

Failure of Conventional Mechanical Ventilation in Morbid Obesity: Is High Frequency Percussive Ventilation an Answer? Case Series and Review of Literature

Sapan Patel¹, Felix Khushid² and Ruth Minkin^{1*}

¹Division of Pulmonary and Critical Care Medicine NewYork Presbyterian Brooklyn Methodist Hospital, Brooklyn, New York, United States

²Department of Respiratory Therapy, NewYork-Presbyterian Brooklyn Methodist, Brooklyn, New York, United States

Abstract

The prevalence of obesity is increasing in the United States and worldwide. Obesity is associated with prolonged hospital and Intensive Care Unit length of stays, and prolonged duration of mechanical ventilation (MV). The difficulty of oxygenation and ventilation in obesity is influenced by altered respiratory physiology. There is no mode of ventilation shown to improve morbidity or mortality in the obese population, nor is there a superior rescue ventilation mode when patients fail conventional MV. We present a series of obese and severely obese patients who improved with high frequency percussive ventilation (HFPV) delivered by Volumetric Diffusive Respirator (VDR) after failing conventional MV.

We performed a retrospective chart review of obese and severely obese patients admitted over 12 months period to our institution's medical ICU requiring MV. Patients with a body mass index (BMI) >30 kg/m² that failed conventional MV were included. Failure was defined as PaO₂ / FiO₂ ratio <0.6 on high positive end expiratory pressure (PEEP) >16 cmH₂O or plateau pressure >40 cmH₂O to maintain a PaO₂/FiO₂ ratio >0.6.

Five patients met our inclusion criteria with BMI between 34.2 and 48.58 kg/m² (mean BMI 39.49 kg/m²). The mean PaO₂ and PEEP were 68 mmHg and 18.8 cmH₂O respectively, prior to transition to VDR. Arterial blood gas analysis within 60 minutes of transitioning to VDR showed a mean PaO₂ 298.4 mmHg. All patients were successfully transitioned back to conventional mode, mean time on VDR 50.3 hours, with eventual liberation from mechanical ventilation.

Our case series showing rapid improvement in ventilation and oxygenation in morbidly obese patients suggest an option for its use as a rescue modality when conventional ventilation fails in obese population.

Keywords: Respiratory failure in obese patients; Mechanical ventilation; High frequency percussive ventilation; Hypoxemic respiratory failure

Introduction

As a consequence of the rise in rate of obesity (Body Mass Index (BMI) >30 kg/m²) and morbid obesity (BMI>40 kg/m²) across the United States and around the world, approximately 20% of the patients admitted to the intensive care unit (ICU) are obese [1]. Health care workers and systems face a major burden of caring for these patients admitted to hospitals and intensive care units. The current knowledge base insufficiently addresses the challenges particular to morbidly obese patients admitted to ICU with acute respiratory failure requiring mechanical ventilation. Changes imposed by alterations in thoraco-abdominal compliance and gas exchange might predispose obese patients to respiratory failure and could affect the response to therapeutic measures. The most significant change in pulmonary mechanics seen in obesity is a decrease in pulmonary compliance which has been attributed to one of several factors: fatty infiltration of the chest wall, increased pulmonary blood volume, and extrinsic compression of the thoracic cage by weight from excess soft tissue [2-4]. In addition, respiratory resistance has been shown to be increased in obese subjects [4,5]. The above described peculiarities frequently pose additional challenge in managing obese and morbidly obese patients requiring mechanical ventilation for acute respiratory failure. When conventional mode of mechanical ventilation is not meeting the goals patients may be considered for a rescue therapy such as extracorporeal membrane oxygenation that may be exceedingly risky for this population. High-Frequency Percussive Ventilation (HFPV) has been

reported to be of benefit in patients that have failed conventional mechanical ventilation. HFPV was developed in the early 1980s by Forrest Bird and was approved for patient use by the US Food and Drug Administration in 1993. It has been mostly reported in the literature as a ventilation mode used for inhalational injury and burns as well as in the pediatric and neonate population with acute respiratory failure [6-8]. HFPV is a flow regulated, pressure limited, and time cycled ventilator mode which delivers a series of high frequency (200-900 cycles/min) subtidal volumes in a successive stepwise pattern which results in the formation of low frequency convective pressure limited breathing cycles (Figure 1) [9]. A Volumetric Diffusion Respirator (VDR) provides this mode of ventilation. HFPV delivers biphasic percussions, which aid in lung recruitment by creating an oscillatory functional residual capacity (FRC) during the expiration resulting in improved gas diffusion. Multiple theories regarding the mechanism for

***Corresponding author:** Ruth Minkin, Division of Pulmonary and Critical Care Medicine NewYork Presbyterian Brooklyn Methodist Hospital, Brooklyn, New York, United States, Tel: (917) 664-7849; E-mail: RUM9030@nyp.org

Received July 28, 2018; **Accepted** September 20, 2018; **Published** September 27, 2018

Citation: Patel S, Khushid F, Minkin R (2018) Failure of Conventional Mechanical Ventilation in Morbid Obesity: Is High Frequency Percussive Ventilation an Answer? Case Series and Review of Literature. Clin Med Case Rep 2: 117.

Copyright: © 2018 Minkin R, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

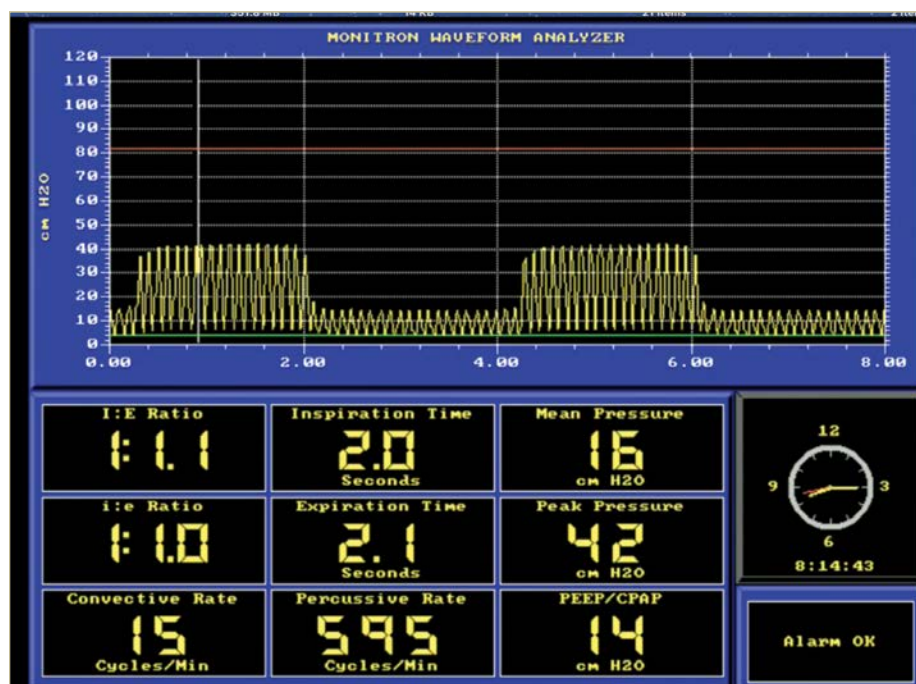


Figure 1: Interface for HFPV.

gas exchange have been postulated; however no single well-accepted theory exists. The VDR instantaneously adapts to changes in lung compliance and airway resistance resulting in reduced mean airway pressures. HFPV improves mucous clearance by directly creating a vibratory effect from successive pressure peaks on bronchial mucosa, by creating the autocephalad flow of gas within the airways and by enhancing mucociliary clearance via elevated flow with percussion [10,11]. HFPV is also beneficial in recruiting atelectatic lung areas.

The studies evaluating HFPV, however, are few in number and nonrandomized [12] found that when 7 patients were changed from conventional mechanical ventilation and high PEEP to HFPV at the same level of airway pressure and FiO_2 , the PaO_2 improved significantly. In a recent RCT [2] compared HFPV and low tidal volume ventilation-based strategies in burn patients with respiratory failure. In the HFPV arm, 12 (39%) of the 31 compared to 14 (45%) of the 31 patients in the low tidal volume group had ALI/ARDS. The investigators found no significant difference between the two groups in primary outcome-mean ventilator free days. There was also no significant difference in secondary outcomes such as, 28-day mortality, days free from non-pulmonary organ failure, ventilator associated pneumonia, and barotrauma. On subgroup analysis, there was significant difference in the need for rescue modality 29% (nine patients) vs 6% (two patients) in the low tidal volume vs HFPV groups respectively. The authors concluded by saying HFPV results in similar outcomes when compared with a low-tidal volume ventilation-based strategy in burn patients with respiratory failure. However, low-tidal volume ventilation strategy failed to achieve ventilation and oxygenation goals in a higher percentage necessitating rescue ventilation.

Several other authors have reported their experience with HFPV in non-inhalational respiratory failure in pediatric patients [3], in pediatric inhalational injury requiring extracorporeal life support [13], and in adults with ARDS who failed CMV [14].

We describe a series of 5 obese and morbidly obese medical patients managed with HFPV delivered by VDR in the Medical ICU team at New York Presbyterian Brooklyn Methodist Hospital over the course of one year after they failed conventional mechanical ventilation (Table 1). Our institution accumulated experience with use of HFPV delivered by VDR as method of ventilation for patients after cardiac surgery who failed mechanical conventional ventilation as well as intermediate modality prior to consideration of extracorporeal membrane oxygenation [15,16]. Our institution has standardized the use of HFPV as an alternative ventilation strategy in adults. In our center use of HFPV is reserved for patients who fail conventional ventilation and decision to transition patient to this mode is made by a multidisciplinary team consistent of an intensivist caring for the patient and adequately trained senior respiratory therapist assigned to the patient.

Case Study

Case 1: 50-year-old male with a BMI 39.80 without major medical history admitted for methadone overdose. He was intubated on presentation due to inability to protect his airways due to altered consciousness. He was placed on conventional mechanical ventilation, pressure regulated volume control (PRVC), with initial settings of Tidal Volume(TV) 550 mls, respiratory rate (RR) 18 breath per minute (BPM), FiO_2 of 60% and positive end expiratory pressure (PEEP) 5 cmH_2O . His initial arterial blood gas (ABG) demonstrated acute respiratory failure with hypoxemia, PaO_2 85 mmHg. During his admission to the ICU, his FiO_2 and PEEP requirements continued to increase and on Day 10 of his admission while on PRVC with FiO_2 100% and PEEP 20 cmH_2O his ABG was still suboptimal with PaO_2 79 mmHg and evidence of reduced lung compliance. He was transitioned to VDR with initial settings of FiO_2 100%, Percussive Rate (PR) 590/min, oscillary CPAP 18, and a convective rate of 15. His ABG after 1 hour on VDR demonstrated marked improvement with PaO_2 431 mmHg. He continued to have

Patient	Cause of respiratory failure	Type of respiratory failure	Age	Gender	BMI kg/m ²	Time to HFPV (days)	Pre-HFPV pO ₂ (mm Hg)	1 h post-HFPV pO ₂ (mmHg)	Time on HFPV (hrs)	Outcome
1	Methadone Overdose	Hypoxemic	50	M	39.8	10	79	431	48.5	Alive
2	Laparotomy for Necrotizing Soft Tissue Infection	Hypoxemic	37	M	37.5	3	45	208	39	Alive
3	Asthma and OHS	Hypoxemic and hypercapnic	38	F	34.2	4	54	171	88	Alive
4	Septic Shock and Acute Renal Failure	Hypoxemic	30	M	48.58	8	68	350	64	Alive
5	Pneumonia	Hypoxemic	40	F	37.8	1	94, PPI>40 cm	332	12	Alive

Table 1: Patients characteristics before and after HFPV use.

decreasing FiO₂ requirement and was transitioned back to conventional mechanical ventilation (PRVC) on Day 13 and subsequently extubated on Day 16 to non-invasive positive pressure ventilation and transitioned to general medical floor. He was ultimately discharged on Day 28.

Case 2: 38-year-old male with a BMI 37.05 and no past medical history admitted for intra-abdominal free air and taken to the operating room for an exploratory laparotomy that revealed a necrotizing infection of the soft tissue. Post procedure, he remained intubated and on mechanical ventilation PRVC with settings TV 460 mls, RR 25 bpm, FiO₂ 50%, PEEP 5 cmH₂O. He underwent a second laparotomy on Day 3 for a supraleator abscess drainage and abdominal washout. Upon returning from the OR, he was found to be hypoxemic despite conventional ventilation on PRVC mode with FiO₂ 100%, PEEP 20 cmH₂O, with subsequent ABG demonstrating severe hypoxemia with PaO₂ 45 mmHg. He was placed on VDR with initial settings of FiO₂ 100%, Percussive Rate 600/min, Oscillatory CPAP 18, and a convective rate of 15. His ABG after 1 hour on VDR demonstrated PaO₂ of 208 mmHg. He continued to have decreasing FiO₂ requirements and was transitioned back to conventional mechanical ventilation (PRVC) on Day 5 and was extubated on Day 9 without complications.

Case 3: 38-year-old female with a BMI 34.20 with past history of asthma, obesity hypoventilation syndrome (OHS), tracheostomy with reversal presented with acute hypoxemic respiratory failure requiring intubation and mechanical ventilation with PRVC mode. During her ICU course, she continued to require high FiO₂ and High PEEP and on Day 4 her ABG still showed hypoxemia with PaO₂ 54 mmHg, on PRVC with, FiO₂ 100%, PEEP 18 cmH₂O. She was transitioned to VDR with initial settings FiO₂ 100%, Percussive Rate 600/min, Oscillatory CPAP 22, and Convective Rate 15. Her subsequent ABG 1 hour later demonstrated PaO₂ 171 mmHg. She continued to have decreasing FiO₂ and PEEP requirements, her ventilation also improved, on Day 9 she was transitioned to conventional mechanical ventilation (PRVC). She eventually required surgical tracheostomy placed on Day 14, however, continued to undergo daily weaning trials. On Day 26, she was transitioned to trach collar and was subsequently discharged.

Case 4: A. 30-year-old male with BMI 48.58 and a past history of asthma, schizoaffective disorder, hypertension, and diabetes mellitus type II presented for septic shock and acute renal failure. On Day 5 he developed respiratory failure, was intubated and placed on conventional mechanical ventilation, PRVC mode. Post intubation he continued to require high PEEP and FiO₂ to maintain oxygenation. On Day 8 he still demonstrated very marginal oxygenation with PaO₂ 68 mmHg on PRVC TV 460 mls, RR 26 bpm, FiO₂ 100%, PEEP 16 cmH₂O. He was placed on VDR with initial settings FiO₂ 100%, Percussive Rate 595/min, Oscillatory CPAP 14, and convective rate 15 and his subsequent ABG 1 hour later showed PaO₂ 350 mmHg. He was transitioned to conventional ventilation on Day 9, however became

hypoxic and required re-initiation of VDR on Day 10. On Day 11, he was transitioned back to conventional ventilation and extubated on Day 16 without complication.

Case 5: 40-year-old female with BMI 37.8 and a past history of OHS, obstructive sleep apnea (OSA) on CPAP, and tracheostomy for ARDS 3 years prior with reversal presented with hypoxic respiratory failure due to pneumonia. She was initially placed on high flow oxygen without improvement in oxygenation and required intubation and mechanical ventilation on Day 2. Post intubation on conventional mechanical ventilation, PRVC, with FiO₂ 100%, PEEP 20 cmH₂O her PaO₂ was 94, however she had poor lung compliance, and plateau pressures (PPI) were persistently elevated over 40cmH₂O. She was transitioned to VDR with initial settings FiO₂ 100%, Percussive Rate 600/min, Oscillatory CPAP 14, and convective rate 15 and her subsequent ABG 45 minutes later showed PaO₂ 332 mmHg. Her FiO₂ was gradually down-titrated and she was transitioned back to PRVC. Her FiO₂ and PEEP were titrated down and she was eventually weaned of the ventilator and successfully extubated.

Discussion and Review of Literature

The prevalence of obesity (BMI between 30 and 39.9 kg/m²) and severe obesity (BMI ≥ 40 kg/m²) has been increasing in the United States. Between 2007 and 2008, 32.2% of American men and 35.5% of American women were found to be obese [17]. There is controversy among the data regarding outcomes for obese and severely obese patients as numerous studies have demonstrated that these patients have longer ICU and hospital length of stays, as well as duration of mechanical ventilation [18-23], but on the other hand several studies have found that obese and severely obese patients may have lower hospital and ICU mortality rates than normal-weight patients [24,25]. It appears that although obesity is not necessarily associated with increased mortality in ICU patients, it is associated with longer ICU length of stay, and duration of mechanical ventilation.

Obesity alone significantly alters respiratory physiology, which contributes to the difficulty of oxygenation and ventilation in patients with acute respiratory failure. The most significant change in obese patients is a decrease in pulmonary compliance, which is attributable to fatty infiltration of the chest wall, increased blood flow through pulmonary vasculature, as well as chest wall compression from excessive fat [26,27]. In obese as compared to normal weight subjects there is increased respiratory rate ranging from (15.3-21 vs. 10-12 breaths per minute), significantly lower tidal volumes and increased minute ventilation that shown to be 11 L/min or greater in most studies [28-30]. Sampson showed that there is a decrease in inspiratory time without a significant change in expiratory time and no change in mean inspiratory flow in obese subjects [29]. Decrease in inspiratory time may result from increased activity of chest wall receptors, whereas decrease in expiratory time could result from reduced respiratory

compliance or persistent diaphragmatic activity extending into exhalation phase. Obese patients also tend to be more hypoxemic than non-obese patients with a widened alveolar-arterial oxygen gradient caused by ventilation-perfusion mismatching [31,32]. Zhi described "Obesity Paradox" in acute respiratory distress syndrome (ARDS) in meta-analysis reviewing data from 24 studies including over nine thousands patients demonstrating that although obesity was associated with increased risk of development of ARDS it was also correlated with reduced ARDS mortality [33]. Zhi proposed that obesity may be "primed" for the development of ARDS, but the innate immunity and the inflammatory response may be attenuated due to obesity associated reduced levels of proinflammatory cytokines (IL-6, IL-8) and surfactant protein D (marker for alveolar injury) [34].

To date, there is no particular mode of ventilation to improve mortality or morbidity in intubated obese and morbidly obese patients. In a meta-analysis of thirteen studies analyzing ventilation strategies in obese patients undergoing surgery Aldenkortt looked for evidence of effective strategies for intraoperative ventilator management in this population [35]. They reported on a variety of ventilation strategies: pressure- or volume-controlled ventilation (PC, VCV), various tidal volumes, and different PEEP or recruitment maneuvers (RM), and combinations of thereof and found no difference in the outcomes when comparing pressure-controlled and volume-controlled modes of ventilation. The studies reviewed demonstrated that RM with PEEP maintained better intraoperative oxygenation and lung compliance compared with PEEP alone.

A more recent literature review by Hu [36] compared multiple ventilation strategies in obese patients undergoing bariatric surgery. Eight strategies were reviewed: RM alone, PEEP alone, RM plus PEEP, induction PEEP, induction PEEP plus intraoperative RM and PEEP, pressure control ventilation (PCV), volume control ventilation (VCV), and equal ratio ventilation. Similar to Aldenkortt consistent positive effects on oxygenation were seen when a recruitment maneuver was immediately followed by PEEP. Talab [37] compared 2 different PEEP levels preceded by the same recruitment maneuver in obese patients undergoing bariatric surgery and found PEEP of 10cmH₂O to be effective at maintaining the recruitment benefit compared to a PEEP of 5cmH₂O. There were no differences found between modes of ventilation used.

Despite growing body of literature there is still no clear understanding of the optimal way to ventilate obese and morbidly obese patients. Even less clarity exists on strategies that could be beneficial for these patients when they fail conventional mechanical ventilation. Novel nonconventional modes of ventilation including volume-assured pressure support (VAPS), adaptive support ventilation (ASV), airway pressure release ventilation (APRV), and neurally adjusted ventilatory assist (NAVA) [38-41] have been described for various etiologies of respiratory failure leading to ARDS, however, none has a proven mortality benefit over conventional modes of ventilation for obese and non-obese patients.

In our prospective observation series of obese and morbidly obese patients with ARDS who failed conventional mode of mechanical ventilation, HFPV delivered via VDR improved both oxygenation as well as CO₂ washout within 1 hour of transitioning to the latter mode. We believe that HFPV eliminated the need for use of supra high PEEP and high FiO₂ in attempt to overcome reduced chest compliance in obese and morbidly obese patients therefore preventing continuous lung injury due to over distention. Our case series showing rapid improvement in ventilation and oxygenation in morbidly obese patients

suggests an option for its use as a rescue modality when conventional ventilation fails in obese population. Our data are limited by a small sample size as well as observational nature, however, safety of HFPV along with accumulated experience and proper use protocol carries a potential for wider application in proper clinical settings.

References

1. Lewandowski K, Lewandowski M (2011) Intensive care in the obese. *Best Pract Res Clin Anaesthesiol* 25: 95-108.
2. Naimark A, Cherniak RM (1960) Compliance of the respiratory system and its components in health and obesity. *J Appl Physiol* 15: 377-382.
3. Barrera F, Hillyer P, Ascanio G, Bechtel J (1973) The distribution of ventilation, diffusion, and blood flow in obese patients with normal and abnormal blood gases. *Am Rev Respir Dis* 108: 819-830.
4. Zerah F, Harf A, Perlemuter L, Lorino H, Lorino AM, et al. (1993) Effects of obesity on respiratory resistance. *Chest* 103: 1470-1476.
5. Pelosi P, Croci M, Ravagnan I, Tredici S, Pedoto A, et al. (1998) The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. *Anesth Analg* 87: 654-660.
6. Rodeberg DA, Housinger TA, Warden GD (1994) Improved ventilation function in burn patients using volumetric diffuse ventilation. *J Am Coll Surg* 179: 518-522.
7. Chung KK, Wolf SE, Renz EM, Allan PF, Aden JK, et al. (2010) High-frequency percussive ventilation and low tidal volume ventilation in burns: a randomized controlled trial. *Crit Care Med* 38: 1970-1977.
8. Rizkalla NA, Dominick CL, Fitzgerald JC, Thomas NJ, Yehya N (2014) High-frequency percussive ventilation improves oxygenation and ventilation in pediatric patients with acute respiratory failure. *J Crit Care* 29: 314e1 – 314e7.
9. Esan A, Hess DR, Raoof S, George L, Sessler CN (2010) Severe hypoxemic respiratory failure: Part 1-Ventilatory strategies. *Chest* 137: 1203-1216.
10. Lucangelo U, Fontanesi L, Antonaglia V, Pellis T, Berlot G, et al. (2003) High frequency percussive ventilation (HFPV) - Principles and technique. *Minerva Anestesiologica* 69: 841-851.
11. Salim A, Marin M (2005) High-frequency percussive ventilation. *Crit Care Med* 33: S241-5.
12. Gallagher TJ, Boysen PG, Davidson DD, Miller JR, Leven SB (1989) High-frequency percussive ventilation compared with conventional mechanical ventilation. *Crit Care Med* 17: 364-6.
13. Yehya N, Dominick CL, Connelly JT, Davis DH, Minneci PC, et al. (2014) High-frequency percussive ventilation and bronchoscopy during extracorporeal life support in children. *ASAIO Journal* 60: 424-428.
14. Velmahos GC, Chan LS, Tatevossian R, Dougherty WR, Escudero J, et al. (1999) High-frequency percussive ventilation improves oxygenation in patients with ARDS. *Chest* 116: 440-446.
15. Wong I, Worku B, Weingarten JA, Ivanov A, Khushid F, et al. (2017) High-frequency percussive ventilation in cardiac surgery patients failing mechanical conventional ventilation. *Interact Cardiovasc Thorac Surg* 25: 937-941.
16. Gulkarov I, Schiftenhaus J, Wong I, Afzal A, Khushid F, et al. (2018) High-frequency percussive ventilation facilitates weaning from extracorporeal membrane oxygenation in adults. *J Extra Corpor Technol* 50: 53-57.
17. Flegal KM, Carroll MD, Ogden CL, Curtin LR (2010) Prevalence and trends in obesity among US adults, 1999-2008. *JAMA* 303: 235-241.
18. Tremblay A, Bandi V (2003) Impact of body mass index on outcomes following critical care. *Chest* 123: 1202-1207.
19. Dossett LA, Heffernan D, Lightfoot M, Collier B, Diaz JJ, et al. (2008) Obesity and pulmonary complications in critically injured adults. *Chest* 134: 974-980.
20. Morris AE, Stapleton RD, Rubenfeld GD, Hudson LD, Caldwell E, et al. (2007) The association between body mass index and clinical outcomes in acute lung injury. *Chest* 131: 342-348.
21. El-Solh A, Sikka P, Bozkanat E, Jaafar W, Davies J (2001) Morbid obesity in the medical ICU. *Chest* 120: 1989-1997.
22. Bercault N, Boulain T, Kuteifan K, Wolf M, Runge I, et al. (2004) Obesity-related

- excess mortality rate in an adult intensive care unit: A risk-adjusted matched cohort study. *Crit Care Med* 32: 998-1003.
23. Martino JL, Stapleton RD, Wang M, Day AG, Cahill NE, et al. (2011) Extreme obesity and outcomes in critically ill patients. *Chest* 140: 1198-1206.
 24. O'Brien JM Jr, Phillips GS, Ali NA, Lucarelli M, Marsh CB, et al. (2006) Body mass index is independently associated with hospital mortality in mechanically ventilated adults with acute lung injury. *Crit Care Med* 34: 738-744.
 25. Garrouste-Orgeas M, Troche G, Azoulay E, Caubel A, de Lassence A, et al. (2004) Body mass index. An additional prognostic factor in ICU patients. *Intensive Care Med* 30: 437-443.
 26. McCallister JW, Adkins EJ, O'Brien JM Jr (2009) Obesity and Acute Lung Injury. *Clin Chest Med* 30: 495-508.
 27. Biring MS, Lewis MI, Liu JT, Mohsenifar Z (1999) Pulmonary physiologic changes of morbid obesity. *Am J Med Sci* 318: 293-297.
 28. Burki NK, Baker RW (1984) Ventilatory regulations in eucapnic morbid obesity. *Am Rev Respir Dis* 129: 538-43.
 29. Sampson MG, Grassino AE (1983) Load compensation in obese patients during quiet tidal breathing. *J Appl Physiology* 55: 1269-76.
 30. Chlif M, Keochkerian D, Choquet D, Vaidie A, Ahmaidi S (2009) Effects on nobesity on breathing pattern, ventilator neural drive and mechanics. *Respir Physiol Neurobiol* 168: 198-202.
 31. Rivas E, Arismendi E, Agustí A, Sanchez M, Delgado S, et al. (2015) Ventilation/Perfusion distribution abnormalities in morbidly obese subjects before and after bariatric surgery. *Chest* 147: 1127-1134.
 32. Ray CS, Sue DY, Bray G, Hansen JE, Wasserman K (1983) Effects of obesity on respiratory function. *Am Rev Respir Dis* 128: 501-506.
 33. Zhi G, Xin W, Ying W, Guohong X, Shuying L (2016) "Obesity Paradox" in ARDS: A Systematic Review and Meta-Analysis. *PLoS One* 11: e0163677.
 34. Stapleton RD, Dixon AE, Parsons PE, Ware LB, Suratt BT, et al. (2010) The association between BMI and plasma cytokine levels in patients with acute lung injury. *Chest* 138: 568-77.
 35. Aldenkortt M, Lysakowski C, Elia N, Brochard L, Tramer MR (2012) Ventilation strategies in obese patients undergoing surgery: quantitative systematic review and meta-analysis. *Br J Anaesth* 109: 493-502.
 36. Hu X (2016) Effective Ventilation Strategies for Obese Patients Undergoing Bariatric Surgery: A Literature Review. *AANA J* 84: 35-45.
 37. Talab HF, Zabani IA, Abdelrahman HS, Bukhari WL, Mamoun I, et al. (2009) Intraoperative ventilatory strategies for prevention of pulmonary atelectasis in obese patients undergoing laparoscopic bariatric surgery. *Anesth Analg* 109: 1511-1516.
 38. Okuda M, Kashio M, Tanaka N, Fujii T, Okuda Y (2012) Positive outcome of average volume-assured pressure support mode of a Respiroics V60 Ventilator in acute exacerbation of chronic obstructive pulmonary disease: A case report. *J Med Case Rep* 6: 284.
 39. Brunner JX, Iotti GA (2002) Adaptive Support Ventilation (ASV). *Minerva Anestesiol* 68: 365-8.
 40. Modrykamien A, Chatburn RL, Ashton RW (2011) Airway pressure release ventilation: An alternative mode of mechanical ventilation in acute respiratory distress syndrome. *Cleve Clin J Med* 78: 101-10.
 41. Terzi N, Piquilloud L, Roze H, Mercat A, Lofaso F, et al. (2012) Clinical review: Update on neurally adjusted ventilatory assist-report of a round-table conference. *Crit Care* 16: 225.