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

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ABSTRACT

Objective: To characterize static and dynamic thoraco-abdominal volumes in obese adolescents and to test the effects of a 3 weeks multidisciplinary body weight reduction program (MBWRP), entailing energy restricted diet, psychological and nutritional counselling, aerobic physical activity and respiratory muscle endurance training (RMET) on these parameters.

Methods: Total chest wall (V_{CW}), pulmonary ribcage ($V_{RC,p}$), abdominal ribcage ($V_{RC,a}$) 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, percentage of body fat: 38.4%) during rest, inspiratory capacity (IC) manoeuvre and incremental exercise on a cycle-ergometer at baseline and after three weeks of MBWRP.

Results: At baseline, the progressive increase in tidal volume was achieved by end-inspiratory V_{CW} increase ($p < 0.05$) due to both ribcage compartments with constant V_{AB} . End-expiratory V_{CW} reduced 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 ribcage hyperinflation was delayed and associated to 15% increased performance and reduced dyspnoea at high workloads ($p < 0.05$) without ventilatory and metabolic changes.

Conclusions: Otherwise healthy obese adolescents adopt a thoraco-abdominal operational pattern characterized by abdominal ribcage hyperinflation occurrence 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 dyspnoea.

KEYWORDS: obesity; pediatrics; exercise; pulmonary physiology; exercise physiology; kinesiology

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INTRODUCTION

Adolescent obesity, one of the 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; Must and McKeown.1996; Sinha et al.2002; Schiel et al.2006; Must et al.2012). The last includes breathing at lower lung volumes, decreased thoracic compliance and increased respiratory resistance secondary from the reduction in lung volumes related to overweight (Babb 1999; DeLorey et al.2005; Parakeswaran 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 have also to overcome higher resistive load (Oppenheimer et al.2014). Respiratory muscles therefore have to cope with increased work of breathing particularly during exercise (Lin & Lin, 2012). The latter is typically associated with an increased ventilatory response for a given metabolic requirement (Lin & Lin, 2012), and with an increased O_2 cost of breathing (Bernhardt et al., 2013; Babb et al., 2008), that can reach values up to three times greater ($\sim 3.0\text{--}3.5 \text{ mL}_{O_2}\cdot\text{L}^{-1}$ of minute ventilation) than those reached by normal-weight subjects.

The assessment of operating volumes of the lung, namely end-expiratory and end-inspiratory, is important to understand how the respiratory muscles and the ventilatory pattern adapt in response to the incremental exercise-induced demands (Babb 1999; Babb et al.2002; DeLorey et al.2005; Parameswaran et al.2006; Ofir et al.2007; Romagnoli et al.2008; Babb et al.2011; Lin and Lin 2012; Babb 2013; 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 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 adult improve their operating lung volumes, 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 not only volume changes of the lung, but also of 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; Aliverti et al.2002) and can be noninvasively assessed by opto-electronic 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; Vogiatzis et al.2005; Georgiadou et al.2007; Aliverti et al.2009; Wilkens et al.2010). Although the dynamical assessment of total and compartmental operational chest wall volumes during exercise is important to understand 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 if 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 diaphragmatic and abdominal muscles and consequently the regulation of the

operating volumes of the two compartments influenced by these muscles, namely abdominal rib cage and abdomen (Ward et al.1982; Kenyon et al.1997; Aliverti et al.2002; Aliverti et al.2003). In addition, it has been recently shown that the inclusion of respiratory muscle endurance training (RMET) into multidisciplinary body weight reduction program (MBWRP) improves exercise performance in overweight and obese adults more than exercise and nutritional program alone (Frank et al.2011). Therefore, we also investigated if a short period of MBWRP including RMET is able to acutely modify the geometry and the operating volumes of the chest wall in these adolescents.

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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 Kgcm⁻², mean age: 15.9 ± 1.3 years) were enrolled in the study.

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

Informed consent statements were signed by participants' parents. The procedures of the investigation were approved by the ethics committee of the

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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 made together with the assessment of fat-mass, fat-free mass and thoraco-addominal perimeters, areas and volumes.

Bioelectric impedance analysis was used to assess fat-free mass. 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 two-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 opto-electronic plethysmography (OEP, Smart System BTS, Milan, Italy) (Aliverti et al. 2002). Eight video cameras, four in front of the subject and four behind, tracked the movement of 89 retro-reflective markers placed anteriorly and posteriorly over the trunk or chest wall which extent 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 levels were considered to compute the resultant perimeter and the enclosed cross sectional area. The total chest wall volume (V_{cw}) was calculated by applying the 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 sitting or standing, during quiet breathing, slow vital capacity maneuvers (Cala et al. 1996), and submaximal and maximal exercise on a cycle ergometer (Kenyon et al., 1997; Layton et al., 2013). In all these conditions, the discrepancy between the two measurements was always <4%. OEP was validated in other postures (Aliverti et al., 2001) and in paralyzed patients while receiving mechanical ventilation (Aliverti et al., 2000), with discrepancies in tidal volume measurements always <5%. Intra-rater and inter-rater reliability of OEP was also evaluated at rest and during cycle-ergometer submaximal exercise (Vieira et al., 2013).

The chest wall was modelled as being composed of three compartments: the pulmonary rib cage ($V_{RC,p}$, volume enclosed by the clavicles and the xiphoidal process of the sternum), the abdominal rib cage ($V_{RC,a}$, volume enclosed by the xiphoidal 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 one second (FEV_1), Tiffenau index (FEV_1/FVC) and peak expiratory flow (PEF) were determined (Med-Graphics CPX/D, Medical Graphic Corp., USA). The test was carried out by the same technician with the participant in standing position, according to the European Respiratory Society (ERS) guidelines (Miller et al. 2005; Miller et al. 2005).

Exercise

After 3 minutes of measurements during resting quiet breathing to familiarize with the equipment, subjects were asked to perform two inspiratory capacity (IC) manoeuvres. After another minute of resting quiet breathing, an incremental exercise test on a mechanically braked cycle ergometer (Monark Ergonomic 839E) started with 2 minutes of warm-up at 30 Watts and then work rate was increased by 20 Watts every minute 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 ($P_{et}CO_2$) were measured on a breath by breath basis using a metabolic unit (MedGraphics CPX/D, Medical Graphics Corp., USA).

The Borg's 0-10 category ratio scale was used to rate the magnitude of dyspnoea and leg discomfort at the end of each workload (Borg GA 1982).

Operational chest wall volume measurements

Thoraco-abdominal volumes were measured by OEP during the IC maneuvers and exercise with the subjects grasping poles sideways positioned to lift 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 on each subject. Starting from chest wall volume traces, an averaged breath was obtained by the last five breaths at the end of the period of quiet breathing and 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 starting 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 of abdominal muscles, respectively. End-inspiratory abdominal rib cage volume is an index of the action of the diaphragm in its area of apposition. End-expiratory abdominal rib cage volume reflects the action of the insertional component of the abdominal muscles.

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

Multidisciplinary body weight reduction program (MBWRP)

Subjects underwent a 3-weeks in-hospital multidisciplinary body mass reduction program (Division of Auxology, Italian Institute for Auxology, Piancavallo, Italy) entailing the following interventions:

- a) personalized diet, daily monitored by a dietician, formulated according to the Italian recommended daily allowances (Società Italiana di Nutrizione Umana), involving an energy intake ~500 kcal lower than the measured resting energy expenditure;
- b) aerobic physical activity program, including two 30-min sessions/day of cycle ergometer pedaling, treadmill walking, and stationary rowing, carried out in the afternoon for 5 days/week. The intensity of exercise was set at an average heart rate (HR) between 60% and 80% of the individual's age predicted maximum HR;

- c) respiratory muscle endurance training (RMET) (Verges et al. 2008) performed for 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 in order to obtain, during rebreathing, pulmonary ventilatory values corresponding to ~50–60% of the maximal ventilatory capacity previously evaluated by spirometry;
- d) psychological and nutritional counselling.

Statistical analysis

The effect of the 3 weeks of MBWRP on anthropometry, body composition, chest wall geometry and spirometry was tested using One 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, dyspnoea 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 to 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, CA, 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 3.4 kg, resulting in a 1% BMI reduction. 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 in the ribcage ($p=0.475$). V_{CW} at FRC and TLC significantly decreased after MBWRP (Table 1 and Figure 1). This was due mainly to V_{AB} that was the only compartment significantly decreasing after MBWRP at both FRC and TLC (Figure 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) (Figure 2).

Spirometry and inspiratory capacity

The Tiffeneau index higher than 80% excluded the presence of obstructive alteration but could indicate the onset of a restrictive pattern. MBWRP improved FVC both as absolute and as percentage value while it had no significant effect on the other spirometric parameters despite their improvement trend (Table 1).

Inspiratory capacity, measured by OEP, reduced by 290 ± 550 mL after MBWRP (Figure 1). The reduction was due to both pulmonary rib cage (240 ± 320 mL) and abdomen (260 ± 480 mL). Inspiratory capacity of abdominal rib cage, conversely, increased (200 ± 320 mL), but not significantly, after MBWRP.

Exercise performance and ventilation

After 3 weeks of MBWRP, peak work rate significantly increased (219 ± 28 Watts) compared to baseline (193 ± 30 Watts, $p=0.003$). During both tests, the progressive increase of minute ventilation was due to similar rates of tidal volume and breathing frequency increase. After MBWRP, at $W_{\max_{\text{PRE}}}$ the same level of ventilation 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 $W_{\max_{\text{PRE}}}$ because of an increased tidal volume ($p=0.0002$) with similar respiratory rate ($p=0.683$) (Figure 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 (Figure 4). After MBWRP, at the two highest levels of exercise end-expiratory chest wall variations were greater compared to baseline (Figure 4).

In Figure 5 operational volumes of the three different chest wall compartments are shown. At baseline, end-expiratory $V_{\text{RC},p}$, $V_{\text{RC},a}$, and V_{AB} variations compared to rest showed three different behaviors. During exercise, end-expiratory volume of both ribcage compartments cage increased. This occurred immediately after exercise onset for $V_{\text{RC},a}$ and only lately for $V_{\text{RC},p}$. End-expiratory volume of the abdomen progressively decreased with exercise progression. After MBWRP, no pulmonary ribcage hyperinflation occurred whereas end-expiratory $V_{\text{RC},a}$ significantly increase later (from 66% $W_{\max_{\text{PRE}}}$). After MBWRP, end-expiratory abdominal volume showed a similar behavior compared to baseline. At peak exercise, end-expiratory V_{AB} variation was higher than $W_{\max_{\text{PRE}}}$. 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 3-week in-hospital MBWRP as shown in Figure 6.

Respiratory and leg muscles perceived exertion

The relationships between minute ventilation and oxygen uptake with the rate of perceived exertion of breathing and legs are shown in Figure 7. After three weeks of MBWRP, with increasing level of exercise both dyspnoea and leg discomfort reduced. While at baseline exercise terminated with similar levels of dyspnoea and leg discomfort fatigue, after MBWRP leg discomfort prevailed significantly ($p < 0.05$) on dyspnoea at peak exercise. Dyspnoea values at both W_{maxPRE} and maximum exercise workload after MBWRP were significantly lower than the value at baseline W_{maxPRE} .

DISCUSSION

The main result of the present study is that a short period of multidisciplinary body weight reduction program including respiratory muscle endurance training applied to otherwise healthy obese adolescents contributes to increase exercise performance by changing static and dynamic chest wall configuration, lowering the abdominal load, unloading the respiratory muscles and reducing dyspnoea.

Baseline

It is well known that breathing at low pulmonary volumes is one of the several respiratory factors that distinguishes obesity and contributes to constrain the ventilatory response to exercise even in presence of otherwise healthy lungs (Babb 1999; Parameswaran et al. 2006; Ofir et al. 2007; Lin and Lin. 2012; Babb 2013; Chlif et al. 2015). For this reason, a beneficial ventilatory strategy for these 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 with end-expiratory chest wall volume slightly decreasing. This means that the increased request of ventilation is mostly fulfilled by recruiting inspiratory reserve volume and, to a lesser extent, by expiratory reserve volume without dynamic hyperinflation. The last finding has already been previously reported by measuring dynamic changes in end-expiratory lung volumes through serial inspiratory capacity manoeuvres (Mendelson et al. 2012). It is known that the assessment of end-expiratory lung volume variations by serial IC manoeuvres is valid under the assumption 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 are instead obtained on a

breath-by-breath basis without requiring any respiratory maneuver during pedaling. Another original finding of the present study is that, for the very first time in obesity, the action of the different respiratory muscles groups on the chest wall and the partitioning of inspiratory and expiratory reserve volumes in the different compartments have been measured in response to incremental exercise. Immediately after exercise onset, end-inspiratory rib cage volume increases and end-expiratory abdominal volume decreases, indicating that inspiratory rib cage muscles and abdominal muscles are immediately recruited, respectively. This is in agreement with early studies performed on 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. 2005; Wilkens et al. 2010). Differently than healthy lean subjects, in our obese adolescents ribcage hyperinflates. The main contribution to hyperinflation is from abdominal ribcage. This is probably a consequence of an early contraction of the diaphragm and a subsequent increase of its appositional force (Ward et al. 1982). It can be hypothesized that the contraction of the abdominal muscles during expiration optimizes the pre-inspiratory fiber length of the diaphragm that can contract earlier in order to prevent excessive lengthening, to overcome the load imposed by the abdominal contents and to further contribute to increase the pressure that expand the abdominal ribcage. It is possible that at higher abdominal ribcage 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 are still obese, having lost only 4 Kg and 1% of BMI. BMI index by definition does not take into account age, sex or muscle mass with the risk to result higher even in presence of low percentage of body fat and high muscle mass, such as heavily muscled athletes. The fact that the percentage of body fat is higher than 25, 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 (Figure 2) and that weight loss is concentrated predominantly in the abdomen (Table 1). Although the total body weight reduction is 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 diaphragm's area of apposition and reduced muscle fiber length of the abdominal muscles (Sieck et al. 2012). In addition, our results show that inspiratory capacity significantly reduces after MBWRP. The reduction of inspiratory capacity 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 inspiratory capacity, which significantly reduces in the pulmonary ribcage and abdomen, while tends to increase in the abdominal ribcage. During incremental exercise, dynamic variations of total and compartmental operating volumes are similar to baseline condition, but shifted at different volume levels for similar ventilation and

workload (Figures 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 have presumably an effect not only on the exercise performance, but also on the perceived sensational effort. At end exercise, breath and leg efforts reach similar high levels at baseline, whereas leg discomfort is higher than dyspnea dyspnoea after MBWRP. Moreover, MBWRP seems to induce improvements in the onset of intolerable symptoms since both dyspnoea and leg discomforts reduce respectively at similar ventilatory demands and oxygen uptake during incremental cycle exercise. Compared to baseline, after MBWRP: 1) $\dot{V}O_2$ and $\dot{V}CO_2$ variations, being the proximate causes of increased ventilatory requirements, does not change; 2) the slope of the $\dot{V}_E/\dot{V}CO_2$ curve does not change, 3) the dyspnoea/ $\dot{V}_E$ and dyspnoea/ $\dot{V}O_2$ slopes are not superimposed but lower. 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. The latter statement is supported by previous studies showing how breathlessness rises at any given ventilation when an external mechanical load is added to the respiratory muscles (O'Donnell et al, 2000; Mendonca et al., 2014). At intense exercise, also leg discomfort reduces on equal levels of leg power output and $\dot{V}O_2$. The delay in the intolerable breath and legs symptoms, therefore, seems more likely to reflect the static and dynamic ameliorative thoraco-abdominal operational volumes combined with mechanical unload of the respiratory muscles. The former, in turn, results from the combination of a better synergy between the diaphragm and the abdominal

muscles, thanks to the 3.2 kg of body mass reduction localized mainly in the abdomen; the latter might be a consequence of specific respiratory muscle trained (RMET).

In their cohort of obese adolescents, Mendelson et al obtained similar improvements in terms of reduction of exertional dyspnoea and better operating lung volume without changes in $\dot{V}O_2$ and $\dot{V}CO_2$, only with exercise training but in a longer period of 12 weeks (Mendelson et al. 2012). Frank and coworkers found that adding RMET to a nutrition and training program reduced the perception of breathlessness during exercise in overweight and obese adults more than diet and exercise alone. Reduced breathlessness was then associated to improved running performance and increased daily physical activity (Frank et al. 2011). Although the present data set on the changes induced by MBWRP cannot allow to distinguish the single contribution of the three components of the multidisciplinary body weight reduction program, supported by the results of Frank on adult, we can speculate that RMET itself (for its specific action) may have played an important role in getting improvements of the ventilator pump in a shorter time compared to Mendelson's data. The increased FVC, the reduced dyspnoea with no changes in $\dot{V}O_2$ and $\dot{V}CO_2$, the higher end-inspiratory chest wall and pulmonary ribcage volume at peak exercise and tidal volume that tended to increase at peak exercise, in fact, are all signs of ameliorative performance of the ventilatory pump in terms of efficiency, efficacy and endurance. Further additional studies, however, are requested on obese adolescents to verify the effects of three weeks of energy restricted diet plus aerobic training alone in comparison with the results obtained in the present study. In a previous study (Salvadego et al. 2015), carried out in a similar

population, it was observed that acute respiratory muscle unloading by normoxic helium-O₂ breathing, determined a reduced O₂ cost of cycling and lower dyspnoea and limb discomfort during moderate-to-heavy-intensity constant work rate exercise. These findings suggest that in the obese population interventions specifically aimed at reducing the mechanical load and/or at increasing respiratory muscles endurance and strength could be recommended to improve exercise tolerance.

The lack of measurements of absolute lung volumes at rest, of maximal inspiratory and expiratory pressures measured at the mouth and of trans-diaphragmatic pressure during exercise represent the limitation of the present study. The first would have shown the improvement in the restrictive lung pattern. The second would have provided information of the MBWP efficacy on the strength and endurance of the different respiratory muscles. The third would have allowed detecting the early activation of the diaphragm. The relative small size of the sample can be considered another limitation of the study, but we have deliberately decided to study a specific population: male adolescent. In fact, according to age and sex, different regulations of end-expiratory lung volume (EELV) have been found in obesity during exercise: 1) no hyperinflation occurrence in obese adolescence (Mendelson et al.2012); 2) hyperinflation only during heavy levels in young obese men (DeLorey et al.2005); 3) hyperinflation since the beginning in the majority of obese adult (Romagnoli et al.2008; Babb et al.2011); 4) no hyperinflation occurrence in obese adult characterized by higher expiratory reserve volume therefore behaving like healthy controls (Romagnoli et al.2008); 5) no hyperinflation occurrence in young obese women (Babb et al.2002); 6) hyperinflation in older obese women (Ofir et al.2007). It would be

therefore interesting to extend the characterization of dynamic chest wall volumes adaptation to incremental exercise to other obese population, older age and/or females, to verify if thoraco-abdominal volume variations mirror the different lung patterns. Another limitation can be 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 been already described (Vogiatzis et al, 2005).

In conclusion, abdominal ribcage hyperinflation occurs during moderate-to-peak 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 an optimization of the synergy between the diaphragm and the abdominal muscles. As a result, the system moves to higher operating volumes to benefit for a greater thoracic compliance. Three weeks of multidisciplinary body weight reduction program are enough to reduce the abdominal load, to recruit lung and chest wall volumes, to improve exercise performance, to reduce dyspnoea and to delay the dynamic abdominal ribcage hyperinflation without ventilatory and metabolic demands. These factors may contribute to improve exercise tolerance in otherwise healthy obese adolescents, therefore breaking the vicious cycle of inactivity and weight gain.

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Table 1: Subjects' characteristics and spirometry

<u>Anthropometry</u>	Baseline	post-MBWRP	p-value
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
<u>Body composition</u>			
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
<u>Trunk geometry</u>			
Chest wall volume at TLC (L) ¹	38.7 ± 6.8	37.2 ± 6.3	0.008
Chest wall volume at FRC (L) ¹	35.5 ± 6.3	34.3 ± 6.1	0.019
Ribcage 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
Ribcage 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
Ribcage 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
<u>Spirometry</u>			
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 (Ls ⁻¹)	7.8 ± 1.5	8.3 ± 1.6	0.231

MBWRP: Multidisciplinary body weight reduction program

FVC: forced vital capacity;

FEV₁: forced expiratory volume in the first second

PEF: peak expiratory flow

¹: measured during inspiratory capacity maneuver

FIGURE LEGEND**Figure 1**

Volumes of the chest wall and its three compartments, namely pulmonary ribcage, abdominal ribcage and abdomen, at total lung capacity (TLC, upper symbols) and at functional residual capacity (FRC, lower symbols) before (white circles) and after (black circles) three weeks of MBWRP. The vertical distance between the two values at TLC and FRC represents inspiratory capacity (IC). Data are expressed as mean $\pm$ standard deviation.

§, §§: $p < 0.05, 0.01$ vs baseline

Figure 2

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

Figure 3

Relationship between tidal volume and breathing frequency at rest, 33%, 66%, peak exercise workload at baseline (white circles) and the corresponding values after three weeks of MBWRP (black circles). The 5th black point refers to the peak exercise value of the test performed after MBWRP. Short dashed lines represent

isopleths of different levels of minute ventilation from 10 to 140 Lmin⁻¹. Data are expressed as mean $\pm$ standard deviation.

Figure 4 End-inspiratory (triangle) and end-expiratory (circle) chest wall volume variations, referred to the volume at baseline functional residual capacity (FRC), plotted versus the corresponding minute ventilation at rest, 33%, 66%, peak exercise workload at baseline (left panel, white symbols) and the corresponding values after three weeks of MBWRP (right panel, black symbols). The 5th black point refers to the peak exercise value of the test performed after MBWRP. The short-dashed lines represent the chest wall volume at FRC, the dash-dotted lines represent the chest wall volume at total lung capacity (TLC). 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.

Figure 5

End-inspiratory (triangle) and end-expiratory (circle) volume variations of pulmonary rib cage (upper panels), abdominal rib cage (middle panels) and abdomen (bottom panels) plotted vs the corresponding minute ventilation at rest, 33%, 66%, peak exercise workload at baseline (left panel, white symbols) and the corresponding values after three weeks of MBWRP (right panel, black symbols). The 5th black point refers to the peak exercise value of the test performed after MBWRP. For each compartment: volumes are referred to the corresponding compartmental volume at baseline functional residual capacity (FRC), the short-dashed lines represent the volume at FRC, the dash-dotted lines represent the

volume at total lung capacity (TLC). 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.

Figure 6

Ventilatory response is shown in the upper panels with minute ventilation plotted vs 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 ($P_{et}CO_2$, bottom right panel) plotted vs the corresponding minute ventilation. Data are reported at rest, 33%, 66%, peak exercise workload at baseline (white circles) and the corresponding values after three 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.

Figure 7

Rate of perceived exertion of breathing-ventilation (top left panel), rate of leg discomfort-workload (top right panel), rate of perceived exertion of breathing-oxygen uptake (bottom left panel) and rate of leg discomfort-oxygen uptake (bottom right panel) relationships at rest, 33%, 66%, peak exercise workload at baseline (white circles) and the corresponding values after three 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 vs rest; #: $p < 0.05$ vs peak exercise workload at baseline; §§, §§§: $p < 0.01$, 0.001 vs baseline;.

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