Respiratory Physiology & Neurobiology 266 (2019) 130–137

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Effect of weight loss via bariatric surgery for class III obesity on exertional breathlessness

Amar Mainra[a], Sara J. Abdallah[a], Ryan E.R. Reid[b], Ross E. Andersen[b,c], Dennis Jensen[a,c,d,*]

[a] *Clinical Exercise and Respiratory Physiology Laboratory, Department of Kinesiology and Physical Education, Faculty of Education, McGill University, Montréal, QC, Canada*

[b] *Health and Fitness Promotion Laboratory, Department of Kinesiology and Physical Education, Faculty of Education, McGill University, Montréal, QC, Canada*

[c] *Research Centre for Physical Activity and Health, Faculty of Education, McGill University, Montréal, QC, Canada*

[d] *Research Institute of the McGill University Health Centre, Translational Research in Respiratory Diseases Program, Montréal, QC, Canada*

ARTICLE INFO

Keywords:
Obesity
Exercise
Breathlessness
Bariatric surgery
Weight loss

ABSTRACT

We examined the impact of bariatric surgery on cardiometabolic, ventilatory and breathlessness responses to incremental cycle exercise testing in adults with class III obesity (*n* = 6). O_2 consumption, CO_2 production, minute ventilation ($\dot{V}$) and breathing frequency were reduced during submaximal exercise after surgery. Inspiratory capacity (IC) and inspiratory reserve volume were lower at rest and any given $\dot{V}_E$ during exercise after surgery. In the transition from rest to peak exercise, dynamic IC decreased by 0.13 L before surgery and increased by 0.21 L after surgery. Breathlessness intensity ratings were lower during exercise at power outputs ≥75-watts after surgery (e.g., by 1.0 and 1.4 Borg 0–10 scale units at 75-watts and the highest equivalent power output of 117-watts, respectively). In contrast, bariatric surgery had no effect on breathlessness-$\dot{V}_E$ relationships during exercise. In conclusion, relief of exertional breathlessness following bariatric surgery could not be explained by improved dynamic breathing mechanics, but reflected the awareness of reduced metabolic and ventilatory requirements of exercise.

1. Introduction

The prevalence of obesity (defined by the World Health Organization as a body mass index [BMI] ≥30 kg/m^2) continues to rise, particularly in high sociodemographic countries like Canada and the United States of America (Collaborators, G.B.D.O. et al., 2017). Epidemiological studies suggest that adults with obesity are two-to-four times more likely than their non-obese counterparts to experience physical activity-limiting breathlessness (Currow et al., 2017; Sin et al., 2002); and that the prevalence of physical activity-limiting breathlessness is positively and independently associated with BMI (Currow et al., 2017; Sin et al., 2002). Despite the high prevalence and burden of breathlessness in obesity, relatively few studies have examined the physiological mechanisms of exertional breathlessness in this growing population.

Ofir et al. (2007) demonstrated that breathlessness intensity ratings are higher at any given power output during incremental cardiopulmonary cycle exercise testing (CPET) in women with vs. without obesity. In contrast, breathlessness-minute ventilation ($\dot{V}_E$) relationships during CPET were not higher in adults with vs. without obesity (Ingle et al., 2012; Ofir et al., 2007; Romagnoli et al., 2008), suggesting that respiratory mechanical factors are not mechanistically linked to the greater perception of exertional breathlessness in obesity. In fact, preservation of breathlessness-$\dot{V}_E$ relationships during exercise in people with vs. without obesity has been attributed to mechanical adaptations of the respiratory system in obesity, including recruitment of a larger resting inspiratory capacity (IC), dynamic lung hyperinflation, and adoption of a relatively rapid and shallow breathing pattern during exercise (Jensen et al., 2009; O'Donnell et al., 2012; Ofir et al., 2007). The combination of these respiratory mechanical adaptations allow for tidal volume (V_T) expansion to occur on the linear (compliant) portion of the respiratory systems sigmoid pressure-volume curve during exercise, while maintaining a larger inspiratory reserve volume (IRV) (Jensen et al., 2009; O'Donnell et al., 2012; Ofir et al., 2007). Under these circumstances, the greater perception of exertional breathlessness in people with vs. without obesity is thought to reflect the awareness of higher $\dot{V}_E$ pursuant to the higher metabolic demands of exercise in obesity (Jensen et al., 2009; O'Donnell et al., 2012; Ofir et al., 2007; Romagnoli et al., 2008). It follows that weight loss, by decreasing the metabolic and ventilatory demands of exercise in people with obesity,

* Corresponding author at: Department of Kinesiology and Physical Education, 475 Pine Avenue West, Montréal, QC, H2W 1S4, Canada.
E-mail address: dennis.jensen@mcgill.ca (D. Jensen).

https://doi.org/10.1016/j.resp.2019.05.007
Received 5 November 2018; Received in revised form 3 May 2019; Accepted 11 May 2019
Available online 14 May 2019

should decrease breathlessness intensity ratings at any given power output during CPET, but have no effect on breathlessness-$\dot{V}_E$ relationships.

The physiological mechanisms responsible for relief of exertional breathlessness following moderate weight loss through diet and exercise (Bernhardt and Babb, 2014) and extreme weight loss through bariatric surgery (Boissiere et al., 2017; Fontana et al., 2019; Karason et al., 2000) in adults with obesity remain unclear. Studies by Babb et al. (2011) and Bhammar et al. (2016) found that moderate weight loss (by ˜7.5 kg) accomplished *via* a 12-week diet and exercise training program in adults with class I and II obesity was associated with (1) reduced rate of O_2 consumption ($\dot{V}O_2$), $\dot{V}_E$ and breathing frequency (f_B) during constant-load CPET at 60-watts and (2) increased dynamic end-expiratory (EELV) and end-inspiratory lung volumes (EILV) at any given $\dot{V}_E$ during incremental CPET. However, the effect of weight loss on breathlessness-power output and breathlessness-$\dot{V}_E$ relationships was not examined in these studies. Seres et al. (2006) reported that more extreme weight loss (by ˜50 kg) following bariatric surgery for class III obesity was associated with marked reductions in $\dot{V}O_2$ and $\dot{V}_E$ during incremental treadmill exercise testing; however, the authors of this study did not examine the impact of surgically-induced weight loss on breathing pattern, operating lung volume and breathlessness responses to exercise.

The aim of this study was to examine the effect of weight loss *via* bariatric surgery for people with class III obesity on cardiac, metabolic, ventilatory, breathing pattern, operating lung volume and breathlessness responses during CPET. We hypothesized that breathlessness-power output relationships would be reduced, while breathlessness-$\dot{V}_E$ relationships would be unchanged during CPET following obesity surgery. In other words, we hypothesized that relief of exertional breathlessness following surgically-induced weight loss would be primarily related to the reduced metabolic and ventilatory requirements of exercise, while changes in breathing pattern and the behaviour of dynamic operating lung volumes would be less important.

2. Methods

2.1. Study design

In this controlled longitudinal study, participants attended the *Clinical Exercise and Respiratory Physiology Laboratory* of McGill University (Montreal, QC, Canada) for experimental testing 4–6 weeks before (PRE) and ˜3 months after (POST) bariatric surgery, i.e., Roux-en-Y Gastric Bypass. PRE and POST visits included: body composition assessment by dual-energy X-ray absorptiometry (DXA) using a Lunar iDXA™ scanner (GE HealthcareTM; Milwaukee, WI, USA) (Carver et al., 2013); pulmonary function testing; and an incremental CPET. Participants were instructed to avoid alcohol, caffeine and strenuous exercise on the day of assessments. The study protocol and consent form were approved by the Institutional Review Board of the Faculty of Medicine at McGill University. All participants provided written informed consent before any assessments were performed.

2.2. Participants

Participants included ambulatory men (n = 2) and women (n = 4) aged 35–52 years scheduled for bariatric surgery for class III obesity (BMI ≥ 40 kg/m^2) at the Bariatric Clinic of the Royal Victoria Hospital (Montreal, QC, Canada). Exclusion criteria were: presence of a medical contraindication(s), as judged by the supervising physician; use of a walking aid; and pre-surgical body mass > 215 kg to accommodate the upper limit of the DXA scanner.

2.3. Pulmonary function testing

Routine spirometry and 15-sec maximal voluntary ventilation maneuvers were performed using automated equipment (Vmax Encore™; CareFusion, Yorba Linda, CA, USA) according to established procedures (Miller et al., 2005). Spirometric parameters were expressed as absolute values and as percentages of predicted normal values (Hankinson et al., 1999).

2.4. Cardiopulmonary exercise testing

Exercise tests were conducted on an electronically braked cycle ergometer (VIAsprint 150 P; Ergoline, Bitz, Germany) using a computerized CPET system (Vmax Encore®; CareFusion, Yorba Linda, CA, USA) and consisted of a steady-state rest period of 3-min followed by 25-watt increases in power output (starting at 25-watts) every 2-min to the point of symptom-limitation.

Standard respiratory and gas exchange parameters were collected breath-by-breath while participants breathed through a mouthpiece and low-resistance flow transducer with nasal passages occluded by a nose clip. Heart rate (HR) and oxyhemoglobin saturation (SpO_2) were monitored continuously by 12-lead ECG (GE Marquette's CardioSoft® 12-lead ECG system; CareFusion) and finger pulse oximeter, respectively. Inspiratory capacity maneuvers were performed at rest, within the last 30-sec of each 2-min interval during CPET, and at end-exercise (Guenette et al., 2013). Assuming that total lung capacity (TLC) did not change during CPET in our participants (Stubbing et al., 1980), changes in IC and IRV (calculated as IC minus V_T) reflect changes in dynamic EELV and EILV, respectively. Using Borg's modified 0–10 category-ratio scale (Borg, 1982), participants rated the intensity of their perceived breathlessness and leg discomfort at rest, within the last 30-sec of each 2-min interval during CPET, and at end-exercise. Participants verbalized their main reason(s) for stopping exercise; quantified the percentage contribution of breathlessness and leg discomfort to exercise cessation; and identified qualitative phrases that best described their breathlessness at end-exercise (O'Donnell et al., 2000).

2.4.1. Analysis of exercise end-points

Physiological parameters measured breath-by-breath were averaged in 30-sec intervals at rest and during CPET. These parameters, collected over the first 30-sec period of the second minute of each 2-min interval during CPET, were linked with symptom ratings and IC-derived parameters collected over the latter 30-sec of the same minute. Measured parameters were examined at rest; at standardized submaximal power outputs completed by all participants during all incremental CPETs; at the highest equivalent submaximal power output completed by a given participant during each of his/her two incremental CPETs; and at peak exercise. Physiological parameters averaged over the last 30-sec of loaded pedalling (i.e., peak exercise) were linked with symptom ratings and IC-derived parameters collected immediately at the end of this period. Peak power output (PPO) was defined as the highest power output a participant was able to sustain for ≥30-sec, while exercise endurance time was defined as the duration of loaded pedaling. The rate of O_2 consumption at peak exercise ($\dot{V}O_{2,peak}$) was referenced to age, sex, height and ideal body mass predicted normal values (Lorenzo and Babb, 2012). Peak heart rate and PPO were referenced to their respective age, sex and height predicted normal values (Jones et al., 1985).

2.5. Statistical analysis

Two-tailed, paired *t*-tests were used to compare PRE and POST measures, including: participant characteristics, including DXA and pulmonary function test-derived parameters; physiological and perceptual parameters measured at rest, at each standardized submaximal power output during CPET, and at peak exercise; and the percentage contribution of breathlessness and leg discomfort to exercise cessation. Fisher's exact test was used to compare the selection frequencies of reasons for stopping exercise as well as the descriptors of breathlessness

Table 1
Participant characteristics before (PRE) and ˜3 months after (POST) bariatric surgery.

Parameter	PRE	POST
Age, yrs	43.7 ± 2.8	–
Height, cm	165.7 ± 1.8	–
Total body mass, kg	129.4 ± 6.2	105.6 ± 5.8*
Body mass index, kg/m^2	47.1 ± 1.6	38.4 ± 1.6*
Lean tissue mass, kg (% total body mass)	62.2 ± 4.1 (48 ± 2)	57.8 ± 4.6* (55 ± 4*)
Fat mass, kg (% total body mass)	61.6 ± 4.6 (49 ± 2)	43.1 ± 4.8* (41 ± 3*)
Pulmonary function test parameters		
FEV_1, L (% predicted)	2.76 ± 0.11 (93 ± 6)	3.04 ± 0.08† (102 ± 4)†
FVC, L (% predicted)	3.35 ± 0.12 (86 ± 5)	3.57 ± 0.11 (91 ± 3)
FEV_1/FVC, % (% predicted)	82.5 ± 1.9 (108 ± 2)	85.1 ± 1.5 (111 ± 2)
PEFR, L/sec (% predicted)	6.99 ± 0.76 (103 ± 14)	8.55 ± 0.62 (123 ± 6)
$FEF_{25-75\%}$, L/sec (% predicted)	3.17 ± 0.24 (97 ± 9)	3.70 ± 0.28 (111 ± 7)
MVV, L/min	109 ± 7	124 ± 5

Values are means ± SEM. Abbreviations: FEV_1, forced expiratory volume in 1-sec; FVC, forced vital capacity; PEFR, peak expiratory flow rate; $FEF_{25-75\%}$, forced expiratory flow rate between 25% and 75% of the FVC maneuver; MVV, maximum voluntary ventilation.
* $p < 0.05$.
† $p = 0.07$ vs. PRE.

at end-exercise between PRE and POST. Data were analyzed using SigmaStat, version 3.5 (Systat Software Inc., San Jose, CA, USA). Statistical significance was set at $p < 0.05$ and data are reported as mean ± standard error of the mean (SEM).

3. Results

3.1. Participant characteristics

Participant characteristics are summarized in Table 1. Body mass, BMI, lean tissue mass and fat mass decreased by 23.8 kg (18%), 8.7 kg/m^2 (18.5%), 4.4 kg (7%) and 18.5 kg (30%) after bariatric surgery, respectively (all $p < 0.05$). Pulmonary function test parameters were within normal predicted ranges and were not significantly different in POST vs. PRE.

3.2. Physiological responses to exercise

The effect of bariatric surgery on metabolic, cardiac and gas exchange responses to exercise are displayed in Fig. 1 and summarized in Table 2. Exercise endurance time and PPO increased by 1.5-min (15%) and 20-watts (14.5%) after bariatric surgery; however, these improvements were not statistically significant (both $p < 0.19$). Despite the 20-watt increase in PPO after bariatric surgery, absolute peak $\dot{V}O_2$ values were comparable in POST vs. PRE. Compared to PRE, mean values of $\dot{V}O_2$, the rate of CO_2 production ($\dot{V}CO_2$) and HR were lower, while O_2 pulse, the ventilatory equivalent for CO_2 ($\dot{V}_E/\dot{V}CO_2$) and end-tidal CO_2 tension were not different at rest and during submaximal exercise.

The effect of bariatric surgery on ventilatory, breathing pattern and operating lung volume responses to exercise are displayed in Figs. 2 and 3, and summarized in Table 2. The $\dot{V}_E$ response to exercise was reduced in POST vs. PRE and reflected a reduced f_B response with no change in V_T expansion. Resting values of IC and IRV decreased after bariatric surgery by 0.33 L (14.4% of forced vital capacity [FVC]) and 0.29 L (12.1% FVC), respectively. Mean values of dynamic IC and IRV referenced to FVC (IC%FVC and IRV%FVC) were consistently lower for any given $\dot{V}_E$ throughout exercise in POST vs. PRE; for example, IRV was 11.6% FVC, 8.0% FVC, 8.0% FVC and 7.6% FVC lower in POST vs. PRE at standardized submaximal levels of $\dot{V}_E$ of 15 L/min ($p = 0.005$), 30 L/min ($p = 0.069$), 45 L/min ($p = 0.008$) and 55.5 L/min ($p = 0.049$), respectively. Dynamic IC decreased by 0.13 ± 0.05 L (3.8 ± 1.5% FVC) from rest-to-peak exercise in PRE, reflecting dynamic lung hyperinflation. In contrast, dynamic IC increased by 0.21 ± 0.01 (6.1 ± 2.7% FVC) from rest-to-peak exercise in POST.

3.3. Perceptual responses to exercise

The effect of bariatric surgery on perceptual responses to exercise are displayed in Fig. 4 and summarized in Table 2. The relationship between increasing intensity ratings of leg discomfort and power output during CPET was not different in PRE vs. POST. Intensity ratings of breathlessness were reduced by an average of ≥1 Borg 0–10 scale units during exercise at standardized submaximal power outputs ≥75-watts in POST vs. PRE; however, these differences did not persist when breathlessness was examined in relation to $\dot{V}_E$. Breathlessness-IRV%FVC curves were rightward shifted throughout exercise in POST vs. PRE, such that breathlessness intensity ratings were lower at any given IRV% FVC during exercise after bariatric surgery.

The distribution of reasons for stopping exercise was similar in PRE vs. POST: breathlessness, $n = 1$ in PRE vs. $n = 1$ in POST; leg discomfort, $n = 3$ in PRE vs. $n = 5$ in POST; combination of breathlessness and leg discomfort, $n = 1$ in PRE vs. $n = 0$ in POST; and other, $n = 1$ in PRE (sore buttocks from bicycle seat) vs. $n = 0$ in POST. The percentage contribution of breathlessness (PRE, 19 ± 15% vs. POST, 18 ± 10%; $p = 0.90$) and leg discomfort (PRE, 54 ± 16% vs. POST, 72 ± 11%; $p = 0.90$) was also similar in PRE vs. POST. The majority of our participants selected descriptor phrases alluding to a heightened sense of *"work/effort of breathing"* (PRE, $n = 4$ vs. POST, $n = 4$), *"heavy breathing"* (PRE, $n = 5$ vs. POST, $n = 5$) and *"inspiratory difficulty"* (PRE, $n = 4$ vs. POST, $n = 4$) at the peak of exercise in both PRE and POST.

4. Discussion

This is the first study to examine the impact of extreme weight loss following bariatric surgery for class III obesity on ventilation, breathing pattern, operating lung volume and breathlessness responses during symptom-limited incremental cycle exercise testing. The main finding is that relief of exertional breathlessness following bariatric surgery could not be explained by improved static and dynamic breathing mechanics, but was primarily related to the reduced metabolic and ventilatory requirements of exercise.

Bariatric surgery decreased body mass by 24 kg (18%) and fat mass by 18.5 kg (30%). Despite a 4.5 kg (7%) decrease in lean tissue (muscle) mass after bariatric surgery, exercise endurance time and PPO increased by an average of 1.5-min (15%) and 20-watts (14.5%) in POST vs. PRE, respectively. Consistent with the results of earlier bariatric surgery studies (Boissiere et al., 2017; Campos et al., 2018; da Silva et al., 2013; de Souza et al., 2009, 2010; Kanoupakis et al., 2001; Maniscalco et al., 2006; Seres et al., 2006), these findings suggest that the exercise capacity of our participants with class III obesity improved following

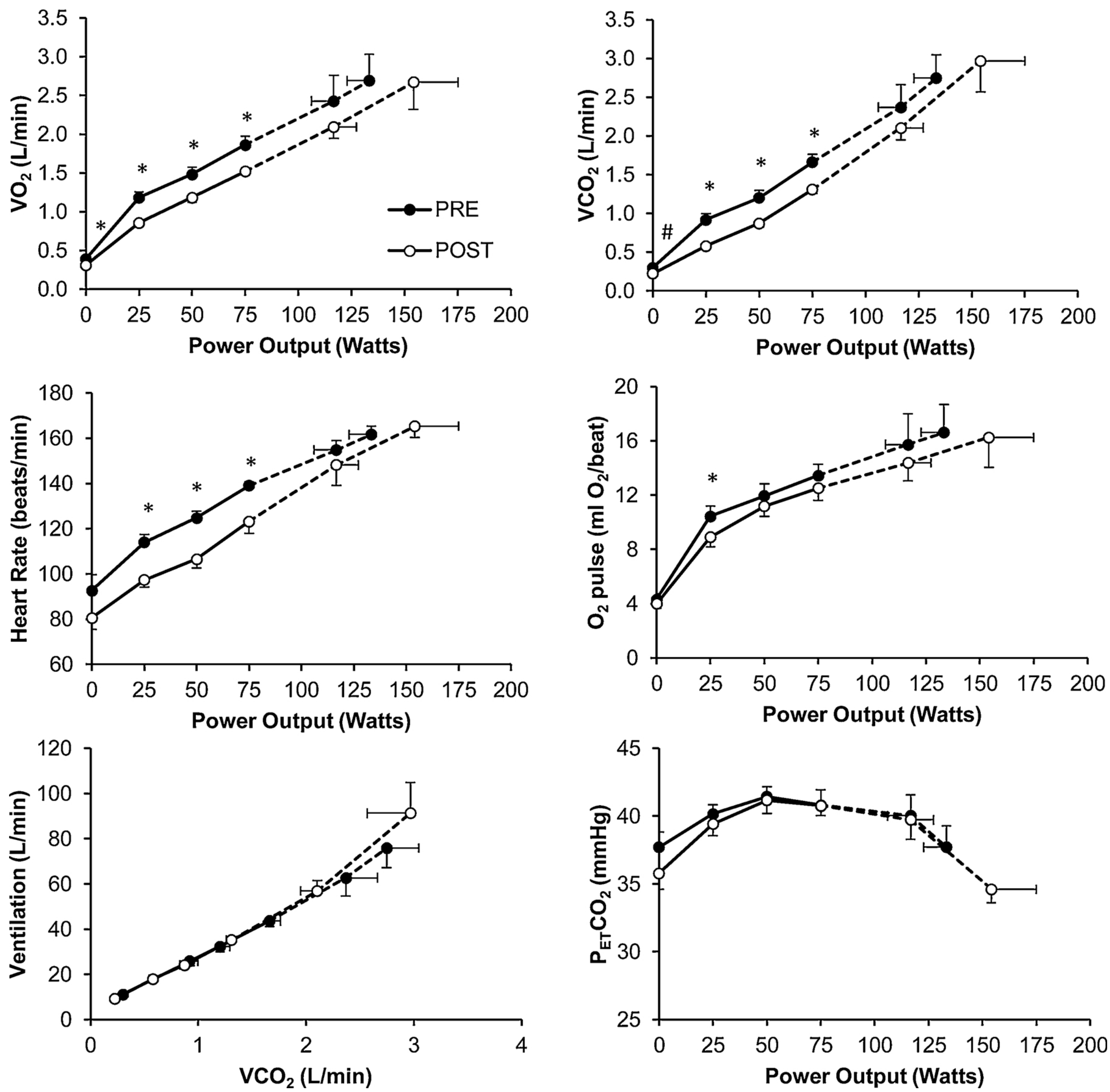

Fig. 1. Metabolic, cardiac and gas exchange responses to symptom-limited incremental cycle exercise testing in adults with class III obesity before (PRE) and ˜3 months after (POST) bariatric surgery. Values are means ± SEM at rest, during exercise at standardized submaximal power outputs, and at peak exercise. Abbreviations: $\dot{V}O_2$, rate of O_2 consumption; $\dot{V}CO_2$, rate of CO_2 production; $P_{ET}CO_2$, end-tidal CO_2 tension. $^*p < 0.05$ and $^{\#}p \leq 0.08$ vs. PRE.

surgically-induced weight loss, even though their peak absolute $\dot{V}O_2$ values were similar in POST vs. PRE.

As a likely result of moving lighter limbs against gravity (secondary to reduced fat and lean tissue mass), cardiac and metabolic responses were consistently reduced at any given submaximal power output during CPET after bariatric surgery. The $\dot{V}_E$ response to exercise was similarly reduced after bariatric surgery and reflected the lower metabolic cost of cycling, as evidenced by relative preservation of the $\dot{V}_E$-$\dot{V}CO_2$ relationship during CPET in POST vs. PRE. These findings confirm and extend the results of earlier studies reporting reduced cardiac, metabolic and ventilatory requirements of exercise following moderate and extreme weight loss *via* lifestyle modification (Bernhardt et al., 2016) and bariatric surgery, respectively (Browning et al., 2017; de Souza et al., 2010; Seres et al., 2006).

Compared with their non-obese counterparts, individuals with obesity tend to adopt a more rapid and shallow breathing pattern to support their exaggerated $\dot{V}_E$ response to exercise (Babb et al., 2002, 1991; Chlif et al., 2015; Ofir et al., 2007). In keeping with the results of Bhammar et al. (2016), the reduced $\dot{V}_E$ response to incremental CPET after extreme weight loss in our study was due to a reduced f_B response to exercise, with no significant change in V_T expansion.

Obesity is characterized by decreases in both EELV and EILV at rest (Babb et al., 1989, 2002; Chlif et al., 2015; DeLorey et al., 2005; Ofir et al., 2007; Romagnoli et al., 2008). These changes, in the setting of a relatively preserved TLC (Jones and Nzekwu, 2006), translate into recruitment of resting IC and IRV (Ofir et al., 2007; Romagnoli et al., 2008). The corollary of these findings is that, in people with obesity, both moderate and extreme weight loss has been shown to decrease IC and IRV at rest by respectively increasing resting EELV and EILV (Babb et al., 2011; Barbalho-Moulim et al., 2013; Bhammar et al., 2016; Boissiere et al., 2017; Campos et al., 2018). In our study, extreme weight loss *via* bariatric surgery was associated with decreases in resting IC (by 0.33 L and ˜15% FVC) and IRV (by 0.29 L and ˜12% FVC). Based on the collective results of earlier studies (Babb et al., 2011, 2008; Bhammar et al., 2016; Ofir et al., 2007; Steier et al., 2014), we speculate that "de-recruitment" of resting IC and IRV after surgically-induced weight loss in our study was primarily due to the combination of increased total respiratory system compliance and reduced intra-abdominal pressures that accompanied reduced total thoracic (abdomen and chest wall) fat mass.

Table 2
Effect of weight loss *via* bariatric surgery on physiological and symptom responses at rest and during exercise in adults with class III obesity.

Parameter	REST PRE	REST POST	75-watts PRE	75-watts POST	PEAK PRE	PEAK POST
Endurance time, min	–	–	–	–	10.1 ± 0.9	11.6 ± 1.5
Power output, watts (% predicted)	–	–	75 ± 0	75 ± 0	133 ± 11 (67 ± 5)	154 ± 21 (86 ± 9*)
Dyspnea Intensity, Borg units	0.7 ± 0.3	0.1 ± 0.1	2.5 ± 0.3	1.5 ± 0.4*	5.8 ± 0.3	6.7 ± 1.5
Leg discomfort, Borg units	0.1 ± 0.1	0 ± 0	3.7 ± 0.8	2.8 ± 1.3	7.3 ± 1.1	8.7 ± 0.7
$\dot{V}O_2$, L/min (% predicted)	0.39 ± 0.03	0.31 ± 0.01*	1.86 ± 0.11	1.52 ± 0.05*	2.69 ± 0.34 (117 ± 10)	2.67 ± 0.35 (124 ± 10)
$\dot{V}CO_2$, L/min	0.30 ± 0.03	0.23 ± 0.01#	1.66 ± 0.10	1.31 ± 0.05*	2.75 ± 0.30	2.97 ± 0.40
RER	0.77 ± 0.04	0.72 ± 0.03	0.89 ± 0.04	0.87 ± 0.03	1.03 ± 0.03	1.11 ± 0.05
Heart rate, beats/min (% predicted)	93 ± 7	81 ± 5	139 ± 2	123 ± 5*	162 ± 4 (89 ± 2)	165 ± 5 (91 ± 3)
O_2 pulse, ml O_2/beat	4.3 ± 0.4	4.0 ± 0.3	13.4 ± 0.9	12.5 ± 0.9	16.6 ± 2.1	16.3 ± 2.2
$\dot{V}_E/\dot{V}CO_2$	37.3 ± 1.6	40.6 ± 1.4*	26.3 ± 0.6	26.9 ± 0.5	27.6 ± 0.8	30.6 ± 0.9#
$P_{ET}CO_2$, mmHg	37.7 ± 1.1	35.8 ± 1.2	40.8 ± 1.2	40.8 ± 0.7	37.7 ± 1.6	34.6 ± 1.0
$\dot{V}_E$, L/min (%MVV)	11.1 ± 0.9	9.2 ± 0.7	43.6 ± 2.6	35.1 ± 1.5*	75.8 ± 8.6 (72 ± 12)	91.3 ± 13.4 (74 ± 10)
V_T, L	0.69 ± 0.09	0.67 ± 0.08	1.37 ± 0.09	1.34 ± 0.08	1.64 ± 0.14	1.81 ± 0.16
V_T, %IC	24.4 ± 3.7	26.1 ± 2.7	49.1 ± 2.7	48.3 ± 1.7	59.6 ± 5.4	65.0 ± 5.2
V_T, %FVC	21.1 ± 3.2	18.6 ± 1.7	41.1 ± 2.7	37.9 ± 2.5#	49.1 ± 3.8	51.0 ± 4.8
f_B, breaths/min	17.2 ± 2.0	14.6 ± 1.6	32.5 ± 1.9	27.2 ± 1.9*	46.4 ± 2.7	50.0 ± 4.3
IC, L	2.90 ± 0.11	2.57 ± 0.11*	2.79 ± 0.10	2.78 ± 0.08	2.77 ± 0.11	2.78 ± 0.08
IC, %FVC	86.6 ± 0.7	72.0 ± 1.8*	83.5 ± 1.2	78.2 ± 3.6	82.8 ± 1.5	78.2 ± 2.9
ΔIC from rest, L	–	–	−0.11 ± 0.05	0.20 ± 0.11*	−0.13 ± 0.05	0.21 ± 0.09*
IRV, L	2.20 ± 0.17	1.91 ± 0.12#	1.42 ± 0.10	1.44 ± 0.06	1.13 ± 0.17	0.97 ± 0.14
IRV, %FVC	65.5 ± 3.2	53.4 ± 3.0*	42.4 ± 2.2	40.4 ± 1.9	33.7 ± 4.8	27.2 ± 4.0#

Values are means ± SEM. Abbreviations: PRE, before bariatric surgery; POST, after bariatric surgery; $\dot{V}O_2$ rate of O_2 consumption; $\dot{V}CO_2$, rate of CO_2 production; RER, respiratory exchange ratio; $\dot{V}_E/\dot{V}CO_2$, ventilatory equivalent for CO_2; $P_{ET}CO_2$, end-tidal CO_2 tension; $\dot{V}_E$, minute ventilation; MVV, maximal voluntary ventilation; V_T, tidal volume; IC, inspiratory capacity; FVC, forced vital capacity; f_B, breathing frequency; Δ, change; IRV, inspiratory reserve volume.

* $p < 0.05$.

\# $p \leq 0.08$ vs. PRE.

Dynamic EELV decreases in the transition from rest-to-moderate intensity exercise in adults with and without obesity (Babb et al., 2002; Chlif et al., 2015; DeLorey et al., 2005). In contrast to non-obese individuals who typically maintain dynamic EELV at or below resting levels during heavy-to-peak exercise, people with obesity tend to dynamically hyperinflate during exercise near the limits of tolerance; that is, their dynamic EELV rises above resting levels during heavy-to-peak exercise (Babb et al., 2002; Chlif et al., 2015; DeLorey et al., 2005; Romagnoli et al., 2008). As reviewed in detail elsewhere (Jensen et al., 2009; O'Donnell et al., 2012) and originally proposed by Ofir et al. (2007), the dynamic increase in EELV during exercise near the limits of tolerance in people with obesity may be mechanically advantageous in as much as it: (1) positions V_T on the linear (compliant) portion of the respiratory systems sigmoid pressure-volume curve where the relationship between increasing contractile respiratory muscle pressure (effort) development and increasing V_T expansion (i.e., neuromechanical coupling of the respiratory system) is preserved; (2) attenuates expiratory flow limitation; and (3) optimizes length-tension relationships of the inspiratory pump muscles, most notably the diaphragm. Furthermore, recruitment of a larger resting IC and adoption of a rapid, shallow breathing pattern combine to accommodate dynamic increases in EELV, while preventing excessive increases in both dynamic EILV

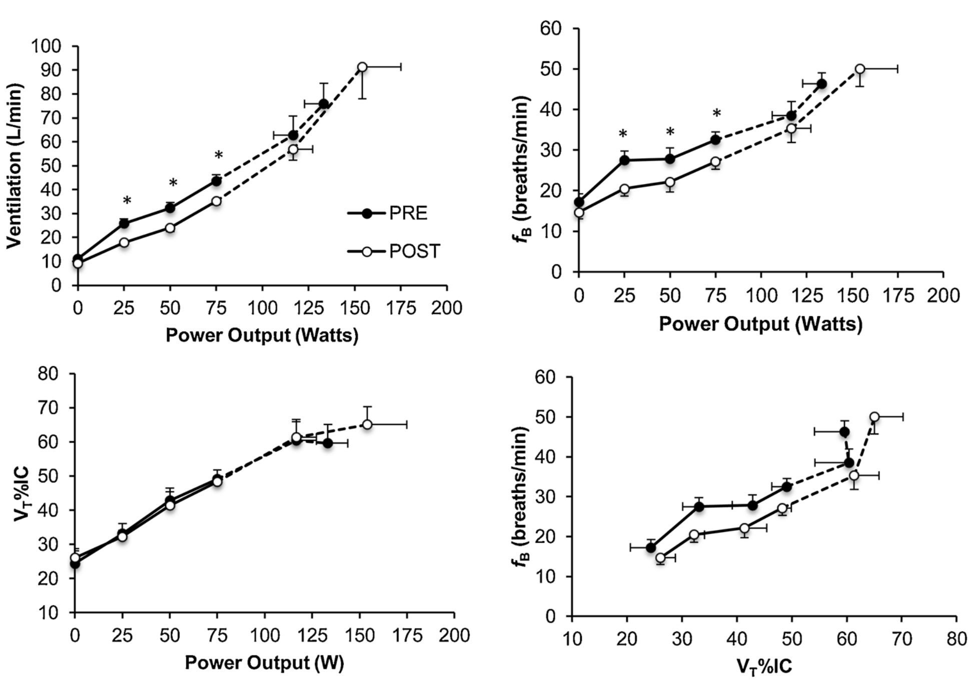

Fig. 2. Ventilatory and breathing pattern responses to symptom-limited incremental cycle exercise testing in adults with class III obesity before (PRE) and ˜3 months after (POST) bariatric surgery. Values are means ± SEM at rest, during exercise at standardized submaximal power outputs, and at peak exercise. Abbreviations: f_B, breathing frequency; V_T, tidal volume; IC, inspiratory capacity. *$p < 0.05$ vs. PRE.

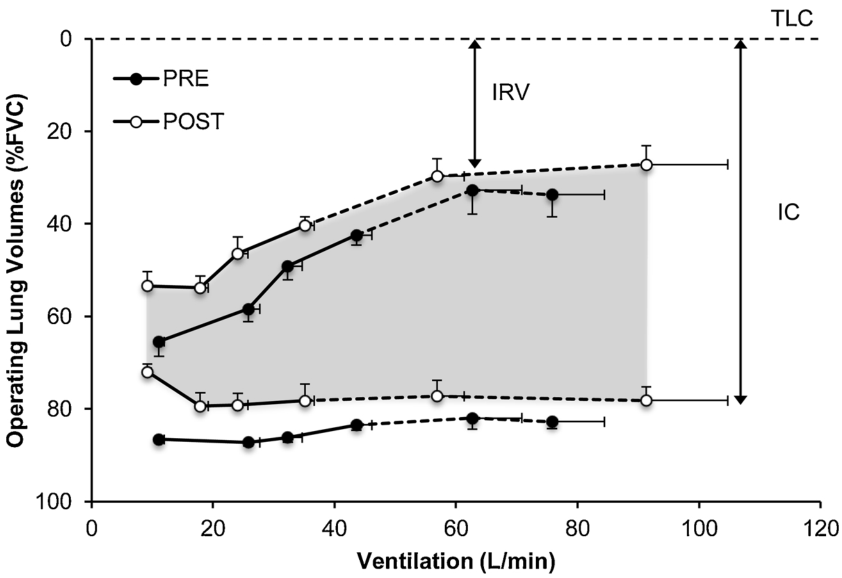

Fig. 3. Dynamic operating lung volume responses to symptom-limited incremental cycle exercise testing in adults with class III obesity before (PRE) and ˜3 months after (POST) bariatric surgery. Values are means ± SEM at rest, during exercise at standardized submaximal power outputs, and at peak exercise. Abbreviations: FVC, forced vital capacity; IRV, inspiratory reserve volume; TLC, total lung capacity; IC, inspiratory capacity.

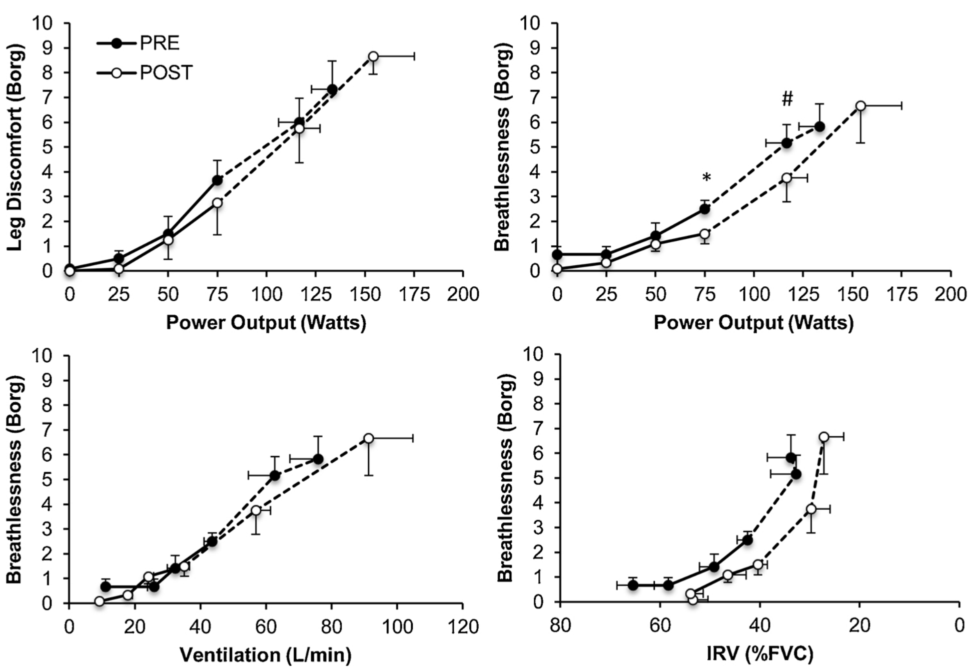

Fig. 4. Perceptual responses to symptom-limited incremental cycle exercise testing in adults with class III obesity before (PRE) and ˜3 months after (POST) bariatric surgery. Values are means ± SEM at rest, during exercise at standardized submaximal power outputs, and at peak exercise. Abbreviations: IRV, inspiratory reserve volume; FVC = forced vital capacity. $^{*}p < 0.05$ and $^{\#}p \leq 0.08$ vs. PRE.

and the elastic work of breathing for any given $\dot{V}_E$ during exercise near the limits of tolerance in adults with vs. without obesity (Babb et al., 2002; Chlif et al., 2015; DeLorey et al., 2005; Ofir et al., 2007; Romagnoli et al., 2008). The collective result of these static and dynamic mechanical adaptations is that V_T expansion is not more mechanically constrained during exercise in people with vs. without obesity.

To our knowledge, only Babb et al. (2011) and Bhammar et al. (2016) have examined the effect of weight loss on operating lung volumes during exercise in men and women with class I and II obesity. In these studies, moderate weight loss (by ˜7.5 kg) increased EELV and EILV at any given submaximal $\dot{V}_E$ during cycle ergometer exercise, but had no effect on the behaviour of dynamic EELV from rest to end-exercise. In keeping with these observations, we are the first to show that IC and IRV were reduced at any given $\dot{V}_E$ during incremental CPET (by 4.5–10% FVC and 6.5–12% FVC, respectively) after more extreme weight loss *via* bariatric surgery for class III obesity. In contrast to the results of Babb et al. (2011) and Bhammar et al. (2016), however, we found that surgically-induced weight loss normalized the behaviour of dynamic EELV during exercise (i.e., prevented dynamic lung hyperinflation), as evidenced by a 0.21 L (˜6% FVC) increase compared with a 0.13 L (˜4% FVC) decrease in dynamic IC from rest-to-peak exercise in POST vs. PRE, respectively. The decrease in dynamic IRV at any given $\dot{V}_E$ during exercise in POST vs. PRE was not due to increased V_T expansion, but reflected the impact of bariatric surgery on static and dynamic IC. It follows that the reduced f_B response to exercise after bariatric surgery could not be explained by release of abnormal restrictive constraints on V_T expansion *via* improved static and dynamic respiratory mechanics.

The collective results of cross-sectional studies by Ofir et al. (2007), Romagnoli et al. (2008) and Ingle et al. (2012), suggest that breathlessness-power output relationships are higher, while breathlessness-$\dot{V}_E$ relationships are not different during incremental CPET in adults with vs. without obesity. Relative preservation of breathlessness-$\dot{V}_E$ relationships during exercise in obesity suggest that the greater intensity ratings of breathlessness reported by individuals with vs. without obesity for a given power output during exercise cannot be explained by abnormal restrictive constraints on V_T expansion (which would be expected to increase breathlessness-$\dot{V}_E$ relationships during exercise (Jensen et al., 2009; Kotrach et al., 2015; Mendonca et al., 2014; O'Donnell et al., 2000, 2009), but that they reflect the awareness of relatively greater $\dot{V}_E$ needed to support the exaggerated metabolic demands of exercise in obesity (Ofir et al., 2007; Romagnoli et al., 2008). Ofir et al. (2007) proposed that the lack of anticipated rise in breathlessness-$\dot{V}_E$ relationships during exercise in people with vs. without obesity may be explained by the aforementioned static and dynamic respiratory mechanical adaptations in obesity, including resting IC recruitment, dynamic lung hyperinflation, and adoption of a more rapid and shallow breathing pattern.

Weight loss through diet and exercise (Bernhardt and Babb, 2014) and bariatric surgery (Boissiere et al., 2017; Karason et al., 2000) is associated with relief of breathlessness in daily life (Boissiere et al., 2017; Karason et al., 2000) and during constant-load cycle exercise testing (Bernhardt and Babb, 2014) in adults with obesity, particularly those who experience more severe activity-related breathlessness before weight loss (Bernhardt and Babb, 2014; Boissiere et al., 2017). We are the first to show that surgically-induced weight loss was associated with clinically meaningful reductions in breathlessness intensity ratings during incremental CPET at standardized submaximal power outputs ≥75-watts: by 1.0 and 1.4 Borg units at 75-watts ($p < 0.05$) and at the highest equivalent power output of 117-watts ($p < 0.08$), respectively. In contrast, extreme weight loss following bariatric surgery had no effect on breathlessness-$\dot{V}_E$ relationships during incremental CPET. The lack of decrease in breathlessness-$\dot{V}_E$ relationships after surgically-induced weight loss may be explained, at least in part, by maintenance of a lower and more mechanically disadvantageous IRV at any given $\dot{V}_E$ during exercise in POST vs. PRE. Indeed, we are the first to show that breathlessness-IRV%FVC curves were rightward shifted throughout exercise in POST vs. PRE, such that breathlessness intensity ratings were lower at any given IRV%FVC during exercise after bariatric surgery; for example, by ˜1.5 Borg units at an IRV of ˜40% FVC. Based on these findings, we concluded that relief of exertional breathlessness following bariatric surgery for class III obesity could not be explained by improved static and dynamic respiratory mechanics, but that it was mechanistically linked to the reduced metabolic and ventilatory requirements of exercise.

4.1. Methodological considerations

Although our sample size was small, it was nevertheless sufficient to detect significant and clinically meaningful differences in a range of key physiological and perceptual outcome variables at rest and during CPET, including $\dot{V}O_2$, $\dot{V}CO_2$, HR, $\dot{V}_E$, f_B, IC, IRV and breathlessness.

Repeated measurements were made just 3-months after bariatric surgery. While this relatively short follow-up period allowed us to isolate the effects of extreme weight loss on physiological and perceptual responses to CPET before any major lifestyle changes to diet and/or physical activity occurred, it also prevented us from commenting on the long(er)-term effects of surgically-induced weight loss on exercise physiological and perceptual responses. However, Fontana et al. (2019) recently reported that participation in moderate-to-intense physical activity after bariatric surgery did not directly influence the perception of breathlessness in people with morbid obesity.

It is reasonable to assume that the observed changes in physiological and perceptual responses to non-weight bearing cycle exercise testing after bariatric surgery may have been further exaggerated during weight bearing exercise (e.g., treadmill walking). In this regard, our results may underestimate the *"true"* impact of extreme weight loss in adults with class III obesity on physiological and perceptual responses during activities of daily life, which are mostly weight bearing (e.g., walking, stair climbing).

4.2. Conclusion and implication

The main results of this study support the hypothesis that relief of exertional breathlessness following weight loss in adults with obesity is primarily related to the reduced metabolic and ventilatory requirements of exercise. The clinical implication of this study is that, in addition to weight reduction and improved body composition, any intervention capable of decreasing the metabolic and ventilatory demands of physical activity (e.g., exercise training) in people with obesity has the potential to increase health-related quality of life by decreasing the burden of breathlessness in daily life.

Author contributions

Conception and design of the study: S.J.A., R.E.R.R., R.E.A., D.J. Collection and assembly of data: S.J.A., R.E.R.R. Analysis of data: A.M., S.J.A., R.E.R.R., D.J. Drafting the article and/or revising it critically for important intellectual content: A.M., S.J.A., R.E.R.R., R.E.A., D.J. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work

Funding

This work was supported by an operating grant to D.J. from the Natural Sciences and Engineering Research Council of Canada (RGPIN 402598-2011). S.J.A. was supported by a Ph.D. Recruitment Award (McGill University), a Ruth Hoyt Cameron Fellowship, a Max Bell Fellowship, and a Frederik Banting and Charles Best Graduate Scholarship – Doctoral Award (CGS-D) from the Canadian Institutes of Health Research (201410GSD-347900-243684). R.E.R.R. was supported by a Bloomberg-Manulife Doctoral Award (McGill University) and a graduate scholarship from the Fonds de Recherche du Québec-Santé. R.E.A. was supported by a Canada Research Chair in Physical Activity and Health (Tier 1) from the Canadian Institutes of Health Research. D.J. was supported by a Chercheurs-Boursiers Junior 1 salary award from the Fonds de Recherche du Québec-Santé, a William Dawson Research Scholar Award from McGill University, and a Canada Research Chair in Clinical Exercise & Respiratory Physiology (Tier 2) from the Canadian Institutes of Health Research.

Conflict of interest

The authors have no real or perceived conflict(s) of interest to disclose.

Acknowledgements

The authors wish to thank the participants for their time and cooperation.

References

Babb, T.G., Buskirk, E.R., Hodgson, J.L., 1989. Exercise end-expiratory lung volumes in lean and moderately obese women. Int. J. Obes. 13, 11–19.
Babb, T.G., Korzick, D., Meador, M., Hodgson, J.L., Buskirk, E.R., 1991. Ventilatory response of moderately obese women to submaximal exercise. Int. J. Obes. 15, 59–65.
Babb, T.G., Wyrick, B.L., DeLorey, D.S., Chase, P.J., Feng, M.Y., 2008. Fat distribution and end-expiratory lung volume in lean and obese men and women. Chest 134, 704–711.
Babb, T.G., Wyrick, B.L., Chase, P.J., DeLorey, D.S., Rodder, S.G., Feng, M.Y., Ranasinghe, K.G., 2011. Weight loss via diet and exercise improves exercise breathing mechanics in obese men. Chest 140, 454–460.
Babb, T.G., DeLorey, D.S., Wyrick, B.L., Gardner, P.P., 2002. Mild obesity does not limit change in end-expiratory lung volume during cycling in young women. J. Appl. Physiol. 92 (1985), 2483–2490.
Barbalho-Moulim, M.C., Miguel, G.P., Forti, E.M., Campos Fdo, A., Peixoto-Souza, F.S., Costa, D., 2013. Pulmonary function after weight loss in obese women undergoing Roux-en-Y gastric bypass: one-year followup. ISRN Obes., 796454 2013.
Bernhardt, V., Babb, T.G., 2014. Weight loss reduces dyspnea on exertion in obese women. Respir. Physiol. Neurobiol. 204, 86–92.
Bernhardt, V., Stickford, J.L., Bhammar, D.M., Babb, T.G., 2016. Aerobic exercise training

without weight loss reduces dyspnea on exertion in obese women. Respir. Physiol. Neurobiol. 221, 64–70.

Bhammar, D.M., Stickford, J.L., Bernhardt, V., Babb, T.G., 2016. Effect of weight loss on operational lung volumes and oxygen cost of breathing in obese women. Int. J. Obes. (Lond.) 40, 998–1004.

Boissiere, L., Perotin-Collard, J.M., Bertin, E., Gaubil, I., Diaz Cives, A., Barbe, C., Dury, S., Nardi, J., Lebargy, F., Deslee, G., Launois, C., 2017. Improvement of dyspnea after bariatric surgery is associated with increased expiratory reserve volume: a prospective follow-up study of 45 patients. PLoS One 12, e0185058.

Borg, G.A., 1982. Psychophysical bases of perceived exertion. Med. Sci. Sports Exerc. 14, 377–381.

Browning, M.G., Franco, R.L., Herrick, J.E., Arrowood, J.A., Evans, R.K., 2017. Assessment of cardiopulmonary responses to treadmill walking following gastric bypass surgery. Obes. Surg. 27, 96–101.

Campos, E.C., Peixoto-Souza, F.S., Alves, V.C., Basso-Vanelli, R., Barbalho-Moulim, M., Laurino-Neto, R.M., Costa, D., 2018. Improvement in lung function and functional capacity in morbidly obese women subjected to bariatric surgery. Clinics (Sao Paulo) 73, e20.

Carver, T.E., Christou, N.V., Andersen, R.E., 2013. In vivo precision of the GE iDXA for the assessment of total body composition and fat distribution in severely obese patients. Obesity 21, 1367–1369 Silver Spring.

Chlif, M., Temfemo, A., Keochkerian, D., Choquet, D., Chaouachi, A., Ahmaidi, S., 2015. Advanced mechanical ventilatory constraints during incremental exercise in class III obese male subjects. Respir. Care 60, 549–560.

Collaborators, G.B.D.O, Afshin, A., Forouzanfar, M.H., Reitsma, M.B., Sur, P., Estep, K., Lee, A., Marczak, L., Mokdad, A.H., Moradi-Lakeh, M., Naghavi, M., Salama, J.S., Vos, T., Abate, K.H., Abbafati, C., Ahmed, M.B., Al-Aly, Z., Alkerwi, A., Al-Raddadi, R., Amare, A.T., Amberbir, A., Amegah, A.K., Amini, E., Amrock, S.M., Anjana, R.M., Arnlov, J., Asayesh, H., Banerjee, A., Barac, A., Baye, E., Bennett, D.A., Beyene, A.S., Biadgilign, S., Biryukov, S., Bjertness, E., Boneya, D.J., Campos-Nonato, I., Carrero, J.J., Cecilio, P., Cercy, K., Ciobanu, L.G., Cornaby, L., Damtew, S.A., Dandona, L., Dandona, R., Dharmaratne, S.D., Duncan, B.B., Eshrati, B., Esteghamati, A., Feigin, V.L., Fernandes, J.C., Furst, T., Gebrehiwot, T.T., Gold, A., Gona, P.N., Goto, A., Habtewold, T.D., Hadush, K.T., Hafezi-Nejad, N., Hay, S.I., Horino, M., Islami, F., Kamal, R., Kasaeian, A., Katikireddi, S.V., Kengne, A.P., Kesavachandran, C.N., Khader, Y.S., Khang, Y.H., Khubchandani, J., Kim, D., Kim, Y.J., Kinfu, Y., Kosen, S., Ku, T., Defo, B.K., Kumar, G.A., Larson, H.J., Leinsalu, M., Liang, X., Lim, S.S., Liu, P., Lopez, A.D., Lozano, R., Majeed, A., Malekzadeh, R., Malta, D.C., Mazidi, M., McAlinden, C., McGarvey, S.T., Mengistu, D.T., Mensah, G.A., Mensink, G.B.M., Mezgebe, H.B., Mirrakhimov, E.M., Mueller, U.O., Noubiap, J.J., Obermeyer, C.M., Ogbo, F.A., Owolabi, M.O., Patton, G.C., Pourmalek, F., Qorbani, M., Rafay, A., Rai, R.K., Ranabhat, C.L., Reinig, N., Safiri, S., Salomon, J.A., Sanabria, J.R., Santos, I.S., Sartorius, B., Sawhney, M., Schmidhuber, J., Schutte, A.E., Schmidt, M.I., Sepanlou, S.G., Shamsizadeh, M., Sheikhbahaei, S., Shin, M.J., Shiri, R., Shiue, I., Roba, H.S., Silva, D.A.S., Silverberg, J.I., Singh, J.A., Stranges, S., Swaminathan, S., Tabares-Seisdedos, R., Tadese, F., Tedla, B.A., Tegegne, B.S., Terkawi, A.S., Thakur, J.S., Tonelli, M., Topor-Madry, R., Tyrovolas, S., Ukwaja, K.N., Uthman, O.A., Vaezghasemi, M., Vasankari, T., Vlassov, V.V., Vollset, S.E., Weiderpass, E., Werdecker, A., Wesana, J., Westerman, R., Yano, Y., Yonemoto, N., Yonga, G., Zaidi, Z., Zenebe, Z.M., Zipkin, B., Murray, C.J.L., 2017. Health effects of overweight and obesity in 195 countries over 25 years. N. Engl. J. Med. 377, 13–27.

Currow, D.C., Dal Grande, E., Sidhu, C., Ekstrom, M., Johnson, M.J., 2017. The independent association of overweight and obesity with breathlessness in adults: a cross-sectional, population-based study. Eur. Respir. J. 50.

da Silva, R.P., Martinez, D., Faria, C.C., de Carli, L.A., de Souza, W.I., Meinhardt, N.G., Souto, K.E., Trindade, M.R., Ribeiro, J.P., 2013. Improvement of exercise capacity and peripheral metaboreflex after bariatric surgery. Obes. Surg. 23, 1835–1841.

de Souza, S.A., Faintuch, J., Fabris, S.M., Nampo, F.K., Luz, C., Fabio, T.L., Sitta, I.S., de Batista Fonseca, I.C., 2009. Six-minute walk test: functional capacity of severely obese before and after bariatric surgery. Surg. Obes. Relat. Dis. 5, 540–543.

de Souza, S.A., Faintuch, J., Sant'anna, A.F., 2010. Effect of weight loss on aerobic capacity in patients with severe obesity before and after bariatric surgery. Obes. Surg. 20, 871–875.

DeLorey, D.S., Wyrick, B.L., Babb, T.G., 2005. Mild-to-moderate obesity: implications for respiratory mechanics at rest and during exercise in young men. Int. J. Obes. (Lond.) 29, 1039–1047.

Fontana, A.D., Lopes, A.D., Lunardi, A.C., 2019. Bariatric surgery associated with practice of moderate to intense physical activity related to weight loss, activity level in daily life, Dyspnea, and quality of life of sedentary individuals with morbid obesity: a prospective longitudinal study. Obes. Surg.

Guenette, J.A., Chin, R.C., Cory, J.M., Webb, K.A., O'Donnell, D.E., 2013. Inspiratory capacity during exercise: measurement, analysis, and interpretation. Pulm. Med., 956081 2013.

Hankinson, J.L., Odencrantz, J.R., Fedan, K.B., 1999. Spirometric reference values from a sample of the general U.S. population. Am. J. Respir. Crit. Care Med. 159, 179–187.

Ingle, L., Cleland, J.G., Clark, A.L., 2012. Body mass index is related to the perception of exertional breathlessness in patients presenting with dyspnoea of unknown origin. Int. J. Cardiol. 157, 300–303.

Jensen, D., Ofir, D., O'Donnell, D.E., 2009. Effects of pregnancy, obesity and aging on the intensity of perceived breathlessness during exercise in healthy humans. Respir. Physiol. Neurobiol. 167, 87–100.

Jones, R.L., Nzekwu, M.M., 2006. The effects of body mass index on lung volumes. Chest 130, 827–833.

Jones, N.L., Makrides, L., Hitchcock, C., Chypchar, T., McCartney, N., 1985. Normal standards for an incremental progressive cycle ergometer test. Am. Rev. Respir. Dis. 131, 700–708.

Kanoupakis, E., Michaloudis, D., Fraidakis, O., Parthenakis, F., Vardas, P., Melissas, J., 2001. Left ventricular function and cardiopulmonary performance following surgical treatment of morbid obesity. Obes. Surg. 11, 552–558.

Karason, K., Lindroos, A.K., Stenlof, K., Sjostrom, L., 2000. Relief of cardiorespiratory symptoms and increased physical activity after surgically induced weight loss: results from the Swedish Obese Subjects study. Arch. Intern. Med. 160, 1797–1802.

Kotrach, H.G., Bourbeau, J., Jensen, D., 2015. Does nebulized fentanyl relieve dyspnea during exercise in healthy man? J. Appl. Physiol. 118, 1406–1414.

Lorenzo, S., Babb, T.G., 2012. Quantification of cardiorespiratory fitness in healthy nonobese and obese men and women. Chest 141, 1031–1039.

Maniscalco, M., Zedda, A., Giardiello, C., Faraone, S., Cerbone, M.R., Cristiano, S., Sofia, M., 2006. Effect of bariatric surgery on the six-minute walk test in severe uncomplicated obesity. Obes. Surg. 16, 836–841.

Mendonca, C.T., Schaeffer, M.R., Riley, P., Jensen, D., 2014. Physiological mechanisms of dyspnea during exercise with external thoracic restriction: role of increased neural respiratory drive. J. Appl. Physiol. 116, 570–581.

Miller, M.R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Crapo, R., Enright, P., van der Grinten, C.P., Gustafsson, P., Jensen, R., Johnson, D.C., MacIntyre, N., McKay, R., Navajas, D., Pedersen, O.F., Pellegrino, R., Viegi, G., Wanger, J., 2005. Standardisation of spirometry. Eur. Respir. 26, 319–338.

O'Donnell, D.E., Hong, H.H., Webb, K.A., 2000. Respiratory sensation during chest wall restriction and dead space loading in exercising men. J. Appl. Physiol. 88, 1859–1869.

O'Donnell, D.E., Ora, J., Webb, K.A., Laveneziana, P., Jensen, D., 2009. Mechanisms of activity-related dyspnea in pulmonary diseases. Respir. Physiol. Neurobiol. 167, 116–132.

O'Donnell, D.E., O'Donnell, C.D., Webb, K.A., Guenette, J.A., 2012. Respiratory consequences of mild-to-moderate obesity: impact on exercise performance in health and in chronic obstructive pulmonary disease. Pulm. Med., 818925 2012.

Ofir, D., Laveneziana, P., Webb, K.A., O'Donnell, D.E., 2007. Ventilatory and perceptual responses to cycle exercise in obese women. J. Appl. Physiol. 102 (1985), 2217–2226.

Romagnoli, I., Laveneziana, P., Clini, E.M., Palange, P., Valli, G., de Blasio, F., Gigliotti, F., Scano, G., 2008. Role of hyperinflation vs. deflation on dyspnoea in severely to extremely obese subjects. Acta Physiol. (Oxf.) 193, 393–402.

Seres, L., Lopez-Ayerbe, J., Coll, R., Rodriguez, O., Vila, J., Formiguera, X., Alastrue, A., Rull, M., Valle, V., 2006. Increased exercise capacity after surgically induced weight loss in morbid obesity. Obesity 14, 273–279 Silver Spring.

Sin, D.D., Jones, R.L., Man, S.F., 2002. Obesity is a risk factor for dyspnea but not for airflow obstruction. Arch. Intern. Med. 162, 1477–1481.

Steier, J., Lunt, A., Hart, N., Polkey, M.I., Moxham, J., 2014. Observational study of the effect of obesity on lung volumes. Thorax 69, 752–759.

Stubbing, D.G., Pengelly, L.D., Morse, J.L., Jones, N.L., 1980. Pulmonary mechanics during exercise in normal males. J. Appl. Physiol. Respir. Environ. Exerc. Physiol. 49, 506–510.