (33±1)</td>
<td>31.5±1.4 (36±2)</td>
<td>65.3±2.8 (66±3)</td>
<td>58.8±3.0 (66±4)</td>
</tr>
<tr>
<td>$P_{\text{ETCO}_2}$, Torr</td>
<td>47.3±1.2</td>
<td>45.2±0.8</td>
<td>39.2±0.9</td>
<td>40.8±1.2</td>
</tr>
<tr>
<td>IC, liters (%predicted)</td>
<td>2.47±0.07 (110±3)</td>
<td>2.68±0.12 (122±5)</td>
<td>2.42±0.05 (105±2)</td>
<td>2.46±0.12 (113±5)</td>
</tr>
<tr>
<td>IRV, liters (%TLC predicted)</td>
<td>1.07±0.07 (21±2)</td>
<td>1.45±0.12† (28±2)†</td>
<td>0.62±0.07 (12±1)</td>
<td>0.84±0.10 (15±2)</td>
</tr>
</tbody>
</table>

Values are means ± SE. FFM, fat-free mass; HR, heart rate; IC, inspiratory capacity; IRV, inspiratory reserve volume; max, maximum; MBC, estimated maximal breathing capacity; $P_{\text{ETCO}_2}$, partial pressure of end-tidal CO$_2$; $V_E$, minute ventilation; VO$_2$, oxygen consumption. Note: resting data have been deleted. *Predicted normal values for VO$_2$ from Wasserman (55). †P < 0.05 obese compared with normal-weight group.
Ventilation was consistently elevated at any given cycle work-rate throughout exercise; at 80 W, \( V'E \) was increased by \( 110 \pm 10 \) l/min or 40% in OB vs. NW (Fig. 1). This excessive \( V'E \), in part, reflected the high metabolic cost of lifting heavy limbs against gravity as well as an increase in the work of breathing: there was an upwards parallel shift of the \( V'O_2 \)/work rate relationship in OB but \( V'E/V'O_2 \) slopes were similar in OB and NW. \( V'E/V'CO_2 \) slopes, estimates of physiological dead space throughout exercise (17), and \( SpO_2 \) measurements were similar in both groups. It is unlikely therefore that increased chemostimulation, as a result of critical arterial oxygen desaturation or inefficiency of CO₂ elimination, contributed to the amplified ventilatory response in OB. Regardless of the mechanism, the accelerated ventilatory response in OB likely contributed to increased intensity of breathing discomfort at a given power output in OB: not only were slopes of Borg dyspnea ratings over \( V'E \) superimposed (Fig. 4) but also Borg ratings at a standardized work rate correlated well with \( V'E/V'CO_2 \) and \( V'E/V'O_2 \) within the OB group and in the total study sample.

To determine the effect of respiratory mechanical factors on exertional breathlessness in OB, we compared dyspnea/\( V'E \) slopes and dyspnea/\( V'O_2 \) slopes with those of the NW group throughout cycle exercise (which would attenuate the increase in \( V'O_2 \) normally associated with weight-bearing exercise in OB). Previous studies have shown that external mechanical loading of the ventilatory muscles causes breathlessness to rise...
at any given $V_e$ during exercise, compared with unloaded control (13, 23, 43, 56). Similarly, studies of mechanical unloading in patients with respiratory diseases demonstrated consistent reductions in dyspnea intensity at any given $V_e$ during cycle exercise (25, 46). Our results showed that breathlessness ratings at any given $V_e$ or $V_O_2$ throughout exercise were not increased in OB compared with NW (Fig. 4). The explanation for this surprising finding becomes evident after detailed analysis of ventilatory mechanics at rest and during exercise in OB.

The nature and severity of the mechanical abnormalities encountered in OB will vary with the extent and anatomical distribution of adipose tissue (14, 31). Our subjects had predominant central fat distribution: waist circumferences exceeded 88 cm in all subjects (range 95–136 cm) and waist-to-hip ratios exceeded 0.8. A reduced plethysmographic EELV in OB reflected decreased respiratory system compliance (40) and the resetting of the relaxation volume (5–7). The finding that plethysmographic EELV correlated with the percentage of trunk fat ($r^2 = 0.62$) supports this notion. As expected, ERV was reduced (by 52%), indicating that EELV was positioned close to RV at the lower extreme of the respiratory system’s sigmoidal pressure-volume relationship. Previous studies have indicated increased respiratory resistance (51, 58) and increased expiratory flow limitation in obesity during resting breathing (5, 6, 19, 50). In the OB group, specific airway conductance was not different than NW, but maximal expiratory flow rates at 75% of the VC tended to be lower. Overlap of resting $V_t$ on the maximal expiratory flow-volume curve averaged 40% in OB compared with zero overlap in NW. We concede that the overlap method of assessment of expiratory flow limitation can lead to overestimation because of volume history and gas compression effects (26, 27). Nevertheless, when flows throughout much of tidal expiration reach or exceed the maximal expiratory flow envelope at that operating volume, it strongly suggests the existence of expiratory flow limitation, particularly when considered in the context of attendant acute increases in EELV.

During incremental exercise in nonobese women, dynamic EELV declined slightly but tended to increase after exceeding the VTh. This behavior of EELV contrasts with previous reports in younger (often more athletic) participants, which showed more consistent reductions in EELV during both treadmill and cycle exercise (5, 6, 24). The different results may be explained by the increased age (range 44–65 yr) of some of our participants. Thus changes in the connective tissue matrix of the lung in older participants would increase the propensity for expiratory flow limitation and dynamic hyperinflation during incremental exercise (26). Despite the lack of decline in EELV, $V_t$ expansion and alveolar ventilation was not compromised in NW, and operating lung volumes were likely maintained in the compliant portion of the respiratory system’s pressure-volume relation (i.e., <80% of the vital capacity). In contrast, OB showed progressive dynamic hyperinflation throughout exercise (Fig. 3): peak IC was reduced by 16% (0.39 liter) of the resting value. Participants with marked obesity showed earlier dynamic hyperinflation than the remainder: changes in IC from rest to VTh correlated with BMI ($r = 0.65, P < 0.01$) and with percent trunk fat ($r = 0.60, P < 0.02$). Dynamic hyperinflation likely arose during exercise because of the combination of slow mechanical time constants for lung emptying (because of the relatively low operating position of EELV) and increased breathing frequency with diminished Te as exercise progressed. Babb et al. (6) showed that younger women (mean age 35 yr) with mild obesity (mean BMI 34 kg/m$^2$) retained the ability to reduce EELV in the early phase of incremental cycle exercise. This difference in the control of EELV early in exercise between the two studies might be explained by higher resting expiratory flow limitation in the obese group in the present study. This could be related to the greater age and severity of obesity, both of which have been reported to affect expiratory flow limitation.

![Fig. 6. Resting, ventilatory threshold (VTh), and peak exercise tidal flow-volume loops are plotted within the respective maximal flow-volume loops in typical OB and NW women. The lean (NW) participant increased $V_t$ (from rest to VTh) by encroaching both on the IRV and EELV. In contrast, the OB female started with significant tidal flow limitation at rest and experienced a significant increase in dynamic EELV from rest to peak exercise. BMI, body mass index.](http://jap.physiology.org/ by 10.220.33.2 on June 12, 2017)
Why did respiratory mechanical factors not contribute importantly to exertional breathlessness in obesity? We propose that, first, dynamic increases in EELV may have had salutary effects on respiratory sensation by attenuating the expected rise in expiratory flow limitation as \( \dot{V}e \) increased during exercise. Dynamic increases in EELV in OB to a level that is closer to the predicted relaxation volume of the respiratory system would improve pressure-volume relations without any disadvantage to the inspiratory muscles. The increase in operating lung volumes in OB preserved their ability to generate the required tidal expiratory flow rates: mean expiratory and inspiratory flow rates at any given \( \dot{V}e \) in OB were comparable to that of NW, supporting this idea.

Second, the recruitment of resting IC in OB, by an average of 0.54 liter (28% predicted) higher than NW, is also likely mechanically advantageous. The increase in IC occurred in obesity because EELV declined to a greater extent than TLC. IC (not vital capacity) represents the true operating limits for expiratory flow limitation as \( \dot{V}e \) increased during exercise. An increased resting IC meant that \( \dot{V}t \) expansion (and the increased demand for \( \dot{V}e \)) could be accommodated within the most compliant portion of the respiratory system’s pressure-volume relation in spite of progressive dynamic hyperinflation. We have previously presented similar arguments for the benefits of resting IC recruitment following bronchodilator therapy in patients with chronic obstructive pulmonary disease (41, 42, 48).

The third possible adaptation is the adoption of a relatively shallow breathing pattern throughout exercise in OB compared with NW. This could represent a behavioral compensatory adjustment which minimized the discomfort associated with increased elastic loading of the inspiratory muscles. True mechanical limitation is a less likely explanation for this shallow breathing pattern in OB because, on average, the minimal IRV was greater in OB than NW: at the V\( \text{Th} \), IRV was significantly higher in OB by 0.37 liter despite similar \( \dot{V}e \) (32 l/min).

Qualitative descriptor choices of breathlessness at peak exercise were remarkably similar across groups, but obese women were more likely to report “shallow” breathing and “expiratory difficulty” at the end of exercise (Fig. 5). These descriptor choices may reflect an awareness of reduced thoracic displacement and expiratory flow limitation, but this remains conjectural. It is noteworthy that increased leg discomfort was a prominent exertional symptom in OB: Borg ratings of leg discomfort were significantly greater in OB throughout exercise, and severe leg discomfort was reported at the peak of exercise. Moreover, 11 of the 18 obese participants listed leg discomfort as a primary or coprimary exercise-limiting symptom. Leg discomfort may simply reflect the higher contractile muscle effort and central motor command output required to mobilize the heavy limbs (20, 34).

In summary, although breathlessness was common in OB it was of mild to moderate severity and, on average, participants could reach their predicted maximal power output and \( \dot{V}O_2 \). During weight-supported cycle exercise, intensity of breathlessness rose in all subjects as ventilation increased. In OB, breathlessness ratings were higher, at any submaximal cycle work rate, reflecting relatively higher ventilation and metabolic cost. Because \( \dot{V}e/\dot{V}O_2 \) slopes were not altered by obesity, we can reasonably predict that an increase in \( \dot{V}O_2 \) with weight-bearing exercise in OB would be associated with higher \( \dot{V}e \) and intensity of breathlessness compared with cycle exercise. Ratings of breathlessness at any given exercise \( \dot{V}e \) and \( \dot{V}O_2 \) were not increased in OB compared with NW, and this strongly suggests that respiratory mechanical factors, per se, contributed little to exertional respiratory discomfort. Three potential ameliorating factors were discovered in OB. First, dynamic increases in EELV attenuated progressive expiratory flow limitation and preserved their ability to increase ventilation in tandem with the increased metabolic demand. Second, despite the increased dynamic EELV, resting IC recruitment permitted expansion of \( \dot{V}t \) within the compliant portion of the respiratory system’s pressure-volume relation where neuromechanical coupling is enhanced. Third, the adoption of a relatively shallow breathing pattern likely further obviated the respiratory discomfort normally associated with excessive elastic loading of the inspiratory muscles.

GRANTS

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REFERENCES


