Differences in respiratory muscle activity during cycling and walking do not influence dyspnea perception in obese patients with COPD

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Ciavaglia CE, Guenette JA, Langer D, Webb KA, Neder JA, O'Donnell DE. Differences in respiratory muscle activity during cycling and abdominal muscles during cycling and walking on intensity and quality and intensity, quality, and affective components of COPD (14, 31). Studies have shown that dyspnea in obese patients with moderate-to-severe COPD is multifactorial and we have argued that increased metabolic requirements (increased carbon dioxide output) related to excessive body weight, which drive increased ventilation ($V_E$) during physical activity, are more important than respiratory mechanical factors, per se, in contributing to exertional dyspnea (31, 39).

In a recent noninvasive study in obese COPD patients, we established that dyspnea/work rate and dyspnea/$V_E$ slopes were not affected by exercise test modality (cycling vs. walking when work rate was controlled), despite consistent intermodality differences in some metabolic factors, e.g., oxygen uptake ($V_O_2$) and arterial oxygen saturation (8). In the present study, we extend our previous work in obese COPD by examining, for the first time, the effect of potential differences in amplitude of central respiratory drive (measured indirectly by diaphragmatic electromyography) and respiratory muscle activity (measured by esophageal and gastric balloons) between exercise modalities on dyspnea across its intensity, quality, and affective dimensions.

A number of studies in nonobese healthy individuals have documented compensatory adjustments in abdominal muscle activity to preserve diaphragmatic function when adopting a standing body position (10, 11, 23, 26, 48). Such studies have, to our knowledge, not been conducted during rest or exercise in obese individuals with COPD. It is reasonable to assume that these normal compensatory adjustments to standing upright may be undermined by exaggerated gravitational effects of abdominal obesity. Thus it is possible that diaphragmatic function may be more compromised during standing and walking (compared with weight-supported cycling) in obese patients, and this may have negative sensory consequences. The corollary is that relatively improved diaphragmatic function during cycling would be associated with favorable effects on dimensions of dyspnea, as has previously been shown in nonobese COPD patients after interventions that improve respiratory muscle function (e.g., leaning forward position, bronchodilators, noninvasive mechanical ventilation) (12, 34, 38). Accordingly, our objectives were to determine whether 1) diaphragmatic function, respiratory muscle activity, and respiratory muscle recruitment pattern were different during walking and cycling in obese COPD patients; and 2) whether such intermodality differences in respiratory muscle activity (and accompanying afferent inputs from muscle mechanoreceptors) had direct sensory consequences when external power output was standardized between tests. We, therefore, compared indirect indexes of central respiratory drive, esophageal (Pes) and transdiaphragmatic pressures (Pdi), diaphragmatic efficiency and intensity, quality, and affective components of...
dyspnea during incremental treadmill and cycle exercise when work rate was carefully matched.

METHODS

Subjects

Twelve clinically stable obese (body mass index ≥30 kg/m²) patients with COPD [forced expiratory volume in 1 s (FEV₁)/forced vital capacity (FVC) <70%] and a postbronchodilator FEV₁ < 80% predicted were included. Exclusion criteria included the following: a significant disease (i.e., metabolic, cardiovascular, neuromuscular, and/or musculoskeletal) that could affect breathlessness or exercise capacity, daytime oxygen therapy, a respiratory disease other than COPD, too breathless to leave the house or not breathless (Medical Research Council dyspnea scale 5 or 1, respectively), and any contraindications to clinical exercise testing (3).

Study Design

This cross-sectional study received ethical approval from Queen’s University and Affiliated Hospitals Research Ethics Board (DMED-1187-09). Patients provided written, informed consent before participation. Patients attended three visits separated by at least 48 h. Visit 1 included medical screening, detailed pulmonary function tests, and familiarization with all exercise testing procedures. At visits 2 and 3, patients were randomized to perform either a cycle or treadmill test with detailed diaphragmatic electromyogram (EMGdi) and pressure-derived respiratory mechanical measurements. Before each visit, patients were instructed to withhold inhaler medication at least 4 h for short-acting β₂-agonists, 6 h for anticholinergics, and 12 h for long-acting bronchodilators. Patients were asked to refrain from the intake of caffeine, heavy meals, alcohol, and from major physical exertion before each visit. At a separate visit, patients underwent dual-energy X-ray absorptiometry scan to quantify body composition.

Procedures

Pulmonary function testing included routine spirometry, body plethysmography, single-breath diffusing capacity for carbon monoxide, maximum inspiratory and expiratory mouth pressures, static lung compliance, and static lung recoil pressure using automated testing equipment (Vmax229; SensorMedics, Yorba Linda, CA). Cardiopulmonary exercise tests were performed on an electronically braked cycle ergometer (Ergometrics 800S; SensorMedics) and on a treadmill (MedTrack ST55; Quinton Instrument, Bothell, WA) using a Vmax229d Cardiopulmonary Exercise Testing System (SensorMedics). Cycle and treadmill exercise tests were both performed with 10-W increments, which increased every 2 min to a symptom-limited peak. The treadmill work rate was adjusted as follows: speed began at 0.8 miles/h (21.46 m/min) and thereafter increased linearly by 0.2 miles/h (5.36 m/min) for every 10-W increment for all subjects; a curvilinear rise in percent grade was calculated for each subject based on the equation by Cooper and Storer [Watts = 0.1634 × speed (m/min) × % grade/100 × body mass (kg)] (9). Breath-by-breath data (cardiopulmonary, EMGdi, and respiratory-mechanical measurements) were analyzed using 30-s averages from each individual at steady-state rest, the first 30-s interval of the last minute from each exercise work rate, and the last 30-s of loaded pedaling (peak). Inspiratory capacity (IC) maneuvers were performed during the steady-state resting period, during the last 30-s of each exercise work rate, and at peak exercise. Operating lung volumes were derived from IC measurements (37): end-expiratory lung volume (EELV) = total lung capacity (TLC) − IC, end-inspiratory lung volume (EILV) = EELV + tidal volume (VT), and inspiratory reserve volume (IRV) = IC − VT. Subjects rated “breathing discomfort,” “leg discomfort,” “work or effort of breathing,” “difficulty breathing in,” and “how unpleasant or bad is your breathing” on a modified 10-point Borg scale at rest, every 2 min of exercise, and at peak exercise (4, 40). Immediately after exercise, subjects were asked why they stopped exercising.

Diaphragm EMG and Respiratory Pressures

A combined EMGdi electrode catheter with esophageal and gastric balloons was inserted nasally and positioned according to the strength of inspiratory EMGdi recordings, i.e., position was optimal when the amplitude of the output of the five electrode pairs was greatest and the middle electrode pair was lowest (22). The raw EMGdi signal was amplified and band-pass filtered between 20 and 1,000 Hz (Bioamplifier model RA-8; Guanzhou Yinghui Medical Equipment, Guangzhou, China) and then sampled at 2,000 Hz (PowerLab, model ML880; ADInstruments, CastleHill, NSW, Australia). This signal was converted to a root mean square and averaged during inspiration between cardiac QRS complexes using a 100-ms time constant and a moving window. The largest value from the five electrode pairs was representative of each inspiration. The highest EMGdi value from either resting/peak sniff maneuvers or resting and exercise IC measurements was used as the maximum EMGdi (EMGdi,max).

Table 1. Subject characteristics

| Means ± SD | Men/women, n   | Age, yr | 67 ± 8
| Height, cm | 167 ± 9
| Weight, kg | 103 ± 25
| BMI, kg/m² | 36.6 ± 5.4
| Resting PLst, cmH2O | 20
| Resting CLst, l/cmH2O | 0.27 ± 0.19
| Resting MEP, cmH2O (%predicted) | 138 ± 56 (81 ± 22)
| Resting Ptot, cmH2O | 20 ± 6
| MIP, cmH2O (%predicted) | 68 ± 27 (89 ± 36)
| MEP, cmH2O (%predicted) | 11.4 ± 4.6 (46 ± 10)
| ERV, liters (%predicted) | 3.30 ± 0.83 (105 ± 20)
| RV, liters (%predicted) | 2.77 ± 0.73 (126 ± 29)
| FRC, liters (%predicted) | 3.00 ± 0.98 (105 ± 20)
| IC, liters (%predicted) | 2.37 ± 0.85 (89 ± 22)
| TLC, liters (%predicted) | 5.67 ± 1.24 (98 ± 10)
| FEV1/FVC, % | 50 ± 11
| FEV1, liters (%predicted) | 1.43 ± 0.44 (60 ± 13)
| FEV1/FVC, % | 1.83 (105 ± 20)
| Values are means ± SD, unless otherwise noted; n, no. of subjects; BMI, body mass index; MRC, Medical Research Council; FEV1, forced expired volume in 1 s; FVC, forced vital capacity; TLC, total lung capacity; IC, inspiratory capacity; FRC, functional residual capacity; RV, residual volume; ERV, expiratory reserve volume; sRaw, specific airway resistance; DLCO, diffusing capacity of the lung for carbon monoxide; MIP, maximal inspiratory pressure measured at TLC; MEP, maximal expiratory pressure measured at TLC; Clst, static lung compliance; Ptot, static lung recoil pressure. *Measurements obtained by dual-energy X-ray absorptiometry scan. †Pulmonary function test measurements are prebronchodilator, except for forced spirometry, which is postbronchodilator.

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The esophageal and gastric balloons were inflated with 1.0 and 1.2 ml of air, respectively, and connected to differential pressure transducers (model DP15-34; Validyne Engineering, Northridge, CA). Pes and gastric pressures (Pga) were continuously recorded at a rate of 200 Hz (PowerLab). Pdi was recorded as the difference between Pga and Pes signals. The PowerLab system received continuous flow signal input from the Vmax229d cardiopulmonary testing system for offline analysis.

Pre- and postexercise inspiratory sniffs were performed to obtain maximum Pes and Pdi. IC maneuvers at rest and throughout exercise were used to obtain dynamic peak inspiratory Pes (PesIC) and Pdi (PdiIC). Pre- and postexercise FVC maneuvers were also performed to obtain dynamic peak expiratory Pes. Tidal Pes swings (Pes(tidal)) were defined as the amplitude between the maximum inspiratory value and minimum inspiratory value for each respiratory cycle and expressed relative to maximum Pes (Pes(max; difference between PesIC and FVC Pes). Similarly, tidal Pdi swings were defined as the excursion between maximum inspiratory (Pdi(insp)) and minimum Pdi during expiration. The inspiratory rise in Pdi (Pdi(insp, rise)) was defined as the increase in Pdi from the onset of inspiratory flow to peak Pdi during inspiration. The peak tidal expiratory Pga and expiratory rise in Pga (Pga(exp, rise)), which is the increase in Pga from the lowest point after onset of expiratory flow to its peak value during expiration, were used to estimate expiratory muscle activation (41). End-inspiratory (EI) and end-expiratory (EE) data points of zero flow for Pes (PesEI and PesEE) and Pga (PgaEI and PgaEE) were collected. The ventilatory muscle recruitment (VMR) index was calculated as the difference between PgaEE and PgaEI divided by the difference between PesEI and PesEE (30): a negative value represents greater diaphragm contribution, and a positive value represents a greater rib cage muscle contribution to inspiration. Finally, neuromuscular efficiency of the diaphragm was defined as the relation between Pdiinsp, rise and EMGdi/EMGdi(max).

Statistical Analysis

This study had a small sample size due to the complexity and invasiveness of the respiratory pressure/EMGdi measurements. However, in a previous study evaluating similar outcome measures, a sample size of 11 was sufficient to show significance within-subject differences in sensory and respiratory mechanical/EMGdi measurements at a standardized work rate across two conditions (22). Comparisons of exercise modalities were made at rest, at standardized work rates (i.e., 10, 20, 30, and 40 W., At peak exercise using paired two-tailed t-tests. Linear interpolation was used to calculate Pdiinsp, rise for both tests at common levels of EMGdi/EMGdi(max) (i.e., 30, 40, and 50%). A two-way ANOVA for repeated measures was used to analyze measurements of respiratory muscle strength pre- and postexercise across test modalities. To evaluate the relationship between dyspnea intensity (dependent variable) and relevant independent variables during exercise, the following were included in a multivariable linear regression model: the independent variable of interest, exercise modality as a categorical effect, an interaction term to determine whether the relationship being tested was similar across test modality (independent variable × modality), and subjects were treated as random effects to account for serial measurements (subject nested within modality). Results are reported as means ± SD, unless specified otherwise. A P < 0.05 was used for statistical significance.

RESULTS

Subject characteristics and resting pulmonary function are presented in Table 1. Subjects fit either Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2 (n = 9) or GOLD 3 (n = 3) spirometric criteria for moderate or severe airflow obstruction, respectively (45). By GOLD recommendations, all subjects were symptomatic (category B or D) with either a modified Medical Research Council grade ≥2 or a COPD Assessment Test score ≥10 (45). The mean body mass index fell within the Class II obesity classification, which is associated with a “very high disease risk” when combined with a waist circumference >88 cm in women and >102 cm in men (47). Waist circumference was elevated by 22 cm in men and 25 cm in women relative to previously defined abdominal obesity criteria (16, 47). Dual-energy X-ray absorptiometry scans were available in nine subjects and revealed that men (n = 4) and women (n = 5) had a similar mean percentage of

Table 2. Cardiopulmonary measurements during rest and peak exercise

<table>
<thead>
<tr>
<th></th>
<th>Cycle</th>
<th>Treadmill</th>
<th>Cycle</th>
<th>Treadmill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Work rate, W</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>75 ± 17</td>
<td>78 ± 22</td>
</tr>
<tr>
<td>Exercise time, min:ss</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>14.09 ± 3.30</td>
<td>15.13 ± 4.41</td>
</tr>
<tr>
<td>Dyspnea, Borg scale</td>
<td>0.1 ± 0.2</td>
<td>0.2 ± 0.2</td>
<td>7.7 ± 2.5</td>
<td>7.1 ± 2.1</td>
</tr>
<tr>
<td>Leg discomfort, Borg scale</td>
<td>0.2 ± 0.3</td>
<td>0.2 ± 0.4</td>
<td>7.6 ± 2.4</td>
<td>5.8 ± 3.1*</td>
</tr>
<tr>
<td>VO2, l/min</td>
<td>0.44 ± 0.14</td>
<td>0.43 ± 0.17</td>
<td>1.55 ± 0.45</td>
<td>1.74 ± 0.59*</td>
</tr>
<tr>
<td>VO2 %predicted</td>
<td>23 ± 6</td>
<td>21 ± 10</td>
<td>84 ± 22</td>
<td>93 ± 25*</td>
</tr>
<tr>
<td>VCO2, l/min</td>
<td>0.37 ± 0.12</td>
<td>0.34 ± 0.13</td>
<td>1.53 ± 0.40</td>
<td>1.61 ± 0.51</td>
</tr>
<tr>
<td>RER</td>
<td>0.83 ± 0.05</td>
<td>0.81 ± 0.11</td>
<td>0.99 ± 0.08</td>
<td>0.93 ± 0.11</td>
</tr>
<tr>
<td>VE, l/min</td>
<td>15.6 ± 3.7</td>
<td>14.9 ± 4.5</td>
<td>49.0 ± 9.7</td>
<td>49.5 ± 13.0</td>
</tr>
<tr>
<td>MVV, %</td>
<td>35 ± 13</td>
<td>34 ± 13</td>
<td>107 ± 20</td>
<td>109 ± 22</td>
</tr>
<tr>
<td>VE/VCO2</td>
<td>43.9 ± 6.0</td>
<td>44.9 ± 8.1</td>
<td>32.9 ± 5.4</td>
<td>31.3 ± 4.7*</td>
</tr>
<tr>
<td>PtcO2, Torr</td>
<td>33.6 ± 2.6</td>
<td>33.1 ± 3.2</td>
<td>36.2 ± 5.9</td>
<td>37.5 ± 5.6*</td>
</tr>
<tr>
<td>VT, liters</td>
<td>0.81 ± 0.24</td>
<td>0.81 ± 0.10</td>
<td>1.34 ± 0.36</td>
<td>1.34 ± 0.45</td>
</tr>
<tr>
<td>fB, breaths/min</td>
<td>21 ± 5</td>
<td>20 ± 6</td>
<td>37 ± 7</td>
<td>38 ± 8</td>
</tr>
<tr>
<td>VT/Tr</td>
<td>35 ± 5</td>
<td>37 ± 4</td>
<td>40 ± 4</td>
<td>41 ± 5</td>
</tr>
<tr>
<td>IC, liters</td>
<td>2.38 ± 0.80</td>
<td>2.37 ± 0.79</td>
<td>1.73 ± 0.34</td>
<td>1.74 ± 0.54</td>
</tr>
<tr>
<td>IRV, liters</td>
<td>1.57 ± 0.69</td>
<td>1.56 ± 0.55</td>
<td>0.38 ± 0.15</td>
<td>0.40 ± 0.18</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>80 ± 8</td>
<td>80 ± 7</td>
<td>120 ± 16</td>
<td>126 ± 18</td>
</tr>
<tr>
<td>Heart rate, %predicted</td>
<td>48 ± 4</td>
<td>48 ± 4</td>
<td>72 ± 9</td>
<td>76 ± 10</td>
</tr>
<tr>
<td>SpO2 (%)</td>
<td>95 ± 2</td>
<td>95 ± 3</td>
<td>91 ± 3</td>
<td>89 ± 4*</td>
</tr>
</tbody>
</table>

Values are means ± SD. VO2, oxygen uptake; VCO2, carbon dioxide production; RER, respiratory exchange ratio; VE, ventilation; MVV, maximal voluntary ventilation; VE/VCO2, ventilatory equivalent for carbon dioxide production; PtcO2, partial pressure of end-tidal carbon dioxide; VT, tidal volume; fB, breathing frequency; VT/Tr, inspiratory duty cycle; IRV, inspiratory reserve volume; SpO2, arterial oxygen saturation by pulse oximetry. *P < 0.05, treadmill vs. cycle test at peak exercise.
total body fat (40 and 42%, respectively) and truncal fat (45 and 42%, respectively) (Table 1).

**Exercise Responses**

Steady-state rest and peak exercise responses are reported in Table 2. Patients exercised to a peak work rate of 73 ± 17 W on the cycle ergometer and 78 ± 22 W on the treadmill (P = 0.27). Exercise duration was longer on the treadmill compared with the cycle ergometer by a mean difference of 67 s, but was not significantly different (P = 0.17). Peak VO\(_2\) during treadmill exercise was significantly higher compared with cycle exercise. \(\dot{V}E\) (Fig. 1A) and carbon dioxide production (\(\dot{V}CO_2\)) were similar at a given work rate and reached similar peak values (Table 2) for both exercise modalities. Moreover, \(\dot{V}E/\dot{V}CO_2\) relationships were superimposed across exercise modalities. For any given \(\dot{V}E\) during exercise, both exercise modalities had similar EMG\(_d\)/EMG\(_d,max\), global respiratory muscle effort (Pes\(_{tidal}\) in absolute terms and relative to Pes\(_{max}\)), breathing pattern, and operating lung volumes (Fig. 1, B and C).

**Inspiratory Muscles**

Raw data tracings from a representative patient are shown in Fig. 2 to illustrate differences in Pga, Pdi, and the VMR at a similar work rate (30 W) and \(\dot{V}E\) (cycle: 24 l/min; treadmill: 26 l/min). Indexes of inspiratory muscle strength were not significantly different across modalities for pre- and postexercise measurements when analyzed by two-way repeated-measures ANOVA; however, postexercise Pdi\(_{IC}\) and Pdi obtained by pre- and postexercise inspiratory sniffs decreased significantly from preexercise values with both modes of exercise (Table 3). Inspiratory Pes in absolute terms or relative to Pes\(_{IC}\) was similar during exercise under both conditions (Fig. 1C, Table 3). Pdi\(_{insp}\) was greater throughout cycle exercise compared with treadmill exercise (Fig. 3A); however, inspiratory diaphragmatic effort (Pdi\(_{insp}\)/Pdi\(_{IC}\)) was similar between both exercise conditions due to a concurrent increase in Pdi\(_{IC}\) during cycle exercise. Pdi\(_{insp, rise}\) was also significantly greater during cycling compared with treadmill exercise (Fig. 3B). Furthermore, the downward displacement of the VMR index during cycling indicates greater use of the diaphragm at rest and at any given work rate compared with treadmill exercise (Fig. 3C). Interpolated values of Pdi\(_{insp, rise}\) at standardized EMG\(_d/\)EMG\(_{d,max}\) of 30, 40, and 50% were greater during cycle compared with treadmill exercise, indicating increased diaphragm efficiency during cycling (Fig. 4).

**Expiratory Muscles**

There was greater abdominal expiratory muscle activity during treadmill compared with cycle exercise as shown by a greater Pga\(_{exp, rise}\) throughout exercise and by a greater proportion of
subjects exhibiting a \(P_{ga_{exp}}\) rise at rest and early in exercise (Fig. 3, E and F). \(P_{ga_{EE}}\) was similar during both modes of exercise, while \(P_{ga_{EI}}\) fell to a significantly greater extent during treadmill walking compared with cycling (Fig. 3D).

Exertional Dyspnea

Subjects reported similar intensity of “breathing discomfort” (Fig. 5A), “work/effort of breathing,” “difficulty breathing in,” and “unpleasantness of breathing” (Fig. 5B) during submaximal and symptom-limited peak exercise for both test modalities. There were no significant differences between modalities for reasons for stopping exercise. Breathing discomfort, alone or in combination with leg discomfort, was reported as the main reason for stopping exercise in 58% of cycle tests and in 83% of treadmill tests. Conversely, leg discomfort, alone or in combination with breathing discomfort, was reported in 75% of cycle tests and in 58% of treadmill tests. Qualitative descriptors of breathlessness at end exercise were similar between modalities. Dyspnea increased similarly in both tests as a function of increasing \(V_e\), \(EMG_{di}/EMG_{dimax}\), and \(Pet_{idal}/Pet_{emax}\) throughout exercise (Fig. 5). Dyspnea intensity during exercise correlated strongly with \(V_e/\)maximal voluntary ventilation, \(Pet_{idal}/Pet_{emax}\), and \(EMG_{di}/EMG_{dimax}\) (all \(P < 0.0005\)); these relationships were similar across testing modality.
Muscle recruitment to achieve a given $V_˙E$ during different modalities was similar at peak exercise, as was peak force-generating capacity ($Pdi_{IC}$) compared with treadmill exercise at that measurement point. Since efferent respiratory neural output ($EMG_{di}/EMG_{dimax}$) was moderately obese with significant abdominal adiposity ($Pdi_{IC}$, obtained by IC maneuvers at rest and throughout exercise; $Pes_{insp}$, tidal esophageal pressure ($Pes$) swings; $Pes_{max}$, maximum $Pes$; $VMR$, ventilatory muscle recruitment; $EMG_{di}/EMG_{dimax}$, ratio of diaphragmatic electromyogram to maximum diaphragmatic electromyogram; $Pdisn$, inspiratory sniffs; $Pdi_{IC}$, obtained by IC maneuvers at rest and throughout exercise; $Pdi_{insp}$, inspiratory $Pdi$; $Pdi_{insp, rise}$, inspiratory rise in $Pdi$; $Pes_{insp}$, inspiratory Pes; $Pga_{exp}$, expiratory gastric pressure ($Pga$); $Pga_{exp, rise}$, expiratory rise in $Pga$; $Pga_{end}$, end-inspiratory $Pga$; $Pga_{exp, end}$, end-expiratory $Pga$. *$P < 0.05$, treadmill vs. cycle exercise at that measurement point.

**DISCUSSION**

The novel findings of this study were as follows: 1) COPD patients with abdominal adiposity had greater diaphragmatic efficiency and less expiratory muscle activity when cycling compared with walking; and 2) differences in respiratory muscle recruitment to achieve a given $V_˙E$ during different exercise modalities did not impact intensity, affective, and qualitative domains of dyspnea. Our results do not support the hypothesis that differences in afferent inputs from the diaphragm and expiratory muscles during walking vs. cycling modulate dyspnea perception in obese patients with COPD, at least in circumstances where $V_˙E$, indirect measures of respiratory neural drive, and dynamic respiratory mechanics are similar across exercise modalities.

Patients in this study had moderate airway obstruction and were moderately obese with significant abdominal adiposity (Table 1). Cardio-respiratory fitness expressed as peak $V_{O2}$ relative to ideal body weight was only modestly reduced. Mechanical constraints on $V_˙E$ were similar at peak exercise, as was peak force-generating capacity ($Pdi_{IC}$) compared with treadmill exercise, suggesting a distinct mechanical advantage (Fig. 3). Since efferent respiratory neural output ($EMG_{di}/EMG_{dimax}$) to the crural diaphragm was similar during both modalities, the greater $Pdi_{insp, rise}$ pressures during cycling suggest greater neuromuscular efficiency of this muscle (Fig. 4). Improved diaphragmatic efficiency (change in $Pdi$ relative to change in $EMG_{di}$) during cycling may reflect relatively improved (reduced) abdominal compliance in this posture, allowing an enhanced fulcrum effect of increased abdominal impedance during diaphragmatic descent (11). A leaning forward position while seated with arms extended grasping the handlebars might improve length-tension relations of the diaphragm or permit
the pectoral and scalene muscles to act as accessory muscles of inspiration (18, 43), as has been previously proposed (11, 12). However, our ergometer and mouthpiece assembly ensured an almost vertical position of the thorax during cycling, suggesting that such factors are not instrumental in improving diaphragmatic efficiency in this circumstance. It is also possible that, with hip flexion during cycling, the proximal thighs supported the lower abdominal wall during the breathing cycle, thus helping to maintain positive intra-abdominal hydraulic pressure to assist the diaphragms inspiratory action (1).

During walking, neuromuscular efficiency of the diaphragm was significantly reduced compared with cycling. Before exercise and consistent with previous studies in health (26), most patients had phasic expiratory muscle activity (Pgaexp.rise) while standing compared with sitting (91 vs. 50%, respectively). However, on average, the magnitude of expiratory muscle activity was similar in both cycle and treadmill positions at rest. During treadmill walking, there was a fall in PgaEI (Fig. 3) and a shift in the respiratory muscle recruitment pattern toward more activity of the inspiratory muscles of the rib cage and expiratory muscles, as indicated by analysis of the VMR plots of Macklem et al. (28). Greater expiratory muscle activity during walking may reflect increased abdominal muscle recruitment to stabilize the trunk. A reduction in PgaEI and increased abdominal volume have been reported during cycle and treadmill exercise in separate studies in healthy individuals and is thought to indicate abdominal wall relaxation during inspiration (2, 42). Whether similar mechanisms are at play during walking in obese COPD patients could not be determined in the absence of concomitant measures of thoraco-abdominal displacements. In contrast to the situation during treadmill exercise, PgaEE and PgaEI were similar in absolute terms throughout submaximal cycle exercise in our patients.

**Fig. 3.** Pdi (A), Pdi inspiratory rise (Pdi.insp.rise; B), VMR index (C), Pga at zero flow (Pga, zero flow; D), expiratory gastric rise (Pga.exp.rise; E), and the frequency of expiratory muscle activity (F) are shown relative to work rate. Values are means ± SE, unless specified otherwise. *P < 0.05, cycle vs. treadmill at a given work rate or at peak exercise. PdiIC, maximum inspiratory Pdi during an IC maneuver; PgaEE, end-expiratory Pga; PgaEI, end-inspiratory Pga.

**Fig. 4.** The Pdi.insp.rise is shown relative to electrical activation of the diaphragm (EMGdi/EMGdi,max). Pdi.insp.rise at 30, 40, and 50 EMGdi/EMGdi,max and at peak exercise was significantly greater during cycle compared with treadmill exercise (*P < 0.05). Values are means ± SE.
suggesting improved (decreased) abdominal compliance. In keeping with the results of a recent study (25), there was no difference in the behavior of EELV, despite the differences in expiratory muscle recruitment between modalities.

Despite differences in respiratory muscle recruitment across tests, global measurements of respiratory muscle activity (tidal swings of Pes) were similar for a given VE. Individual respiratory muscle contributions to VE may vary such that reduced diaphragmatic contributions during treadmill is likely counter-balanced by increased contribution of other respiratory muscles to maintain the VE dictated by the VCO2. Based on a previous study (25), we believe that the relatively increased expiratory muscle activity during treadmill testing in the present study is unlikely to translate into increased ventilatory output in the presence of expiratory flow limitation.

A related question is why relatively increased diaphragmatic activity during cycling compared with walking did not translate into increased VE for a given work rate? In line with the argument above, one possibility is that increased diaphragmatic activity is linked to a corresponding reduction in activity of the other respiratory muscles (as suggested by our VMR analysis) such that VE, as dictated by the prevailing VCO2, remains constant. A second possibility is that, even in the face of increased inspiratory muscle activity during cycling, further increases in VE are not possible, particularly at higher exercise intensities where significant restrictive respiratory mechanical constraints are present (Fig. 1F).

The similarity in ventilatory response during the two exercise modalities, despite differences in the contribution of various respiratory muscles to support VE, is also explained by metabolic factors. Thus the ventilatory response to exercise, regardless of the test modality, was ultimately determined by VCO2. As highlighted in our laboratory’s previous study (8), it is clear that net VCO2/work rate responses and VE/VCO2 (and consequent Ve/work rate) slopes were similar across tests, notwithstanding differences in VO2 and respiratory exchange ratio.

**Mechanisms of Exertional Dyspnea**

**Increased central neural drive.** Current concepts of the neurophysiology of exertional dyspnea in COPD emphasize the key role of increased respiratory neural drive from cortical and medullary centers in the brain and the attendant increased central corollary discharge to the somatosensory cortex (36, 40). We extended the results of our previous study by demonstrating that, not only ventilatory parameters, but also respiratory neural drive (EMGdi/EMGdimax) and global respiratory effort were similar during both exercise modalities and increased as a function of increasing VCO2. Thus we confirmed that the association between dyspnea intensity and measures of central respiratory drive was not influenced by differences in VO2 requirements and arterial O2 saturation at a standardized external power output during walking and cycling. The inter-modality differences in arterial O2 saturation are expected and are thought to reflect differences in alveolar VE, as previously described (8, 29). The small decreases in arterial O2 saturation during walking are well below the threshold required to stimulate peripheral chemoreceptors or to directly influence respiratory sensation. The strong correlations (independent of exercise modality) between dyspnea intensity and the three indirect indexes of increasing respiratory neural drive (i.e., VE/maximal voluntary ventilation, EMGdi/EMGdimax and effort, and Pes_tidal/Pes_max) support the hypothesis that amplitude of central respiratory drive (and central corollary dis-
charge) is an important determinant of dyspnea, regardless of the nature of the physical task that provokes the symptom.

**Altered afferent sensory inputs.** The previously established relationship between increase in dyspnea intensity and reduction of dynamic IRV toward its minimal value (34) has been shown to be independent of exercise modality (8). It is widely accepted that alteration of peripheral afferent inputs from the respiratory system (lung, chest wall, and respiratory muscles) can influence dimensions of dyspnea during exercise. For example, increased VT and IRV following pharmacological lung deflation, or changes in posture at rest, can affect (reduce) activity-related dyspnea intensity perception, presumably by altering peripheral afferent sensory inputs from the respiratory system and by partially reducing neuromechanical dissociation (33). It has long been postulated that afferent information from abundant sensory receptors in the respiratory muscles represents the proximate source of feedback regarding the status of the respiratory system and the appropriateness of its response to the prevailing central neural drive (7). In this context, it is reasonable to assume that, during exercise, alteration of afferent inputs from various active respiratory muscle groups (which sense tension and displacement) will modulate dyspnea perception. The present study design allowed us, for the first time, to evaluate the sensory consequences of body position-related changes in diaphragmatic efficiency and in expiratory muscle recruitment in relative isolation, in a setting where intensity of respiratory neural drive and global contractile respiratory muscle effort was constant. The finding that intensity, affective, and qualitative domains of dyspnea were unaffected by test-specific alterations in respiratory muscle activity required to support a given VE argues against a specific dyspneogenic role for mechanoreceptors in respiratory muscles of the chest wall and abdomen, at least under the experimental conditions of our study. The lack of a further increase in dyspnea as a result of greater diaphragmatic dysfunction during treadmill walking may reflect the relative paucity of spindles in this muscle, which provide sensory information about length and displacement (44). The lack of influence of increased expiratory muscle recruitment on dyspnea during treadmill walking is in keeping with the results of a recent study, which shows no association between increased expiratory effort and dyspnea during exercise in COPD (25).

To the extent that between-test differences in the respiratory muscle activity required to generate a given VE had no measurable effect on dimensions of dyspnea, it would seem that there is substantial redundancy in the peripheral sensory systems. “Sense of effort,” as estimated by $P_{esdav}/P_{esmax}$, which was similar at a given VE during both test modalities, may be more closely linked to amplitude of central corollary discharge than to the pattern of afferent inputs from contracting respiratory muscles, per se (6, 13, 17, 24). Thus afferent inputs from other sources, such as pulmonary vagal receptors and chest wall mechanoreceptors, which are likely similar between tests (given the similarity of VT and operating lung volumes), may represent the primary source of peripheral afferent feedback to the somatosensory cortex, at least under the current experimental conditions.

**Limitations**

The focus of the present study was to evaluate sensory-mechanical relations in patients with combined COPD and obesity; therefore, the results may not be generalizable to nonobese patients who are more likely to have reduced resting IC. The lack of measurements of thoraco-abdominal excursions and tonic and phasic EMG recordings from respiratory muscles other than the diaphragm precludes definitive conclusions about variability in the complex respiratory muscle coordination strategies employed as a result of positional differences during exercise.

**Conclusions**

The present study shows, for the first time, that diaphragmatic and expiratory muscle activity is different during cycling and walking in obese individuals with COPD. However, despite the relatively reduced neuromuscular efficiency of the diaphragm during weight-bearing treadmill exercise compared with weight-supported cycling, perceived respiratory discomfort was not increased. Our results further indicate that exertional dyspnea intensity is ultimately dictated by the amplitude of respiratory neural drive and concomitant dynamic restrictive mechanical constraints (decreasing IRV). Moreover, under conditions where respiratory neural drive and the volume and timing components of breathing were constant, body position-related alterations in activity of major respiratory muscles to achieve a similar VE during different exercise modalities had no measurable effects on the intensity and quality of dyspnea.

**Implications**

Clinicians involved in laboratory cardiopulmonary exercise testing should be aware of the fundamental physiological differences between cycling and treadmill in obese COPD patients. Either test modality is suitable for evaluation of dyspnea, which, regardless of physical task, rises in association with increasing central neural drive. An important clinical implication is that interventions that reduce central respiratory drive (e.g., reduction of $V_{CO2}$ by manipulation of energy substrate or exercise training) should successfully relieve exertional dyspnea in obese patients with COPD.

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**AUTHOR CONTRIBUTIONS**

REFERENCES


