Mechanical Ventilation in the Critically Ill Obese Patient

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Preface

There is no doubt that obesity has become one of the leading public health threats worldwide. The number of obese subjects has doubled during the last 25 years to reach more than 600 million subjects in 2015. Considering the 100 million obese children in the world, obesity's future is assured at least for the next generation. Of course, the continuously increasing incidence of the disease is problematic, but the new alarming phenomenon is the explosion of the cases of massively obese individuals. Indeed, the higher the severity of obesity according to body mass index, the higher the incidence of obesity-associated cardio-respiratory disorders and metabolic diseases. Obesity-induced chronic respiratory failure—commonly referred to as obesity hypoventilation syndrome—is encountered in more than half of the superobese patients with a BMI exceeding 50 $kg \cdot m^{-2}$. The management of these patients in the emergency setting is often challenging and raises specific problems that must be addressed and overcome at the bedside in a short time. At the interface between multiple health specialties, the obese patient usually requires a time-consuming multidisciplinary approach involving different stakeholders in respiratory care, cardiovascular diseases, endocrinology, surgery, anesthesiology, and also a necessary implication of the nursing staff. This book is intended to highlight the critically ill obese patient's specificities that must be taken into account when mechanical ventilation is part of the therapeutic management of such a patient. Given the singularity of the massively obese critically ill patient, it can be assumed that an individualizing care approach is particularly adapted for this topic. Good knowledge of the respiratory physiology and cardio-respiratory interactions appears to be an essential prerequisite to the management of a critically ill obese patient, especially when oxygenation and mechanical ventilation are needed. The first part of the book is devoted to delivering insight into the basic understanding of the physiological characteristics of the respiratory system of the obese patient and their implications for mechanical ventilation. The second part deals with the comorbidities of the obese patient and the causes of acute respiratory failure that can impact on the outcome. The third part of the book includes chapters about preoxygenation, positioning, recruitment strategy, sedation and analgesia during invasive mechanical ventilation, and its associated complications. Another part is about noninvasive ventilation and the promising technique of high-flow oxygen via nasal cannula, which both have the potential to avoid the resort to invasive mechanical ventilation in many situations. Finally, nutritional support and outcome after mechanical ventilation are two main issues that are developed in the last part. We are convinced that this book provides a useful didactic tool for an everyday practice of critical care medicine in obese patients with respiratory failure.

Both editors are very grateful to all authors for their valuable contribution to the book. We are deeply aware of the time they spent in writing the chapters, making it possible to share their knowledge and expertise with the readers. We greatly appreciate having so many internationally recognized experts in the field of obesity and mechanical ventilation who accepted to participate in the writing of this book.

Lens, France Malcolm Lemyze, M.D.
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Abbreviations

ABG	Arterial blood gas
AECOPD	Acute exacerbation of chronic obstructive pulmonary disease
AHI	Apnea-hypopnea index
AHRF	Acute hypercapnic respiratory failure
APACHE II	Acute physiology and chronic health evaluation II
ARF	Acute respiratory failure
ASPEN	American Society for Parenteral and Enteral Nutrition
ASV	Adaptive servoventilation
AVAPS	Average volume-assured pressure support
BMI	Body mass index
BNP	Brain natriuretic peptide
BPAP	Bi-level positive airway pressure
bpm	Breath per minute
CF	Cystic fibrosis
CHF	Congestive heart failure
CI	Confidence interval
CKD	Chronic kidney disease
CO_2	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CRF	Chronic respiratory failure
CSA	Central sleep apnea
CVEs	Cardiovascular events
DLCO	Carbon monoxide diffusion capacity
ECG	Electrocardiogram
EN	Enteral nutrition
EPAP	Expiratory positive airway pressure
ERV	Expiratory reserve volume
ETO_2	End-tidal oxygen concentration
FAO_2	Fraction of alveolar oxygen
FEO_2	Fraction of expired oxygen
FEV_1	Forced expiratory volume in 1 s
FFM	Full face mask
FiO_2	Fraction of inspired oxygen

FRC	Functional residual capacity
FVC	Forced vital capacity
HDU	High dependency unit
HF	Heart failure
HFNC	High-flow nasal cannulae
HFpEF	Heart failure with preserved ejection fraction
HFrEF	Heart failure with reduced ejection fraction
hsCRP	High-sensitivity C-reactive protein
IC	Indirect calorimetry
ICU	Intensive care unit
IMV	Invasive mechanical ventilation
IPAP	Inspiratory positive airway pressure
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
MV	Mechanical ventilation
NIPPV	Noninvasive positive pressure ventilation
NIV	Noninvasive ventilation
NMD	Neuromuscular diseases
NPPV	Noninvasive positive pressure ventilation
OHS	Obesity hypoventilation syndrome
OR	Operating room
OSA	Obstructive sleep apnea
$PaCO_2$	Arterial partial pressure of carbon dioxide
PACU	Postanesthesia care unit
PAD	Peripheral artery disease
PaO_2	Arterial partial pressure of oxygen
PAP	Positive airway pressure
PE	Pulmonary embolism
PEEP	Positive end-expiratory pressure
PN	Parenteral nutrition
PSV	Pressure support ventilation
RCT	Randomized controlled trials
RM	Recruitment maneuver
RMs	Recruitment maneuvers
RR	Risk ratio
RV	Residual volume
SAP	Safe apnea period
SCCM	Society of Critical Care Medicine
SpO_2	Peripheral oxygen saturation
SRBD	Sleep-related breathing disorders
TLC	Total lung capacity
TVB	Tidal volume breathing
VC	Vital capacity
VO2max	Maximal oxygen consumption
Vt	Tidal volume
VtPS	Volume-targeted pressure support

Part I

Effects of Obesity on Respiratory Physiology

Control of Ventilation in Obesity

1

Nikolaos Markou, Heleni Stefanatou, and Maria Kanakaki

1.1 Introduction

The literature on the control of ventilation in obesity suggests a fundamental dichotomy: eucapnic subjects tend to maintain normal or augmented chemosensitivity, whereas hypercapnic subjects have a blunted chemosensitivity [1, 2]. Yet existing studies often pose methodological problems. Thus, they do not always take into account other factors which may also affect chemical control of breathing like gender or the coexistence of sleep-disordered breathing (SDB), which is very common in obese subjects. Furthermore, although most of these studies utilize rebreathing assessments of chemoreflex sensitivity, they do not always use the same rebreathing protocols. Additionally the output of the ventilatory center is not uniformly evaluated: some investigators measure minute ventilation (VE) alterations, while others evaluate neural drive more directly, in terms of alterations in mouth occlusion pressure (P0,1) or in diaphragmatic electromyogram activity (EMGdi). Finally, practically all studies deal with chemical control of breathing only at the awake state, with very few data on chemosensitivity during sleep.

In the rest of the chapter, we shall initially present data on the neural control of breathing at rest. Then we shall discuss data on the hypercapnic ventilatory response (HCVR) and the hypoxic ventilatory response (HOVR) in eucapnic and in hypercapnic obesity (obesity hypoventilation syndrome—OHS), with emphasis on studies accounting for the coexistence of obstructive sleep apnea (OSA). Finally we shall discuss the cause of alterations in the chemical control of breathing in OHS and the possible consequences of these alterations.

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1.2 Respiratory Neural Drive at Rest in Obesity

In otherwise healthy eucapnic obese adults, measurements of P0,1 and EMGdi suggest that respiratory neural drive at rest is increased compared to nonobese controls or to reference values [3–8]. Even in hypercapnic obesity, some limited data suggest that P0,1 at rest is not reduced and may even be increased relative to normal reference values [9, 10]. In eucapnic obesity, respiratory drive at rest seems to be closely related to indices of body weight [4, 7]. In a large cohort of 245 obese subjects with no obstructive or restrictive syndrome or neuromuscular impairment, P0,1 at rest was independently associated with severity of obesity (defined as percentage of body fat) and inversely associated with minimum oxygen saturation during sleep, total lung capacity, partial pressure of end-tidal CO_2, and leptin levels [6].

In normal subjects, external elastic loading is known to augment neural drive by activating neural load-compensating mechanisms [11–13]. The increase of neural drive at rest in obesity seems to represent a similar compensatory mechanism in order to maintain an adequate minute ventilation in the face of increased mechanical loading due to weight gain [1, 2, 14]. From another viewpoint, an increased EMGdi in obesity might also indicate a reduced ventilatory reserve, that is, an inability in obese subjects to adequately augment their neural drive when needed, which might predispose to hypoventilation and hypercapnia in situations of increased work of breathing [7].

1.3 Chemical Control of Breathing in Eucapnic Obesity

In normal volunteers, the application of external elastic loading results in compensatory increases of neural drive responses to CO_2 rebreathing and to exercise. The range of these neural adjustments may vary with load size and type of load—e.g., loading of the rib cage compartment might elicit more intense responses, than loading of the abdominal compartment [11–13, 15]. Similar compensatory mechanisms have been reported to be operative in eucapnic obesity as well [2, 16], and they probably contribute to the increased sensation of dyspnea often encountered in these subjects [17]. In spite of this neural adjustment, in obesity the final output in terms of minute ventilation response may remain unaffected or even decreased. Thus, Lopata et al. report that obese eucapnic subjects without OSA had an increased response of respiratory neural drive (evaluated as EMGdi) to CO_2 rebreathing compared with normal controls, whereas the VE response was decreased. They conclude that compensatory adjustments in respiratory neural drive are not always adequate to completely overcome the increased mechanical load in obesity [3]. Eucapnic subjects with less preserved HCVR may be more prone to ventilatory compromise: Sampson et al. have observed an impairment of the VE response to CO_2 rebreathing in eucapnic massively obese patients who had previously suffered an episode of transient hypercapnia at the time of a respiratory insult, compared with carefully matched controls who had never been hypercapnic [4].

Yet, perhaps because of methodological differences, not all studies on chemosensitivity in eucapnic obesity come to the same conclusions. A shortcoming of many of these studies is that they do not account for the frequent coexistence of obstructive sleep apnea (OSA) in obesity. Yet, OSA has also been associated with increased chemosensitivity [18–22]—although the literature again is not unanimous [23–27], with an increased gain of the central controller of breathing implicated in OSA pathogenesis [28–30].

In studies addressing the question of chemosensitivity in eucapnic obesity without taking into account the possible presence of sleep-disordered breathing (SDB), the HCVR has been reported to be normal [5, 31] or increased [4, 32, 33] or even gender-depended, with normal responses for males and increased responses for females [34].

An association has also been suggested between an increased HCVR in obesity and the percentage and distribution of body fat [32]. The HOVR has similarly been reported as normal [31] or increased [5, 32–34]. Before and after studies with weight loss after surgical treatment of obesity conclude that eucapnic obesity is associated with an augmented HCVR [17, 35].

Methodological problems are encountered in some of these studies, like a great imbalance as regards age and gender between obese subjects and normal controls [5] or the measurement of HCVR without a hyperoxic background mixture, which may have contributed to the finding of an augmented HCVR in another study [33].

1.4 Chemical Control of Breathing in Eucapnic Obesity Without OSA

Studies of eucapnic obese subjects in whom OSA had been rigorously excluded with polysomnography also provide somewhat conflicting data.

Thus, Lopata et al. [3] report a lower VE response to CO_2 rebreathing compared with normal controls in spite of a normal or increased response in terms of mouth occlusion pressure and EMGdi. According to Narkiewicz et al., eucapnic obese subjects without OSA had a higher HCVR compared to normal controls matched for age and sex but a similar HOVR [36]. Buyse et al. on the other hand, compared the chemosensitivity of 138 healthy obese subjects without OSA (21 men and 117 women) of whom more than half had morbid obesity ($BMI > 40$), with reference values from their laboratory, and concluded that in obesity, chemosensitivity is affected by gender differences [37]. Obese women had an increased response of VE normalized for vital capacity and of P0,1 to hyperoxic hypercapnia and an even more increased response to hypoxia. HCVR and HOVR slopes correlated with BMI. On the contrary, obese men did not have an altered chemosensitivity. Women deemed to be menopausal in this study had lower HCVR and HOVR than women deemed to be premenopausal. Estrogen and progestin are known to augment respiratory drive [38], and an augmented chemosensitivity in obese women may be associated with increased estrogen production from fat tissue in the premenopausal period [37].

An interplay between weight increase and sex on chemosensitivity is further corroborated by the findings of Sin DD et al. in a large cohort of 219 patients (many of them obese) who underwent polysomnography under suspicion for OSA and in whom HCVR independently correlated with BMI in women and with age in men [39].

Finally, in a study of obese adolescents, it was found that after exclusion of OSA, obese subjects in the awake state had a higher VE response to CO_2 than age-matched lean subjects but that this difference did not persist during sleep [40].

1.5 Chemical Control of Breathing in Eucapnic Obesity with OSA

Coexistence of OSA seems to blunt neural drive responses and to diminish the VE response to CO_2 in the study of Lopata et al. [3]. A blunting effect of coexisting OSA on HCVR has also been confirmed by Gold et al. in eucapnic obese males, while HOVR was not affected by the coexistence of OSA [41].

On the other hand, in a case-control comparison of 21 men and 34 women with obesity and OSA matched 1:1 with obese subjects without OSA, on the basis of age, height, and BMI, coexistence of OSA resulted in a higher VE/VC and P0,1 response to hypoxia (but not hypercapnia) in women, while it did not affect chemosensitivity in obese men [37].

Finally, in obese adolescents, coexistence of OSA did not affect the HCVR in the awake state. Nevertheless, during sleep, obese subjects with OSA had blunted ventilatory responses to CO_2 administration compared both to normal controls and to obese subjects without OSA, although the neural drive response was not evaluated [40]. The blunted response during sleep might conceivably result in prolonged respiratory events in these subjects (promoting nocturnal hypercapnia), while the enhanced response during wakefulness might lead to an inappropriately high ventilatory response upon arousal from apnea with concomitant ventilatory instability because of fluctuations in $PaCO_2$ [40].

1.6 Chemical Control of Breathing in Hypercapnic Obesity (Obesity Hypoventilation Syndrome)

The simplest evidence for a defective central respiratory drive in OHS is that most of these patients are able to voluntarily hyperventilate to eucapnia, implying that impairments in respiratory system mechanics alone do not explain the hypoventilation [42].

This impression is further confirmed by several small studies that report a blunted HCVR in OHS compared to normal weight subjects [3, 43] or subjects with eucapnic obesity [44], at least in the absence of OSA [3]. Interestingly, Lopata et al. report that in eucapnic obesity coexisting with OSA, the HCVR is similarly blunted [3], but this finding has not been confirmed by Garay et al., who report a substantially higher HCVR in eucapnic obesity compared with OHS [23].

Data on HOVR in OHS are fewer, but it seems that HOVR is also decreased compared with lean controls [43]. A trend for lower HOVR has also been observed in hypercapnic compared with eucapnic obese subjects with OSA [21], while in another study of OSA patients not necessarily obese, this difference in HOVR between hypercapnic and eucapnic subjects was significant [45].

This blunted chemosensitivity in OHS is not likely to be associated with genetic influences: HCVR and HOVR were similar between first-degree relatives of patients with OHS and controls matched for age and weight [46]. It should be noted that neither the decreased drive observed in hypercapnic OSA can be attributed to genetic influences [45].

The demonstration of increases in HCVR and HOVR as early as 2 weeks from initiation of treatment of OHS with continuous positive airway pressure (CPAP) or noninvasive positive pressure ventilation (NIPPV) [10, 46–48] constitutes additional evidence that blunting of chemosensitivity does not preexist but is a secondary effect of the syndrome, probably mediated by hypercapnia, which is similarly reversed with CPAP or NIPPV treatment. This improvement in HCVR is probably confined to subjects with substantially blunted chemosensitivity, in whom an increase of 47% has been reported after NIPPV [49].

Blunted HCVR has also been observed in patients with hypercapnic OSA (many of whom are obese and suffering in fact from OHS) compared with normal controls [19, 23] or with eucapnic OSA patients [45, 47, 48] and is similarly reversed—together with hypercapnia—by effective OSA treatment.

A weak but significant inverse association between HCVR and $PaCO_2$ has been demonstrated in a large cohort of 219 patients who underwent polysomnography under suspicion of OSA, although only a few of them had severe obesity or hypercapnia [40].

Development of nocturnal hypercapnia is believed to be a critical factor toward the establishment of a blunted HCVR in obesity as well as in isolated OSA. Notably, the study of Chouri-Pontarollo N et al. confirms that in patients with OHS, the HCVR correlates moderately with the amount of nocturnal hypoventilation during REM sleep [49].

Obesity may promote nighttime hypercapnia by increasing metabolic rate and CO_2 production [50] while at the same time imposing increases in elastance and resistance of the respiratory system and perhaps impairing respiratory muscle function [1, 2]. During sleep these effects may promote nocturnal alveolar hypoventilation, more pronounced during REM sleep. Additionally, obesity often compromises upper airway patency causing OSA, which is in fact present in 90% of patients with OHS [1]. Most individuals with OSA can sufficiently hyperventilate after apneas to eliminate the accumulated CO_2 and therefore can maintain overall eucapnia during sleep [51–53]. Yet in obesity, this interapnea elimination of CO_2 can be impaired due to mass loading and reduced FRC, or because the ventilatory response to accumulated CO_2 during sleep may be blunted [41, 52].

Once nocturnal hypercapnia develops, kidneys retain at night small amounts of bicarbonate to buffer the decrease in pH. This increase in serum bicarbonate is not always corrected before the next sleep period as the time constant of bicarbonate excretion is longer than that of CO_2. The result will be a net gain of bicarbonate which will cause a secondary depression of central respiratory drive [53–55] and will promote further CO_2 accumulation at night [51].

Thus a vicious circle begins, with more severe exposure to hypoxemia and hypercapnia and further attenuation of central drive, with a decreased HCVR during daytime and maintenance of the state of hypoventilation during the day as well [1, 2, 56].

A blunted HOVR may also contribute to daytime hypercapnia in obesity. Blunted HOVR may be caused by sleep desaturation in the settings of OSA or of alveolar hypoventilation during sleep: this nocturnal hypoxemia may lead to depression of HOVR, in way similar to that seen in high-altitude hypoxia [57]. Sustained hypoxia may also impair the arousal response to external resistive loading, and this may worsen sleep-associated airway occlusion [58]. Nocturnal hypoxemia in obese patients may thus further impair the compensatory hyperventilation between apneic events, contributing to nocturnal rise in CO_2 [1].

There are some indirect indications of a poor correlation of central drive at the awake state with central drive during sleep [40, 51]. This might explain why some patients with OHS may still have normal HCVR. Regrettably data on respiratory drive during sleep are scarce in obesity [40] and nonexistent in OHS, and it remains unclear if what matters more is respiratory drive during wakefulness or during sleep.

In addition to its contribution to the establishment and maintenance of OHS, an impaired chemosensitivity may be responsible for the worsening of hypercapnic acidosis observed in a randomized crossover study of patients with OHS after breathing an oxygen mixture with an FiO2 0,5 [59]. It has also been found that OHS patients with the lowest HCVR responses had a greater propensity for increased objective sleepiness, while they also demonstrated significant improvement in objective daytime sleepiness with NIPPV [49].

Respiratory stimulants (medroxyprogesterone, acetazolamide) have occasionally been used in the past in OHS in order to reverse CO_2 retention [60–63]. Yet experience remains limited, and such drugs do not currently constitute a part of the mainstream approach in OHS, which remains based on application of CPAP or NIPPV during sleep.

1.7 The Role of Leptin in Alterations of Chemosensitivity in Obesity

Neurohormonal changes may also be implicated in alterations of chemosensitivity in obesity. In this context, the interplay between obesity, leptin, and ventilatory drive seems to play an important although not fully clarified role.

Leptin is a satiety hormone produced by adipocytes that, in addition to reducing appetite and weight via receptors in the hypothalamus, increases ventilation in animal models by stimulating central respiratory centers after penetrating the blood-brain barrier [64].

Leptin levels rise in proportion to body fat and obese subjects usually have high leptin levels, while hypoxia (in the context of OSA and OHS) also seems to exert an influence on leptin production [1, 2].

The association of leptin with chemosensitivity in humans is not absolutely clear. In mostly nonobese eucapnic OSA patients, both HCVR and leptin levels were higher than in matched healthy controls, and a significant correlation existed between HCVR and leptin levels [20]. Yet hypercapnic OSA patients, in spite of a significantly lower HCVR, had leptin levels similar to those found in eucapnic OSA [20].

High serum leptin concentrations have been associated with the presence of hypercapnia in obesity [65] and OSA [66]. In obese subjects leptin was a better predictor of hypercapnia than the degree of adiposity [65], while in OSA leptin was the only independent predictor of hypercapnia [66]. Furthermore, serum leptin levels are inversely associated with respiratory drive (P0,1) at rest in obese subjects [6].

In order to explain the paradox of a depressed ventilatory drive and hypercapnia in the presence of high leptin levels, it has been suggested that in some obese subjects, central resistance to ventilatory stimulatory effects of leptin may develop [2]. Leptin has to penetrate the blood-brain barrier in order to affect the respiratory center. The finding that obese individuals have leptin levels three times higher compared to lean controls while their leptin CSF/serum ratio is fourfold lower [67] suggests that such resistance may be the result of reduced leptin CSF penetration [1]. The observation that NIPPV use significantly reduces leptin levels [68] has led to the hypothesis that the improvement noted with positive pressure treatment in the central chemosensitivity of OHS patients [10, 47, 48] may be mediated through a reduced leptin resistance.

Yet the hypothesis of leptin resistance is not uniformly supported by all studies. Redolfi et al. [69] found that leptin levels were considerably elevated in OHS patients compared with reference values but remained much lower than those observed in matched obese eucapnic controls. Several months after initiation of NIPPV, $PaCO_2$ was normalized in these patients, HCVR was increased by 100%, and leptin levels were increased by 50%, although they still remained significantly lower than in eucapnic obesity. More study is therefore needed in order to clarify the exact role of leptin in the control of ventilation in obesity.

Conclusion

Eucapnic obesity may be associated with an augmented chemosensitivity which represents a compensatory response to mass loading of the respiratory system. Yet, a small subset of obese subjects who develop daytime hypercapnia demonstrates a blunted respiratory drive. Although secondary to nocturnal hypoventilation and the subsequent development of daytime hypercapnia, this blunted chemosensitivity contributes to the establishment and maintenance of daytime hypercapnia.

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Obesity, Respiratory Mechanics and Its Impact on the Work of Breathing, Neural Respiratory Drive, Gas Exchange and the Development of Sleep-Disordered Breathing

2

Culadeeban Ratneswaran, Patrick Murphy, Nicholas Hart, and Joerg Steier

2.1 Respiratory Mechanics and Obesity

2.1.1 Background

Obesity reduces life expectancy and increases morbidity and mortality [1, 2]. It causes serious health risks including diabetes, cardiovascular disease and cancer [3]. Despite this, the worldwide prevalence of obesity has doubled since the 1980s [4]. Although there is extensive knowledge about the cardiovascular and metabolic risks of obesity, respiratory comorbidities of obesity are less well understood.

The degree of obesity can be measured using the body mass index (BMI), often used due to its ease of use and correlation with adverse health outcomes. BMI, however, is not a good measure of body fat distribution. There is ongoing discussion whether indices of fat distribution may be better predictors of morbidity [5] and whether they are of greater relevance to the development of sleep-disordered breathing, but this has not been born out by prospective studies [6, 7].

2.1.2 Non-communicable Disease

According to the World Health Organization (WHO), non-communicable disease (NCD) contributes to the majority of mortality worldwide. NCD is commonly

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attributable to one of the following four factors: alcohol, tobacco, unhealthy diet and physical inactivity [8]. The trend to lead a more sedentary lifestyle with reduced metabolic needs, while energy intake increases, results in a general rise in body weight with age [9, 10]. The population most at risk of obesity-related ill health therefore tends to be middle-aged.

2.1.3 The Respiratory Muscle Pump

Effects of obesity can impact on the respiratory mechanics, as well as on neural respiratory drive. The respiratory muscle pump sums up all muscle groups that contribute to ventilation; it contains the diaphragm, chest wall muscles, neck and shoulder muscles and the abdominal muscles. Different parts of the respiratory muscle pump are active during inspiration, expiration, awake at rest, during exercise or while asleep. The most important muscle for inspiration is the diaphragm, which separates the thoracic from the abdominal cavity. It delivers the majority of the work of breathing in healthy individuals [11]. Due to its contribution to intrathoracic and intra-abdominal pressure swings while breathing, it impacts on various effects associated with ventilation. The diaphragm is made of three parts, the costal part, the crural part and a central tendon (Fig. 2.1).

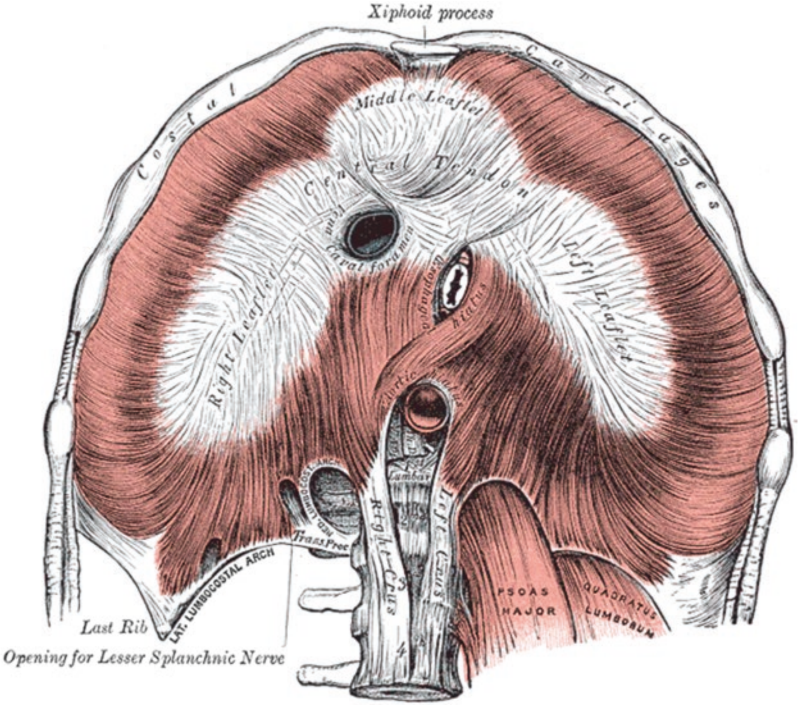

Fig. 2.1 The human diaphragm (reproduced from Gray's Anatomy, 20th US edition, originally published in 1918)

Contraction of the diaphragm results in caudal movement of the dome-like structure in addition to expansion of the ribcage which is supported by other inspiratory muscle groups like the parasternal intercostal muscles, the scalenes and accessory muscle groups. The resulting negative intrathoracic pressure results in inspiratory airflow. In expiration, the diaphragm is largely relaxed and positive intra-abdominal pressures will push it back up into the thoracic cavity. Elevated intra-abdominal pressures in obesity significantly impact on the function of the diaphragm by increasing the load during inspiration and expiration (Fig. 2.2).

2.1.4 Gas Exchange in Obesity

Gas exchange is typically measured using the diffusing capacity of the lungs for carbon monoxide (DLCO). The DLCO is relatively well preserved in mild obesity [12–16], but the pattern in severe obesity is less well understood [16, 17]. However, intra-abdominal pressures in obesity impact on the diaphragm and the intrathoracic

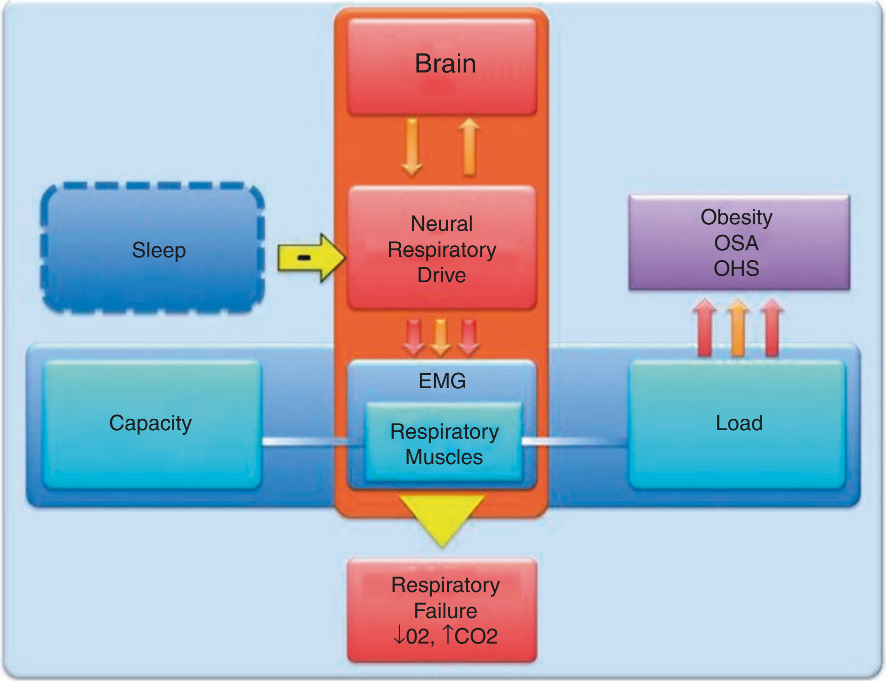

Fig. 2.2 The load-capacity ratio of the respiratory muscle pump, simplified scheme. Multiple factors in obesity contribute to an increased load that leads to an elevated neural respiratory drive to recruit from the capacity of the respiratory muscle pump. If the elevated level of neural drive cannot be sustained (e.g., fatigue) or is influenced by other factors (e.g., sleep, drugs), an imbalance between load and capacity will develop and cause symptoms and respiratory failure when awake and sleep-disordered breathing when asleep

cavity, particularly in supine posture, and contribute to a ventilation-perfusion mismatch in the posterobasal compartments of the lung, and this mismatch contributes to the effect of alveolar hypoventilation.

2.1.5 Lung Volumes in Obesity

Lung volumes in obesity are either relatively normal or slightly reduced, indicating a restrictive ventilatory defect (Fig. 2.3). The forced expiratory volume in 1 s (FEV_1) is lower in obesity compared to nonobese subjects [19, 20], suggesting that in addition to an increased elastic load, obese subjects must overcome an increased airway resistance which is a consequence of the reduction in operational lung volumes (Figs. 2.4 and 2.5). The expiratory reserve volume (ERV) is low in morbidly obese subjects, and the functional residual capacity (FRC) is close to the residual volume (Fig. 2.3).

2.1.6 Respiratory Mechanics and Changes in Obesity

During normal inspiration, the diaphragm descends and the decrease in intrathoracic pressures initiates inspiratory airflow; in parallel, the diaphragm descent draws blood into the vena cava and the right side of the heart. During expiration, an increase in intrathoracic pressures leads to air being expelled from the lungs. While inspiration is generally an active process, expiration follows passively due to the elastic recoil of the chest compartment and positive intra-abdominal pressures, and, unless enforced, expiration does not require significant muscle activity in the normal subject at rest.

In obesity, many factors related to the respiratory system change. Intra-abdominal pressures are high, particularly with visceral obesity, and this causes an increased preload on the diaphragm movement, specifically in supine posture. The abdominal pressures are transmitted to the thoracic cavity where they result in reduced transpulmonary pressures [18]. Due to the reduced pressure gradient, it is more likely that obese subjects breathe close to the residual volume (RV) with the functional residual capacity (Fig. 2.2) which leads to increased airway resistance due to the closing volume of the small airways [21]. This effect increases the work of breathing due to a low compliance [22] (Figs. 2.4 and 2.5). In supine posture, the work of breathing increases further [18, 23, 24], the intra-abdominal pressure impacts directly on the diaphragm, and an intrinsic positive end-expiratory pressure (PEEPi) develops [24, 25]. Neural respiratory drive increases to recruit force, but it can be offset by inflating the chest with continuous positive airway pressure (CPAP; Fig. 2.6) [24]. However, without noninvasive support, patients with obesity are prone to develop a restrictive spirometry. With sleep onset, neural respiratory drive falls and the required minute ventilation is no longer maintained, which results in hypoventilation and the development of hypercapnia.

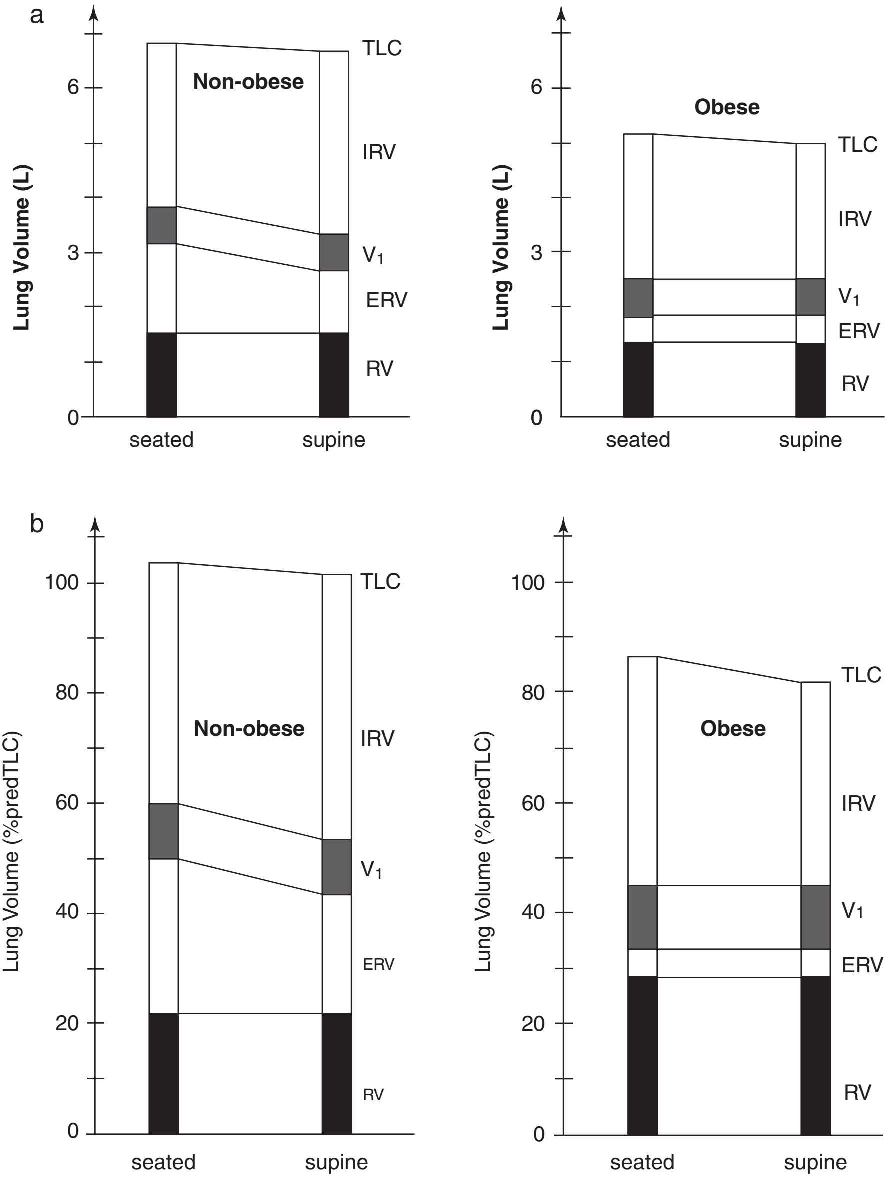

Fig. 2.3 Simplified schematic illustration of lung volumes seated and supine in normal and obese subjects, expressed as litres (*upper panel*) and per cent predicted TLC (*lower panel*). *TLC* total lung capacity, *IRV* inspiratory reserve volume, V_t tidal volume, *ERV* expiratory reserve volume, *RV* residual volume. With friendly permission from Thorax [18]

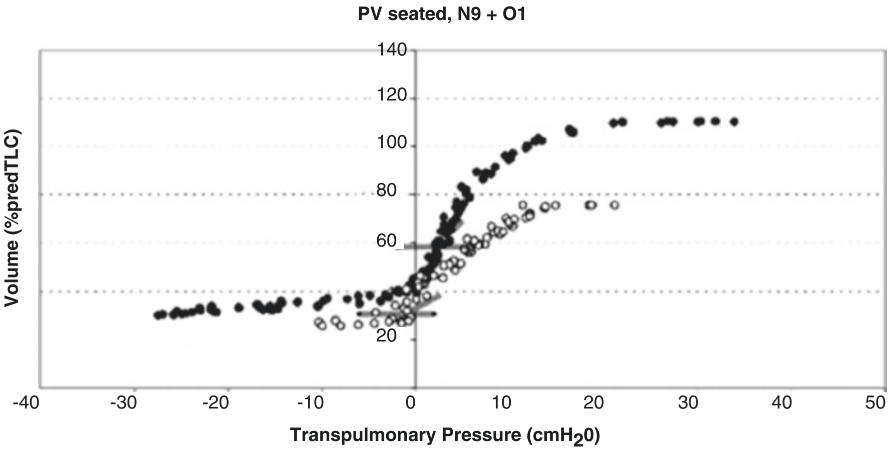

Fig. 2.4 Pressure–volume (PV) curves seated of a normal (N9, male, 66 years, 1.72 m, body mass index (BMI) 23.3 kg/m^2; filled circles) and matched obese (01, male, 60 years, 1.73 m, BMI 34.4 kg/m^2; open circles) subject. Functional residual capacity (FRC) levels and dynamic compliance are indicated by *bold grey bars*. The PV curve in the obese is restricted in lung volume and diminished in slope, the FRC is low. Despite the differences in the slope of the static PV curves, the dynamic compliance, illustrated by the *diagonal grey bars*, is not substantially different between the obese and normal subject. With friendly permission from Thorax [18]

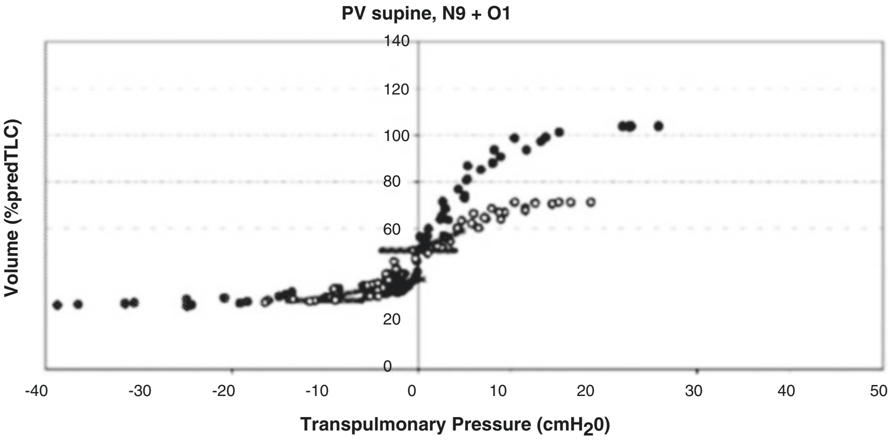

Fig. 2.5 Pressure–volume curves supine of a normal (N9, *filled circles*) and matched obese (01, *open circles*) subject. Compared with the seated posture, the slope of the curves is diminished, in the obese functional residual capacity approximates residual volume. Dynamic compliance is lower than when seated and more different between obese and normal subject. With friendly permission from Thorax [18]

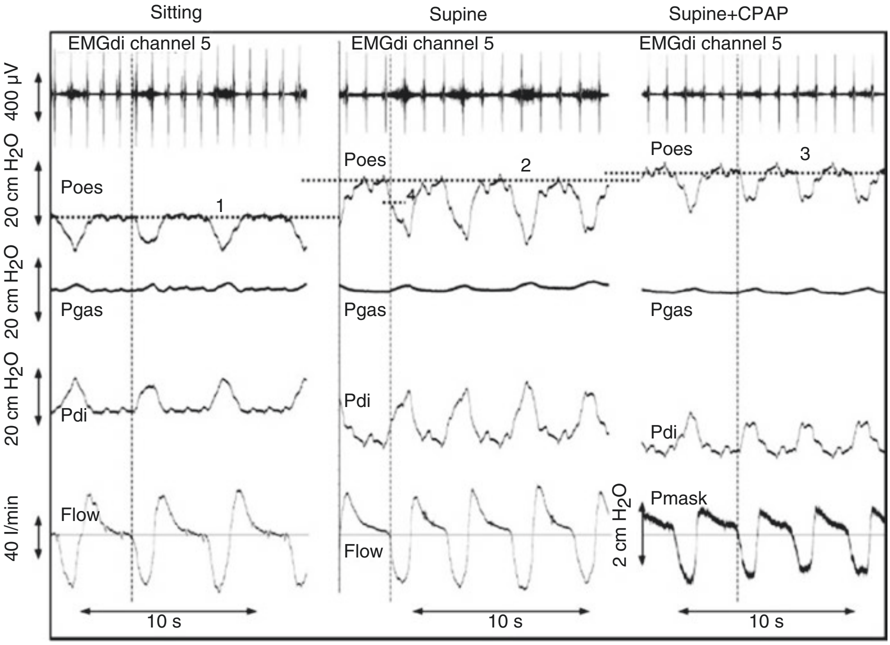

Fig. 2.6 Resting breathing in an obese subject (body mass index 42 kg/m^2, neck circumference 43 cm) when seated (*left*), supine without CPAP (*middle*) and with CPAP (*right*). The change in end-expiratory oesophageal baseline pressure is reflected by the *horizontal dotted lines* (nos 1–3). There is PEEPi of approximately 6 cm H_2O (*vertical lines* indicate the start of inspiratory flow, difference between *horizontal dotted lines* 2 and 4 = PEEPi). Zero flow is indicated by the *horizontal line*. The right panel shows the same patient supine breathing with CPAP of 6 cm H_2O (*full facemask*). Neural respiratory drive to the diaphragm increases when changing posture from sitting to supine and decreases with CPAP; PEEPi is offset with CPAP and pressure swings of Poes and Pdi are smaller. Note that on the lower right trace we do not measure flow but mask pressure because flow is predominantly inspiratory when receiving CPAP. The inspiratory deflection in mask pressure was chosen instead of flow to mark the beginning of inspiration (*vertical line*). *CPAP* continuous positive airway pressure, *EMGdi* electromyogram of the diagram (channel 5 records the biggest EMG signal; *Poes* oesophageal pressure, *Pgas* gastric pressure; *Pdi* transdiaphragmatic pressure (Pdi = Pgas − Poes); PEEPi, intrinsic positive end-expiratory pressure; EMGdi in μV, all pressures in cm H_2O, flow in l/min. With friendly permission from Thorax [24]

2.2 Sleep-Disordered Breathing

2.2.1 Fat Distribution

Sleep-disordered breathing relates to abnormal breathing when asleep; the most common types of abnormal breathing during sleep in obesity are obstructive sleep apnoea (OSA), obesity hypoventilation syndrome (OHS) and an overlap syndrome (OSA/OHS). Neck circumference is a predictor of OSA which suggests that upper