Respiratory complications of obesity: from early changes to respiratory failure

Neeraj M. Shah[1,2,3] and Georgios Kaltsakas[1,2,3]

[1]Lane Fox Respiratory Service, St Thomas' Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK. [2]Lane Fox Clinical Respiratory Physiology Centre, Guy's and St Thomas' NHS Foundation Trust, London, UK. [3]Centre for Human and Applied Physiological Sciences (CHAPS), King's College London, London, UK.

Corresponding author: Neeraj M. Shah (neeraj.shah@gstt.nhs.uk)

Shareable abstract (@ERSpublications)
Obesity has significant and wide-ranging effects on respiratory function, and is an important contributor to morbidity and mortality https://bit.ly/3k8bGmX

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Abstract

Obesity is a significant and increasingly common cause of respiratory compromise. It causes a decrease in static and dynamic pulmonary volumes. The expiratory reserve volume is one of the first to be affected. Obesity is associated with reduced airflow, increased airway hyperresponsiveness, and an increased risk of developing pulmonary hypertension, pulmonary embolism, respiratory tract infections, obstructive sleep apnoea and obesity hypoventilation syndrome. The physiological changes caused by obesity will eventually lead to hypoxic or hypercapnic respiratory failure. The pathophysiology of these changes includes a physical load of adipose tissue on the respiratory system and a systemic inflammatory state. Weight loss has clear, well-defined benefits in improving respiratory and airway physiology in obese individuals.

Educational aims

- Provide an understanding of the physiological changes that obesity causes on the respiratory system.
- Describe the mechanisms that explain why obesity is a risk factor for the development of various respiratory conditions.
- Explain the association between obesity and obstructive sleep apnoea, obesity hypoventilation syndrome and respiratory failure.
- Provide an overview of the benefits of weight loss on the respiratory system.

Introduction

The accumulation of adipose tissue above socially accepted norms has been recognised as a significant contributor to numerous chronic diseases since the classical age [1]. Despite this, being overweight has been considered a sign of wealth and wellbeing for much of human history [2]. Only in the past century have perceptions changed. Obesity was finally recognised as a disease state by the National Institutes of Health in 1998 [3]. While the association of increasing body mass index (BMI) with cardiovascular comorbidity and glucose dysfunction is recognised and has become embedded into clinical practice, obesity is also associated with a systemic inflammatory state, gastrointestinal disorders, malignancy, psychological and importantly, respiratory comorbidity [4]. The pathophysiology of these complications is less well known and understood and therefore deserves attention. Respiratory complications of obesity include airway disorders, impaired physiology, pulmonary vascular disease, respiratory tract infections and ultimately ventilatory failure (figure 1). This review uses a systematic approach to describe the pathophysiological processes that lead to these complications and the impact of potential treatments. Although the respiratory complications of obesity have been recognised in the literature throughout history, only in the past 30–40 years have these been actively considered and acted upon by clinicians and public health organisations [5].

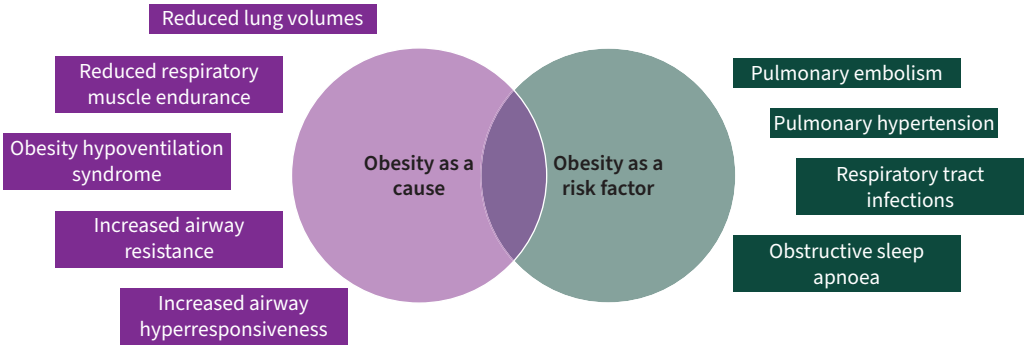

FIGURE 1 Associations between the respiratory system and obesity, delineating where obesity is causative and where obesity is a risk factor.

Epidemiology

Obesity is classified into categories based on BMI, into moderate (BMI 30–35 $kg \cdot m^{-2}$), severe (BMI 35–40 $kg \cdot m^{-2}$) and morbid obesity (BMI >40 $kg \cdot m^{-2}$). In addition, a supranormal BMI of 25–30 $kg \cdot m^{-2}$ is considered as overweight. With increasing BMI, come increasing severity of complications, in both cardiovascular and respiratory function [4]. The pattern of obesity also has an impact on respiratory comorbidity. Individuals with an abdominal pattern are more likely to suffer from respiratory compromise than those with a peripheral pattern, due to the physical constraints central adipose tissue places on the diaphragm [6]. Global obesity prevalence has increased from 3.2% in 1975 to 10.8% in 2014 in men, and from 6.4% to 14.9% in women [7]. All classes of obesity are becoming more prevalent [8, 9]. It is therefore imperative that all clinicians are aware of the impact obesity can have on their patients' respiratory physiology, as they are almost always going to be treating overweight individuals on a regular basis.

Pulmonary physiology

The impact of obesity on lung volumes stems primarily from its impact on thoracic compliance. Thoracic, or chest wall, compliance is attenuated in obese patients due to the physical limitation on chest wall expansion and diaphragm contraction that abdominal and chest wall adipose tissue places [10–12]. Lung compliance is also reduced in obesity mainly due to an increase in pulmonary blood flow [13], but also due to closure of the peripheral airways leading to a consequent chronic microatelectasis [14]. Additionally, reduction of functional residual capacity (FRC) may lead to increased alveolar surface tension further decreasing the lung compliance [8]. However, the contribution of reduced lung compliance appears to be less important than thoracic compliance [15].

The earliest and most commonly reported effect of obesity on static lung volumes is a reduction in expiratory reserve volume (ERV), usually with a conserved residual volume, which ultimately results in a reduction in FRC [16, 17]. Increasing severity of obesity is exponentially correlated with reducing ERV [16], and inversely proportional to other static lung volumes and capacities [16, 18]. A similar relationship is observed with end-expiratory lung volume [19]. Total lung capacity (TLC) tends to be normal, except in morbidly obese individuals where it can reduce by up to 20% [16], resulting in a restrictive defect. Therefore, if TLC is reduced in individuals with a BMI of up to 40 $kg \cdot m^{-2}$, an alternative or additional respiratory condition should be sought, as obesity alone is unlikely to be causing this degree of respiratory compromise [12]. The effects on static lung volumes are observed far more frequently in those with an abdominal pattern of obesity compared to those with a gynaecoid pattern, due to its impact on the diaphragm [6].

Vital capacity (VC), forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV_1) tend to be mildly reduced in obese individuals, resulting in a normal or close to normal FEV_1/FVC ratio [17, 18, 20]. Maximum expiratory flow 25–75% of FVC can be considerably reduced [18], reflecting small airway obstruction, and can be an early indicator of respiratory compromise in the context of obesity. Diffusion capacity tends to be normal or increased, reflecting the increase in pulmonary blood flow observed in obesity [13].

The sparse literature on the effects of obesity on respiratory muscle strength suggest that it remains mostly normal [20–23]. Posture appears to have an effect on respiratory muscle strength. In obese individuals, in

the supine position maximal inspiratory pressure is significantly reduced compared with the upright position [24, 25]. Respiratory muscle endurance, evidenced by the maximum voluntary ventilation, is reduced with increasing BMI [26–28]. This is most likely because of reduced lung volumes and chest wall compliance and the subsequent increase in load on the respiratory system [29]. The direct impact of obesity on the structure of respiratory muscles remains unclear. Animal studies have suggested that the diaphragm thickens and has an increased concentration of type I and type IIb fibres [30, 31], which would increase its contractility. Animal studies have also demonstrated a fast-to-slow shift in myosin heavy chain phenotype [31, 32], which increases the endurance of the diaphragm. In summary, obesity contributes to a decrease in compliance and static lung volume, with mild impairment in FEV_1/FVC and sparing of the respiratory musculature (table 1).

Breathlessness on exertion is often described by overweight individuals without any respiratory compromise [33, 34]. The exact mechanisms to explain this are yet to be understood. In some early studies of overweight individuals with apparently normal respiratory physiology (*i.e.* normal spirometry), those reporting breathlessness on exertion were more likely to have a reduced maximum voluntary ventilation [35, 36]. Therefore, in some individuals, with unexplained breathlessness, further physiological investigations may reveal deficits. However, there is a cohort of overweight individuals in whom extensive cardiopulmonary investigation does not reveal any cause of breathlessness. Traditionally, breathlessness in these individuals was attributed to cardiopulmonary deconditioning. However, several studies have demonstrated normal aerobic capacity in these individuals. In individuals reporting exertional breathlessness, the sensation of the work of breathing is increased, compared with individuals without breathlessness, without any difference in the oxygen cost of breathing [37]. A potential explanation for this is a change in the "respiratory gate", a subcortical mechanism designed to filter out insignificant respiratory stimuli. Obese individuals may have a lower threshold in this respiratory gate, allowing less important respiratory stimuli to stimulate the cortex, giving rise to the sensation of breathlessness [38]. This is a poorly investigated field and so managing breathlessness in obese individuals without any respiratory compromise can be challenging. In these individuals, psychophysiological factors contributing to the perception of breathlessness should be explored.

Airway limitation

Airway narrowing and a subsequent increase in resistance is a common feature in obese individuals, despite a preserved FEV_1/FVC [39]. Body plethysmography demonstrated increasing airway resistance with increasing BMI [18]. Forced oscillation technique revealed almost double the airway resistance in obese individuals compared with controls [40, 41]. Furthermore, obese individuals displayed increased ΔX_{rs} (difference between inspiratory and expiratory reactance), independent of the effect of low FRC, suggesting an additional mechanism causing airway flow limitation [42]. In patients with morbid obesity, negative expiratory pressure assessment revealed expiratory flow limitation in the supine position, when compared with age-matched controls [43]. The pathophysiology of airway narrowing in obese individuals can be classified into mechanical causes and hyperresponsiveness due to a pro-inflammatory state.

Lung volume is an important determinant of airway calibre [44]. In individuals with normal respiratory physiology, lung inflation causes a dose-dependent increase in airway calibre; the change in airway diameter is proportional to the cube root of the lung volume [45]. As obese individuals tend to breathe at

TABLE 1 The impact of obesity on parameters of respiratory physiology

Parameter	Effect
Expiratory reserve volume	Reduction
Functional residual capacity	Reduction
Total lung capacity	Reduction (only in the morbidly obese)
Vital capacity/forced vital capacity	Mild reduction
Forced expiratory volume in 1 s	Mild reduction
Maximal expiratory flow at 25–75% of forced vital capacity	Reduction
Diffusion capacity	Reduction/no change/increase
Respiratory muscle strength	No change
Respiratory muscle endurance	Reduction
Airway resistance	Increase
Airway reactance	Increase
Neural respiratory drive	Increase

lower FRC, the airway smooth muscles may be unloaded, allowing them to shorten excessively, causing airway narrowing. In addition, normal breathing imposes a tidal strain on airway smooth muscles, resulting in a bronchodilating effect. As obese individuals tend to breathe at a lower FRC, this bronchodilating effect is diminished, resulting in airway narrowing [46].

Obesity is associated with a systemic pro-inflammatory state (raised leukocytes, cytokines and chemokines) [47] and this has been demonstrated to be a contributor to a number of complications, including cardiovascular disease [48], glucose intolerance [49] and malignancy [50]. This pro-inflammatory state is also a potential cause of airway hyperresponsiveness in obese individuals. Airway eosinophils and neutrophils are not significantly increased in obese individuals; thus, this inflammatory state appears to be systemic [39]. Serum tumour necrosis factor (TNF)-α is increased in obese individuals. TNF-α receptors are found on airway smooth muscles, and *in vitro*, administration of TNF-α results in increased contractility of airway smooth muscles [51]. Leptin is a pro-inflammatory hormone produced by adipose cells that acts centrally to reduce hunger. Monocytes and macrophages respond to leptin with increased production of cytokines. As serum leptin levels are considerably increased in obese individuals, it is believed that airway hyperresponsiveness observed in obesity is at least partially caused by leptin [52]. Adiponectin is another hormone produced by adipose tissue, although serum adiponectin levels appear to be reduced in obese individuals [53]. Adiponectin inhibits TNF-α and so its reduction may have downstream effects on the contractility of airway smooth muscle [54]. Of note, bariatric surgery can result in a reduction in airway hyperresponsiveness and is associated with an increase in serum adiponectin and decrease in serum leptin [55]. In addition to those already discussed, there are probably many more molecular pathways contributing to airway hyperresponsiveness in obesity which will be elucidated with further work [56].

Asthma and COPD

Obesity has a considerable impact on both asthma and COPD; this is unsurprising as both conditions involve airway inflammation and changes to respiratory physiology.

The prevalence of asthma increases with BMI [57], as does its severity [58]. Asthma prevalence is 11% in obese individuals compared with only 7% in those with BMI <25 $kg \cdot m^{-2}$ [59]. Obese individuals are more likely to be hospitalised with an asthma exacerbation [60], and are less likely to respond to conventional inhaled corticosteroid therapy [61]. This is believed to be secondary to the pro-inflammatory state caused by obesity. Inhaled corticosteroids exert their effect on mitogen-activated protein kinase phosphatase-1 (MKP-1). The proinflammatory state in obesity appears to downregulate MKP-1, attenuating the impact of corticosteroids [62].

The interaction between obesity and COPD is less dose responsive. Although the prevalence of COPD does increase with increasing BMI [63], the severity of COPD adds complexity. In a study from the Netherlands, among patients with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage 1 and 2 COPD the prevalence of obesity was 16–24%, whereas in patients with GOLD stage 4 COPD the prevalence of obesity was 6%. This was compared with a national prevalence of 10% [64, 65]. Studies of the mechanisms to explain the interaction between COPD and obesity are scarce, aside from the interactions in sleep disordered breathing. Both have an impact on pulmonary mechanics and ventilatory demand, and are likely to mutually amplify their effects. There is an "obesity paradox" phenomenon reported in COPD: increased BMI appears to be protective against all-cause mortality. The annual decline in FEV_1 in men was lower in obese individuals with COPD than non-obese [66]. This is probably a reflection of the well-established causality between reduced BMI and all-cause mortality in COPD [67]. This paradox is not universal and is influenced by the heterogeneous phenotypes that characterise COPD. In patients with advanced COPD, obesity appears to be protective, when a low BMI is a significant contributor to all-cause mortality. By contrast, in patients with mild COPD, obesity appears to increase the risk of cardiovascular morbidity which in turn is a greater contributor to mortality than low BMI [68].

Pulmonary vascular disease

Obesity appears to be associated with an increased risk of developing pulmonary vascular disorders such as pulmonary hypertension and pulmonary embolism. Obesity has been demonstrated to be an independent risk factor for the development of all classes of pulmonary hypertension [69]. The literature suggests that obesity is associated with worse outcomes in patients with pulmonary arterial hypertension (PAH). A meta-analysis revealed that the response to treatment in patients with PAH was attenuated in those with increasing BMI [70] and health-related quality of life was worse in individuals with a raised BMI [71]. The effect of obesity on mortality in PAH remains unclear. Some studies report that obesity does not have any impact on mortality [72, 73], while others report a survival obesity paradox [69, 71, 74]. Mechanisms

for an association between obesity and the development of pulmonary hypertension remain unclear [75], but have been postulated as being related to the presence of obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS) and the cardiomyopathy of obesity [76]. Murine data appear to suggest that pulmonary hypertension is associated with reduced serum adiponectin levels, which is a consequence of obesity, and that the administration of adiponectin is protective against the development of PAH [77]. Human studies have yet to be conducted, so the clear mechanism and potential therapeutic target for the development of pulmonary hypertension in obese individuals remains elusive.

Several large registry studies have demonstrated the strong association between obesity and the incidence of venous thromboembolism (VTE) [78–81]. Obesity is not only associated with an increased risk of primary VTE, but also recurrent VTE [82]. In addition, increasing BMI is proportional to increasing risk of VTE [83]. Although there is a strong relationship between incidence of VTE and BMI, its impact on outcome remains unclear. Studies have reported an obesity survival paradox in VTE [79, 84], but others have questioned whether these data reflect a true survival benefit or whether they reflect methodological challenges impacting the interpretation of their results [85, 86].

Respiratory tract infections and acute respiratory distress syndrome

Although obesity appears to cause a systemic pro-inflammatory state, until the coronavirus disease 2019 (COVID-19) pandemic, the association between obesity and respiratory tract infections remained unclear due to conflicting data. Mechanistic studies investigating the impact of obesity in animal models of influenza suggested that the presence of obesity results in an attenuated antiviral host response [87, 88]. This appeared to correlate with observational data from the H1N1 influenza epidemic reporting that obesity is a risk factor for the severity of disease [89–91] and admission to critical care and death [92]. This association between obesity and viral respiratory disease has been compellingly confirmed during the COVID-19 pandemic, with multiple reports demonstrating that obesity was a poor prognostic marker, with an increase in the development of COVID-19 pneumonitis [93], and increased risk of hospitalisation and death [94].

Several mechanisms to explain the association between obesity and COVID-19 have been explored. A well described mechanism is the impact of obesity on the angiotensin-converting enzyme 2 (ACE2) receptor. ACE2-R is an attachment site for the viral spike protein on the surface of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [95], allowing the virus to enter cells. The ACE2-R is found on lung epithelial cells as well as adipocytes, and is therefore upregulated in obese individuals [96]. Adipocytes act as a reservoir and replication site for SARS-CoV-2 [97], and so could result in prolonged viral shedding, as has been observed influenza [98]. Another mechanism is related to expression of interleukin-6 (IL-6). IL-6 is an independent risk factor for severity of COVID-19 [99]. Adipose tissue is a source of IL-6 secretion [100] and so it follows that obesity is likely to contribute to the impact of IL-6 on COVID-19 severity. Leptin is a pro-inflammatory molecule that stimulates production of pro-inflammatory cytokines such as TNF-α and IL-6. As already described, leptin is overexpressed in obesity and so may be an important contributor to the inflammatory response [101], and subsequent cytokine storm that is associated closely with morbidity and mortality [96, 102]. Several other molecular mechanisms remain under investigation, without definitive answers. To summarise, obesity results in a pro-inflammatory state through numerous mechanisms, which increases the degree of inflammatory response in COVID-19. In addition, obese individuals are more likely to suffer from other chronic conditions such as hypertension, cardiovascular disease, chronic kidney disease and type 2 diabetes mellitus which are all associated with increased morbidity and mortality in COVID-19 [103].

By contrast, the evidence of an association between obesity and bacterial pneumonia remains equivocal. While some studies have reported that obesity is associated with self-reported incidence of respiratory tract infection [104], and an increased risk of hospitalisation [105], many other studies have reported on the obesity survival paradox from bacterial pneumonia. A meta-analysis of 12 observational studies including 1.5 million patients [106], and subsequent studies [107, 108], have demonstrated that although obesity is associated with an increased risk of contracting a bacterial respiratory tract infection, it appears to be inversely proportional to mortality. No satisfactory mechanistic explanation has been elicited for this disparity in outcomes between viral and bacterial respiratory tract infections in obese individuals. While many theories have been speculated, none are yet supported by compelling evidence [109]. Obesity is an independent risk factor for the development of acute respiratory distress syndrome [110]. Despite this, obesity has been associated with an equivalent or better survival outcome compared with individuals with a normal BMI [111–113]. This is an example of the so-called obesity survival paradox, which states that somewhat counterintuitively, patients admitted to the intensive care unit are less likely to die if they have a raised BMI when compared with those with either a normal or low BMI.

Respiratory failure

Ultimately, the combination of these physiological changes can result in the development of ventilatory failure in obese individuals. The load–capacity–drive relationship is a useful framework to discuss the pathophysiology of alveolar hypoventilation and consequent hypercapnic respiratory failure in obesity [114]. Increased load on the respiratory system and a failure to adequately increase neural respiratory drive ultimately results in alveolar hypoventilation (figure 2), As discussed earlier, respiratory muscle capacity does not tend to be affected in obese individuals.

Load on the respiratory system is the combination of resistive load (increased resistance to airflow), elastic load (inversely proportional to compliance) and threshold load (intrinsic positive end-expiratory pressure ($PEEP_i$)). As described earlier, airway resistance is increased in obese individuals, thus increasing resistive load. Both lung and chest wall compliance are reduced in obesity. Lung compliance due to breathing at lower lung volume which causes microatelectasis, and chest wall compliance due to the physical pressure of adipose tissue on the expansive ability of the rib cage [115]. Reduced pulmonary compliance results in an increase in elastic load. $PEEP_i$ is increased in obese individuals [23, 116], particularly in the supine position [43], demonstrating increased threshold load. This may be explained by expiratory flow limitation in the supine position, causing gas trapping at the end of expiration and thereby generating $PEEP_i$ [43].

Neural respiratory drive is the mechanism by which the medullary respiratory centre controls the rate and work of breathing in response to pH and arterial carbon dioxide tension. Obese individuals tend to exhibit increased neural drive, in order to increase minute ventilation and overcome the increased load on the respiratory system [20, 23, 43, 117]. This is often associated with an increased perception of breathlessness [114]. With increasing BMI, there is an increased risk of being unable to raise respiratory drive to compensate for the added load [118, 119]. Without this compensatory mechanism, increasing respiratory load will result in alveolar hypoventilation and consequent hypercapnic respiratory failure. Obese individuals who suffer from daytime hypercapnia in the absence of other causes of hypercapnia are considered to have OHS [5].

OSA

OSA is a relatively common condition associated with recurrent apnoeas during sleep caused by intermittent closure of the upper airway. Obesity has a very close relationship with OSA; 60–70% of OSA patients are obese [120, 121]. Further, an increase in BMI appears to increase the risk of developing OSA. A 10% weight gain results in a six-fold increase in the likelihood of developing OSA [122]. Obesity appears to contribute to OSA by two primary mechanisms:

1) the deposition of adipose tissue on the anterior neck results in a physical obstruction of an already floppy airway during sleep;

2) as described earlier, obese individuals breathe at reduced lung volumes, and this reduces airway calibre. Reduced airway calibre results in an increased likelihood of airway collapse during sleep [123].

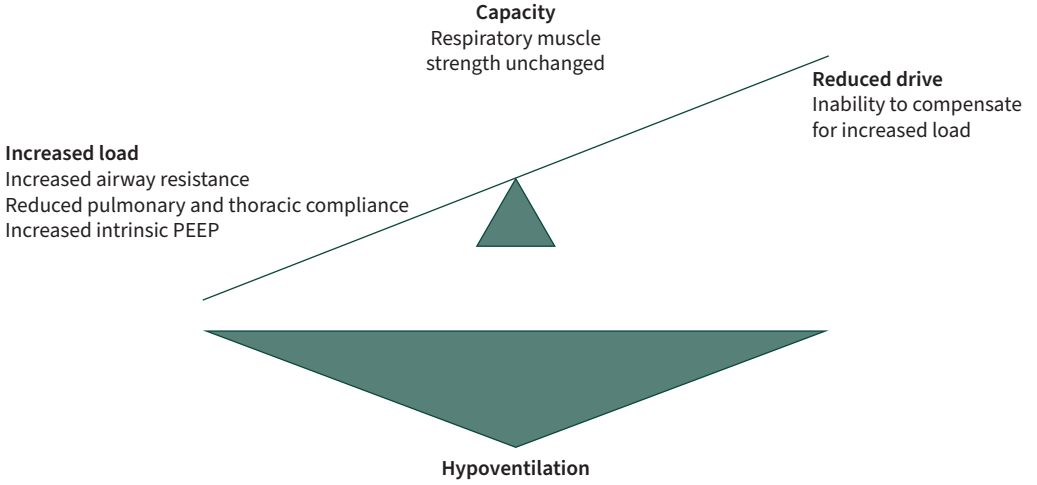

FIGURE 2 The effect of pathophysiological changes of obesity on load–capacity–drive and their contribution to the development of hypoventilation. PEEP: positive end-expiratory pressure.

In addition, poor sleep as a consequence of OSA may contribute to increasing BMI, which in turn worsens the degree of OSA. Poor sleep is associated with reduced serum leptin, which is an appetite suppressant [124]. Reducing serum leptin may increase appetite resulting in an increase in oral intake and therefore weight gain [125]. Finally, weight loss appears to improve the symptoms and severity of OSA [126, 127], further cementing the relationship between weight gain and the development of OSA.

OHS

Individuals with OHS are categorised into those with associated OSA (90%) and those without (10%) [128–130]. Lone OHS is caused by the inability to compensate for the increased load on the respiratory system, resulting in alveolar hypoventilation. In patients with OSA, intermittent ceased ventilation, continued metabolic production of carbon dioxide (CO_2) and increased work of breathing against an occluded airway can result in hypercapnia. Ordinarily, this is compensated for by an increase in alveolar ventilation [131]. In patients with superimposed OHS, the time period between apnoeas tends to be shorter [130], resulting in inadequate CO_2 clearance. This compounds the effects of the changes to the pulmonary mechanics already described, resulting in alveolar hypoventilation and hypercapnia. Hypercapnia during sleep effects an increase in bicarbonate to buffer the CO_2. As this is a slow process, raised serum bicarbonate persists during wakefulness, blunting the ventilatory response to CO_2 in subsequent sleep, making hypoventilation worse and exacerbating hypercapnia [132]. This will eventually lead to daytime hypercapnia.

Weight loss

The impact of weight loss, whether by controlled diet or bariatric surgery, on respiratory physiology in both eucapnic and hypercapnic individuals has been investigated extensively, but mostly in small observational studies. The data is convincing on the positive impact of weight loss on ERV [26, 29, 133–137], TLC [29, 133, 135, 138–140], FRC [29, 135, 138, 140, 141] and FVC [135, 138–140, 142–144]. A modest increase in respiratory muscle strength [29] has been reported, albeit from normal strength at baseline [141], with more convincing data to suggest an increase in respiratory muscle endurance [29, 138, 141, 145]. In eucapnic obese individuals, neural respiratory drive was reduced [146], while in hypercapnic obese individuals, neural drive was increased [145]. The positive impact of all of these physiological changes is illustrated by the clear reduction in hypercapnia observed after weight loss [147].

Summary

Obesity is a significant contributor to respiratory morbidity. Increasing BMI has deleterious effects on static and dynamic pulmonary volumes and causes airway flow limitation and increased airway hyperresponsiveness. Obesity increases the risk of pulmonary hypertension, pulmonary embolism, respiratory tract infections and subsequent hypoxic respiratory failure and ventilatory failure. The core mechanisms of how obesity causes this broad spectrum of respiratory complications include the addition of the physical load of adipose tissue onto the respiratory system and the systemic inflammatory state that it induces. Obesity has a close relationship with OSA and OHS; it is both causative and adds complexity to their disease progression and management. Weight loss is an important therapeutic strategy to ameliorate and resolve these deleterious effects. As the prevalence of obesity increases, a core understanding of its impact on the respiratory system will become increasingly relevant to all healthcare professionals.

Key points

- The prevalence of obesity, and therefore obesity-related respiratory complications, is increasing and deserves close consideration by all healthcare professionals.
- The effects of obesity on the respiratory system can be explained by the physical load that additional central adipose tissue has on the system, and a systemic inflammatory response that is induced with increased BMI.
- Obesity causes reduced lung volumes and airway calibre, and increased airway hyperresponsiveness.
- Obesity is a risk factor for, and exacerbates, respiratory tract infections, pulmonary vascular disease and ventilatory failure.
- Weight loss is a key treatment modality for improving respiratory function in patients with raised BMI.

Self-evaluation questions

1. A decrease in which of the following parameters is an early sign of respiratory compromise due to obesity?
    a) Total lung capacity
    b) Respiratory muscle strength
    c) Forced vital capacity
    d) Expiratory reserve volume

2. Which of the following biomarkers tends to be reduced in obese individuals?
    a) Cytokines
    b) Leptin
    c) Adiponectin
    d) Tumour necrosis factor-α
3. Obesity is an independent risk factor for which of the following conditions? Select all that apply.
    a) Lung cancer
    b) Pulmonary embolism
    c) Idiopathic pulmonary fibrosis
    d) Acute respiratory distress syndrome
4. In obese patients suffering from ventilatory failure, neural respiratory drive is:
    a) Increased
    b) Decreased
    c) Unchanged

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Suggested answers

1. d.
2. c.
3. b and d.
4. b.