Respiration

Review

Respiration 2020;99:856–866
DOI: 10.1159/000509735

Received: May 1, 2020
Accepted: June 23, 2020
Published online: November 26, 2020

Obesity and the Lung: What We Know Today

Judith Maria Brock[a] Adrian Billeter[b] Beat Peter Müller-Stich[b] Felix Herth[a]

[a]Department of Pneumology and Critical Care Medicine, Thoraxklinik and Translational Lung Research Center Heidelberg (TLRCH), University of Heidelberg, Heidelberg, Germany; [b]Department of General, Visceral and Transplantation Surgery, University of Heidelberg, Heidelberg, Germany

Keywords
Lung diseases · Obesity · Adiposity · Bariatric surgery

Abstract
Obesity is becoming more and more prevalent especially in Western industrial nations. The understanding of adipose tissue as an endocrine organ as well as the detection of adipocytokines – hormones that are secreted from the adipose tissue – gave reason to examine the interactions between adipose tissue and target organs. These efforts have been intensified especially in the context of bariatric surgery as promising weight loss therapy. Interactions between the lung and adipose tissue have rarely been investigated and are not well understood. There are obvious mechanical effects of obesity on lung function explaining the associations between obesity and lung diseases, in particular obesity hypoventilation syndrome, obstructive sleep apnea syndrome, asthma, and chronic obstructive pulmonary disease. The rise in the prevalence of obesity affects the epidemiology of pulmonary diseases as well. The aim of this review is to summarize the current knowledge on interactions, associations, and consequences of obesity and weight loss on lung function and lung diseases. Based on these data, areas for future research are identified.

Introduction

The number of overweight and obese patients in developed countries has considerably risen in the past years. In this context, many efforts have been made to understand the mechanisms of weight gain and weight loss. The adipose tissue – in former times considered as passive repository organ – is now increasingly recognized as a large endocrine organ with secretion of adipocytokines and other hormones that are responsible for metabolic effects. Bariatric surgery is the most effective method for weight reduction in severe obese patients. Interactions of adipose tissue and target organs as well as the changes induced by bariatric surgery are object of medical research. Chronic inflammatory diseases of many different organ systems are seen in a new light due to the understanding of obesity as state of chronic inflammation [1].

As chronic respiratory diseases account for many deaths worldwide, the influence of obesity on respiratory diseases and vice versa require a better understanding. Mechanical effects of obesity on the lung are well known, especially regarding obesity hypoventilation syndrome (OHS) and obstructive sleep apnea syndrome (OSAS) [2]. The association between asthma and obesity is also confirmed, but not completely understood. In contrast, we

karger@karger.com
www.karger.com/res

Judith Maria Brock
Department of Pneumology and Critical Care Medicine, Thoraxklinik and Translational Lung Research Center Heidelberg (TLRCH), University of Heidelberg
Röntgenstraße 1, Heidelberg, DE–69126 (Germany)
Judith.Brock@gmx.de

cannot fully explain the "positive" effect of obesity on chronic obstructive pulmonary disease (COPD) which is known as the "obesity paradox" [3].

Therefore, investigating the crosstalk between adipose tissue and the lung as well as understanding the interactions between obesity and lung diseases is of much interest. There are already numerous reviews on specific respiratory diseases and their link to obesity. Franssen et al. [4] already presented a great overview of the increasingly recognized relationship between obesity and COPD. Others focused on the link between asthma and obesity as Peters et al. [5] or Carpaji and Van Den Berge [6], or the connection between OHS [7], respectively, OSAS [8] and obesity. These reviews allow us to focus on one specific respiratory disease. In contrary, the aim of this review is to present and summarize the current understanding of all the interactions between obesity and different lung diseases to provide a complete overview and to show up further areas of research. Furthermore, it is an update to former reviews including insights into weight loss effects through bariatric surgery.

Importance of Obesity

The obesity prevalence has increased over the past 50 years in pandemic dimensions in every single country albeit with regional differences. Importantly, the difference between "overweight" (body mass index [BMI] 25–30 kg/m^2) and "obese" (grade I BMI 30–35 kg/m^2, grade II BMI 35–40 kg/m^2, and grade III BMI >40 kg/m^2) as measured by BMI should be considered when the prevalence of obesity is discussed [9]. The most important risk factor for the metabolic syndrome and cardiovascular diseases is the fat distribution according to the "android" obesity type – also called abdominal or central or visceral obesity – in contrary to the "gynoid" obesity type (peripheral obesity with mostly subcutaneous fat). It can be estimated by measuring the waist-to-hip ratio. Other methods to quantify visceral fat are magnetic resonance imaging (MRI) and bioimpedance analysis (BIA). Waist circumference correlates better with the visceral fat area in MRI than BMI does [10, 11].

In 2017-2018, 42.4% of the population were obese in the USA [9]. Latest estimates show that 30–70% of Europeans are overweight and 10–30% are obese [12]. In 2015, the mean worldwide prevalence of obesity in adults was 19,5% with a prevalence of 23.6% in Germany [13]. The results of the German Health Interview and Examination Survey for Adults (DEGS1) gave an insight into the distribution of severity: while 53% of women and 67.1% of men, respectively, have a BMI above 25 kg/m^2, 29 and 43.8% are overweight, 15.9 and 18.1% suffer from obesity I°, 5.2 and 3.9% II°, and 2.8 and 1.2% III° [14].

Obesity is a major global health challenge. In 2010, about 3.4 million deaths and 3.9% of years of life lost were associated with overweight and obesity [15]. Annual health care costs and medication costs increase by 36 and 77% for obese people compared with people of average weight. Obesity is associated with many comorbidities and complications reducing quality of life and life expectancy, such as type 2 diabetes mellitus, hypertension, coronary heart disease, stroke, and some cancers [16]. To reduce the burden, obesity needs to be understood better and the interactions with the associated comorbidities need to be evaluated and understood.

Importance of Lung Diseases

Chronic respiratory diseases are accounting for 7% of all deaths worldwide. In 2017, 3.91 million deaths were correlated to chronic respiratory disease. From 1990 to 2017, deaths and loss of health related to chronic respiratory diseases increased. In contrast, age-standardized mortality rate of chronic respiratory diseases decreased overall, with a decreasing trend for asthma, COPD, and pneumoconiosis and an increasing trend for interstitial lung disease and pulmonary sarcoidosis [17].

However, there are differences among the countries with higher mortality and higher index for disability-adjusted life years in regions with low sociodemographic index. Main risk factors are smoking, air pollution, and high BMI [17].

Moderate-to-high weight gain (>1 kg/year) is accompanied by a decline in lung function, while losing weight in obese patients is related to significant improvements in lung function parameters [18], demonstrating the importance of investigating lung function and lung diseases in relation with body weight.

The Adipose Tissue as Endocrine Organ

In former times, adipose tissue was seen as passive reservoir for energy storage. With the identification of different adipocytokines, the adipose tissue was more and more considered as an endocrine organ itself whose >100 products have metabolic and cardiovascular effects.

Besides the important secretory function, the adipose tissue contains a variety of receptors (e.g., cytokine receptors, catecholamine receptors, and insulin receptors) through which it forms an interactive network that not only stores fat but also has important immunologic, neuroendocrine, and metabolic functions. There is a crosstalk between adipose tissue and other organs, especially insulin-dependent organs.

Excess of adipose tissue as seen in obesity is considered as a chronic and low-grade state of inflammation. Obesity leads to insulin resistance, hyperglycemia, dyslipidemia, hypertension – the metabolic syndrome – and ultimately to cardiovascular complications [1, 19]. If a relevant crosstalk between adipose tissue and lung exists and if the adipose tissue directly influences the lung, it is essentially unknown.

Can the Lung Become Fat Itself?

Organs such as the liver or the pancreas "fatten up" in obesity resulting in nonalcoholic fatty liver disease (NAFLD) or pancreatic lipomatosis. To our current knowledge, the lung itself does not fatten up in a comparable manner to the other organs. Nevertheless, a very interesting aspect is the concept of "fatty airways." Postmortem analyses showed that adipose tissue accumulates in the outer wall of large airways and is associated with BMI, wall thickness, and number of inflammatory cells. This could be a new mechanism for the pathophysiology of airway inflammation [20].

Especially in asthma, these "fatty airways" are described in association with airway inflammation and disease severity. Fatty airways could influence immunologic processes and produce adipocytokines that influence inflammatory pathways and therefore airway inflammation [21]. The lung tissue itself has thus far not been shown to be affected by even severe obesity.

Is the Lung an Endocrine Organ?

In principle, the lung is not producing hormones itself, but it is influenced by hormones. The organ has different ways to deal with arriving hormones: inactivation or transformation and activation or no influence at all. Since the lung has a huge surface for blood exchange, it is likely a good place for hormones to pass and to be filtered, transformed, or inactivated [22].

A further hint that lung could in principle be an endocrine organ is the fact that pleural diseases produce hormones or are influenced by them. Hypothyroidism, thyrotoxicosis, thyroid cancer, and breast cancer can produce pleural effusion; catamenial pneumothorax can produce recurrent pneumothorax. In thyrotoxicosis, high concentrations of thyroid hormones are found in the pleural effusion. Another lung disease that is correlated with hormones is lymphangioleiomyomatosis (LAM). Abnormal smooth-muscle-like cells growing within the lungs – called LAM cells – express estrogen and progesterone receptors and the disease itself seems to correlate with endocrine status as it is more present in women in reproductive years, during pregnancy or while taking exogenous estrogens. Solitary fibrous tumors of the pleura can also lead to paraneoplastic syndromes such as osteoarthropathy (increase in growth hormone releasing factor), gynecomastia (increase in beta human chorionic gonadotropin), and hypoglycemia (increase in insulin-like growth factor 2) [23]. Hence, the lung is obviously interacting with many hormones like essentially any human organ and its endocrine interactions should be investigated more detailed.

Can the Lung Interact with Adipose Tissue?

In the context of obesity, the most important clue that shows us the crosstalk between adipose tissue and the lung as a possibly endocrine organ is the presence and interactions of adipocytokines. The adipose tissue secrets adipokines (bioactive peptides) and inflammatory cytokines (e.g., tumor necrosis factor-alpha [TNF-α], interleukin-6 [IL-6], and monocyte chemoattractant protein-1), which together are called adipocytokines. Adipocytokines are the key factor of obesity-induced metabolic disorders as they represent the mediators between adipose tissue and target organs (especially liver, muscle, pancreas, and central nervous system). Adipokines regulate food intake, blood pressure, insulin sensitivity, and reproduction. They have paracrine and autocrine functions.

Most recognized representatives of this group are leptin – the saturation hormone – and adiponectin. Leptin has effects via hypothalamic pathways as well as direct effects on peripheral tissues. It suppresses food intake and acts anti-diabetic. Leptin correlates with fat mass and is therefore high in obese patients and low in underweight and weight loss. However, leptin secretion can also be stimulated by insulin or glucocorticoids.

Adiponectin has anti-atherogenic and anti-inflammatory effects and improves insulin sensitivity. The two adiponectin receptors 1 and 2 are expressed primarily in the muscle and liver. Adiponectin levels are low in insulin resistance and obesity and increase while weight reduction or improved insulin sensitivity [1, 24, 25]. Among the >50 known adipokines, the most famous ones include visfatin (critical for beta cell function), resistin (related to obesity, insulin resistance, and inflammation), omentin (anti-inflammatory and insulin-sensitizing), chemerin (regulates adipogenesis), apelin (inhibits insulin secretion), and vaspin (decreases food intake and improves hyperglycemia) [26].

The role of adipocytokines in the pathophysiology of respiratory diseases is currently under investigation. Visfatin and leptin are listed as possible markers for COPD; leptin and resistin are named as proinflammatory factors in tumor cachexia; the apelin-adiponectin axis is researched in pulmonary hypertension, and many adipocytokines are examined in the context of asthma. Despite these promising findings, the data are controversial and limited [27].

The most researched adipocytokines in lung disease are leptin and adiponectin, in particular in connection with OSAS/OHS and asthma [28–34]. In OSAS, lower levels of adiponectin and higher levels of leptin have been observed and are directly associated with the apnea-hypopnea index (AHI), duration of hypoxemia, and BMI. After treatment with continuous positive airway pressure (CPAP) therapy, leptin levels in OSAS patients seem to fall. Resistin levels are higher in OSAS too. Inflammatory cytokines such as TNF- α or interleukins are increased in OSAS patients and reduced after starting CPAP therapy [8]. Another study showed elevated levels of, for example, chemerin and vaspin in severe OSAS, which were furthermore risen after sleep [33].

Adiponectin is mostly reported to be decreased in asthma. While the results of the studies are not uniform, it remains unclear whether the modulation of adiponectin in asthma disease is independent of obesity. It has been hypothesized that low adiponectin levels can be used as a marker for uncontrolled asthma [3]. The leptin/adiponectin ratio has also been shown to correlate with the severity of asthma [35].

In COPD patients, adiponectin is increased. A lower leptin/adiponectin ratio is associated with a decline of forced expiratory volume in 1 sec (FEV1). The higher the BMI in COPD, the lower are the adiponectin levels. Perhaps, an adiponectin increase may reflect a compensatory response to the inflammatory processes in COPD. The level of adiponectin correlates with severity of disease, frequency of exacerbations, and FEV1 decline [3].

During acute exacerbation of idiopathic pulmonary fibrosis (IPF), adiponectin and leptin are found in higher levels than in initial diagnosis of IPF. The adiponectin/leptin ratio was correlated with C-reactive protein level (CRP) in acute exacerbated IPF and with worse survival. Furthermore, the progression of IPF is associated with weight loss [36].

In the research of obesity and bariatric surgery, the glucagon-like peptide-1-(GLP-1)-receptor gets a lot of attention. GLP-1-receptor seems to have a role in obesity-related asthma [37], in exacerbation of COPD (mouse study) [38], and in sleep quality in OSAS patients (the lower the GLP-1, the higher the AHI) [39]. The GLP-1-receptor is widely distributed in the lung within the alveoli, septa, airways, and vascular smooth muscle, but its function is not completely understood [40, 41].

About 40% of OSAS patients suffer of impaired glucose tolerance. Incretin hormones such as GLP-1 stimulate insulin secretion from pancreatic beta cells and are inactivated by dipeptidyl peptidase-4 (DPP-4). Therefore incretin-based therapies with DDP-4 inhibitors and GLP-1 analogs are commonly used in the therapy of diabetes mellitus type 2. Studies are now examining the levels of GLP-1 and DPP-4 in OSAS [42] and test liraglutide (GLP-1-receptor analog) as a possible drug in obese OSAS patients with promising initial results [43].

In view of these findings, there are interesting ideas to use adipocytokines in various lung diseases, especially COPD and asthma, as diagnostic marker for early diagnosis or specific phenotype and therapeutic marker [3]. Research in this field is controversial, and associations are not completely understood. The data from these clinical studies clearly suggest that there *are* interactions between the lung, adipose tissue, and adipose tissue hormones that warrant be further researched [28–30, 37].

Effects of Obesity on the Lung

Obesity causes changes in the mechanics of the lung and chest wall. Fat accumulates in the thoracic and abdominal cavities which increases intra-abdominal and intrathoracic pressure and impedes inflation of the lung. The results are minimal lower FEV1 and lower functional ventilatory capacity (FVC), small effects of ≈ 10% on residual volume (RV) and total lung capacity (TLC), and large effects concerning functional residual capacity (FRC) and expiratory reserve volume (ERV) which are both reduced to ≈ 34% of

the expected value. Tidal volume is also decreased, which is compensated by a higher respiratory rate. The compliance of the whole respiratory system is reduced. Via these mechanical effects, obesity leads to airway narrowing and closure of small airways which produces air trapping and inhomogeneity of ventilation.

It is not completely understood how respiratory system resistance is increased in obesity. It is important to keep in mind that deep, forced tidal breaths as performed with the usual spirometry examination may mask the effect. Changes related to breathing at lower lung volumes and low functional residual capacity caused by mechanical compression of the lung are overlooked. Possibly, measurements with the newer method of oscillometry, where breathing maneuvers are performed in the resting breathing position, could show the true effects of obesity on lung function. In particular, we would expect an increased respiratory system resistance as a sign of increased airway closure.

The relationship between obesity and airway hyperresponsiveness (AHR) is unclear. Some studies showed increased AHR in obesity. One idea is that breathing at low FRC with raised breathing frequency affects the contractility of airway smooth muscles and leads to stiffening. These effects are possibly better seen in oscillometry than in spirometry measurements.

Obesity can also cause hypoxemia in the lung via hypoventilation, associated comorbidities, reduction of FRC, shunt, and ventilation/perfusion imbalance. The association between hypoxemia and obesity as well as measurements of the lung's diffusing capacity for carbon monoxide (DLCO) in obese patients is reported controversially in different studies [6, 10, 44, 45].

It is important to notice that pulmonary tests are mainly performed in the sitting position. There is little and controversial reporting on the influence of body position on lung function in obese patients. No statistically significant changes are seen in FVC, FEV1, VC, TLC, FRC, and RV for different body positions. Few studies show that FRC and FEV1 are higher in the sitting vs. supine position. This could be due to the cephalic displacement of the diaphragm as a result of the abdominal pressure, increased pulmonary blood volume, and limited expiratory flow with increased airway resistance in more recumbent positions [46].

Duration of obesity seems to play a role in development of respiratory effects. Pulmonary function tests showed significantly lower values in patients with obesity lasting >15 years than in patients with obesity lasting <5 years [47].

Furthermore, studies with children show that age of obesity onset seems to have an effect on severity of lung function changes – although there are conflicting results – especially in parameters of airflow limitation (FEV1 and FVC) with greater changes the earlier the onset. In contrast to adults having higher FEV1 and FVC, FEV1/FVC is lower in children with higher weight, suggesting an obstructive rather than a restrictive disease. This could be explained by the airway dysanapsis seen in childhood obesity that is caused by the incongruence between growth of lung parenchyma and caliber of the airways [5].

In summary, obese patients have to breathe more often, have to exert more effort to overcome the resistance of the airways, and are more often hypoxic. Probably, the respiratory effects are worse; the earlier the obesity onset, the longer the duration of obesity. Whether this is actually reflected for the patient with increased dyspnea or reduced physical resilience remains unclear. It is also unknown whether it makes a difference how fast the weight increase occurred.

Effects of Weight Loss on the Lung

Weight loss can be achieved by conservative strategies, which consist of a combination of diet, exercise, and psychological intervention as well as by bariatric surgery. There are several different types of bariatric operations. The most commonly used procedures, and which are considered in this article, are the Roux-en-Y gastric bypass and sleeve gastrectomy.

Indication for bariatric surgery is BMI > 50 kg/m^2, BMI > 40 kg/m^2 with diabetes mellitus 2, BMI > 40 kg/m^2 without comorbidities after failing of conservative strategies, and BMI > 35 kg/m^2 with 1 or more comorbidities (e.g., diabetes mellitus 2, coronary artery disease, hypertension, OSAS, OHS, and asthma) after failing of conservative strategies. Conservative strategies regularly fall and are considered failed after 6 months of lifestyle intervention if the weight change is <15–20% [48]. Therefore, bariatric surgery gets more and more focus and most research concerning lung and weight loss is performed in the field of surgery.

Most of the changes seen in lung functions of obese patients resolve after significant weight loss. In patients without lung disease, improvements in ERV, FRC, TLC, and RV as well as FEV1 are seen and dyspnea is also improved [49]. There are some studies investigating changes in lung function after bariatric surgery [50–56]. Most

of them examine patients 6 months after surgery when significant weight loss is already achieved.

A review from 2018 reported 23 studies with 1,013 participants: patients with and without lung diseases. Overall pulmonary function score – as a result of dynamic and static lung volume tests, arterial blood gases, and gas diffusing capacity – was improved in 11 studies after bariatric surgery with no difference in type of bariatric surgery [50].

The biggest of these studies from Norway with 139 participants (76 bariatric surgeries and 63 conservative treatments) observed effects of bariatric surgery versus conservative treatment on pulmonary function. After 1 year, greater improvements were seen after bariatric surgery than after lifestyle intervention in FVC, FEV1, TLC, VC, FRC, ERV, and pO_2 in arterial blood. This effect is most likely associated to greater weight loss in surgical procedures (30% weight loss vs. 8% weight loss in conservative treatment). The effects did not differ between participants with or without asthma. Changes in levels of CRP and adiponectin did not correlate with changes in arterial blood gas or the pulmonary function test [57]. Changes in lung function parameters are in the range of 12% improvement in FEV1, 9% improvement in FVC, 15% improvement in peak expiratory flow (PEF), and 30% improvement in FEV – as reported in a cohort of 104 obese patients [58].

One study examined 19 lung-healthy patients with BMI >40 kg/m^2 5 weeks after surgery. Five weeks after surgery, weight loss was mild (11.5 ± 2.5 kg) with no effects in spirometry and plethysmography except FRC, but changes in the oscillometry were already observed (respiratory system resistance in the supine position). Furthermore, sleep quality and responsiveness to bronchodilators in the upright position were improved [55]. Despite little weight loss after 5 weeks, the metabolic effects of bariatric surgery have already occurred. It would be interesting in the future to investigate early effects of bariatric surgery in order to determine to what extent do mechanical effects of weight loss and metabolic effects contribute to improved lung function.

Other studies focused on "lung age" (3.56 × height – (40 × FEV1) – 77,280 in women) before and 14 ± 18.7 months after bariatric surgery. The idea is that mechanical and inflammatory processes age the lung. Before surgery, lung age was about 12 years older than chronological age. They found functional pulmonary rejuvenation after surgery resulting in a normalization of lung age in relation to chronological age [53].

Another method to specify weight loss is to measure the subcutaneous and visceral fat area which is a good measurement for abdominal obesity. This is performed via MRI in the supine position (centered on the L4-5 intervertebral disc). Tu et al. [56] found an association between loss of the visceral fat area (about 70.9% loss after bariatric surgery) and improved pulmonary function (increases in FEV1 and FVC) in 32 patients 6 months after surgery.

Small studies show other interesting ideas and results: a possibility to quantify improvements after bariatric surgery is to measure "lung tissue volume" (volume of the lung that is not occupied by air = parenchymal tissue, small pulmonary vessels, and capillaries) in computed tomography. The lung tissue volume is elevated at baseline and decreased by 8% 53 weeks after bariatric surgery in obese women. The mechanisms of this decrease are not understood. Perhaps the extravascular lung water decreases after weight reduction due to the lower systemic inflammatory activity after bariatric surgery. Alternatively, there may be a reduction in perivascular adipose tissue [59].

In 19 obese women, mild-to-moderate shunt and ventilation/perfusion imbalances were seen that resolved after bariatric surgery (measured via the multiple inert gas elimination technique and thermodilution) [60]. Furthermore, there are reports in the literature of bariatric surgery conducted in patients with interstitial lung disease. The aim is to improve candidacy for lung transplantation in obese ILD patients. Ardila-Gatas et al. [61] reported 25 patients with a median BMI of 39 kg/m^2 undergoing bariatric surgery. Six out of 7 patients became lung transplant candidates, and in one of them, it has already been performed. Furthermore, 1 year after surgery, FVC and DLCO were significantly improved. Hence, bariatric surgery seems to be an interesting therapy option in patients with ILD not suitable for lung transplantation. However, the risks of the bariatric operation have to be evaluated in more detail.

In conclusion, most studies show significant improvements in lung function after weight loss. Since bariatric surgery achieves superior weight loss than conservative studies, most research has been conducted in this field. To our knowledge, there are no data on pathological persistent remodeling of the lung in obese patients.

OHS and OSAS – the Obvious Obesity-Associated Lung Diseases

The estimated OHS prevalence is 0.4% in the adult population, while 8–20% of patients with obesity suffer from OHS [7]. Under therapy with CPAP, the results re-

garding weight trends are controversial. Most studies describe that patients gain weight under CPAP therapy, while others found that patients lose weight [62–67]. Therefore, it is more likely that weight changes are a result of eating behavior than of CPAP use [67]. CPAP is believed to improve insulin sensitivity [68] and seems not to be associated with higher rates of cardiovascular complications [69]. Conservative weight loss strategies in OHS achieve a weight loss of 6–7%, but have no significant effect on severity of OHS. In contrast, bariatric surgery leads to 15–64.4% weight loss with a reduction in the apnea-hypopnea index and daytime sleepiness, lowering of pulmonary artery pressure, and improved gas exchange. In some patients, OHS may even resolve fully. In conclusion, a weight loss of about 25–30% is necessary that OHS improves [70]. Visceral fat is the main risk factor for OSAS, and visceral fat area size correlates with the apnea-hypopnea index although the relationship is not completely understood [8].

About 50% of OSAS patients are obese. About 40–90% of overweight people suffer from OSAS. Oxidative stress (created by decline in oxygen levels via apnea), metabolic dysregulation (such as insulin resistance), inflammation (e.g., vascular endothelial and systemic inflammation), and lifestyle factors are seen as possible factors for the development of OSAS. Recent studies even suggest that gut microbiota may contribute to inflammation and obesity and therefore also to OSAS. First of all, there are mechanical and anatomical changes in obesity causing collapse of upper airways through fat accumulation in the face, neck, pharynx, chest wall, and diaphragm. Abdominal pressure is increased due to visceral fat accumulation. OSAS is believed to contribute to weight gain, while obesity also leads to OSAS [71]. OSAS is strongly associated with metabolic diseases such as insulin resistance, type 2 diabetes mellitus, NAFLD, and obesity which represent high-risk factors for cardiovascular disease, hypertension, arrhythmia, stroke, and coronary heart disease [8, 72].

Bariatric surgery improves arterial oxygenation, respiratory function, and polysomnography in patients with OSAS. Most patients suffering of OSAS, OHS, and COPD do no longer require CPAP therapy after bariatric surgery [73]. Lifestyle modification therapies in OSAS reach a weight loss of 3–18% and an improvement of AHI of 3–62%. The large variability of success reflects the great variability of weight loss in conservative treatments and the variability of OSAS response to weight loss. There are hints that losing >5% of initial weight leads to improvements in sleep quality and duration.

Weight loss surgery improves AHI, sleep quality, and sleep duration and modifies sleep architecture. Surprisingly, the effects of bariatric surgery are not always correlated to the amount of weight loss strongly indicating that other aspects than mechanical ones must be taken into consideration [74].

Obese Phenotype in Asthma

The risk of developing asthma is increased 1.5–2.5-fold in overweight people as well as the risk of being hospitalized is 4–6-fold higher for obese than slim asthma patients. In obese asthma patients, exacerbations are more frequent and asthma is less under control while quality of life is reduced. The treatment with anti-inflammatory medicine (e.g., inhaled corticosteroids) seems less effective [5, 6]. Perhaps this observation could be explained by less effective dosage with rising weight. Another explanation could be that airway narrowing and closure caused by obesity impede delivery of inhaled medications to the small airways [5]. Asthma patients with BMI >30 kg/m^2 have a higher symptom score which was reflected in reduced spirometry results but did not lead to reduced work ability as Klepaker et al. [75] showed.

Obesity can promote development of asthma via lung volume reduction and chest wall compliance reduction. The systemic inflammation caused by obesity and increased oxidative stress may further induce asthma in obese patients. With significantly reduced ERV as explained before, patients breathe at lower lung volumes which increases the probability of hyperinflation during bronchoconstriction. It seems that bronchial hyperresponsiveness is only weakly affected by obesity [6].

Besides the mechanical effects, obesity contributes to a phenotype of asthma that is difficult to treat, called "extra obese asthma phenotype." The obese phenotype of asthma is characterized by less eosinophils and more neutrophils in the sputum, suggesting a different type of airway inflammation [5, 6]. Nevertheless, these findings are controversial and in 2 studies, airway wall biopsies showed higher numbers of eosinophils in obese compared with lean asthma controls where the number of sputum eosinophils was reduced [76, 77]. The discrepancy between sputum, blood, and airway wall biopsies needs to be further researched and shows the necessity for investigating different compartments of eosinophils.

Physical inactivity was cited as possible cause of obesity development in asthma, and insulin resistance/diabetes mellitus appears to contribute to the development of

asthma symptoms in obese patients. Moreover, asthma and OSAS are both risk factors for developing the other disease [6]. Relationship between asthma and obesity probably represents a combination of mechanical and inflammatory processes [78].

Asthma symptoms and lung function are improved both via dietary intervention as well as via bariatric surgery. This is already achieved with a weight loss of 5–10%. Bariatric surgery improves asthma control, for example, no longer needing oral corticosteroids, decreasing use of inhaled corticosteroids, and less bronchial hyperresponsiveness [6].

The results show improvements in peak flow, spirometry lung function, and ERV. The airway hyperresponsiveness is demonstrated to resolve in some studies. However, the effects of weight loss depend most likely on the specific asthma phenotype. The most effective intervention is bariatric surgery reducing the numbers of exacerbations and resulting in better asthma control and better lung function [5].

Data suggest that some asthma patients benefit from bariatric surgery in the way that they have a better disease control, lower exacerbation risk, less medication use, and improved quality of life. To date, there is not enough evidence to suggest bariatric surgery as a primary treatment for asthma without any other indications. Future research should focus on the question whether different asthma phenotypes benefit differently from bariatric surgery [79].

COPD and Obesity Paradox

Current data on the relationship between obesity and COPD are inconsistent. Obesity seems more prevalent in early COPD stages GOLD I-II and less prevalent in COPD GOLD IV. The prevalence of obesity in COPD ranges between 18 and 54%. Whether obesity is really more prevalent in COPD patients as reported in some studies remains unclear. It is both possible that COPD is a risk factor for obesity or vice versa. While some studies suggest that obesity leads to more dyspnea in COPD, other studies found no effect [45].

While obesity usually is associated with higher mortality rates, an obesity survival paradox has been found in patients with COPD. The obesity paradox describes the protective effect for some diseases of being overweight. There is evidence of an obesity paradox in COPD and different explanations for it. In leaner patients as well as in elderly patients, there is significant loss of muscle mass which would be needed for breathing efforts and endocrine secretion. Therefore, obese patients with more muscle mass have likely better outcome. Furthermore, BMI does not necessarily reflect the composition of the body, which could be responsible for conflicting results. For future research, other measurements of body composition than BMI as, for example, BIA measurement to differentiate between fat mass and muscle mass should be undertaken [3]. Another explanation for the obesity paradox could be the relatively less hyperinflation of the lung in obese patients.

Some studies suggest that BMI > 32 kg/m^2 has more negative than positive effects on COPD. Obesity has negative effects on exercise capacity when measured in weight-bearing tests such as 6-minute-walk. However, in weight-supported exercises such as cycling, this observation has not been made. On the one hand, obesity correlates with more severe exacerbations in COPD; on the other hand, obesity shows better survival after exacerbation and lower risk of early readmission to the hospital [45].

Usually, obesity in COPD is linked to the blue bloater phenotype, although many different attempts to classify COPD further in clinical phenotypes have been made. Depending on the number of phenotypes suggested, 1 or 2 of them are associated with severe obesity, less emphysema, higher cardiovascular risk profile, and more systemic inflammation. Metabolic syndrome is found in 34–38% of patients with COPD with primarily hypertension, hyperglycemia, and abdominal obesity. Diabetes leads to a higher rate of pulmonary infections, higher rate of exacerbations, and adverse COPD outcomes. In COPD, the increased content of abdominal fat mainly consists of visceral fat. An interesting finding is that the visceral fat area was not decreased with the severity of emphysema [80].

Most studies concern cachexia and gaining weight in COPD. There is rarely literature for bariatric surgery in patients with COPD.

Goto et al. [81] reported a case series of 481 patients with COPD undergoing bariatric surgery. The risk of emergency department visit or hospitalization for AECOPD significantly declined during the first 12 months after bariatric surgery and remained low for the following months.

However, it should be critically reviewed whether obesity should be treated in COPD because of the obesity paradox. There are reports of 28 COPD patients with BMI > 30 kg/m^2 who were treated over 12 weeks with a conservative weight reduction program. BMI reduced from an initial value of 36.3 kg/m^2 by 2.4 kg/m^2 without a loss of skeletal muscle mass, while clinical outcomes such as exercise capacity and dyspnea improved [82].

Conclusion

Obesity and lung diseases are frequent diseases. Via mechanical and probably metabolic effects, lung mechanics are altered in the presence of obesity. We should consider using oscillometry in addition to spirometry to detect the changes in lung function parameters. These effects on lung function resolve with weight loss. Because bariatric surgery is much more effective than conservative strategies, most studies focus on effects after surgery.

In OSAS and OHS, the correlation of the disease and obesity is obvious. Most effects are mechanically based, but open questions remain. In asthma, the connection to obesity is also clear, although there seems to be a special asthma phenotype that reacts particularly to increased adipose tissue. Identifying and clearly describing this phenotype represents a challenge for future research. In COPD, we experience an opposite effect of obesity called obesity paradox. Patients seem to profit from mild overweight. Up to which BMI these benefits are seen and at which point one has to recommend weight loss to COPD patients is a question to answer in the future.

BMI is not always the best instrument to describe overweight. As we recognize that distribution of body composition in fat mass, muscle mass, and other compartments is more relevant than weight alone, we should use better and more accurate instruments to describe overweight and obesity, for example, measuring body composition via bioimpedance analysis or imaging methods in addition to BMI and waist/hip ratio.

Bariatric surgery can serve as a model for understanding the consequences of weight loss and metabolic effects. To distinguish between mechanical and metabolic effects, early investigations in the short term after bariatric surgery are needed. Which patients with lung diseases could profit from this approach should be an issue of research as well as we should evaluate the positive and negative effects on the lung following bariatric surgery. The interactions of the lung and adipose tissue should be taken more into consideration in future research as crosstalk is supposed to occur and proven interactions could lead the way to new therapeutic options.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors did not receive any funding.

Author Contributions

B.-P. Müller-Stich conceived the presented ideas. He and F. Herth supervise and direct the projects in this field. J. Brock took the leading in writing the manuscript, while A. Billeter mainly contributed with his ideas to the final version of the manuscript. All authors provided critical feedback and helped shape the research and manuscript.

References

1 Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab. 2004;89(6):2548–56.
2 Ghimire P, Kaul P. Pickwickian syndrome. Treasure Island, FL: StatPearls; 2020.
3 Bianco A, Nigro E, Monaco ML, Matera MG, Scudiero O, Mazzarella G, et al. The burden of obesity in asthma and COPD: role of adiponectin. Pulm Pharmacol Ther. 2017;43:20–5.
4 Franssen FM, O'Donnell DE, Goossens GH, Blaak EE, Schols AM. Obesity and the lung: 5. Obesity and COPD. Thorax. 2008;63(12):1110–7.
5 Peters U, Dixon AE, Forno E. Obesity and asthma. J Allergy Clin Immunol. 2018;141(4):1169–79.
6 Carpaij OA, Van Den Berge M. The asthma-obesity relationship: underlying mechanisms and treatment implications. Curr Opin Pulm Med. 2018;24(1):42–9.
7 Masa JF, Pépin JL, Borel JC, Mokhlesi B, Murphy PB, Sánchez-Quiroga MÁ. Obesity hypoventilation syndrome. Eur Respir Rev. 2019;28(151):180097.
8 Li M, Li X, Lu Y. Obstructive sleep apnea syndrome and metabolic diseases. Endocrinology. 2018;159(7):2670–5.
9 Centers for Disease and Control Prevention. Available from: https://www.cdc.gov/obesity/index.html.
10 Dixon AE, Peters U. The effect of obesity on lung function. Expert Rev Respir Med. 2018;12(9):755–67.
11 Fang H, Berg E, Cheng X, Shen W. How to best assess abdominal obesity. Curr Opin Clin Nutr Metab Care. 2018;21(5):360–5.
12 World Health Organization. Available from: http: //www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics.
13 Blüher M. Obesity: global epidemiology and pathogenesis. Nat Rev Endocrinol. 2019;15(5):288–98.
14 Mensink GBM, Schienkiewitz A, Haftenberger M, Lampert T, Ziese T, Scheidt-Nave C. Übergewicht und Adipositas in Deutschland: Ergebnisse der Studie zur Gesundheit Erwachsener in Deutschland (DEGS1). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2013;56:786–794.
15 Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766–81.
16 Apovian CM. Obesity: definition, comorbidities, causes, and burden. Am J Manag Care. 2016;22(7 Suppl):s176–85.

17 Li X, Cao X, Guo M, Xie M, Liu X. Trends and risk factors of mortality and disability adjusted life years for chronic respiratory diseases from 1990 to 2017: systematic analysis for the Global Burden of Disease Study 2017. BMJ. 2020;368:m234.
18 Peralta GP, Marcon A, Carsin A-E, Abramson MJ, Accordini S, Amaral AF, et al. Body mass index and weight change are associated with adult lung function trajectories: the prospective ECRHS study. Thorax. 75(4):313–20.
19 Eugen JV. Das viszerale Fettgewebe: basis für chronisch entzündliche Erkrankungen. Entzündung und Ernährung. 2008;11–15.
20 Elliot JG, Donovan GM, Wang KCW, Green FHY, James AL, Noble PB. Fatty airways: implications for obstructive disease. Eur Respir J. 2019;54(6):1900857.
21 Brightling CE, Tobin AB, Milligan G. Fatty airways: a source of good and bad fats? Eur Respir J. 2019;54(6):1902060.
22 Ben-Harari RR, Youdim MB. The lung as an endocrine organ. Biochem Pharmacol. 1983; 32(2):189–97.
23 Sorino C, Negri S, Spanevello A, Feller-Kopman D. The pleura and the endocrine system. Eur J Intern Med. 2020;72:34–7.
24 Cao H. Adipocytokines in obesity and metabolic disease. J Endocrinol. 2014;220(2):T47–59.
25 Armani A, Mammi C, Marzolla V, Calanchini M, Antelmi A, Rosano GM, et al. Cellular models for understanding adipogenesis, adipose dysfunction, and obesity. J Cell Biochem. 2010;110(3):564–72.
26 Fasshauer M, Blüher M. Adipokines in health and disease. Trends Pharmacol Sci. 2015; 36(7):461–70.
27 Chwalba A, Machura E, Ziora K, Ziora D. The role of adipokines in the pathogenesis and course of selected respiratory diseases. Endokrynol Pol. 2019;70(6):504–10.
28 Dubey A, Kant S, Tiwari S, Agarwal S, Mahdi AA. Leptin level correlates with obesity and health related quality of life in obstructive sleep apnea syndrome patients. Indian J Tuberc. 2015;62(2):105–9.
29 Lu M, Fang F, Wang Z, Wei P, Hu C, Wei Y. Association between serum/plasma levels of adiponectin and obstructive sleep apnea hypopnea syndrome: a meta-analysis. Lipids Health Dis. 2019;18(1):30.
30 Lykouras D, Theodoropoulos K, Sampsonas F, Lagiou O, Lykouras M, Spiropoulou A, et al. The impact of obstructive sleep apnea syndrome on renin and aldosterone. Eur Rev Med Pharmacol Sci. 2015;19(21):4164–70.
31 Madaeva IM, Berdina ON, Sholokhov LF, Semenova NV, Kolesnikova LI. Pathophysiological aspects of neuro-endocrine regulation system in patients with obstructive sleep apnea syndrome. Z Nevrol Psikhiatr Im S S Korsakova. 2018;118(4):55–9.
32 Santis S de, Cambi J, Tatti P, Bellussi L, Passali D. Changes in ghrelin, leptin and pro-inflammatory cytokines after therapy in Obstructive Sleep Apnea Syndrome (OSAS) patients. Otolaryngol Pol. 2015;69:1–8.
33 Xu T, Lin Y, Sun S, Zhang Q. Changes in four plasma adipokines before and after sleep in OSAS patients. Clin Respir J. 2017;11(6):968–74.
34 Yang Y, Yang S, Jiao X, Li J, Wu H, Sun H, et al. Targeted sequencing analysis of the adiponectin gene identifies variants associated with obstructive sleep apnoea in Chinese Han population. Medicine. 2019;98(16):e15219.
35 Nasiri Kalmarzi R, Ataee P, Mansori M, Moradi G, Ahmadi S, Kaviani Z, et al. Serum levels of adiponectin and leptin in asthmatic patients and its relation with asthma severity, lung function and BMI. Allergol Immunopathol. 2017;45(3):258–64.
36 Enomoto N, Oyama Y, Yasui H, Karayama M, Hozumi H, Suzuki Y, et al. Analysis of serum adiponectin and leptin in patients with acute exacerbation of idiopathic pulmonary fibrosis. Sci Rep. 2019;9(1):10484.
37 Nguyen DV, Linderholm A, Haczku A, Kenyon N. Glucagon-like peptide 1: a potential anti-inflammatory pathway in obesity-related asthma. Pharmacol Ther. 2017;180:139–43.
38 Viby NE, Isidor MS, Buggeskov KB, Poulsen SS, Hansen JB, Kissow H. Glucagon-like peptide-1 (GLP-1) reduces mortality and improves lung function in a model of experimental obstructive lung disease in female mice. Endocrinology. 2013;154(12):4503–11.
39 Reutrakul S, Sumritsopak R, Saetung S, Chanprasertyothin S, Anothaisintawee T. The relationship between sleep and glucagon-like peptide 1 in patients with abnormal glucose tolerance. J Sleep Res. 2017;26:756–63.
40 Körner M, Stöckli M, Waser B, Reubi JC. GLP-1 receptor expression in human tumors and human normal tissues: potential for in vivo targeting. J Nucl Med. 2007;48(5):736–43.
41 Rogliani P, Calzetta L, Capuani B, Facciolo F, Cazzola M, Lauro D, et al. Glucagon-like peptide 1 receptor: a novel pharmacological target for treating human bronchial hyperresponsiveness. Am J Respir Cell Mol Biol. 2016;55(6):804–14.
42 Matsumoto T, Harada N, Azuma M, Chihara Y, Murase K, Tachikawa R, et al. Plasma incretin levels and dipeptidyl peptidase-4 activity in patients with obstructive sleep apnea. Ann Am Thorac Soc. 2016;13(8):1378–87.
43 Blackman A, Foster GD, Zammit G, Rosenberg R, Aronne L, Wadden T, et al. Effect of liraglutide 3.0 mg in individuals with obesity and moderate or severe obstructive sleep apnea: the SCALE Sleep Apnea randomized clinical trial. Int J Obes. 2016;40(8):1310–9.
44 Littleton SW, Tulaimat A. The effects of obesity on lung volumes and oxygenation. Respir Med. 2017;124:15–20.
45 Zewari S, Vos P, Van Den Elshout F, Dekhuijzen R, Heijdra Y. Obesity in COPD: revealed and unrevealed issues. COPD. 2017; 14(6):663–73.
46 Katz S, Arish N, Rokach A, Zaltzman Y, Marcus EL. The effect of body position on pulmonary function: a systematic review. BMC Pulm Med. 2018;18(1):159.
47 Santamaria F, Montella S, Greco L, Valerio G, Franzese A, Maniscalco M, et al. Obesity duration is associated to pulmonary function impairment in obese subjects. Obesity. 2011; 19(8):1623–8.
48 . Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie: S3-Leitlinie: Chirurgie der Adipositas und metabolischer Erkrankungen: Version 2.3. AWMF; 2018.
49 Littleton SW. Impact of obesity on respiratory function. Respirology. 2012;17(1):43–9.
50 Alsumali A, Al-Hawag A, Bairdain S, Eguale T. The impact of bariatric surgery on pulmonary function: a meta-analysis. Surg Obes Relat Dis. 2018;14(2):225–36.
51 Boissière L, Perotin-Collard JM, Bertin E, Gaubil I, Diaz Cives A, Barbe C, et al. Improvement of dyspnea after bariatric surgery is associated with increased Expiratory Reserve Volume: a prospective follow-up study of 45 patients. PLoS One. 2017;12(9): e0185058.
52 Campos E., Peixoto-Souza F., Alves V., Basso-Vanelli R., Barbalho-Moulim M., Laurino-Neto R., et al. Improvement in lung function and functional capacity in morbidly obese women subjected to bariatric surgery. Clinics. 2018;73:1.
53 Melo SM, Argentino PA, Oliveira MM, Melo GN, Souza Neto GL. Functional lung rejuvenation in obese patients after bariatric surgery. Rev Assoc Med Bras. 2016;62(2):157–61.
54 Pazzianotto-Forti EM, da Costa Munno CM, Merino DFB, Simões da Rocha MR, Mori TA de, Júnior IR. Effects of inspiratory exercise with linear and nonlinear load on respiratory variables post-bariatric surgery. Respir Care. 2019;64(12):1516–22.
55 Peters U, Hernandez P, Dechman G, Ellsmere J, Maksym G. Early detection of changes in lung mechanics with oscillometry following bariatric surgery in severe obesity. Appl Physiol Nutr Metab. 2016;41(5):538–47.
56 Tu Y, Yu H, Bao Y, Zhang P, Di J, Han X, et al. Baseline of visceral fat area and decreased body weight correlate with improved pulmonary function after Roux-en-Y gastric bypass in Chinese obese patients with BMI 28–35 kg/m2 and type 2 diabetes: a 6-month follow-up. BMC Endocr Disord. 2015;15:26.
57 Gabrielsen AM, Lund MB, Kongerud J, Viken KE, Røislien J, Hjelmesaeth J, et al. Pulmonary function and blood gases after gastric bypass and lifestyle intervention: a comparative study. Clin Obes. 2013;3(5):117–23.

58 Nguyen NT, Hinojosa MW, Smith BR, Gray J, Varela E. Improvement of restrictive and obstructive pulmonary mechanics following laparoscopic bariatric surgery. Surg Endosc. 2009;23(4):808–12.
59 Santos A, Rivas E, Rodríguez-Roisin R, Sánchez M, Ruiz-Cabello J, Arismendi E, et al. Lung tissue volume is elevated in obesity and reduced by bariatric surgery. Obes Surg. 2016;26(10):2475–82.
60 Rivas E, Arismendi E, Agustí A, Sanchez M, Delgado S, Gistau C, et al. Ventilation/perfusion distribution abnormalities in morbidly obese subjects before and after bariatric surgery. Chest. 2015;147(4):1127–34.
61 Ardila-Gatas J, Sharma G, Nor Hanipah Z, Tu C, Brethauer SA, Aminian A, et al. Bariatric surgery in patients with interstitial lung disease. Surg Endosc. 2019;33(6):1952–8.
62 Drager LF, Brunoni AR, Jenner R, Lorenzi-Filho G, Benseñor IM, Lotufo PA. Effects of CPAP on body weight in patients with obstructive sleep apnoea: a meta-analysis of randomised trials. Thorax. 2015;70(3):258–64.
63 Myllylä M, Kurki S, Anttalainen U, Saaresranta T, Laitinen T. High adherence to CPAP treatment does not prevent the continuation of weight gain among severely obese OSAS patients. J Clin Sleep Med. 2016;12(4):519–28.
64 Redenius R, Murphy C, O'Neill E, Al-Hamwi M, Zallek SN. Does CPAP lead to change in BMI? J Clin Sleep Med. 2008;4(3):205–9.
65 Aro M, Anttalainen U, Kurki S, Irjala K, Polo O, Saaresranta T. Gender-specific change in leptin concentrations during long-term CPAP therapy. Sleep Breath. 2020;24(1):191–9.
66 Rishi MA, Copur AS, Nadeem R, Fulambarker A. Effect of positive airway pressure therapy on body mass index in obese patients with obstructive sleep apnea syndrome: a prospective study. Am J Ther. 2016;23(2):e422–8.
67 Tachikawa R, Ikeda K, Minami T, Matsumoto T, Hamada S, Murase K, et al. Changes in energy metabolism after continuous positive airway pressure for obstructive sleep apnea. Am J Respir Crit Care Med. 2016;194(6):729–38.
68 Isobe Y, Nakatsumi Y, Sugiyama Y, Hamaoka T, Murai H, Takamura M, et al. Severity indices for obstructive sleep apnea syndrome reflecting glycemic control or insulin resistance. Intern Med. 2019 Nov 15;58(22):3227–34.
69 Baratta F, Pastori D, Fabiani M, Fabiani V, Ceci F, Lillo R, et al. Severity of OSAS, CPAP and cardiovascular events: a follow-up study. Eur J Clin Invest. 2018;48(5):e12908.
70 Tamae Kakazu M, Soghier I, Afshar M, Brozek JL, Wilson KC, Masa JF, et al. Weight loss interventions as treatment of obesity hypoventilation syndrome: a systematic review. Ann Am Thorac Soc. 2020;17(4):492–502.
71 Kuvat N, Tanriverdi H, Armutcu F. The relationship between obstructive sleep apnea syndrome and obesity: a new perspective on the pathogenesis in terms of organ crosstalk. Clin Respir J. 2020;14(7):595–604.
72 Ryan S, Arnaud C, Fitzpatrick SF, Gaucher J, Tamisier R, Pépin JL. Adipose tissue as a key player in obstructive sleep apnoea. Eur Respir Rev. 2019;28(152):190006.
73 Martí-Valeri C, Sabaté A, Masdevall C, Dalmau A. Improvement of associated respiratory problems in morbidly obese patients after open Roux-en-Y gastric bypass. Obes Surg. 2007;17(8):1102–10.
74 Xanthopoulos MS, Berkowitz RI, Tapia IE. Effects of obesity therapies on sleep disorders. Metab Clin Exp. 2018;84:109–17.
75 Klepaker G, Svendsen MV, Hertel JK, Holla ØL, Henneberger PK, Kongerud J, et al. Influence of obesity on work ability, respiratory symptoms, and lung function in adults with asthma. Respiration. 2019;98(6):473–81.
76 Desai D, Newby C, Symon FA, Haldar P, Shah S, Gupta S, et al. Elevated sputum interleukin-5 and submucosal eosinophilia in obese individuals with severe asthma. Am J Respir Crit Care Med. 2013;188(6):657–63.
77 van der Wiel E, Ten Hacken NH, van den Berge M, Timens W, Reddel HK, Postma DS. Eosinophilic inflammation in subjects with mild-to-moderate asthma with and without obesity: disparity between sputum and biopsies. Am J Respir Crit Care Med. 2014;189(10):1281–4.
78 Simpson JL, Scott HA. What does the increasing prevalence of obesity mean for the management of asthma and airways disease? J Bras Pneumol. 2020;46(1):e20200048.
79 Chaaban TA. Bariatric surgery: a potential cure for asthma? Eur Respir Rev. 2019;28(152):190003.
80 Wouters EFM. Obesity and metabolic abnormalities in chronic obstructive pulmonary disease. Ann Am Thorac Soc. 2017;14(Suppl_5):S389–94.
81 Goto T, Tsugawa Y, Faridi MK, Camargo CA, Hasegawa K. Reduced risk of acute exacerbation of COPD after bariatric surgery: a self-controlled case series study. Chest. 2018;153(3):611–7.
82 McDonald VM, Gibson PG, Scott HA, Baines PJ, Hensley MJ, Pretto JJ, et al. Should we treat obesity in COPD? The effects of diet and resistance exercise training. Respirology. 2016;21(5):875–82.