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Effects of a multidisciplinary body weight reduction program on static and dynamic thoraco-abdominal volumes in obese adolescents

Antonella LoMauro, Ambra Cesareo, Fiorenza Agosti, Gabriella Tringali, Desy Salvadego, Bruno Grassi, Alessandro Sartorio, and Andrea Aliverti

Abstract: The objective of this study was to characterize static and dynamic thoraco-abdominal volumes in obese adolescents and to test the effects of a 3-week multidisciplinary body weight reduction program (MBWRP), entailing an energy-restricted diet, psychological and nutritional counseling, aerobic physical activity, and respiratory muscle endurance training (RMET), on these parameters. Total chest wall (V_{CW}), pulmonary rib cage ($V_{RC,p}$), abdominal rib cage ($V_{RC,a}$), and abdominal (V_{AB}) volumes were measured on 11 male adolescents (Tanner stage: 3–5; BMI standard deviation score: >2 ; age: 15.9 ± 1.3 years; percent body fat: 38.4%) during rest, inspiratory capacity (IC) maneuver, and incremental exercise on a cycle ergometer at baseline and after 3 weeks of MBWRP. At baseline, the progressive increase in tidal volume was achieved by an increase in end-inspiratory V_{CW} ($p < 0.05$) due to increases in $V_{RC,p}$ and $V_{RC,a}$ with constant V_{AB} . End-expiratory V_{CW} decreased with late increasing $V_{RC,p}$, dynamically hyperinflating $V_{RC,a}$ ($p < 0.05$), and progressively decreasing V_{AB} ($p < 0.05$). After MBWRP, weight loss was concentrated in the abdomen and total IC decreased. During exercise, abdominal rib cage hyperinflation was delayed and associated with 15% increased performance and reduced dyspnea at high workloads ($p < 0.05$) without ventilatory and metabolic changes. We conclude that otherwise healthy obese adolescents adopt a thoraco-abdominal operational pattern characterized by abdominal rib cage hyperinflation as a form of lung recruitment during incremental cycle exercise. Additionally, a short period of MBWRP including RMET is associated with improved exercise performance, lung and chest wall volume recruitment, unloading of respiratory muscles, and reduced dyspnea.

Key words: obesity, pediatrics, exercise, pulmonary physiology, exercise physiology, kinesiology.

Résumé : Cette étude a pour objectif de déterminer les volumes thoraco-abdominaux statiques et dynamiques chez des adolescents obèses et d'évaluer sur ces variables les effets de 3 semaines d'un programme multidisciplinaire de perte de poids (MBWRP) comprenant un régime restrictif, du counseling psychologique et nutritionnel, de l'activité physique aérobie et un entraînement en endurance des muscles respiratoires (RMET). On mesure les volumes de la cage thoracique totale (V_{CW}), du compartiment pulmonaire ($V_{RC,p}$), du compartiment abdominal ($V_{RC,a}$) et de l'abdomen (V_{AB}) de 11 adolescents mâles (stade de Tanner : 3–5, IMC > 2 écarts-types, âge $15,9 \pm 1,3$ ans, pourcentage de gras corporel : 38,4 %) au repos, la capacité inspiratoire (IC), une manœuvre de capacité inspiratoire (IC) et un test d'effort progressif sur cycloergomètre au début et après 3 semaines de MBWRP. Au début, le volume courant s'accroît progressivement par l'augmentation de V_{CW} à la fin de l'inspiration ($p < 0,05$) due à l'agrandissement des deux compartiments de la cage thoracique, V_{AB} demeurant constant. V_{CW} à la fin de l'expiration diminue en présence d'une augmentation tardive de $V_{RC,p}$ avec hyperinflation dynamique de $V_{RC,a}$ ($p < 0,05$) et une diminution graduelle de V_{AB} ($p < 0,05$). Après le MBWRP, la perte de poids se concentre à l'abdomen et l'IC totale diminue. Au cours de l'exercice physique, l'hyperinflation de la cage thoraco-abdominale est retardée et associée à une augmentation de la performance de 15 % et à une diminution de la dyspnée à de fortes charges de travail ($p < 0,05$) sans variations ventilatoires et métaboliques. Des adolescents obèses en bonne santé par ailleurs adoptent une modalité de fonctionnement thoraco-abdominale caractérisée par l'occurrence d'une hyperinflation de la cage thoracique pour ainsi solliciter les poumons au cours de l'épreuve d'effort progressif sur cycloergomètre. De plus, un MBWRP de courte durée incluant un RMET est associé à une amélioration de la performance à l'effort, à une sollicitation volumique des poumons et de la cage thoracique, à une décharge des muscles respiratoires et à un allègement de la dyspnée. [Traduit par la Rédaction]

Mots-clés : obésité, pédiatrie, exercice physique, physiologie pulmonaire, physiologie de l'exercice, kinésiologie.

Introduction

Adolescent obesity, a major health concern that has reached a worldwide epidemic dimension (Brennan et al. 2015), is frequently associated with early cardiovascular risk, diabetes, sleep-disordered

breathing, and impaired ventilatory function (Must et al. 1992, 1996; Must and McKeown 2000; Sinha et al. 2002; Schiel et al. 2006). The last includes breathing at lower lung volumes, decreased thoracic compliance, and increased respiratory resistance secondary to the

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reduction in lung volumes related to overweight (Babb 1999; DeLorey et al. 2005; Parameswaran et al. 2006; Babb et al. 2011; Chlif et al. 2015). These features suggest that in addition to an augmented elastic load due to the mass burdening on the chest wall, obese subjects also have to overcome a higher resistive load (Oppenheimer et al. 2014). Respiratory muscles therefore have to cope with increased work of breathing, particularly during exercise (Lin and Lin 2012). The latter is typically associated with an increased ventilatory response for a given metabolic requirement (Lin and Lin 2012) as well as an increased oxygen cost of breathing (Bernhardt et al. 2013; Babb et al. 2008), which can reach values up to 3 times greater (~ 3.0 – 3.5 mL of O_2/L of minute ventilation) than those reached by normal-weight subjects.

The assessment of operating volumes of the lung, namely end-expiratory and end-inspiratory volumes, is important for understanding how the respiratory muscles and the ventilatory pattern adapt in response to incremental exercise-induced demands (Babb 1999, 2013; Babb et al. 2002, 2011; DeLorey et al. 2005; Parameswaran et al. 2006; Ofir et al. 2007; Romagnoli et al. 2008; Lin and Lin 2012; Chlif et al. 2015). Obese adolescents do not hyperinflate, i.e., they do not increase their end-expiratory lung volume, in response to increasing exercise (Mendelson et al. 2012). This finding is in contrast with studies demonstrating that young obese men hyperinflate during heavy levels of exercise, whereas their end-expiratory lung volume does not change during moderate exercise (DeLorey et al. 2005). Both obese adolescents and adults improve their operating lung volume, by increasing their end-expiratory lung volume, after a period of exercise training and diet (DeLorey et al. 2005; Babb et al. 2011; Mendelson et al. 2012).

The respiratory response to exercise involves volume changes of not only the lung but also the chest wall. The distribution of the latter into the different thoraco-abdominal compartments is determined by the action of different respiratory muscle groups (Aliverti et al. 1997, 2002) and can be noninvasively assessed by optoelectronic plethysmography (Cala et al. 1996). Distinct altered patterns of chest wall operating volumes during exercise have been described in chronic obstructive pulmonary disease, pulmonary fibrosis, and cystic fibrosis (Aliverti et al. 2004, 2009; Vogiatzis et al. 2005a; Georgiadou et al. 2007; Wilkens et al. 2010). Although the dynamical assessment of total and compartmental operational chest wall volumes during exercise is important for understanding which factors contribute to exercise limitation, to date there is a lack of investigations regarding obesity.

The major aim of the present study is to verify whether thoraco-abdominal volumes of male obese adolescents during exercise are characterized by specific features eventually adopted to cope with the increasing ventilatory demands. The main hypothesis was that the abdominal volume (mass) would affect the action of the diaphragm and abdominal muscles and consequently the regulation of the operating volumes of the 2 compartments influenced by these muscles, namely the abdominal rib cage and abdomen (Ward et al. 1992; Kenyon et al. 1997; Aliverti et al. 2002, 2003). In addition, it has been recently shown that the inclusion of respiratory muscle endurance training (RMET) in a multidisciplinary body weight reduction program (MBWRP) improves exercise performance in overweight and obese adults more than exercise and nutritional counseling alone (Frank et al. 2011). Therefore, we also investigated whether a short period of MBWRP including RMET can acutely modify the geometry and operating volumes of the chest wall in these adolescents.

Materials and methods

Subjects and protocol

Eleven otherwise healthy male obese adolescents (Tanner stage: 3–5; BMI standard deviation score >2 according to the published Italian standards (Cacciari et al. 2006); mean BMI: 36 ± 5 kg/m²; mean age: 15.9 ± 1.3 years) were enrolled in the study.

On the second day of hospitalization, after spirometry and measurements of height and weight, body composition, and chest wall geometry, the subjects performed incremental exercise until exhaustion on a cycle ergometer. Afterward they participated in a 3-week in-hospital MBWRP (see below for a detailed description). All the tests performed at baseline were repeated at the end of the MBWRP.

Informed consent statements were signed by participants' parents. The procedures of the investigation were approved by the ethics committee of the Italian Institute for Auxology, Piancavallo, Italy, and were performed in agreement with the recommendations set forth in the Helsinki Declaration.

Anthropometry, body composition, and chest wall geometry

Standard measures of height, weight, and body mass index (calculated as body weight/height²) were taken together with the assessment of fat mass, fat-free mass, and thoraco-abdominal perimeters, areas, and volumes.

Bioelectric impedance analysis was used to assess fat-free mass (Kyle et al. 2004). Whole-body resistance to an applied current (50 kHz, 0.8 mA) was measured with a tetrapolar device (Human IM, Dietosystem, Italy). Fat-free mass was calculated with equations derived with a 2-compartment model (Gray et al. 1989). Fat mass was calculated as the difference between total body mass and fat-free mass. Thoraco-abdominal perimeters, areas, and volumes were measured by optoelectronic plethysmography (OEP) (Smart System BTS, Milan, Italy) (Aliverti et al. 2002). Eight video cameras, 4 in front of the subject and 4 behind, tracked the movement of 89 retroreflective markers placed anteriorly and posteriorly over the trunk or chest wall, extending from clavicles to pubis, with the subject seated on the cycle ergometer. The position of each marker was reconstructed and used to characterize chest wall geometry and calculate thoraco-abdominal volumes. At the end of resting expiration, the coordinates of the markers at the xiphoid process and the umbilical level were used to compute the resultant perimeter and the enclosed cross-sectional area. The total chest wall volume (V_{CW}) was calculated by applying Gauss's theorem to the three-dimensional coordinates of the markers. The accuracy of the system has been previously tested by simultaneous measurements with a spirometer in healthy subjects while they were sitting or standing, during quiet breathing, during slow vital capacity maneuvers (Cala et al. 1996), and during submaximal and maximal exercise on a cycle ergometer (Kenyon et al. 1997; Layton et al. 2013). In all these conditions, the discrepancy between the 2 measurements was always $< 4\%$. OEP has been validated in other postures (Aliverti et al. 2001) and in paralyzed patients receiving mechanical ventilation (Aliverti et al. 2000), with discrepancies in tidal volume measurements always $< 5\%$. Intra-rater and inter-rater reliability of OEP has also been evaluated at rest and during submaximal cycle-ergometer exercise (Vieira et al. 2013).

The chest wall was modeled as being composed of 3 compartments: the pulmonary rib cage ($V_{RC,p}$, volume enclosed by the clavicles and the xiphoid process of the sternum), the abdominal rib cage ($V_{RC,a}$, volume enclosed by the xiphoid process of the sternum and the lower costal margin of the rib cage where the diaphragm is apposed), and the abdomen (V_{AB} , volume enclosed by the lower costal margin of the rib cage and the iliac crests) (Kenyon et al. 1997; Aliverti et al. 2002).

Spirometry

Forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), Tiffeneau index (FEV₁/FVC), and peak expiratory flow (PEF) were determined (MedGraphics CPX/D, Medical Graphics Corp., Saint Paul, Minn., USA). The test was carried out by the same technician with the participant in standing position, accord-

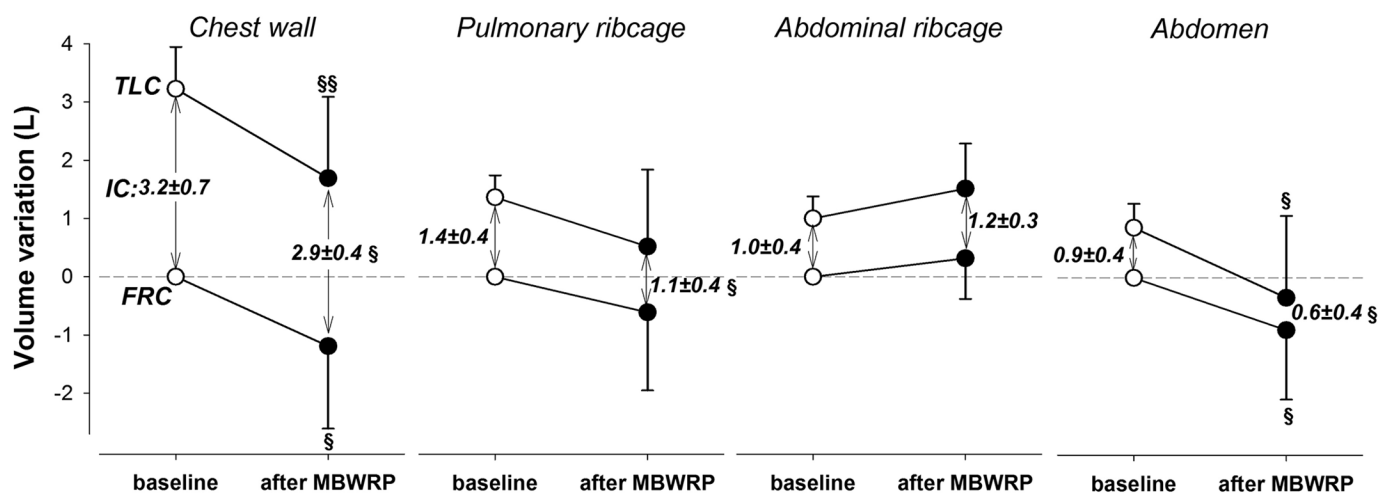
Table 1. Subjects' characteristics and spirometry results.

Characteristic	Baseline	Post-MBWRP	p value
Anthropometry			
Age (years)	15.9±1.3	16.0±1.3	0.341
Stature (m)	1.7±0.05	1.7±0.05	Not tested
Body mass (kg)	107.8±16.4	104.3±15.9	>0.001
Body mass index (kg/m ²)	36.4±5.0	35.2±4.8	>0.001
Body composition			
Fat-free mass, total body (kg)	66.3±9.6	64.4±9.1	0.002
Fat-free mass (% of body mass)	61.6±2.1	61.8±1.9	0.661
Fat mass, total body (kg)	41.4±7.4	39.9±7.3	0.019
Fat mass (% of body mass)	38.4±2.1	38.2±1.9	0.692
Trunk geometry			
Chest wall volume at TLC (L) ^a	38.7±6.8	37.2±6.3	0.008
Chest wall volume at FRC (L) ^a	35.5±6.3	34.3±6.1	0.019
Rib cage volume (L)	22.1±3.4	21.8±3.3	0.475
Abdominal volume (L)	13.4±3.2	12.5±3.2	0.031
Rib cage circumference (m)	1.10±0.04	1.09±0.04	0.067
Abdominal circumference (m)	1.15±0.07	1.12±0.07	0.002
Rib cage cross-sectional area (cm ²)	861.6±73.0	840.4±79.4	0.062
Abdominal cross-sectional area (cm ²)	980.2±108.4	920.0±110.7	>0.001
Spirometry			
FVC (L)	4.9±0.8	5.1±0.9	0.025
FVC (% predicted)	95.0±11.7	99.3±13.9	0.019
FEV ₁ (L)	4.2±0.7	4.3±0.6	0.268
FEV ₁ (% predicted)	94.5±11.1	96.1±9.4	0.246
FEV ₁ /FVC (%)	86.1±6.9	84.1±6.6	0.119
PEF (L/s)	7.8±1.5	8.3±1.6	0.231

Note: MBWRP, multidisciplinary body weight reduction program; TLC, total lung capacity; FRC, functional residual capacity; FVC, forced vital capacity; FEV₁, forced expiratory volume in the first second; PEF, peak expiratory flow.

^aMeasured during inspiratory capacity maneuver.

Fig. 1. Volumes of the chest wall and its 3 compartments, namely the pulmonary rib cage, abdominal rib cage, and abdomen, at total lung capacity (TLC, upper symbols) and functional residual capacity (FRC, lower symbols) before (white circles) and after (black circles) 3 weeks of a multidisciplinary body weight reduction program (MBWRP). The vertical distance between the 2 values at TLC and FRC represents inspiratory capacity (IC). Data are expressed as mean ± standard deviation. §, §§: $p < 0.05, 0.01$ vs. baseline



ing to the European Respiratory Society guidelines (Miller et al. 2005a, 2005b).

Exercise

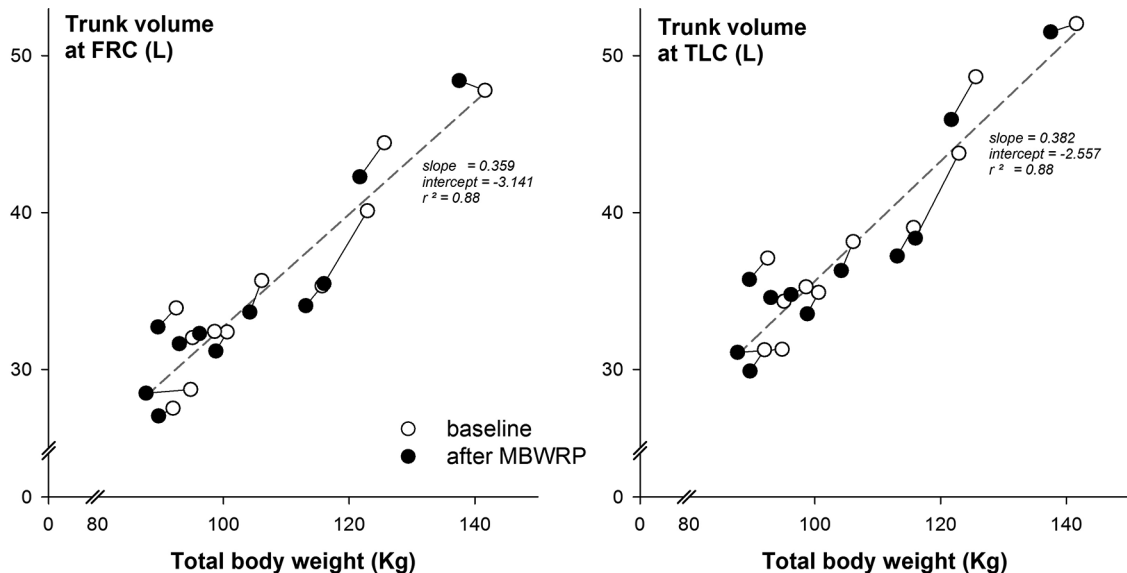
After 3 min of measurements during resting quiet breathing to familiarize subjects with the equipment, the subjects were asked to perform 2 inspiratory capacity (IC) maneuvers. After another minute of resting quiet breathing, an incremental exercise test on a mechanically braked cycle ergometer (Monark Ergonomic 839E) was started. Following 2 min of warm-up at 30 W, the work rate was increased by 20 W/min to the limit of tolerance while pedaling frequency was maintained between 60 and 70 rpm. Oxygen

uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), ventilatory equivalents for oxygen ($\dot{V}_E/\dot{V}O_2$), ventilatory equivalents for carbon dioxide ($\dot{V}_E/\dot{V}CO_2$), end-tidal oxygen tension ($P_{ET}O_2$), and end-tidal carbon dioxide tension ($P_{ET}CO_2$) were measured on a breath-by-breath basis using a metabolic unit (MedGraphics CPX/D, Medical Graphics Corp., Saint Paul, Minn., USA). Borg's 0–10 category ratio scale was used to rate the magnitude of dyspnea and leg discomfort at the end of each workload (Borg 1982).

Operational chest wall volume measurements

Thoraco-abdominal volumes were measured by OEP during the IC maneuvers and exercise with the subjects grasping poles posi-

Fig. 2. Relationship between body weight and trunk volume at functional residual capacity (FRC, left panel) and total lung capacity (TLC, right panel) for each subject at baseline (white circles) and after 3 weeks of MBWRP (black circles). The dashed grey line represents the correlation between the 2 measurements, and its parameters are also reported.



tioned to keep the arms away from the rib cage in order not to cover lateral markers. Total and compartmental chest wall volumes at functional residual capacity (FRC) and total lung capacity (TLC) were determined on the best maneuver for each subject. Starting from chest wall volume traces, an averaged breath was obtained from the last 5 breaths at the end of the period of quiet breathing and at the end of each exercise workload. From the averaged breath, tidal volume, breathing frequency, and minute ventilation were determined. End-expiratory and end-inspiratory volumes of the chest wall and its compartments were also measured and reported as variations from the baseline volumes at FRC before subjects started pedaling. End-inspiratory and end-expiratory pulmonary rib cage volumes are indexes of the action of inspiratory and expiratory rib cage muscles, respectively. End-inspiratory and end-expiratory abdominal volumes are indexes of the action of the diaphragm and abdominal muscles, respectively. End-inspiratory abdominal rib cage volume is an index of the action of the diaphragm in its area of apposition, while end-expiratory abdominal rib cage volume reflects the action of the insertional component of the abdominal muscles.

Data were collected during resting quiet breathing (rest); at 33%, 66%, and 100% of peak exercise workload at baseline ($W_{max,PRE}$); and at peak exercise workload after the 3 weeks of MBWRP.

Multidisciplinary body weight reduction program

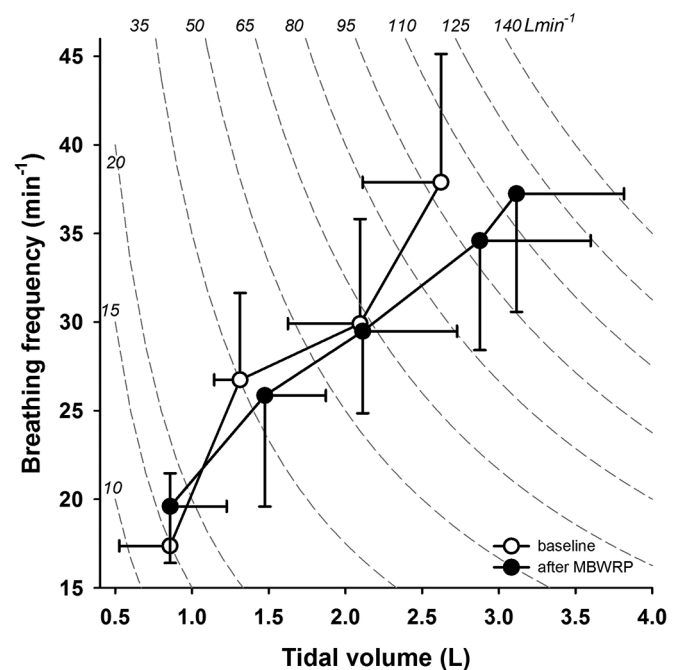
Subjects underwent a 3-week in-hospital MBWRP (Division of Auxology, Italian Institute for Auxology, Piancavallo, Italy) entailing the following interventions:

(a) personalized diet, monitored daily by a dietician, formulated according to the Italian recommended daily allowances (Società Italiana di Nutrizione Umana), and involving an energy intake ~ 500 kcal lower than the measured resting energy expenditure;

(b) aerobic physical activity, including two 30-min sessions/day of cycle ergometer pedaling, treadmill walking, and stationary rowing, carried out in the afternoon 5 days/week; the intensity of exercise was set to achieve an average heart rate between 60% and 80% of the individual's age-predicted maximum heart rate;

(c) RMET (Verges et al. 2008) performed 5 days/week, 1 session/day, 12–18 min/session, ~ 25 respiratory acts/session using a commercially available device (Spiro 141 Tiger, Idiag, Fehraltorf, Switzerland); the volume of the bag was chosen to obtain, during rebreathing, pulmo-

Fig. 3. Relationship between tidal volume and breathing frequency at rest and at 33%, 66%, and 100% of peak exercise workload at baseline (white circles) and after 3 weeks of MBWRP (black circles). The 5th black point refers to the peak exercise value of the test performed after MBWRP. Dashed lines represent isopleths of different levels of minute ventilation from 10 to 140 L/min. Data are expressed as mean \pm standard deviation.



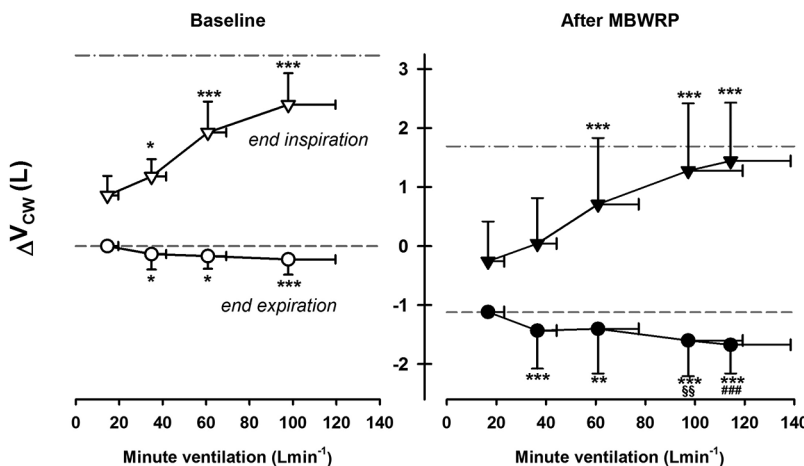
nary ventilatory values corresponding to $\sim 50\%$ – 60% of the maximal ventilatory capacity previously evaluated by spirometry;

(d) psychological and nutritional counseling.

Statistical analysis

The effect of the 3 weeks of MBWRP on anthropometry, body composition, chest wall geometry, and spirometry was tested us-

Fig. 4. End-inspiratory (triangles) and end-expiratory (circles) chest wall volume variations, relative to the volume at baseline functional residual capacity (FRC), plotted versus the corresponding minute ventilation at rest and at 33%, 66%, and 100% of peak exercise workload at baseline (left panel, white symbols) and after 3 weeks of MBWRP (right panel, black symbols). The 5th black point refers to the peak exercise value of the test performed after MBWRP. The dashed lines represent the chest wall volume at FRC and the dashed-dotted lines represent the chest wall volume at total lung capacity. Data are expressed as mean \pm standard deviation. *, **, ***: $p < 0.05, 0.01, 0.001$ vs. rest; ###: $p < 0.001$ vs. peak exercise workload at baseline; §§: $p < 0.01$ vs. baseline.



ing 1-way repeated-measures analysis of variance (RM ANOVA) or the Friedman RM ANOVA on ranks with the time of intervention (i.e., baseline and after MBWRP) as independent factor.

A linear mixed model with repeated measures was used to describe the effect of the 3 weeks of MBWRP on breathing pattern, pulmonary gas exchange, dyspnea, and leg discomfort. Total and compartmental chest wall volumes were tested as absolute values and as variations relative to resting values. Peak exercise values at baseline were compared with both iso-workload and peak exercise values of the test performed after MBWRP.

ANOVA was carried out using SigmaStat version 11.0 (Systat Software, San Jose, Calif., USA), whereas linear mixed model analysis was performed with R (R Foundation for Statistical Computing, Austria). Data are presented as mean \pm standard deviation with the level of significance set at $p < 0.05$.

Results

Anthropometry, body composition, and chest wall geometry

Table 1 reports anthropometric, body composition, chest wall geometry, and spirometric data at baseline and after MBWRP. After MBWRP, subjects significantly decreased their body weight, with an average loss of 3.5 kg, resulting in a BMI reduction of 1%. The body mass loss resulted from a reduction of both fat mass and fat-free mass and was due to a significant reduction of volume in the abdomen ($p = 0.031$) rather than the rib cage ($p = 0.475$). V_{CW} at FRC and TLC significantly decreased after MBWRP (Table 1 and Fig. 1). This was due mainly to V_{AB} , which was the only compartment that significantly decreased after MBWRP at both FRC and TLC (Fig. 1). Body weight before and after MBWRP linearly correlated with total trunk volume measured by OEP at FRC and TLC ($p < 0.001$ in both cases) (Fig. 2).

Spirometry and inspiratory capacity

The Tiffeneau index was higher than 80%; this excluded the presence of obstructive alterations but could indicate the onset of a restrictive pattern. MBWRP improved FVC (when expressed both as absolute and percentage of predicted values), while it had no significant effect on the other spirometric parameters, despite their increase (Table 1).

Inspiratory capacity, measured by OEP, was reduced by 290 \pm 550 mL after MBWRP (Fig. 1). The reduction was due to decreases in

IC of both the pulmonary rib cage (240 \pm 320 mL) and the abdomen (260 \pm 480 mL). Conversely, IC of the abdominal rib cage increased (200 \pm 320 mL), though not significantly, after MBWRP.

Exercise performance and ventilation

After 3 weeks of MBWRP, peak work rate significantly increased (219 \pm 28 W) compared with baseline (193 \pm 30 W, $p = 0.003$). At baseline and after MBWRP, the progressive increase of minute ventilation was due to similar rates of increase of tidal volume and breathing frequency. After MBWRP, the level of ventilation at $W_{max_{PRE}}$ was the same as that at baseline but was achieved with a higher tidal volume ($p = 0.046$) and lower respiratory rate ($p = 0.042$). At maximum workload after MBWRP, minute ventilation was higher ($p = 0.0009$) than that at baseline $W_{max_{PRE}}$ because of an increased tidal volume ($p = 0.0002$) with similar respiratory rate ($p = 0.683$) (Fig. 3).

Operational chest wall volume measurements

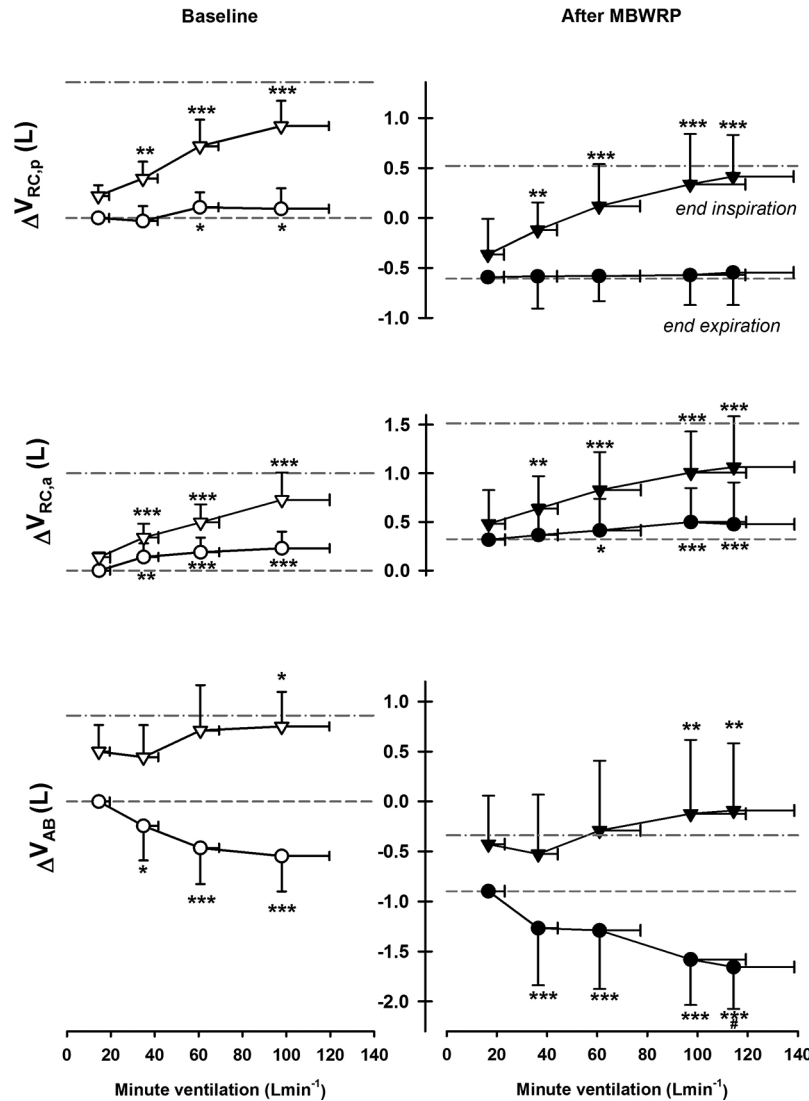
The progressive increase in tidal volume was achieved by chest wall volume progressively increasing at end-inspiration and progressively decreasing at end-expiration (Fig. 4). At the 2 highest levels of exercise, end-expiratory chest wall variations were greater after MBWRP compared with baseline (Fig. 4).

Operational volumes of the 3 different chest wall compartments are shown in Fig. 5. At baseline, end-expiratory $V_{RC,p}$, $V_{RC,a}$, and V_{AB} variations compared with rest showed different behaviors. During exercise, the end-expiratory volume of both rib cage compartments increased. This occurred immediately after the onset of exercise for $V_{RC,a}$ and only later for $V_{RC,p}$. End-expiratory V_{AB} progressively decreased with exercise progression. After MBWRP, no pulmonary rib cage hyperinflation occurred, whereas end-expiratory $V_{RC,a}$ significantly increased later (from 66% $W_{max_{PRE}}$). After MBWRP, end-expiratory V_{AB} showed a similar behavior compared with baseline. End-expiratory V_{AB} variation was higher at peak exercise than at $W_{max_{PRE}}$. No differences were found in end-inspiratory compartmental volumes before and after MBWRP.

Pulmonary gas exchange

MBWRP had no effect on metabolic responses, since $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, $P_{ET}O_2$, and $P_{ET}CO_2$ were similar at baseline and after the 3-week in-hospital MBWRP, as shown in Fig. 6.

Fig. 5. End-inspiratory (triangles) and end-expiratory (circles) volume variations of the pulmonary rib cage (upper panels), abdominal rib cage (middle panels), and abdomen (bottom panels) plotted against the corresponding minute ventilation at rest and at 33%, 66%, and 100% of peak exercise workload at baseline (left panels, white symbols) and after 3 weeks of MBWRP (right panels, black symbols). The 5th black point refers to the peak exercise value of the test performed after MBWRP. For each compartment, volumes are relative to the corresponding compartmental volume at baseline functional residual capacity (FRC), the dashed lines represent the volume at FRC, and the dashed-dotted lines represent the volume at total lung capacity. Data are expressed as mean \pm standard deviation. *, **, ***: $p < 0.05, 0.01, 0.001$ vs. rest; #: $p < 0.05$ vs. peak exercise workload at baseline.



Respiratory and leg muscle perceived exertion

The relationships between minute ventilation, oxygen uptake, or leg power output and the ratings of perceived exertion for breathing and legs are shown in Fig. 7. After 3 weeks of MBWRP, both dyspnea and leg discomfort were reduced at higher levels of exercise. At baseline, exercise terminated with similar levels of dyspnea and leg discomfort, whereas after MBWRP, leg discomfort was significantly ($p < 0.05$) greater than dyspnea at peak exercise. Dyspnea values at both $W_{\text{max_PRE}}$ and maximum exercise workload after MBWRP were significantly lower than the value at baseline $W_{\text{max_PRE}}$.

Discussion

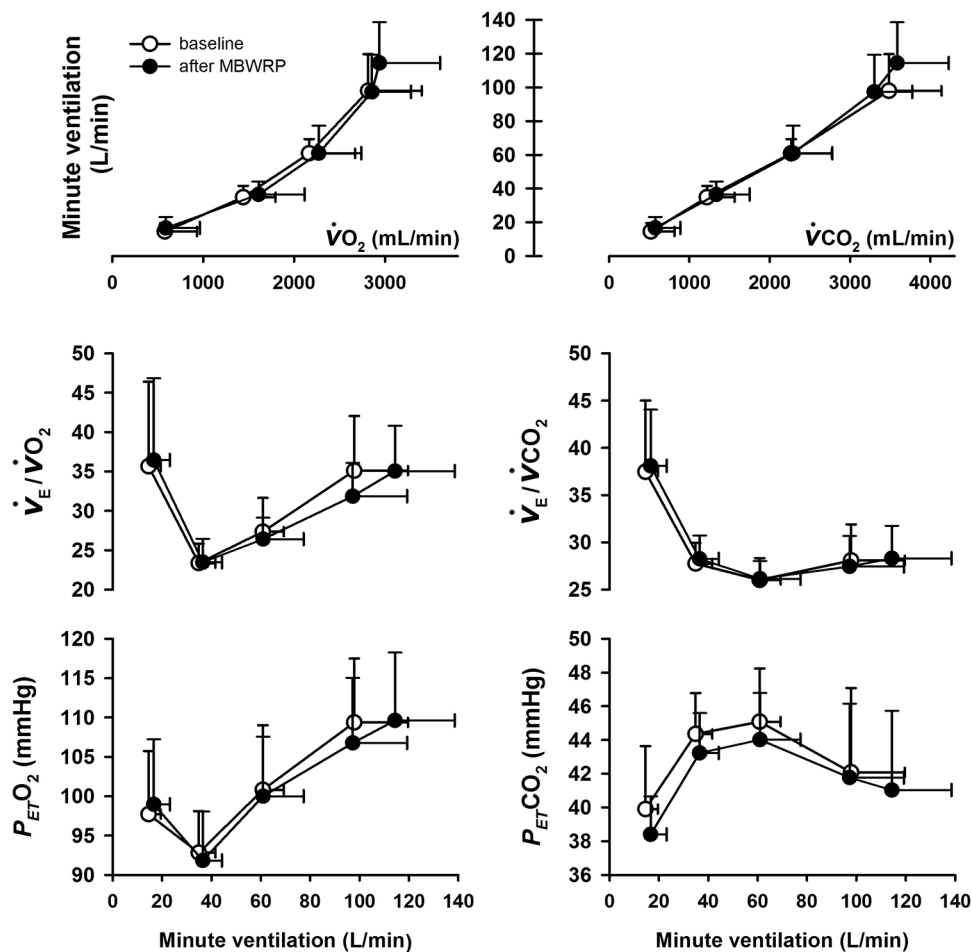
The main result of the present study is that a short multidisciplinary body weight reduction program including respiratory muscle endurance training applied to otherwise healthy obese adolescents contributes to increased exercise performance by changing static and dynamic chest wall configuration, lower-

ing the abdominal load, unloading the respiratory muscles, and reducing dyspnea.

Baseline

Breathing at low pulmonary volumes is one of several respiratory factors that distinguish obesity and contribute to a constrained ventilatory response to exercise even in the presence of otherwise healthy lungs (Babb 1999, 2013; Parameswaran et al. 2006; Ofir et al. 2007; Lin and Lin 2012; Chlif et al. 2015). For this reason, a beneficial ventilatory strategy for obese subjects would be to move towards higher lung volumes. Our data show that the increase of tidal volume during pedaling is achieved by a progressive increase of end-inspiratory chest wall volume and a slight decrease of end-expiratory chest wall volume. This means that the increased ventilatory demand is mostly fulfilled by recruiting inspiratory reserve volume and, to a lesser extent, expiratory reserve volume without dynamic hyperinflation. This finding was previously reported by Mendelson et al. (2012), who measured dynamic changes in end-expiratory lung

Fig. 6. Ventilatory response is shown in the upper panels with minute ventilation plotted against the corresponding oxygen uptake ($\dot{V}O_2$, left) and carbon dioxide output ($\dot{V}CO_2$, right). Ventilatory equivalents for oxygen ($\dot{V}_E/\dot{V}O_2$, middle left panel), ventilatory equivalents for carbon dioxide ($\dot{V}_E/\dot{V}CO_2$, middle right panel), end-tidal oxygen tension ($P_{ET}O_2$, bottom left panel), and end-tidal carbon dioxide tension ($P_{ET}CO_2$, bottom right panel) are plotted against the corresponding minute ventilation. Data are reported at rest and at 33%, 66%, and 100% of peak exercise workload at baseline (white circles) and after 3 weeks of MBWRP (black circles). The 5th black point refers to the peak exercise value of the test performed after MBWRP. Data are expressed as mean \pm standard deviation.



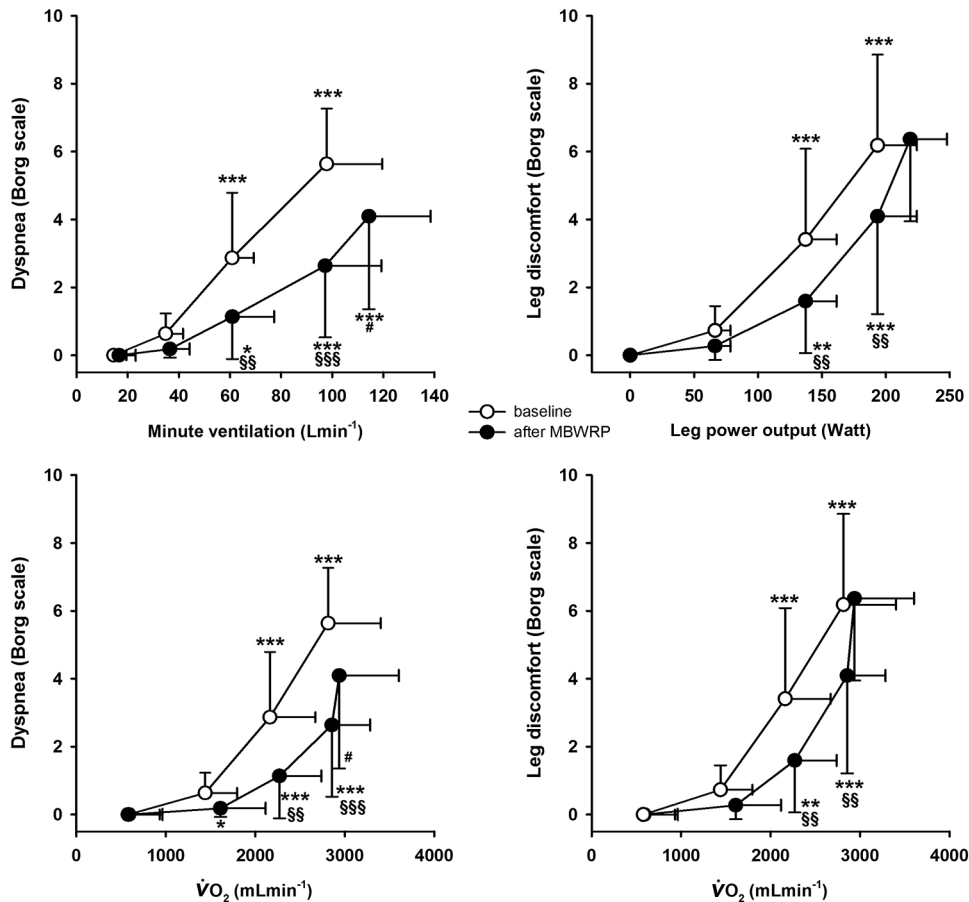
volumes through serial IC maneuvers. The assessment of end-expiratory lung volume variations by serial IC maneuvers is valid under the assumptions that total lung capacity does not change appreciably during exercise and that subjects perform maximal maneuvers at each step (Yan et al. 1997). Our results were instead obtained on a breath-by-breath basis without requiring any respiratory maneuvers during pedaling. Another original aspect of the present study is that, for the first time in obese subjects, the action of the different respiratory muscle groups on the chest wall and the partitioning of inspiratory and expiratory reserve volumes in the different compartments in response to incremental exercise have been measured. Immediately after the onset of exercise, end-inspiratory rib cage volume increases and end-expiratory abdominal volume decreases, indicating that inspiratory rib cage muscles and abdominal muscles are immediately recruited. This is in agreement with earlier studies of healthy lean subjects showing that inspiratory reserve volume is entirely located in the rib cage, whereas expiratory reserve volume is in the abdomen (Aliverti et al. 2002; Vogiatzis et al. 2005b; Wilkens et al. 2010). However, in contrast to findings in healthy lean subjects, in our obese adolescents the rib cage hyperinflates. The main contribution to hyperinflation is from the abdominal rib cage. This is probably a consequence of an early contraction of the diaphragm and a subsequent increase of its appositional force (Ward et al. 1992). It can be hypothesized that the contraction of the

abdominal muscles during expiration optimizes the pre-inspiratory fiber length of the diaphragm, which can contract earlier to prevent excessive lengthening, overcome the load imposed by the abdominal contents, and further contribute to increasing the pressure that expands the abdominal rib cage. It is possible that at higher abdominal rib cage volumes, the lung is recruited and the respiratory system returns to a more normal position on its pressure–volume curve, characterized by higher compliance, as already suggested by other authors (DeLorey et al. 2005; Ofir et al. 2007; Babb et al. 2008; Mendelson et al. 2012; Babb 2013).

MBWRP effect

After 3 weeks of MBWRP, our adolescents were still obese, having lost only 3.5 kg and 1% of BMI. BMI does not take into account age, sex, or muscle mass; therefore, it may be high in individuals with a low body fat percentage and high muscle mass, such as heavily muscled athletes. However, the fact that the body fat percentage was higher than 25, both before and after MBWRP, confirms the diagnosis of mild obesity according to the ideal body fat percentage chart, taking into account the sex and the age of the subjects (McCarthy et al. 2006). Our OEP measurements indicate that trunk or chest wall volume highly correlates to total body weight (Fig. 2) and that the weight loss was concentrated predominantly in the abdomen (Table 1). Although the total body weight

Fig. 7. Relationships between rate of perceived exertion (RPE) for breathing and ventilation (top left panel), rating of leg discomfort and workload (top right panel), RPE for breathing and oxygen uptake (bottom left panel), and rating of leg discomfort and oxygen uptake (bottom right panel) at rest and at 33%, 66%, and 100% of peak exercise workload at baseline (white circles) and after 3 weeks of MBWRP (black circles). The 5th black point refers to the peak exercise value of the test performed after MBWRP. Data are expressed as mean \pm standard deviation. *, **, ***: $p < 0.05, 0.01, 0.001$ vs. rest; #: $p < 0.05$ vs. peak exercise workload at baseline; §§, §§§: $p < 0.01, 0.001$ vs. baseline.



reduction was small, it can still have important consequences on the respiratory system. In fact, lower abdominal volume, suggesting a reduction in abdominal mass, determines a reduced mechanical load, shortened diaphragmatic sarcomeres, a decreased area of apposition of the diaphragm, and reduced muscle fiber length of the abdominal muscles (Sieck et al. 2013). In addition, our results show that IC is significantly reduced after MBWRP. The reduction of IC indicates that the volume of the lungs at functional residual capacity increases and therefore the diaphragm lowers to a more physiologic position. The new configuration of the diaphragmatic-abdominal compartment at rest modifies the starting point of the system before exercise, as confirmed by the reduction of IC, which is significantly reduced in the pulmonary rib cage and abdomen but tends to increase in the abdominal rib cage. During incremental exercise, dynamic variations of total and compartmental operating volumes are similar to those at baseline but are shifted to different volume levels for similar ventilation and workload (Figs. 4 and 5). After MBWRP, pulmonary rib cage hyperinflation disappeared, while abdominal rib cage hyperinflation occurred later (i.e., at higher workload).

The new static and dynamic chest wall configurations presumably have an effect not only on exercise performance but also on perceived effort. At the end of exercise, dyspnea and leg discomfort reached similar levels at baseline, whereas leg discomfort was higher than dyspnea after MBWRP. Moreover, MBWRP seems to delay the onset of intolerable symptoms, since both dyspnea and leg discomfort were lower at similar ventilatory demands and oxygen uptake during incremental cycle exercise after MBWRP. Compared with

baseline, after MBWRP: (i) $\dot{V}O_2$ and $\dot{V}CO_2$ variations, being the proximate causes of increased ventilatory requirements, do not change; (ii) the slope of the $\dot{V}_E/\dot{V}CO_2$ curve does not change; and (iii) the dyspnea/ \dot{V}_E and dyspnea/ $\dot{V}O_2$ slopes shift downward. Our interpretation is that although there are no MBWRP-induced changes in the ventilatory and metabolic demands of incremental cycle exercise in obese adolescent males, the respiratory muscles are mechanically unloaded. This interpretation is supported by previous studies showing how breathlessness increases at any given ventilation when an external mechanical load is added to the respiratory muscles (O'Donnell et al. 2000; Mendonca et al. 2014). During intense exercise after MBWRP, compared with baseline, leg discomfort is lower at equal levels of leg power output and $\dot{V}O_2$. The delay in the onset of intolerable symptoms, therefore, seems more likely to reflect the static and dynamic ameliorative thoraco-abdominal operational volumes combined with mechanical unloading of the respiratory muscles. The former, in turn, results from increased synergy between the diaphragm and the abdominal muscles owing to the 3.5 kg of body mass reduction localized mainly in the abdomen; the latter might be a consequence of specific RMET.

In their cohort of obese adolescents, Mendelson et al. (2012) obtained similar improvements in terms of reduction of exertional dyspnea and better operating lung volume without changes in $\dot{V}O_2$ and $\dot{V}CO_2$ with exercise training alone over a longer period of 12 weeks. Frank and coworkers (2011) found that a nutrition and training program with RMET reduced the perception of breathlessness during exercise in overweight and obese adults more than diet

and exercise alone. Reduced breathlessness was then associated with improved running performance and increased daily physical activity (Frank et al. 2011). Although the present data on the changes induced by MBWRP do not allow us to distinguish the individual contributions of the 3 components of the MBWRP, based on the results of Frank et al., we can speculate that RMET itself may have played an important role in generating improvements of the ventilator pump in a shorter time compared with the study of Mendelson et al. The increased FVC, the reduced dyspnea without changes in $\dot{V}O_2$ and $\dot{V}CO_2$, the higher end-inspiratory chest wall and pulmonary rib cage volumes at peak exercise, and tidal volume that tended to increase at peak exercise are all signs of ameliorative performance of the ventilatory pump in terms of efficiency, efficacy, and endurance. However, additional studies of obese adolescents are needed to determine the effects of 3 weeks of energy-restricted diet plus aerobic training alone in comparison with the results obtained in the present study. In a previous study (Salvadeo et al. 2015) carried out in a similar population, it was observed that acute respiratory muscle unloading by normoxic helium- O_2 breathing determined a reduced oxygen cost of cycling and lower dyspnea and limb discomfort during moderate-to-heavy-intensity exercise at a constant work rate. These findings suggest that in the obese population, interventions specifically aimed at reducing the mechanical load and (or) increasing respiratory muscle endurance and strength could be recommended to improve exercise tolerance.

A limitation of the present study is the lack of measurements of absolute lung volumes at rest, maximal inspiratory and expiratory pressures at the mouth, and trans-diaphragmatic pressure during exercise. The first set of measurements would have shown improvements in the restrictive lung pattern. The second set would have provided information on the effect of MBWRP on the strength and endurance of the different respiratory muscles. The third set would have allowed detection of early activation of the diaphragm. The relatively small sample size can be considered another limitation of the study, but we deliberately decided to study a specific population: male adolescents. In fact, differences in the regulation of end-expiratory lung volume during exercise have been found among obese subjects of different ages and sexes: (i) no hyperinflation in obese adolescents (Mendelson et al. 2012); (ii) hyperinflation only during heavy levels of exercise in young obese men (DeLorey et al. 2005); (iii) hyperinflation from the beginning of exercise in the majority of obese adults (Romagnoli et al. 2008; Babb et al. 2011); (iv) no hyperinflation in obese adults characterized by higher expiratory reserve volume, similar to healthy controls (Romagnoli et al. 2008); (v) no hyperinflation in young obese women (Babb et al. 2002); and (vi) hyperinflation in older obese women (Ofir et al. 2007). It would therefore be interesting to extend the characterization of dynamic chest wall volume adaptation to incremental exercise to other obese populations, older individuals, and (or) females to verify whether thoraco-abdominal volume variations mirror the different lung patterns. Another limitation of our study is the lack of an age-matched, non-obese control group, even if the regulation of total and compartmental end-inspiratory and end-expiratory chest wall volumes in healthy, young, and lean subjects has already been described (Vogiatzis et al. 2005b).

In conclusion, abdominal rib cage hyperinflation occurs during moderate-to-peak-intensity incremental exercise in male obese adolescents to recruit lung volume. This can be considered a dynamic adaptation of the ventilatory pump to cope with the obesity-related chest wall loading through optimization of the synergy between the diaphragm and the abdominal muscles. As a result, the system moves to higher operating volumes to achieve greater thoracic compliance. Three weeks of a multidisciplinary body weight reduction program are enough to reduce the abdominal load, recruit lung and chest wall volumes, improve exercise performance, reduce dyspnea, and delay dynamic abdominal rib cage hyperinflation without ventilatory and metabolic demands. These factors may contribute to

improved exercise tolerance in otherwise healthy obese adolescents, therefore breaking the vicious cycle of inactivity and weight gain.

Conflict of interest

The authors declare that there are no conflicts of interest.

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