Obesity and ARDS

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Obesity prevalence continues to increase globally, with figures exceeding 30% of some populations. Patients who are obese experience alterations in baseline pulmonary mechanics, including air-flow obstruction, decreased lung volumes, and impaired gas exchange. These physiologic changes have implications in many diseases, including ARDS. The unique physiology of patients who are obese affects the presentation and pathophysiology of ARDS, and patients who are obese who have respiratory failure present specific management challenges. Although more study is forthcoming, ventilator strategies that focus on transpulmonary pressure as a measure of lung stress show promise in pilot studies. Given the increasing prevalence of obesity and the variable effects of obesity on respiratory mechanics and ARDS pathophysiology, we recommend an individualized approach to the management of the obese patient with ARDS. *CHEST 2012; 142(3):785–790*

Abbreviations: ALI = acute lung injury; FRC = functional residual capacity; OSA = obstructive sleep apnea; PEEP = positive end-expiratory pressure; TLC = total lung capacity; VC = vital capacity; $\dot{V}/\dot{Q}$ = ventilation/perfusion

The obesity pandemic continues, with rising prevalence reported throughout the world. In the United States, recent data show that more than two-thirds of US citizens are either obese or overweight (BMI > 25 kg/m²). Approximately 33% of adults in the United States are obese (BMI > 30 kg/m²), and in some areas of the country the prevalence of obesity reaches > 40%.¹ In Europe, obesity prevalence varies by country but ranges from 9% to 30%, and is steadily increasing.² All of these statistics emphasize the importance of obesity and related conditions in patient care. Even in a state of relative health, obesity has major effects on cardiopulmonary physiology. ARDS continues to be both prevalent and very morbid, with an estimated age-adjusted incidence of 86.2 per 100,000 patient years, and reported in-hospital mortality of nearly 40%.³ Data from the 2009 influenza A(H1N1) pandemic suggested that

patients who are obese represent a unique patient population in ARDS. Among patients with severe or fatal 2009 influenza A(H1N1), rates of severe and morbid obesity (BMI > 35 kg/m² and > 40 kg/m², respectively) were five to 15 times higher than the general population.^{4,5} This finding, with other data, suggests a potential link between ARDS and obesity, and at a minimum demonstrates that when critical illness is coincident with obesity, there are additional considerations for disease mechanism, management, and prognosis.⁶ Such inpatients are often challenging to manage due to issues including line placement, transportation, drug dosing, and imaging (Table 1).

CHANGES IN BASELINE PHYSIOLOGY

Even without the additional pathophysiology of ARDS, patients who are obese experience a number of changes in their physiology compared with lean control subjects. Some of the baseline alterations in respiratory mechanics of the patient who is obese include a decrease in total lung capacity (TLC), functional residual capacity (FRC), and vital capacity (VC) as well as increases in pleural pressure and upper and lower airway resistance.

The decreased TLC, FRC, and VC are due to an overall decrease in respiratory system compliance, which in turn is secondary to increased weight of the chest wall and increased abdominal pressure from

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Table 1—Effects and Complications of Obesity

Type	Chronic Effect	Acute Management Issues
Neurologic	Increased ICP, cerebrovascular disease, disordered breathing, anxiety, depression	Sedation, abnormal respiratory control
Cardiovascular	Ischemic heart disease hypertension,	Hemodynamic instability, monitoring problems, elevated filling pressures when measured relative to atmosphere
Pulmonary	OSA, obesity hypoventilation, atelectasis	Aspiration risk, complicated intubations, impaired ventilation and gas exchange
Body habitus	Chest wall restriction, limited mobility	Transport and positioning, procedural difficulties (vascular access, imaging)
GI/renal	Cholelithiasis, nonalcoholic steatosis, pancreatitis, glomerulosclerosis	Altered pharmacokinetics, malnutrition, abdominal compartment syndrome
Endocrine	T2DM, hyperlipidemia	Glucose disturbances

ICP = intracranial pressure; OSA = obstructive sleep apnea; T2DM = type 2 diabetes mellitus.

obesity (Fig 1). One key physiologic parameter in patients who are obese is the transpulmonary pressure, which is the distending pressure across the lung (ie, airway opening pressure minus pleural pressure) and which is distinguished from *trans*-chest wall pressure (the difference between pleural and atmospheric pressures).⁷ With the increased pleural pressure experienced in obesity, transpulmonary pressure becomes less positive (or more negative), that is, lung parenchyma experiences less distending (and more collapsing) pressure. Patients who are obese, therefore, have considerable atelectasis. Gravitational variations in pleural pressure likely allow some units to remain patent (eg, in nondependent lung) while others may be collapsed (eg, in dependent lung). Atelectasis in obesity results in impaired gas exchange and decreased lung compliance.⁸⁻¹¹

Some authors have questioned the occurrence of negative transpulmonary pressures in obesity (ie, pleural pressure in excess of pressure measured at the airway opening). Such pleural pressure elevations without complete lung collapse are possible, as commonly occurs during forced exhalation when pleural pressure is raised by expiratory muscle activity and airway opening pressure remains atmospheric. Other situations in which pleural pressure elevations may be sustained are conditions of expiratory flow limitation or airway closure, in which pleural pressure elevations (ie, pressure outside the major airways) lead to airway narrowing/collapse allowing alveolar pressures to exceed those at the airway opening. Thus, negative transpulmonary pressures are commonly seen clinically even if not directly measured. As described here, the resultant atelectasis is an important consideration in patients who are obese, even in the absence of additional lung pathology.

FEV₁ and FVC are reduced in proportion to each other in patients who are obese, but there is also evidence of small airways dysfunction in patients who are obese and, in some, expiratory flow limitation. This phenomenon can result in development of intrinsic

positive end-expiratory pressure (PEEP) at rest, and during exercise can cause air trapping and dynamic increase in end-expiratory lung volume.¹² Even in the absence of increased end-expiratory lung volume, alveolar pressure may be elevated at end-exhalation secondary to the increased intraabdominal pressure seen in obesity. These changes, combined with the intrinsic mechanical loading of inspiratory muscles in obesity, increase the work and oxygen cost of breathing both at rest and during exercise.¹³⁻¹⁵

A decrease in compliance and increase in resistance have been observed in sedated, paralyzed patients who are morbidly obese without underlying lung pathology.⁹ These mechanical influences have implications for the mechanics of ventilating a patient who is obese, particularly in the setting of ARDS or other lung pathology. Patients who are obese additionally often have arterial hypoxemia and an elevated alveolar to arterial oxygen (A-a) gradient. This

FIGURE 1. Components of lung volume. Patients who are obese have reduced lung volume components (TV, ERV, and RV), which results in lower VC, FRC, and TLC. ERV = expiratory reserve volume; FRC = functional reserve capacity; IRV = inspiratory reserve volume; RV = residual volume; TLC = total lung capacity; TV = tidal volume; VC = vital capacity.

finding is hypothesized to be due to a combination of atelectasis with shunting and ventilation/perfusion ($\dot{V}/\dot{Q}$) mismatch due to airway narrowing and variations in lung perfusion.

Obesity has many important effects on nonpulmonary physiology, including vascular physiology and endocrine function, and is accompanied by comorbidities that complicate critical illness in the patient who is obese (Table 1). These issues are complex—for example, measured intrathoracic vascular pressures are higher in patients who are obese, which reflects both issues of accurate measurement as well as actual physiologic changes—and are reviewed extensively elsewhere in the literature.¹⁶

OBESITY AS A RISK FACTOR FOR ACUTE LUNG INJURY

In addition to the changes in respiratory mechanics, patients who are obese experience chronic alterations in circulating inflammatory mediators derived from adipose tissue (collectively known as adipokines). Patients who are obese have increased circulating levels of cytokines (including tumor necrosis factor- α and IL-6), increased chemokine production (including IL-8), and altered levels of hormones produced by adipocytes such as leptin and adiponectin. A causal link between this inflammatory milieu in patients who are obese and asthma or airway hyper-responsiveness has been more thoroughly explored than the potential link with lung injury.¹⁷

Some animal studies have suggested mechanisms for increased lung injury risk with obesity, but no causal relationship has been established between the baseline effects of obesity and the pathogenesis of lung injury in patients who are obese.¹⁸ Additionally, the magnitude of the baseline inflammatory effects of obesity is unknown and there has also been limited comparison of these pathways in patients with acute lung injury (ALI)/ARDS who are obese and nonobese. Currently, the role of adipokines in perpetuating lung injury pathogenesis remains under active investigation.

AIRWAY MANAGEMENT

Airway management, including intubation and extubation, is a key issue in patients with lung injury who are obese. Even relatively healthy patients who are obese and who undergo surgery have an increased risk of complications and respiratory failure perioperatively. There is ongoing discussion about the degree to which obesity predicts difficult endotracheal intubation, and other predictive tools such as the Mallampati scale may trump BMI as a prognostic tool. One recent retrospective study found that patients with obstructive sleep apnea (OSA) do experience

a higher rate of perioperative complications.¹⁹ Although not all patients with obesity have OSA, anatomic changes that result in OSA (increased soft tissue in the neck, decreased airway diameter, and increased airway collapsibility) can make intubation of patients who are obese difficult.^{20,21} With sedation and paralytics, the critical closing pressure of the upper airway (ie, the pressure that must be overcome to keep the airway open) increases as muscle tone decreases, and is affected by other factors such as airway structure.^{22,23} Thus, complete airway closure is common during intubation of patients who are obese following muscle relaxation.²⁴

Other sequelae of obesity such as impaired gas exchange with atelectasis, $\dot{V}/\dot{Q}$ mismatch, and the increased prevalence of gastroesophageal reflux disease can also complicate intubation, particularly with the underlying insult of ALI/ARDS. Although many patients will do well with the standard practice of “rapid sequence intubation” (with use of short-acting neuromuscular blockade, short-acting sedatives, and standard technique of preoxygenation), if there are additional issues that may lead to difficult intubation then it is reasonable to pursue an awake fiberoptic intubation.²⁵

There are additional issues with the extubation of patients who are obese, especially those with OSA, in whom there is an increased propensity for airway collapse and risk of reintubation. Residual effects of sedatives and muscle relaxants may be pronounced in patients who are obese given their unique pharmacodynamics, including delayed clearance of lipophilic drugs, and the difficulty of dosing by weight in patients who are obese. For example, some drugs should be dosed by ideal body weight or by lean body weight and others should be dosed by total body weight.²⁶ In addition to decreased wakefulness as sedatives wear off, the residual effects of the recent presence of an endotracheal tube can blunt upper airway reflexes that normally help to maintain airway patency.^{27–29} Noninvasive positive pressure ventilation can assist in successful extubation and can help to prevent reintubation in high-risk patients. Notably, use of noninvasive ventilation after postextubation respiratory distress develops (rescue strategy) has been shown to delay but not prevent reintubation and is also associated with higher mortality.³⁰ As summarized in recent practice guidelines, we recommend against the use of noninvasive ventilation in patients who experience respiratory failure following extubation.³¹ Conversely, preemptive noninvasive ventilation at the time of extubation of patients at high risk has been shown to shorten the duration of invasive mechanical ventilation without increasing the risk of reintubation, ICU length of stay, or mortality.³² These data suggest that noninvasive ventilation may be useful in patients

who are at high risk of extubation failure, though this strategy is not specific to the obese patient. We recommend extubation to noninvasive ventilation (preemptive strategy) in patients with known OSA, those with a history of failed extubation, and in patients in whom there is coexisting CO₂ retention due to either obstructive airways disease or obesity hypoventilation syndrome.

VENTILATOR MANAGEMENT OF ARDS IN PATIENTS WHO ARE OBESE

When obesity is coincident with respiratory failure (eg, ARDS), there are specific issues for mechanical ventilation and management. With increased abdominal pressure and concomitant elevated pleural pressure, even in a state of relative health, patients who are obese develop atelectasis and, therefore, a more heterogeneous lung, with some areas of well-aerated lung and other areas of relatively collapsed lung. One study of patients who were obese without lung injury and also of patients with ascites demonstrated that a reverse Trendelenburg position, in which the supine patient's head was placed higher than the feet at an angle of 45 degrees, facilitated liberation from the ventilator.³³ This finding is presumably due to a reduction in *trans*-diaphragmatic pressure, decreased atelectasis, and improved gas exchange with the postural change and resulting gravitational unloading.

The heterogeneity normally seen in patients who are obese is compounded in ARDS, in which increased pleural pressure is combined with increased surface tension due to surfactant dysfunction such that obese patients with ARDS can experience considerable atelectasis and alveolar flooding with resultant gas exchange abnormalities. Atelectasis also predisposes patients with ARDS to ventilator-associated lung injury, which results in part from the shear stresses that occur at the intersection of open and closed alveoli (ie, junctions between normal and abnormal lung). On conventional ventilator settings, the effective pressures generated in these heterogeneous areas are estimated theoretically to exceed 100 cm H₂O, which greatly surpasses the generally accepted "safe" maximum transpulmonary pressure of 25 cm H₂O.⁷

These mechanisms of lung injury have led to an "open lung" strategy of ventilation, in which attempts are made to create parenchymal homogeneity. Strategies to achieve this end have included recruitment maneuvers (eg, applying sustained high airway pressures of 40 cm H₂O, for brief periods) and PEEP titration to optimize respiratory mechanics. This "open lung" strategy has traditionally been balanced with attempts to minimize airway pressures, which

are also thought to contribute to ventilator-associated lung injury. Focus has shifted from simply reducing airway pressures to reducing transpulmonary pressures, the distending pressure across the lung itself.⁷ With the increased pleural pressures that obese patients experience, a high level of PEEP may be necessary to overcome these collapsing influences and prevent derecruitment. In the setting of obesity with raised pleural pressure, high peak airway pressures (>30 cm H₂O) can be applied without lung overdistention since transpulmonary pressures <25 cm H₂O at end inspiration are generally considered safe.^{34,35}

Failure to account for increased pleural pressure, which is rarely measured directly, can result in an undertitration of PEEP and increased shear stress and lung injury. In some cases, empirical titration of PEEP (without consideration of pleural pressure) can lead to PEEP overtitration with resulting hemodynamic compromise. One strategy that may safely guide PEEP titration in patients with ARDS, and especially patients who are obese, is the use of esophageal manometry. Since pressure measured by an esophageal balloon estimates pleural pressure, transpulmonary pressure can be estimated and PEEP can be titrated based on the physiologic requirements of the afflicted individual to achieve a positive transpulmonary pressure at end-exhalation. This strategy, in a primarily surgical ARDS population, resulted in improved gas exchange and a trend to improved 28-day mortality.³⁶ There have long been concerns that esophageal balloon pressures are confounded in critically ill and recumbent patients, and that the measured value may reflect the effects of the weight of the mediastinum, for example. However, detailed studies of esophageal balloons in obese patients and in patients with ALI have demonstrated esophageal pressure values consistent with physiologic expectations and predictions of pleural pressure.^{37,38} Additionally, the lung parenchymal stress measured directly as end-inspiratory transpulmonary stress was less than stress inferred from conventional measurements.³⁸ These data suggest that, although not perfect, esophageal pressure measurements by experienced operators may allow for safe titration of PEEP to overcome the challenges of the obese patient with ALI, as well as patients with ARDS generally. However, multicenter trials and more widespread experience will be required before such strategies can be generally recommended.

Recognizing that data are not definitive, if there is local expertise with the technique, we recommend use of esophageal manometry to guide PEEP titration in patients who are obese with ARDS and ongoing hypoxemia. However, if there is not institutional experience in placing esophageal balloons and interpreting the data, we recommend that practitioners

titrate PEEP based on other physiologic indices of recruitability. These include use of the airway pressure-time curve profile (stress index) and titration of PEEP according to tidal compliance.^{39,40} The latter is a relatively simple bedside maneuver—with the patient receiving a set tidal volume, plateau pressure is measured as PEEP is increased. If the plateau decreases, stays the same, or rises minimally this finding suggests improved lung compliance and an element of recruitable lung. However, if the plateau pressure increases by the same or greater amount than the increase in PEEP, this situation implies that recruitment did not occur and that there may in fact be areas of overdistention or hyperinflation.

In addition to titration of PEEP, prone positioning may be an important recruitment strategy in patients who are obese with lung injury. Prone positioning allows the weight of mediastinal tissue to be supported by the sternum, and thus less lung tissue may be susceptible to collapsing forces. This situation is especially relevant in patients who are obese, but is not the only potential mechanism of improved oxygenation with proning, which has also been shown to improve $\dot{V}/\dot{Q}$ matching and decrease shunt.⁴¹ One multicenter study showed improved oxygenation with proning, but no mortality benefit.⁴² Another meta-analysis found a mortality benefit of proning only in patients with ARDS with severe hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 100$ mm Hg), but not in moderate hypoxemia ($\text{PaO}_2/\text{FiO}_2 < 300$).⁴³ Prone positioning, including assessment of duration of positioning and appropriate PEEP titration, requires further study.^{44,45} Additionally, the feasibility and impact of proning in patients who are obese has not yet been studied systematically, and will likely be impacted by specifics such as degree of familiarity of nursing and physicians with proning and availability of appropriate resources. Additionally, the impact of obesity and fat distribution with resulting influences on position-induced changes in abdominal pressure has not yet been studied, and may be a critical variable explaining some of the variance in clinical trials. Other rescue measures for patients with ARDS and ongoing hypoxemia include inhaled nitric oxide, which can be appealing in patients with coexisting pulmonary hypertension due to COPD, OSA, and other comorbidities. However, there are insufficient data to support the routine use of inhaled nitric oxide in patients with ALI.⁴⁶

Importantly, even though high airway pressures can be tolerated in obesity, the strategy of low tidal volume ventilation is still paramount, and tidal volumes should be based on ideal body weight. This recommendation is because as body weight increases, lung size does not increase concomitantly and, therefore, individuals of the same height and different

weights should receive the same tidal volume (about 6 mL/kg IBW).^{35,47} It must be noted that this low tidal volume strategy is frequently accompanied by hypercapnia, which in patients who are obese may reflect both the acute illness and chronic hypoventilation.

CONCLUSION

A thorough understanding of the physiologic considerations related to patients who are obese with lung injury is becoming essential for optimal patient care given the obesity pandemic and ongoing prevalence of ARDS. An individualized approach to the care of these patients can be invaluable, since a “one size fits all” approach may be problematic for some patients. We support further clinical trials using individual patient measurements/responses to guide therapy, rather than simplified algorithms that are likely to provide heterogeneous results.

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