Effects of weight change and weight cycling on lung function in overweight and obese adults

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Abstract

Background: Epidemiological studies have reported on the detrimental effects on lung function after natural, thus limited, weight gain in time in unselected populations. Studies on bariatric surgery, on the other hand, have indicated large improvements of lung function after substantial weight loss.

Objective: To study the associations between a profound weight loss or gain and pulmonary function within the same population. A second objective was to investigate the effect of weight cycling on pulmonary function.

Methods: We selected records from our lung function database, on subjects in the follow-up of CPAP therapy for sleep apnea, with a weight change ≥ 20 kg within 5 years. Lung function (n= 255) at baseline was normal, except for a tendency of mild restriction in morbid obesity. Within this selection, 73 subjects were identified with significant "weight cycling", defined as a $\geq$ 10 kg opposite change in body weight prior to or following the $\geq$ 20 kg weight change.

Results: Weight change affected pulmonary function more in males than in females ($p< 0.001$). In males, FVC increased on average 1.4% predicted/BMI after weight loss, and the reverse after weight gain, whereas females exhibited a smaller change of 0.9% predicted/BMI. Weight loss slightly increased the FEV_1/FVC-ratio and decreased the specific airway resistance, whereas the opposite occurred with weight gain. Larger effects of weight change on lung function were observed in leaner subjects ($p= 0.02$) and in older subjects ($p< 0.002$). Changes in TLC followed that of FVC with no change in RV, while the largest change was observed in FRC. In subjects with weight cycling, the improvement in lung function due to weight loss was reversed by subsequent weight gain and vice versa.

Conclusion: This study provides evidence that the detrimental effect of obesity on lung function is a passive and reversible process.

Introduction

Overweight and obesity are global challenges in health care with a worldwide increasing prevalence of 39% in the adult population in 2016 (1). For adults, the World Health Organization defines overweight and obesity as a body mass index (BMI) $\geq$ 25 and $\geq$ 30 kg/m^2, respectively (1). Obese people often experience breathlessness and other respiratory symptoms during daily activities (2). The excess adipose tissue around the chest wall and abdomen increases the mechanical load on the respiratory system and decreases the functional residual capacity (FRC) (3). An increase in BMI has a larger effect on the FRC than on residual volume (RV) and total lung capacity (TLC) (4). The forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) are slightly lower in obese subjects than in normal subjects (4-8). Obesity minimally affects the diffusion capacity of the lung (4, 9).

Whereas a consistent but weak association has been reported between obesity and lung function in cross-sectional studies, longitudinal studies have reported a strong detrimental effect on lung function after naturally occurring weight gain, with larger effects in males than females (10-14). Intervention studies on weight reduction, on the other hand, have reported positive effects on spirometric values and lung volumes (15-18). However, the change in FVC per kilogram weight change varies a lot between the different studies, ranging from 9 to 26 ml in males and from 5 to 14 ml in females (10-16, 18-21). This may be due to the weight change involved in the natural increase with age which is much less than that involved with intervention in obesity.

To our knowledge, the effect of a profound weight reduction and a profound increase, i.e. ≥ 20 kg of the body weight, within the same population has not been studied yet. To this

end, we analyzed our lung function database on male and female outpatients with sleep disordered breathing (SDB) in their annual follow-up of continuous positive airway pressure (CPAP) therapy. Furthermore, we analyzed the effect of weight cycling, i.e. the cyclical loss and gain of weight (22) and *vice versa*, on dynamic and static lung volumes. Some of the results of this study were previously reported in the form of an abstract (23).

Materials and methods

Subjects

The retrospective analysis of our lung function database of the department of Respiratory Medicine of the Antwerp University Hospital included data from 2003 until January 2019. The selection included data on clinically stable, adult subjects with predominantly obstructive sleep apnea who presented for an annual follow-up visit for assessment of CPAP compliance and counseling and who experienced a substantial weight change ≥ 20 kg between two visits within a 5 year-period. Within this time frame, the visits with the largest weight change were selected.

Subjects who exhibited an inverse weight change of $\geq$ 10 kg in body weight prior to or following the weight loss or gain $\geq$ 20 kg were selected to study the effect of weight cycling.

The medical records were investigated for prescribed medication, smoking history and comorbidities. A doctor's diagnosis of asthma or COPD was an exclusion criterion but smoking was not. Subjects with a self-reported history of asthma and those with prescribed asthma medication but without a history of asthma were not withheld from the study. Recent pneumonia, intellectual disability and congestive heart failure were reasons for exclusion. Other comorbidities that led to exclusion: neuromuscular disease and/or chest

wall deformation and thoracic or abdominal carcinoma. Patients who were treated during daytime with bilevel positive airway pressure (BiPAP) therapy for alveolar hypoventilation and those who underwent thoracic surgery, radiation- or chemotherapy between the two visits were also excluded.

The study protocol was approved by the Ethics Committee of the Antwerp University Hospital and the University of Antwerp (EDGE No. 001127, EC No. 20/20/255).

Measurements

Height and weight were measured at each visit to our lung function laboratory. Lung function testing was performed by experienced technicians according to the ERS '93 and ERS/ATS '05 guidelines (24-26). Measurements were obtained with a MasterScreen PFT for spirometry and MasterScreen Body (Jaeger, Würzburg, Germany) for lung volume measurements and airway resistance (Raw, measured as total airway resistance). All setups were equipped with Jaeger/CareFusion JLAB software from 2003 to 2017 and SentrySuite from 2017 on. The following lung function parameters were included in the present analysis: FEV_1, FVC, FEV_1/FVC ratio from the spirometric records, and RV, FRC, TLC as well as Raw and sRaw (specific airway resistance, i.e. Raw x FRC) as obtained by body plethysmography.

Statistical analysis

Lung function data were expressed as percent predicted (% pred) according to the Global Lung Function Initiative 2012 (GLI '12) predicted values for spirometry (27), whereas ERS '93 predicted values were used for data on lung volumes (24).

Normal distribution of relevant parameters was tested by employing the Kolmogorov-Smirnov test. The differences between parameters before and after weight change were analyzed with Paired Student *t*-tests. Pearson correlation coefficient or Spearman's rho were computed to assess relations between variables. Significance was accepted at $p< 0.05$. Statistical analyses were performed using SPSS (IBM Corp. Released 2015. IBM SPSS statistics for Windows, Version 23.0. Armonk, NY: IBM Corp).

Multiple linear regression (MLR) analysis was performed to assess the impact of independent variables on the association between weight change and lung function change. Sex, direction of the weight change (*i.e.* gain or loss), age at baseline, and BMI and lung function at baseline were considered as possible explanatory modifiers based on the strength of their relation with the change in lung function per unit BMI change. In separate MLR analyses these variables and their interaction with weight change were included one by one. The MLR analyses were performed using R (RStudio Version 1.1.447).

Results

Our database consisted of 255 subjects (79% males) who lost or gained ≥ 20 kg in a 5 years' period. Smoking status was not reported in 27% of them, while 15%, 34% and 24% were current smokers, ex-smokers or lifetime nonsmokers, respectively. Males and females were separated into 2 groups: weight loss and weight gain (75% and 25% of the subjects, respectively). The average time interval between two visits in the groups with weight loss and weight gain was 2.2 (1.3 (SD)) years and 3.5 (1.4) years, respectively.

Anthropometric characteristics of the subjects and lung function data at baseline are reported in Table 1. Data on static lung volumes on both visits were available in 93% of the

subjects. Subjects with weight loss were initially morbidly obese and lung function data at baseline showed a slight tendency towards a restrictive pattern with an average FEV_1 and FVC of 92.1 (13.7) %pred and TLC of 94.8 (10.8) %pred. Only 5% of the subjects in this group had combined values of FVC and TLC below the lower limit of normal (27). The FRC was lower than predicted with an average value of 83.9 (13.7) %pred ($p< 0.001$). The FEV_1/FVC ratio and RV data were within the normal range. Subjects before weight gain were on average mildly obese and their lung function data exhibited normal spirometry and lung volumes at baseline.

The changes in body weight and dynamic and static lung volumes according to sex are reported in Table 2. The magnitude of weight loss was larger than that of weight gain ($p<0.001$ and $p= 0.001$, for males and females, respectively). Significant improvements in FEV_1, FVC, FRC and TLC were observed in both males and females who lost weight, whereas opposite changes occurred after weight gain. Figure 1 depicts the change in FEV_1 and FVC after weight change in the male subjects, with the 2 groups (n= 148 and n=53, with weight loss and weight gain, respectively) divided into subgroups based on the baseline BMI. The subjects with weight gain exhibited a similar but inverse change in FEV_1 and FVC compared to those with weight loss. The magnitude of the change in FEV_1 and FVC was associated to the change in body weight ($p< 0.001$, see Figure 2). The expected changes in lung volumes after a standardized change in BMI of 10 kg/m^2 were calculated to adjust for the different magnitudes of weight change (see Figure 3). Compared to females with weight loss, in males the changes in FEV_1 and FVC were larger: 10.7 (6.6) *versus* 15.8 (9.4) %pred for FEV_1 and 9.8 (6.4) *versus* 14.5 (8.9) %pred for FVC, respectively. Similar graphs as those depicted in Figures 1 & 3 were obtained when using z-scores to express the change in FEV_1 and FVC instead of %pred (data not shown).

The MLR-analyses revealed that the inverse effects of weight loss and gain on FEV_1 and FVC were of similar magnitude ($p= 0.68$ and $p= 0.95$, respectively), but males exhibited a considerably larger effect of weight change than females ($p< 0.001$ and $p< 0.01$, respectively, see Table 3 for results on FVC). Further analyses on the effect of independent variables on the relationship between change in weight and FVC revealed that both leaner subjects (baseline BMI, $p= 0.02$) and older subjects (baseline age, $p= 0.002$) exhibited a larger effect of weight change on lung function. However, the baseline value of FVC (expressed as %predicted) did not significantly influence the relationship between change in weight and FVC ($p= 0.81$).

The increase in FVC as observed in the subjects with weight loss was associated with an average increase in TLC of 8% predicted in both sexes (see Table 2). Weight gain had the opposite effect, a decrease in FVC and a decrease in TLC. The largest improvement in static lung volumes after weight loss was observed in FRC with an average increase of 25.5 (15.4) %pred and 22.5 (14.7) %pred in males and females, respectively. Weight change did not alter RV.

An average decrease of 30% in Raw was observed after weight loss, while the opposite (an average increase of 20%) occurred after weight gain ($p< 0.001$, see Table 4). Corrected for the lung volume at which Raw was measured, specific airway resistance (sRaw) decreased on average by 14% after weight loss ($p< 0.001$), whereas a small but non-significant increase of 8% in sRaw was observed after weight gain.

Among the 255 subjects with weight loss and gain, a subgroup (n= 73 subjects; M: F = 58: 15) exhibited weight cycling. In two thirds of them, the initial weight loss was followed by weight regain (-26 (9) and +20 (5) kg, respectively), whereas in the remaining one third the initial

increase in body weight was followed by weight reduction (+18 (7) and -28 (14) kg, respectively). In both groups, the magnitude of the weight loss was larger than that of the weight gain ($p< 0.01$ and $p< 0.05$, respectively). The time interval of the weight cycling process was similar in both groups and amounted 6 (2) years. Figure 4 depicts the initial and final changes in FVC in the subgroups of females and males with weight cycling. The change in FVC followed the cyclical weight changes such that the improvement in lung function due to weight reduction was lost by the subsequent weight regain and vice versa. In 92% of the subjects with weight cycling, static lung volumes and Raw were available at all time points. Figure 5 depicts the effects of weight cycling on the static lung volumes. Consistent with the findings after a single weight change, weight cycling did not affect RV ($p= 0.58$) whereas the increase in TLC after weight loss and decrease after weight gain mirrored the changes in VC. The most pronounced effects of weight change on the static lung volumes were observed on FRC. The initial and subsequent weight change during the weight cycling process, corrected for its magnitude, induced similar but opposite changes in FRC and TLC ($p= 0.12$ and $p= 0.50$, respectively). Airway resistance decreased after (initial or subsequent) weight loss whereas an increase in Raw was observed after weight gain ($p< 0.001$). Similarly, sRaw decreased or increased after weight loss or gain, respectively, but the relative changes were 50% smaller than those of Raw.

Discussion

We have demonstrated that a profound weight reduction or increase, i.e. ≥ 20 kg of body weight within 5 years, has large effects on lung function in obese patients. After weight loss FEV_1, FVC, TLC and FRC improved, while the opposite occurred when body mass increased.

The effect of weight changes on lung function was most pronounced in males. In a subset of males and females weight cycling occurred and the effects on lung function confirm that the beneficial effect of weight loss on lung function is reversed by subsequent weight regain.

The effect of substantial weight loss or gain in an outpatient population with sleep apnea and obesity was studied, with the assumption that included subjects had normal lung function. The group with weight gain exhibited completely normal baseline lung function data, whereas the group with weight loss exhibited a mild restrictive pattern. The tendency to lung function restriction in morbid obesity has been well documented in the literature (4, 15, 17, 28, 29). The subsequent weight loss that we observed in the latter group revealed that the restrictive pattern disappeared with weight loss. Recently, the GLI study group has published new reference data on static lung volumes (30). When we expressed our data relative to the GLI predictions, both baseline data and the change induced by weight change were not significantly altered, except for baseline RV of the groups with weight loss and gain who both exhibited larger values than expected. This is in line with our recent observation that the GLI prediction for RV is too low for a healthy Belgian population (31).

In accord with previous studies, we observed a larger effect of weight change on pulmonary function in males than in females (10-14, 20). Differences in the regional patterns of fat distribution between the sexes is the most likely explanation for this finding since independent effects of obesity itself and the body fat distribution on lung function impairment have been described (5, 32). Males and post-menopausal females have increased visceral obesity compared to pre-menopausal females. Increased visceral adiposity exacerbates the secretion of pro- inflammatory molecules into systemic circulation which

adversely affects the risk of cardiovascular events (33). Pre-menopausal females are better protected against complications of obesity such as hyperglycemia, hyperinsulinemia and hypertension than males (34). This has been attributed to the female sex hormone estrogen which regulates body fat distribution (35).

The waist-hip ratio (WHR) is often used as a measure of abdominal adiposity, with men exhibiting larger values than women. In cross-sectional studies, WHR and baseline pulmonary function were strongly inversely associated in males, whereas a less prominent decline in lung function with increase in WHR has been observed in females (5, 36, 37).

There are only a few longitudinal studies where, next to weight changes, changes in body fat distribution were related to pulmonary function decline. Longitudinal analysis in a general-population cohort attributed the larger lung function decline in their male population to the larger increase in WHR in males compared to females (12). Unfortunately, data on the change of WHR in our population were not available. Future studies should include measures of fat distribution to gain further insight into the mechanism of weight change on lung function.

The difference between the sexes depends on the unit used to express the change in lung function. Expressed as an absolute change in FVC per BMI, males exhibited more than twice the effects compared to females (64 ml/BMI and 30 ml/BMI, respectively, $p< 0.001$). Expressing the change in terms of kilogram body weight reduced the gap, as females are generally shorter than males. We preferred to express the change in pulmonary function as % predicted as it corrects for anthropometric variables such as sex, height and age (27).

Furthermore, this way also corrects for the expected natural decline in the measurement interval (27, 30).

As previous studies on the effect of weight change have published their results in different units, a comparison is difficult to establish. Table 5 summarizes previously published values on the effect of weight loss or gain on spirometry with respect to our data. Studies on the effects of bariatric surgery in obese populations have reported similar weight reductions, but generally report far less improvement in lung function than what we have observed (14, 15, 20, 21). Investigations on the effects of weight gain are generally studies on the natural weight gain in unselected populations or selected patient cohorts, and thus, have observed an average weight gain far less than we did. Two studies (10, 19) have reported comparable effects on lung function to what we observed, while others found about half the effect (11-14).

Our data not only showed that weight loss (or gain) was linearly related to improvement (or decline) in lung function, but also that more marked effects occurred in leaner subjects. The latter result is in line with some previously published data (10), but contradicts others (12-14). This may partly be due to inclusion characteristics of the subjects under study: in underweight and normal weight subjects weight gain can be beneficial for lung function whereas in subjects with overweight and obesity weight gain has a detrimental effect. We also observed stronger effects of weight change on lung function with increasing age, likely because the distribution of body mass changes at middle and advanced age (12, 32, 36).

Obesity imposes a mechanical load to the thorax and abdomen, where the increased abdominal mass may limit the movement of the diaphragm, thus decreasing TLC. The most marked and consistently reported effect of obesity is a reduction in FRC (4, 38, 39). Indeed, we observed that FRC was the most affected lung volume at baseline in the subjects with morbid obesity and benefited most from a decrease in body weight. The reduction in FRC associated with obesity passively affects airway caliber since Raw is largely dependent on the operating lung volume. Previous studies have found that the increase in resistance in obesity is larger than expected on the basis of the reduced operating lung volume (26). This may, at least partly, be explained by the recent finding that greater adiposity in the airway wall, especially in the large airways, was associated with airway wall thickness and increase in BMI (40). As expected, we observed a significant increase in Raw in the subjects with weight gain and the reverse in the subjects with weight loss. However, the changes in Raw were larger than the changes in FRC such that sRaw significantly decreased in subjects with weight loss. In subjects with weight gain, sRaw increased to a lesser extend (and the change was not significant). The smaller effect in the latter group may be explained by the magnitude of the gain in weight which was less than that of weight loss (on average +23 kg and -30 kg, respectively). Therefore, our data strongly suggest that the increase in sRaw due to obesity is reversible and not caused by persistent remodeling of the bronchial wall.

The major strengths of our study are the longitudinal design of the study, the relatively large numbers of included subjects with substantial weight loss, or the opposite weight gain, and that the weight changes were of similar magnitude. The results in the subgroups, males *vs.* females and weight loss *vs.* weight gain, were consistent throughout: weight loss was

associated with improvements in FEV_1 and FVC, resulting from an improvement in TLC whereas RV remained unchanged, and weight gain deteriorated lung volumes. Moreover, we identified a large subgroup with weight cycling. The changes in lung volumes followed the cyclical weight changes such that the improvement in lung function due to weight reduction was lost by the subsequent weight regain and vice versa. This is in line with recent results from a large prospective epidemiological study in adults that indicated that moderate and high weight gain over a long period of time was associated with accelerated lung function decline, while weight loss was related to its attenuation (41).

Our study also has some limitations. Firstly, the number of included females was limited compared to the number of males. This is inherent to the study population since obstructive sleep apnea is more common in males (42). The ratio of males *vs.* females receiving CPAP therapy for SDB at the Antwerp University Hospital over the last 2 decades was 4:1. This ratio is reflected in the sex ratio of our study population (see Table 1). This ratio differs from data on the prevalence of SDB in a general population with ratios of male vs. female of 3:1 (43) to 2:1 (44). There is most likely a sex-related bias in referral for polysomnography to our hospital. This bias may, at least partly, be explained by the fact that females have a different clinical presentation of SDB: they less often present with a primary complaint of witnessed apnea and are more likely to have a history of depression (45). Another sex-related bias was probably introduced by our inclusion criterion of $\geq$ 20 kg weight loss or gain within 5 years. In our study population, the average change in BMI was 8.7 (2.8) kg/m^2 in the males *vs*. 9.7 (3.2) kg/m^2 in the females (Table 1). A change in BMI threshold for inclusion would have favored more females in the study.

A second limitation is that the smoking history of the included subjects was not well-documented. In 27% of the subjects, the smoking status was not reported in the medical records and in more than two-third of the current or ex-smokers, the smoking history in terms of packyears was not documented. Recent evidence suggests that both current and ex-smokers with preserved spirometry experience an accelerated decline in lung function compared to never-smokers (46). In our data, smoking status was not significantly associated with baseline lung function, after adjustment for baseline weight. Furthermore, smoking status did not modify the effect of weight loss (or gain) on FEV_1 and FVC. Further research is needed to explore the interaction of smoking history and weight change on lung function.

Obesity is one of the most important risk factors for the development of this obstructive sleep apnea (42) and weight reduction is a standard recommendation (47). In our population, weight loss was induced by bariatric surgery, lifestyle interventions, other reasons or unknown in 56%, 30%, 4% and 10% of the subjects, respectively. The weight loss method did not significantly modify the effect of weight change on pulmonary function.

The prevalence of obesity and asthma has increased over the last decades suggesting an association between the two, although a causal link is still controversial (48). Recent studies have revealed that asthma in obese adults is over-diagnosed when taking a positive bronchodilator test or provocation test as the gold standard (49, 50). We excluded all subjects with a doctor's-diagnosis of asthma, confirmed by lung function, since the variable airways obstruction characteristic of asthma would interfere with our research question (51). However, to avoid excluding too many subjects, we've included subjects with

a patient-reported history of asthma but without documented variable airway obstruction and those without a history of asthma but with prescribed asthma medication (5% and 11% of our population, respectively). The effect of weight change on pulmonary function was not different between these subjects and the rest of the population.

In summary, in an obese outpatient population, we have observed that profound weight loss resulted in an improvement in FEV_1 and FVC, with more marked effects in males than in females. The increase in FEV_1 was slightly larger than that of FVC, resulting in an increase in FEV_1/FVC ratio and a concomitant decrease in sRaw. The change in FVC resulted from an increase in TLC, whereas FRC exhibited the largest increase. Weight gain had opposite effects but similar in magnitude. The reversible nature of the change in lung volumes was confirmed by subjects who exhibited weight cycling. Larger effects of weight change on lung function were observed in leaner subjects and in older subjects. Our results strongly suggest that the detrimental effect of obesity on lung function is a passive and reversible process. This further supports clinicians to encourage obese patients to lose weight, especially those with respiratory constraints.

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Table 1. Anthropometric characteristics and lung function values at baseline.

	Males		Females	
	Weight loss	Weight gain	Weight loss	Weight gain
n	148	53	44	10
Age (yrs)	51.6 (10.4)	49.3 (11.3)	51.5 (11.3)	54.0 (11.4)
Height (cm)	178.7 (6.4)	180.2 (6.67)	164.0 (6.6)	166.0 (4.6)
Weight (kg)	127.3 (19.0)	105.2 (16.2)	113.8 (18.0)	91.3 (19.1)
BMI (kg/m²)	39.8 (5.2)	32.4 (5.0)	42.2 (5.7)	33.1 (6.1)
FEV_1 (% pred)	92.2 (13.3) $	102.5 (15.0)	91.9 (15.1) $	97.5 (12.2)
FEV_1 (z-score)	-0.55 (0.97) $	0.20 (1.11)	-0.57 (1.08) $	-0.15 (0.89)
FVC (% pred)	92.7 (13.0) $	101.5 (13.5)	90.8 (15.1) $	100.2 (12.7)
FVC (z-score)	-0.53 (0.96) $	0.11 (0.99)	-0.65 (1.09) $	0.03 (0.90)
FEV_1/FVC (%)	78.3 (5.9)	79.5 (4.5)	81.2 (4.8)	77.8 (8.1)
FEV_1/FVC (z-score)	-0.05 (0.87)	0.08 (0.74)	0.12 (0.76)	-0.29 (1.12)
FRC (% pred)	84.4 (14.1) $	98.3 (17.2)	81.9 (14.0) $	102.7 (21.7)
FRC (z-score)	-0.92 (0.84) $	-0.09 (1.05)	-0.99 (0.77) $	0.15 (1.22)
RV (% pred)	98.2 (16.8)	99.7 (16.6)	96.4 (15.8)	103.1 (19.5)
RV (z-score)	-0.09 (0.89)	0.01 (0.92)	-0.17 (0.80)	0.17 (1.02)
TLC (% pred)	94.5 (10.6) $	100.8 (11.1)	95.8 (11.6) §	103.9 (15.3)
TLC (z-score)	-0.57 (1.11) $	0.10 (1.19)	-0.34 (0.97) §	0.35 (1.34)

Values are expressed as mean (standard deviation). Data on static lung volumes were available in 93% of the subjects.

$, §: significantly different from predicted with $p< 0.001$, $p< 0.05$, respectively.

Table 2. Changes in anthropometrics and lung function after weight change.

	Males		Females	
	Weight loss	Weight gain	Weight loss	Weight gain
n	148	53	44	10
Interval (yr)	2.2 (1.3)	3.5 (1.4)	1.9 (1.1)	3.7 (1.3)
ΔWeight (kg)	-29.4 (9.3) $	23.7 (4.3) $	-31.5 (8.8) $	21.8 (3.0) $
ΔBMI (kg/m²)	-9.2 (3.0) $	7.4 (1.7) $	-11.7 (3.3) $	7.9 (1.4) $
ΔFEV_1 (% pred)	14.1 (8.2) $	-10.4 (8.5) $	12.6 (8.1) $	-5.6 (3.8)¶
ΔFVC (% pred)	13.0 (8.0) $	-8.1 (7.4) $	11.4 (8.0) $	-5.2 (7.0)§
ΔFEV_1/FVC (%)	0.5 (3.3)	-2.3 (3.3) $	0.5 (3.1)	-1.5 (4.9)
ΔFRC (% pred)	25.5 (15.4) $	-13.0 (12.7) $	22.5 (14.7) $	-10.7 (13.6) §
ΔRV (% pred)	-0.8 (13.6)	-0.3 (15.6)	4.5 (15.6)	-7.8 (9.7) §
ΔTLC (% pred)	7.9 (5.8) $	-4.4 (6.0) $	8.4 (5.7) $	-6.1 (3.4) $

Values are expressed as mean (standard deviation). Δ: change after weight loss or gain.

$, ¶, §: Significant change from baseline with $p< 0.001$, $p< 0.01$, and $p< 0.05$ respectively (paired t-test). Data on static lung volumes were available in 93% of the subjects.

Table 3: Multiple linear regression models for the determinants of the change in FVC expressed as percent-predicted.

	B	SE	p-value
ΔBMI	-0.827	0.123	< 0.001
Sex	-0.200	1.542	0.897
ΔBMI x Sex	-0.413	0.140	< 0.01
ΔBMI	-0.323	0.262	0.219
Age	0.051	0.051	0.311
ΔBMI x Age	-0.016	0.005	< 0.01
ΔBMI	-2.017	0.363	< 0.001
BMI	0.016	0.112	0.886
ΔBMI x BMI	0.023	0.010	< 0.05

Sex: 0= female, 1= male; Age: age at baseline (years);

B: regression coefficient; BMI: body mass index at baseline (kg/m^2); SE: standard error.

Table 4. Airway resistance and specific airway resistance before and after weight change.

Weight loss	pre		post		Δ (%)	
Males (n= 139)						
Raw (kPa·s/L)	0.333	(0.105)	0.223	(0.077)	-31.5	(20.0) $
sRaw (kPa·s)	1.147	(0.369)	0.952	(0.336)	-14.9	(23.2) $
Females (n= 41)						
Raw (kPa·s/L)	0.404	(0.112)	0.292	(0.117)	-27.9	(19.2) $
sRaw (kPa·s)	1.043	(0.260)	0.917	(0.322)	-12.8	(18.4) $
Weight gain	pre		post		Δ (%)	
Males (n= 49)						
Raw (kPa·s/L)	0.260	(0.085)	0.305	(0.102)	+22.0	(34.3) $
sRaw (kPa·s)	1.015	(0.292)	1.057	(0.336)	+7.3	(28.6)
Females (n= 9)						
Raw (kPa·s/L)	0.329	(0.074)	0.388	(0.081)	+19.0	(16.5) §
sRaw (kPa·s)	1.034	(0.174)	1.114	(0.162)	+9.0	(15.9)

Values are expressed as mean (standard deviation).

Δ: percent change from baseline.

$, §: $p< 0.001$ and $p< 0.05$, respectively.

Raw: airway resistance; sRaw: specific airway resistance.

Table 5. Overview on published data on the effect of weight change on FEV_1 and FVC. Data are expressed relative to the present data.

					Males		Females	
	population	Interval (yrs)	n	Δweight (kg)	$\Delta FEV_1/\Delta$weight	ΔFVC/ Δweight	ΔFEV_1/ Δweight	ΔFVC/ Δweight
Weight Loss								
Present study	Obese CPAP	2	192	-30	100	100	100	100
Thomas et al. (15)	Obese – bar surg	2	29	-34			44	55
Hewitt et al. (20)	Obese – bar surg	5	113	-41	40	48	31	48
Fenger et al. (14)	epidemiological	5	2294		84	107	54	62
Rivas et al. (21)	Obese – bar surg	1	19	-36			59	82
Weight Gain								
Present study	Obese CPAP	4	63	+23	100	100	100	100
Chen et al. (10)	epidemiological	6	703	+2	106	75	75	102
Chinn et al. (19)	shipyard	7	1005	+2	81			
Wise et al. (11)	COPD	5	1170	+7	51	47	47	78
Carey et al. (12)	epidemiological	7	3391	+3	44	43	43	
Bottai et al. (13)	epidemiological	8	1131	+2	28	48	48	51
Fenger et al. (14)	epidemiological	5	2294		61	40	40	48

Data of the present study are: weight loss in males: $\Delta FEV_1/\Delta$weight= -15.8 ml/kg (-0.49 %pred/kg); ΔFVC/Δweight= -19.2 ml/kg (-0.46 %pred/kg), weight gain in males: $\Delta FEV_1/\Delta$weight= -21.8 ml/kg (-0.43 %pred/kg); ΔFVC/Δweight= -21.8 ml/kg (-0.34 %pred/kg), weight loss in females: $\Delta FEV_1/\Delta$weight= -9.0 ml/kg (-0.40 %pred/kg); ΔFVC/Δweight= -10.5 ml/kg (-0.37 %pred/kg), weight gain in females: $\Delta FEV_1/\Delta$weight= -12.0 ml/kg (-0.27 %pred/kg); ΔFVC/Δweight= -13.6 ml/kg (-0.25 %pred/kg).

Figure legends

Figure 1. Relationship between change in body weight (expressed as body mass index, BMI) and FEV_1 (top panel) and FVC (bottom panel) in male subjects divided into subgroups based on the initial body weight. Weight loss (n= 148): 4 subgroups with intervals of baseline BMI of 5 kg/m^2, weight gain (n= 53): 2 subgroups with initial BMI < or ≥ 30 kg/m^2.
Error bar represents 1 SE.

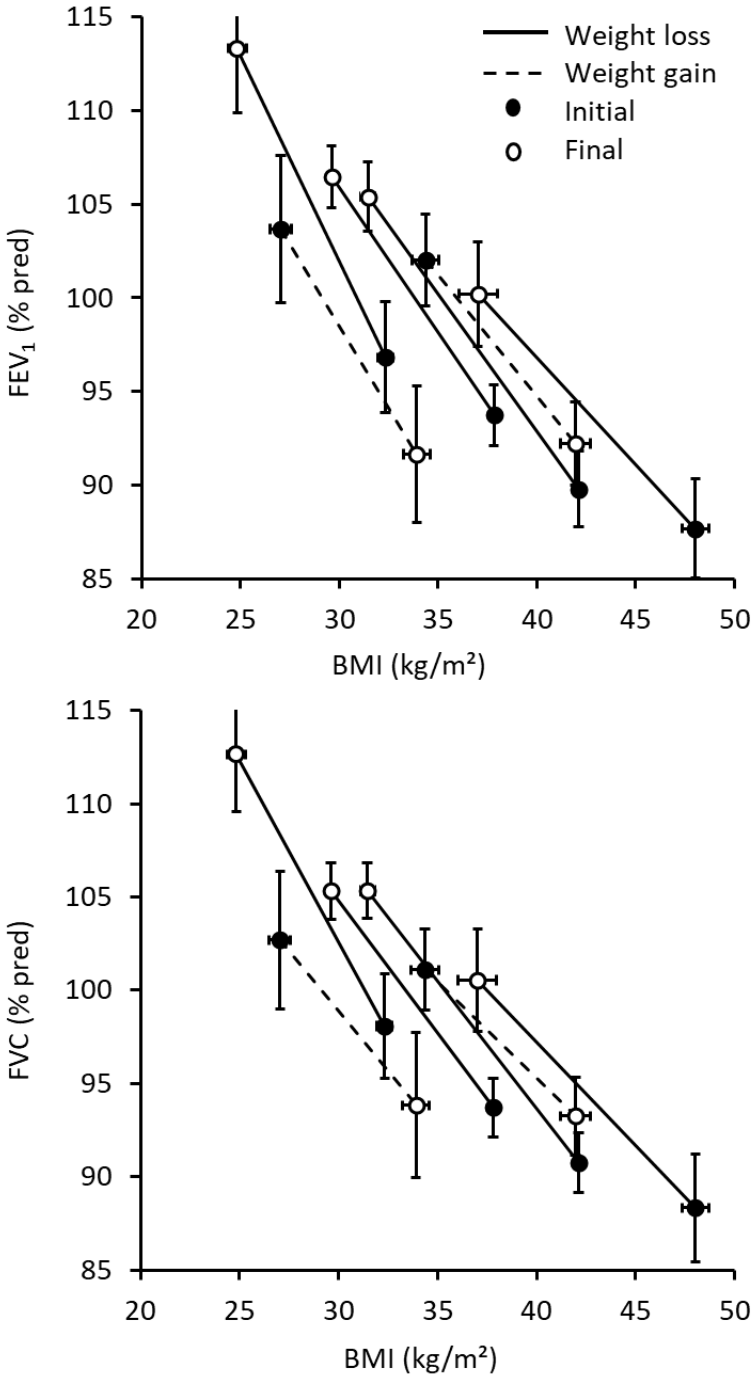
Figure 2. Relationship between change in body mass index (BMI, with intervals of 2 kg/m^2) and change in FVC (expressed as % predicted) in male subjects who lost or gained weight.
Error bar represents 1 SE.

Figure 3. Estimated change in FEV_1 and FVC (expressed as % predicted) after a standardized change in BMI of 10 kg/m^2 in sleep apnea subjects who lost or gained weight. Comparisons between the sexes were performed using multiple regression analysis.
Error bar represents 1 SE.

***, **: $p< 0.001$ and $p< 0.01$, respectively.

Figure 4. Relationship between average weight change (expressed in BMI) and change in FVC (expressed as % predicted) in subjects who exhibited weight loss but weight gain thereafter (n = 12 females, n= 38 males) or vice versa (n= 3 females, n= 20 males). Open symbol: initial starting point; solid line: initial weight change; broken line: subsequent weight change.

Figure 5. Changes in total lung capacity (TLC), functional residual capacity (FRC) and residual volume (RV) (top to bottom) as a function of the change in body mass index (BMI) in subjects who exhibited weight cycling. The intermediate BMI during the weight cycling process was taken as a reference point. To the left of the reference point is the initial weight and volume change, to the right the subsequent change. Closed symbols: weight loss followed by weight gain: n= 45 subjects; open symbols: weight gain followed by weight loss: n= 22 subjects. $|\Delta$ BMI$|$: absolute change in BMI; error bar represents 1 SE.



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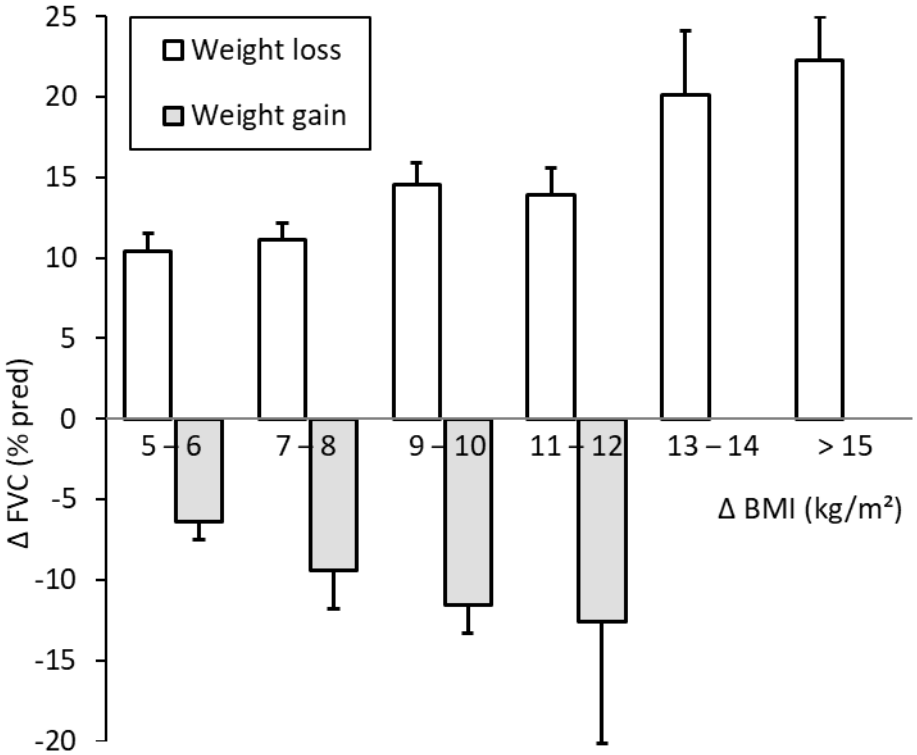

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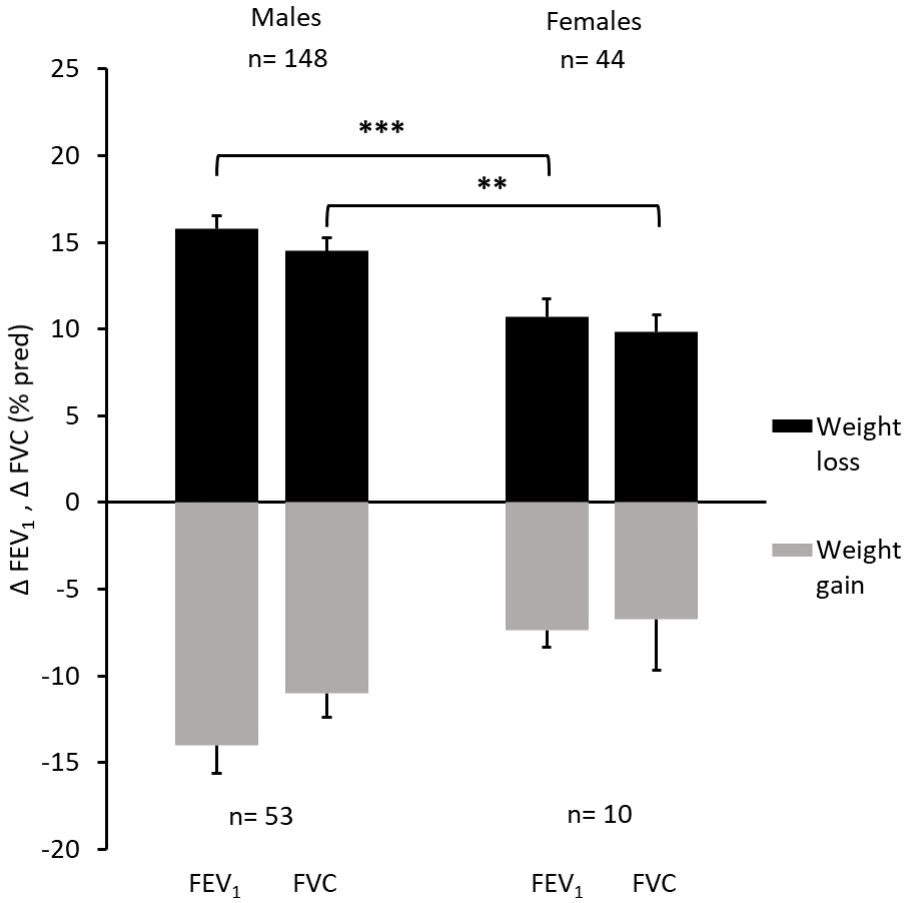

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Error bar represents 1 SE.

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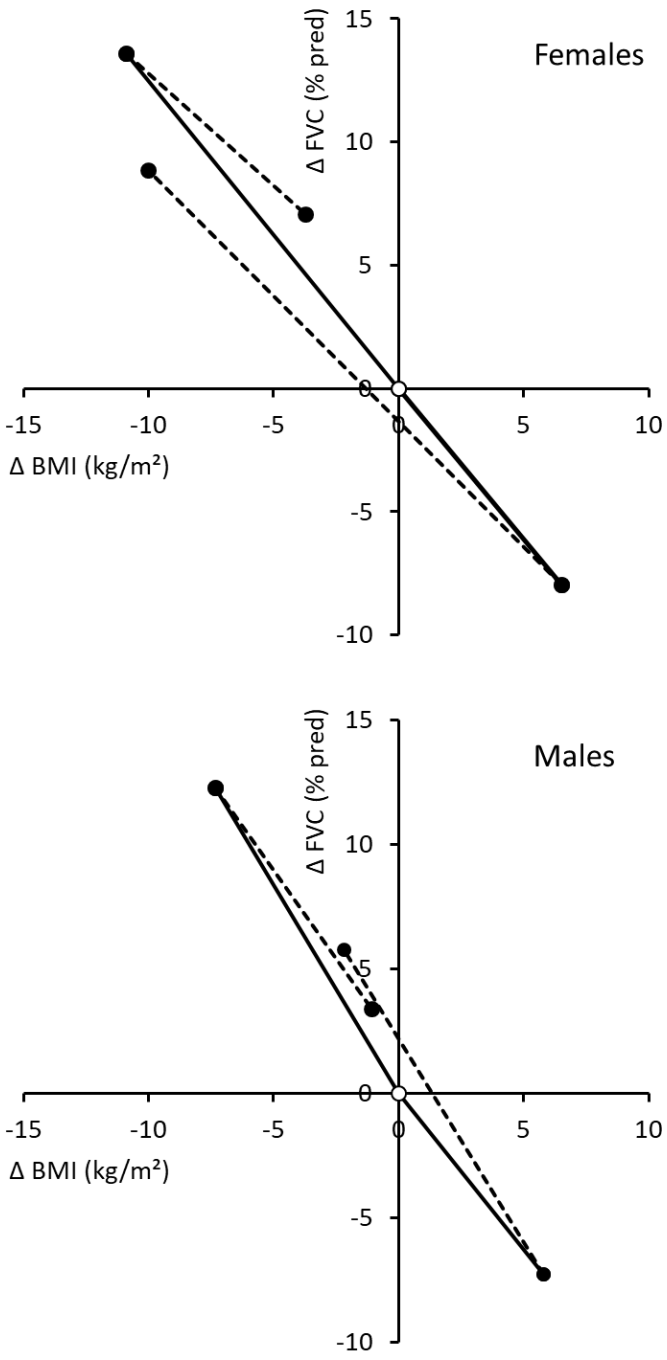

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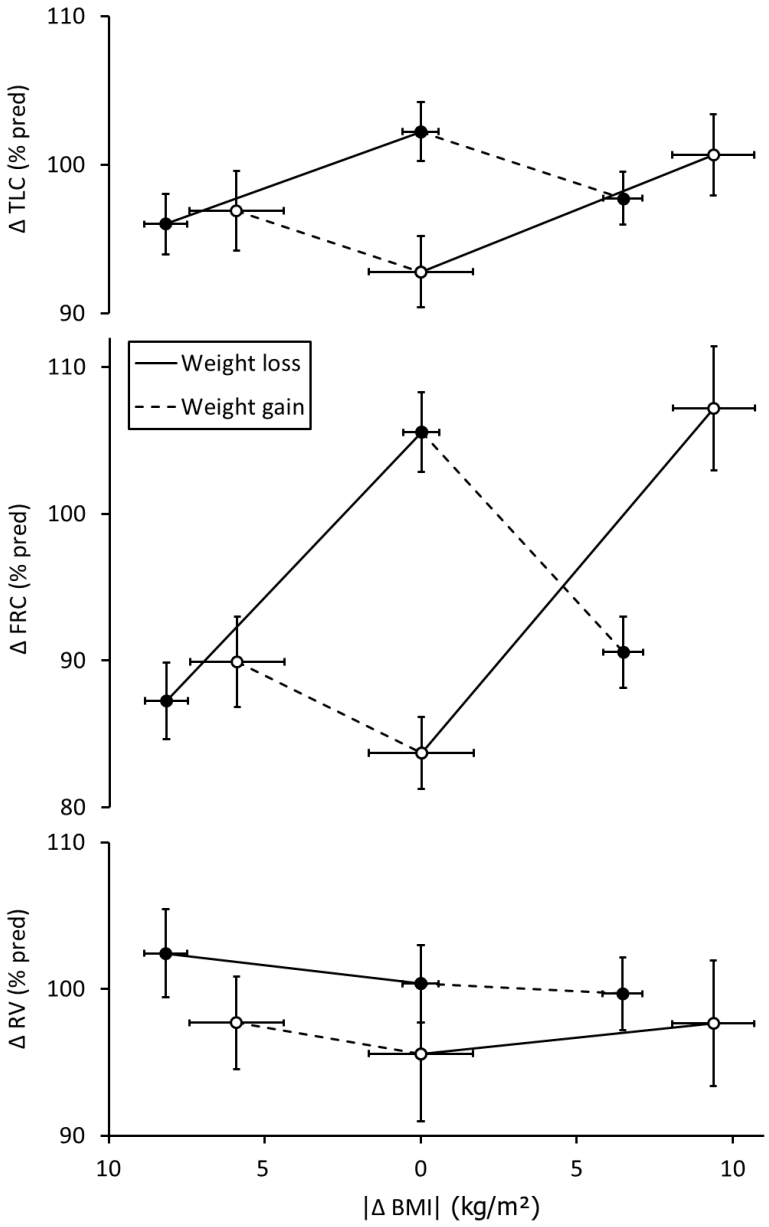

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