Transpulmonary Pressure-Guided Lung-Protective Ventilation Improves Pulmonary Mechanics and Oxygenation Among Obese Subjects on Mechanical Ventilation

Daniel D Rowley, Susan R Arrington, Kyle B Enfield, Keith D Lamb, Alexandra Kadl, John P Davis, and Danny J Theodore

BACKGROUND: Transpulmonary pressure (P_L) is used to assess pulmonary mechanics and guide lung-protective mechanical ventilation (LPV). P_L is recommended to individualize LPV settings for patients with high pleural pressures and hypoxemia. We aimed to determine whether P_L-guided LPV settings, pulmonary mechanics, and oxygenation improve and differ from non-P_L-guided LPV among obese patients after 24 h on mechanical ventilation. Secondary outcomes included classification of hypoxemia severity, count of ventilator-free days, ICU length of stay, and overall ICU mortality. METHODS: This is a retrospective analysis of data. Ventilator settings, pulmonary mechanics, and oxygenation were recorded on the initial day of P_L measurement and 24 h later. P_L-guided LPV targeted inspiratory P_L < 20 cm H_2O and expiratory P_L of 0–6 cm H_2O. Comparisons were made to repeat measurements. RESULTS: Twenty subjects (13 male) with median age of 49 y, body mass index 47.5 kg/m^2, and SOFA score of 8 were included in our analysis. Fourteen subjects received care in a medical ICU. P_L measurement occurred 16 h after initiating non-P_L-guided LPV. P_L-guided LPV resulted in higher median PEEP (14 vs 18 cm H_2O, $P = .009$), expiratory P_L (–3 vs 1 cm H_2O, $P = .02$), respiratory system compliance (30.7 vs 44.6 mL/cm H_2O, $P = .001$), and P_{aO_2}/F_{IO_2} (156 vs 240 mm Hg, $P = .002$) at 24 h. P_L-guided LPV resulted in lower F_{IO_2} (0.53 vs 0.33, $P < .001$) and lower P_L driving pressure (10 vs 6 cm H_2O, $P = .001$). Tidal volume (420 vs 435 mL, $P = .64$) and inspiratory P_L (7 vs 7 cm H_2O, $P = .90$) were similar. Subjects had a median of 7 ventilator-free days, and median ICU length of stay was 14 d. Three of 20 subjects died within 28 d after ICU admission. CONCLUSIONS: P_L-guided LPV resulted in higher PEEP, lower F_{IO_2}, improved pulmonary mechanics, and greater oxygenation when compared to non-P_L-guided LPV settings in adult obese subjects. *Key words: mechanical ventilation; obesity; respiratory mechanics; esophageal pressure; transpulmonary pressure; respiratory support; lung-protective ventilation; PEEP*. [Respir Care 2021;66(7):1049–1058. © 2021 Daedalus Enterprises]

Introduction

The morbidly obese patient represents a unique challenge in mechanical ventilation. The prevalence of obesity in the ICU, as defined as a body mass index (BMI) ≥ 30 kg/m^2, is increasing globally.[1,2] An estimated one third of all ICU admissions meet criteria for obesity, and up to 7% meet criteria for morbid obesity (BMI ≥ 40 kg/m^2).[3-5] Optimal mechanical ventilation in these patients is difficult to monitor using traditional methods. The use of esophageal pressure manometry to obtain transpulmonary pressure (P_L) measurements to optimize and individualize mechanical ventilator settings in patients with suspected high pleural pressures and refractory hypoxemia has been recommended[6]; however, esophageal pressure manometry is less commonly used internationally.[7] P_L manometry was incorporated into our lung-protective mechanical ventilation clinical practice guideline (see the supplementary materials at http://www.rcjournal.com) in 2018. We describe observations associated with a P_L-guided lung-protective ventilation (LPV) strategy applied to morbidly obese patients on mechanical ventilation. Our primary objective was to determine whether non-P_L-guided LPV ventilator settings, pulmonary mechanics, and oxygenation differ 24 h after applying P_L-

guided LPV. Secondary outcomes included ventilator-free days, ICU length of stay, and overall ICU mortality.

Methods

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We conducted a retrospective analysis of quality improvement data collected at the University of Virginia Medical Center in Charlottesville, Virginia. Data were reviewed as part of an ongoing quality improvement project that monitors respiratory therapist adherence to our LPV guideline and associated clinical outcomes on a monthly basis. The University of Virginia Institutional Review Board for Health Sciences Research approved this project (IRB HSR #22249) with waiver of patient consent. Between April 2019 and July 2020, data were recorded in electronic medical records (Epic, Verona, Wisconsin) by a respiratory therapist assigned to care for each patient.

Patients

Adult patients $\geq$ 18 y old who met the following criteria were included in our analysis: BMI ≥ 30 kg/m^2, admission to the medical ICU or surgical/trauma ICU, need for mechanical ventilation, and a respiratory therapy consult to obtain P_L measurements by a licensed independent practitioner (eg, physician, nurse practitioner, or physician assistant). Patients who had one or more of the following characteristics prompted a P_L measurement consult: obesity, ARDS that requires $F_{IO_2} \geq 0.60$ and/or set PEEP > 10 cm H_2O, airway driving pressure > 15 cm H_2O with plateau pressure ≥ 30 cm H_2O despite tidal volume (V_T) ≤ 6 mL/kg predicted body weight (PBW), and extrinsic pathology resulting in decreased chest wall-abdominal compliance to assess for optimal set PEEP and V_T. Patients were excluded if they met any contraindication for esophagogastric tube insertion (see the supplementary materials at http://www.rcjournal.com). A total of 20 patients between April 2019 and July 2020 were found to be eligible for analysis.

QUICK LOOK

Current knowledge

Obesity is a growing problem globally, and it is complicating lung-protective mechanical ventilation management because external pressure from the chest wall and abdomen are not accounted for when measuring airway pressure as a surrogate for alveolar stress. Esophageal pressure manometry has been proposed as an adjunct to assess transpulmonary pressures to guide lung-protective ventilation.

What this paper contributes to our knowledge

Transpulmonary pressure manometry can be used to customize and optimize lung-protective mechanical ventilation settings for morbidly obese patients. An F_{IO_2}/expiratory transpulmonary pressure combination table can be used to optimize PEEP settings and may improve pulmonary mechanics and oxygenation for this patient population. This approach resulted in higher PEEP, lower F_{IO_2}, improved pulmonary mechanics, and better oxygenation.

Procedure and Measurements

Subjects who met the inclusion criteria had a 5-French esophageal balloon catheter (Cooper Surgical, Trumbull, Connecticut) placed by a registered respiratory therapist with specialty credentials in adult critical care. All subjects were supine with the head of the bed elevated to 30 degrees. The esophageal balloon catheter was inserted through the nose or mouth and positioned in the esophagus according to the esophageal catheter insertion procedure described by Talmor et al.[8] The appropriate position of the esophageal catheter were confirmed by performing an expiratory airway occlusion maneuver with a simultaneous gentle chest compression. Changes in esophageal and airway pressures resulting from the occlusion maneuver were recorded. The

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Mr Rowley presented a version of this paper as an Editors' Choice abstract at AARC Congress 2020 LIVE!, held virtually November 18, 2020.

Supplementary material related to this paper is available at http://www.rcjournal.com.

This work was supported in part by the Pulmonary Diagnostics & Respiratory Therapy Services Department at the University of Virginia Medical Center. Mr Rowley has disclosed relationships with Philips, Ikaria, and Draeger. Mr Lamb discloses a relationship with Fisher & Paykel.

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DOI: 10.4187/respcare.08686

Table 1. Subject Characteristics

Age, y	49 (39–64)
Subjects	20 (100)
Male	13 (65)
Female	7 (35)
Body mass index, kg/m^2	47.5 (37.4–55.7)
SOFA score	8 (6–11)
Primary diagnosis	
Acute hypoxemic respiratory failure	12 (60)
Cardiogenic shock	2 (10)
Septic shock	4 (20)
Other	2 (10)
Subject care unit	
Medical ICU	14 (70)
Surgical ICU	6 (30)
Mechanical ventilation duration before P_L measurement, h	16 (8–21)
Hypoxemia classification	
None (P_{aO_2}/F_{IO_2} > 300 mm Hg)	2 (10)
Mild hypoxemia (P_{aO_2}/F_{IO_2} < 300 mm Hg)	2 (10)
Moderate hypoxemia (P_{aO_2}/F_{IO_2} < 200 mm Hg)	12 (60)
Severe hypoxemia (P_{aO_2}/F_{IO_2} < 100 mm Hg)	4 (20)
Vasoactive drug requirement	12 (60)
Sedation	20 (100)
Neuromuscular blockade	12 (60)

Data are presented as *n* (%) or median (interquartile range).
SOFA = Sequential Organ Failure Assessment
P_L = transpulmonary pressure

esophageal catheter was considered to be in an appropriate position when the ratio between change in esophageal pressure and change in airway pressure equaled 0.8–1.2 during the occlusion maneuver.[9] Visualization of cardiac artifact on esophageal pressure waveform was also used to qualitatively confirm appropriate catheter position.

All P_L data were measured using one of 2 options. The preferred option was to use a 5-French balloon-tipped catheter (Cooper Surgical) in conjunction with a Hamilton G5 ventilator (Hamilton Medical, Reno, Nevada). The Hamilton G5 ventilator can display esophageal pressure and P_L measurement graphics, in addition to respective numerical output on the ventilator's display screen. The second option used a 5-French esophageal balloon-tipped catheter (Cooper Surgical) in conjunction with a bedside monitor and a disposable pressure transducer (Edwards Lifesciences, Irvine, California) configuration as described by the Cooper Surgical procedure guideline for catheter preparation.[10]

Mechanical ventilator settings, airway pressures, pulmonary mechanics, and oxygenation variables were recorded immediately before P_L-guided LPV and 24 h after P_L guided LPV. Berlin classification for mild hypoxemia (P_{aO_2}/F_{IO_2} < 300 mm Hg), moderate hypoxemia (P_{aO_2}/F_{IO_2} < 200 mm Hg), and severe hypoxemia (P_{aO_2}/F_{IO_2} < 100 mm Hg) was also recorded. Ventilator management was customized in consideration of P_L and airway pressure measurement data. Mechanical ventilator settings were adjusted to target an inspiratory P_L < 20 cm H_2O and an expiratory P_L target of 0–6 cm H_2O. A F_{IO_2}/P_L table (see the supplementary materials at http://www.rcjournal.com) was used to determine optimal expiratory P_L in relationship to set F_{IO_2}.[11] The use of sedation and neuromuscular blockade was at the discretion of the treating licensed independent practitioner.

Statistical Analysis

Data were collected from electronic medical records by study investigators (DDR and SA) and transferred to SPSS 25 (IBM, Armonk, New York) for storage and analysis. The Kolmogorov-Smirnov test was used to evaluate for normality of distribution for continuous variables. Continuous variables were described as median and interquartile range (IQR). Repeat measures for before P_L and after P_L measurements were compared using the Wilcoxon signed-rank test. Categorical variables were described as frequency count and percentage. The McNemar test was applied to evaluate for repeat measurement group difference after binning hypoxemia severity to compare no hypoxemia and mild hypoxemia classifications to moderate hypoxemia and severe hypoxemia classifications, respectively. The Friedman 2-way analysis of variance was applied to compare baseline S_{pO_2}/F_{IO_2} to S_{pO_2}/F_{IO_2} at 24 h, 48 h, 72 h, and 96 h, respectively. Alpha (2-tailed) ≤ .05 was considered significant. For the Friedman test, Bonferroni correction was applied for multiple comparisons, with an adjusted *P* (2-tailed) ≤ .01 being considered statistically significant.

Results

Subject characteristics are shown in Table 1. Our analysis consisted of 20 subjects (13 male) who were morbidly obese (Class 3) with a median BMI of 47.5 kg/m^2 (IQR 37.4–55.7). Median Sequential Organ Failure Assessment (SOFA) score was 8 (IQR 6–11). Most subjects were cared for in our medical ICU (n = 14), and the median duration of mechanical ventilation before a respiratory therapy consult was received for a P_L measurement was 16 h (IQR 8–21). The Hamilton G5 ventilator method for obtaining P_L measurement was used with the majority of our subjects (15 of 20). Sixteen of 20 subjects had either moderate hypoxemia (n = 12) or severe hypoxemia (n = 4), and 12 of 20 subjects received a vasoactive drug at the time of baseline P_L measurement.

Ventilator Settings and Pulmonary Mechanics

P_L manometry resulted in significant ventilator setting adjustments, improved pulmonary mechanics, and oxygenation (Table 2, Fig. 1). Set PEEP adjustment occurred in 19 of

Table 2. Ventilator Settings, Airway Pressures, Pulmonary Mechanics, Oxygenation, and Events Before and After P_L Measurements

Variable	Before P_L-Guided Ventilator Setting Adjustment	After P_L-Guided Ventilator Setting Adjustment	*P*
F_{IO_2}	0.53 (0.40–0.81)	0.33 (0.30–0.40)	< .001
Frequency, breaths/min	26 (22–31)	24 (20–29)	.19
Tidal volume, mL	420 (365–454)	435 (380–460)	.64
Tidal volume, mL/kg PBW	6.0 (5.6–6.0)	6.0 (6.0–7.0)	.17
Set PEEP, cm H_2O	14 (14–20)	18 (16–23)	.009
Peak inspiratory pressure, cm H_2O	39 (32–42)	37 (33–43)	.66
Inspiratory P_{plat}, cm H_2O	30 (27–33)	28 (26–36)	.96
Total PEEP, cm H_2O	15 (14–22)	19 (17–23)	.049
C_{RS}, mL/cm H_2O	30.7 (26.6–41.5)	44.6 (37.6–51.0)	.001
Driving pressure, cm H_2O^*	13 (10–15)	10 (8–11)	.006
Inspiratory P_L, cm H_2O	7 (2–11)	7 (5–9)	.90
Expiratory P_L, cm H_2O	–3 (–5 to 1)	1 (–1 to 3)	.02
P_L driving pressure, cm $H_2O^\dagger$	10 (7–12)	6 (4–8)	.001
P_{aO_2}/F_{IO_2}, mm Hg	156 (97–190)	240 (207–266)	.002
Vasoactive drug requirement	12 (60)	10 (50)	.53

Data are presented as median (interquartile range) or *n* (%). *N* = 20 subjects. $P \leq .01$ is considered to be statistically significant.

* Driving pressure is calculated as the difference between P_{plat} and $PEEP_{total}$.

† P_L driving pressure is calculated as the difference between inspiratory P_L and expiratory P_L.

PBW = predicted body weight

P_{plat} = plateau pressure

C_{RS} = respiratory-system compliance

P_L = transpulmonary pressure

20 subjects; 14 subjects had set PEEP increase, and 5 subjects had set PEEP decrease. Median set PEEP increased significantly from 14 cm H_2O (IQR 14–20) to 18 cm H_2O (IQR 16–23) ($P = .009$), and median F_{IO_2} decreased from 0.53 (IQR 0.40–0.81) to 0.33 (IQR 0.30–0.40) ($P < .001$). Median expiratory P_L increased from –3 cm H_2O (IQR –5 to 1) to 1 cm H_2O (IQR –1 to 3) ($P = .02$) after P_L-guided set PEEP adjustment. Median V_T increased from 420 mL (IQR 365–454) to 435 mL (IQR 380–460), but the difference was not significant ($P = .64$). Median V_T as mL/kg PBW (6.0 [IQR 5.6–6.0] vs 6.0 [IQR 6.0–7.0], $P = .17$) and median inspiratory P_L (7 cm H_2O [IQR 2–11] vs 7 cm H_2O [IQR 5–9], $P = .90$) did not change significantly after P_L-guided set PEEP or V_T increase. Nine of 12 subjects receiving vasoactive drug prior to set PEEP increase remained on vasoactive drug, and 1 subject was started on vasoactive drugs after set PEEP increase ($P = .53$). No pneumothorax resulted from P_L-guided set PEEP or V_T increase.

Exploratory analysis of pulmonary mechanics and oxygenation response to P_L-guided ventilator setting adjustment detected a significant median increase in respiratory system compliance of 30.7 mL/cm H_2O (IQR 26.6–41.5) vs 44.6 mL/cm H_2O (IQR 37.6–51.0) ($P = .001$), a median decrease in P_L driving pressure of 10 cm H_2O (IQR 7–12) vs 6 cm H_2O (IQR 4–8) ($P = .001$), and a median increase in P_{aO_2}/F_{IO_2} of 156 (IQR 97–190) vs 240 (IQR 207–266) ($P = .002$) (Fig. 2). A majority of our subjects demonstrated either moderate hypoxemia ($n = 12$) or severe hypoxemia ($n = 4$) before P_L-guided ventilator setting adjustment, whereas after P_L-guided ventilator setting adjustment none experienced severe hypoxemia, 7 subjects experienced moderate hypoxemia, and a greater number of subjects experienced either mild hypoxemia ($n = 8$) or no hypoxemia ($n = 5$). While a majority of subjects experienced less severe hypoxemia after P_L-guided ventilator setting adjustment, the difference between before and after P_L-guided ventilator setting adjustment was not statistically significant when comparing no hypoxemia and mild hypoxemia to moderate hypoxemia and severe hypoxemia classifications ($P = .71$) (Fig. 3). No significant difference was found in S_{pO_2}/F_{IO_2} when comparing baseline S_{pO_2}/F_{IO_2} (192 mm Hg [IQR 122–243]) and 24-h S_{aO_2}/F_{IO_2} (310 mm Hg [IQR 245–330], $P = .18$), whereas a significant and sustained oxygenation difference was detected in the 48-h S_{aO_2}/F_{IO_2} (300 mm Hg [IQR 245–376], $P = .006$), the 72-h S_{aO_2}/F_{IO_2} (319 mm Hg [IQR 266–393], $P < .001$), and the 96-h S_{aO_2}/F_{IO_2} (283 mm Hg [IQR 277–363], $P < .001$) after P_L-guided LPV (Fig. 4).

ICU Outcomes and Mortality

The median ICU length of stay was 14 d (IQR 10–25), and the median number of ventilator-free days was 7 d (IQR 6–10). All-cause ICU mortality was 15% ($n = 3$). Two subjects died after being transitioned to comfort care due to devastating neurologic injury, and 1

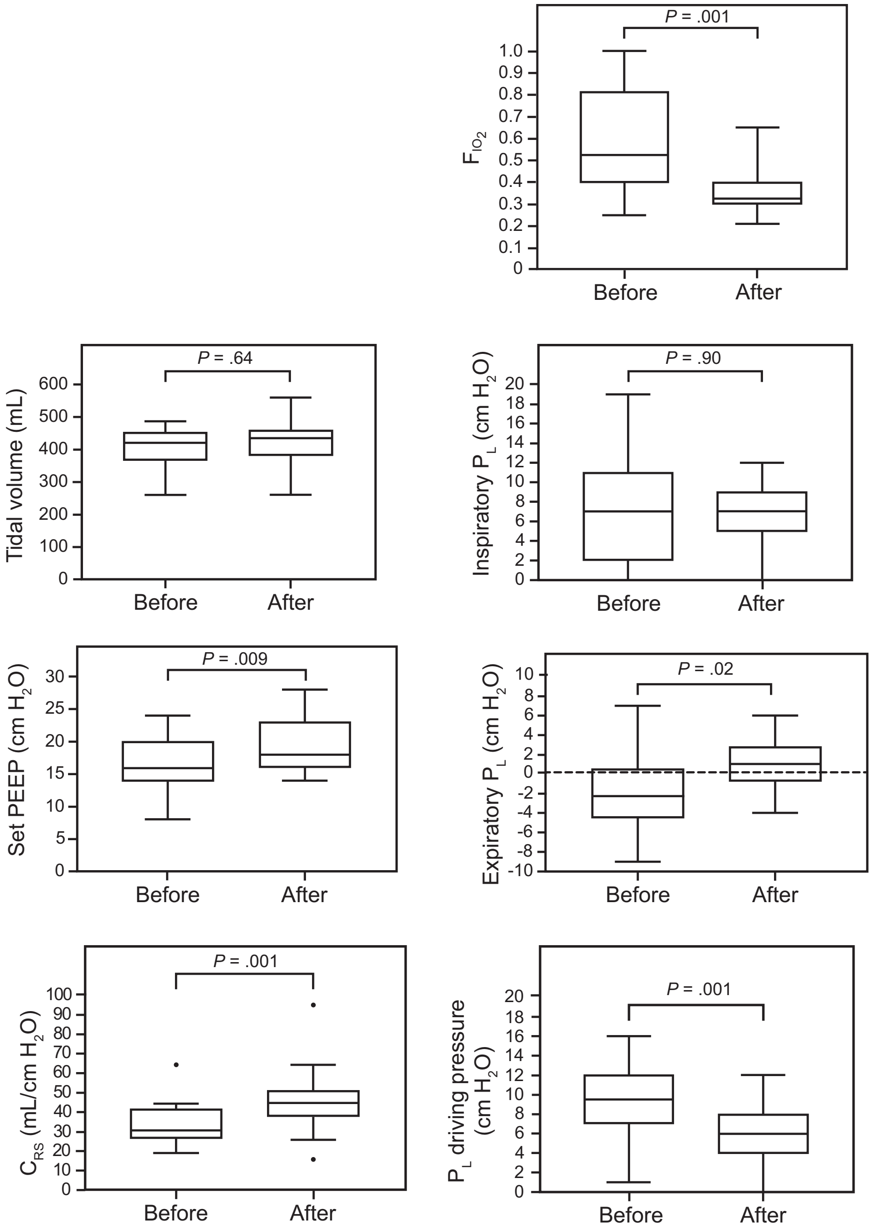

Fig. 1. Box plots of mechanical ventilator settings and pulmonary mechanics before and after P_L-guided ventilator setting adjustment. $P < .05$ is considered significant. Black circle indicates outlier extending > 1.5 box lengths from the edge of box. P_L = transpulmonary pressure; C_{RS} = respiratory-system compliance.

subject was withdrawn from mechanical ventilation due to multi-organ dysfunction.

Discussion

The primary findings of implementing P_L-guided LPV in morbidly obese subjects was significant adjustments to mechanical ventilator settings that resulted in increased respiratory system compliance and oxygenation and decreased driving pressure when compared to a conventional non-P_L-guided LPV ventilator management strategy.

Obesity is a global problem in health care, and up to one third of patients admitted to the ICU are obese.[12] Taking care of obese patients in the ICU can be challenging. One of the main challenges is management of the ventilator to optimize the respiratory system. Obese patients exhibit altered pulmonary mechanics compared to non-obese patients. Obesity lends itself to normal chest-wall elastance and decreased lung elastance, but increased thoracoabdominal wall pressure caused by obesity increases end-expiratory esophageal pressure and decreases P_L, promoting loss of lung volume and atelectasis.[13-15] Despite the high

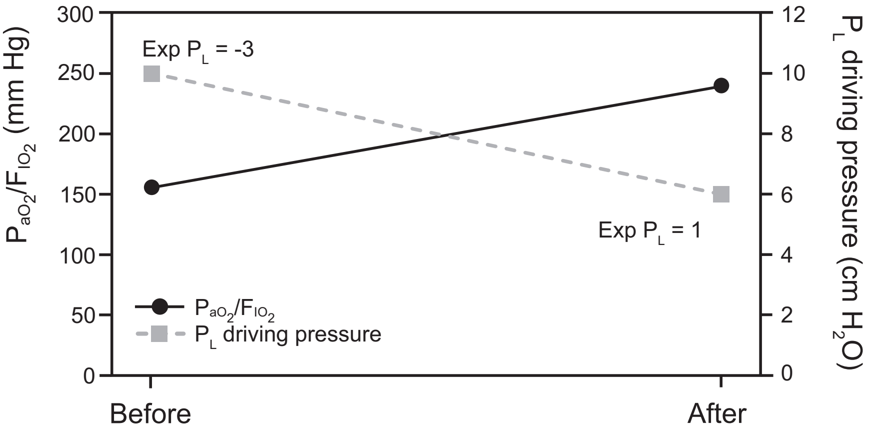

Fig. 2. P_{aO_2}/F_{IO_2} and P_L driving pressure response to P_L-guided set PEEP adjustment. Change in P_{aO_2}/F_{IO_2} ($P = .002$) and change in P_L driving pressure ($P = .001$). $P < .05$ is considered significant. P_L = transpulmonary pressure.

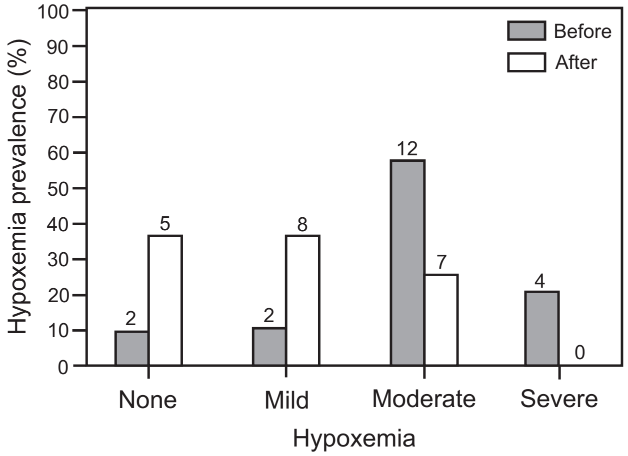

Fig. 3. Distribution of hypoxemia severity before and after P_L-guided mechanical ventilator setting adjustment. Hypoxemia severity classification: None = $P_{aO_2}/F_{IO_2} > 300$ mm Hg; Mild = $P_{aO_2}/F_{IO_2} < 300$ mm Hg; Moderate = $P_{aO_2}/F_{IO_2} < 200$ mm Hg; Severe = $P_{aO_2}/F_{IO_2} < 100$ mm Hg. Frequency count is at the top of the hypoxemia classification bars. P_L = transpulmonary pressure.

prevalence of obesity and the changes in respiratory function observed in this population, very few studies have investigated how to optimize mechanical ventilation in the ICU.

In a recent editorial published in RESPIRATORY CARE, Diehl et al[16] suggested that monitoring esophageal pressure to set optimal PEEP while aiming to achieve a positive end-expiratory P_L could improve the prognosis of obese and severely obese patients with ARDS. However, optimal set PEEP for obese patients remains unclear. Pirrone et al[17] reported that clinician-driven set PEEP (11.6 ± 2.9 cm H_2O) was inadequate for morbidly obese subjects in the ICU. We know that higher set PEEP is needed to offset the pressure from the chest wall mass and abdominal pressure causing atelectasis.[18] The PROBESE study noted no difference between set PEEP 4 cm H_2O versus recruitment maneuvers and set PEEP 12 cm H_2O during general anesthesia in obese subjects without ARDS.[19] These studies bring to light the lack of customized mechanical ventilation management strategies in morbidly obese patients.

P_L manometry has been studied since 1970, when Agostoni et al[20,21] reported that tidal changes in esophageal pressure correlated with pleural pressures applied to the lung surface. This enables a valid estimate of P_L based on the difference between alveolar and esophageal pressure. Since then, multiple studies have evaluated the use of P_L manometry to guide ventilation management based on physiologic parameters in ARDS, but few have looked at its utility in the morbidly obese population.

Florio and colleagues[22] published the first observational study looking at the impact of different mechanical ventilator strategies on Class 3 obese subjects with ARDS. Their lung rescue team incorporated P_L manometry into their assessment for best-PEEP versus following a standard mechanical ventilation protocol approach that utilized the ARDSNet low PEEP/F_{IO_2} combination table.[23] The authors concluded that individualized titration of mechanical ventilation that utilized P_L measurements to guide set PEEP was associated with decreased mortality when compared to the use of the ARDSNet low PEEP/F_{IO_2} table.[22]

In our cohort, 19 of the 20 subjects required PEEP adjustment after initiating P_L guided LPV. The median set PEEP was increased from 14 cm H_2O to 18 cm H_2O to a obtain a slightly positive expiratory P_L. Fumagalli et al[24] described P_L during decremental PEEP titration among extremely obese subjects with mean BMI of 58.6 kg/m^2 who received care in ICU. They reported that set PEEP of 21.7 ± 3.7 cm H_2O resulted in the lowest elastance of the respiratory system and corresponded to a positive end-expiratory P_L. This allowed for restoration of end-expiratory lung volume and improved oxygenation. Fumagalli et al[24] also reported that, in extremely obese subjects, a negative

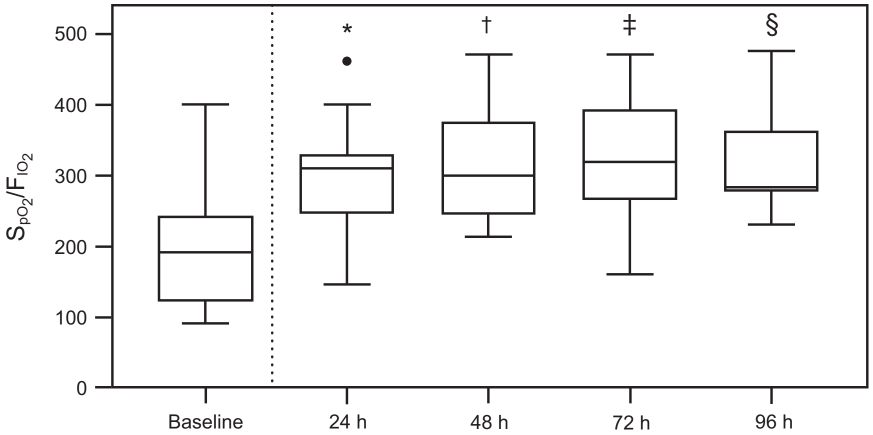

Fig. 4. S_{pO_2}/F_{IO_2} trend after P_L-guided mechanical ventilator setting adjustment Black circle indicates outlier extending > 1.5 box lengths, and asterisk indicates outlier extending > 3 box lengths from the edge of box. Adjusted $P \leq .01$ is significant. *$P = .18$ (Baseline vs 24 h); †$P = .006$ (Baseline vs 48 h); ‡$P = .001$ (Baseline vs 72 h); §$P < .001$ (Baseline vs 96 h).

P_L predicted lung collapse and decruitment. In addition, Eichler et al[25] observed that laparoscopic bariatric subjects in the operating room require high levels of set PEEP to maintain positive P_L. set PEEP of 16.7 cm H_2O before and 23.8 cm H_2O during capnoperitoneum were necessary to achieve positive expiratory P_L. These numbers were confirmed with electrical impedance tomography. Both studies align with our results indicating that morbidly obese patients need a higher level of set PEEP to establish and maintain a positive P_L in order to optimize lung-protective mechanical ventilation.

Our findings are in agreement with those of Pirrone et al[17] and Florio et al[22] in that set PEEP for mechanically ventilated obese patients in the ICU appears to be underestimated both when it is empirically set and when providers use the ARDSNet low PEEP/F_{IO_2} table to guide best set PEEP in this patient population. When extrapolating our preP_L-guided LPV strategy to the ARDSNet high PEEP/F_{IO_2} table,[26] we would have been directed to increase PEEP from 14 cm H_2O up to 16–20 cm H_2O. Our P_L-guided set PEEP was increased to 18 cm H_2O, which falls within the ARDSNet high PEEP/F_{IO_2} set PEEP range for our median F_{IO_2} of 0.53. It is plausible, had we referred to the ARDSNet high PEEP/F_{IO_2} table to determine initial set PEEP at the onset of mechanical ventilation, that we may have achieved similar oxygenation and pulmonary mechanics results. However, median F_{IO_2} was decreased to 0.33 within 24 h after increasing set PEEP to 18 cm H_2O; while expiratory P_L remained slightly positive, the high PEEP/F_{IO_2} table indicates that PEEP should be set at 12–14 cm H_2O. We speculate that decreasing set PEEP as directed by the ARDSNet high PEEP/F_{IO_2} table would have resulted in a negative expiratory P_L and subsequent dorsal lung region atelectasis, worsening oxygenation, and increased risk for ventilator-induced lung injury due to atelectrauma.

As LPV has evolved, it is recognized that PEEP is used not only to recruit atelectactic lung tissue but also to stabilize dependent lung regions and guard against atelectrauma that may occur when dorsal pleural pressure exceeds alveolar pressure at end-exhalation, such as what may occur in obese patients. Future studies should seek to develop BMI-adjusted set PEEP/F_{IO_2} combination tables that are distinguished by obesity classification categories and derived from P_L or electrical impedance tomography measurements to determine if meaningful prognostic and other important clinical outcome differences result.

Higher driving pressure in patients with ARDS has been found to increase mortality.[27] In obese patients with and without ARDS, this relationship has not been well studied. The respiratory physiology changes of obese patients differ from those of non-obese patients. The transthoracic pressure, which consists of the chest and abdomen, is higher in obese patients than in non-obese patients.[28] A P_L-driven LPV strategy resulted in a median decrease in driving pressure from 13 cm H_2O to 10 cm H_2O in our subjects. De Jong et al[29] hypothesized that, in obese subjects with ARDS, driving pressure would not represent the real pressure applied to the lungs and would not be associated with mortality. They found that driving pressure at day 1 was not significantly different in survivors at day 90 (13.7 ± 4.5 cm H_2O) when compared to nonsurvivors (13.2 ± 5.1 cm H_2O. Our all-cause ICU mortality was 15%, but this consisted of obese subjects with and without refractory hypoxemia. More studies are needed to establish the relationship of driving pressure and mortality in obese patients without ARDS.

In the EPVent trial,[8] the use of higher set PEEP based on P_L improved P_{aO_2}/F_{IO_2} and respiratory system compliance. Our findings were similar, with a significant increase in respiratory system compliance and P_{aO_2}/F_{IO_2} and a decreased driving pressure with higher set PEEP. We also noted a shift from moderate and severe hypoxemia to mild or no hypoxemia. Baedorf Kassis et al[30] also reported that set PEEP driven to target positive P_L improved elastance and driving pressures.

Results from a multicenter study of subjects with ARDS indicated that $V_T > 6.5$ mL/kg PBW at the onset of ARDS was associated with a greater risk of ICU mortality when compared to subsequent V_T values.[31] Our subjects had a median V_T of 6 mL/kg PBW at the onset of mechanical ventilation, and median airway driving pressure was 13 cm H_2O when measured just prior to baseline P_L measurement. Inspiratory P_L was 7 cm H_2O before and after any V_T increase. In a recent study by Kalra et al,[32] 53% of subjects characterized with Class 3 obesity (BMI $>$ 40 kg/m^2) received $V_T > 8$ mL/kg PBW and had an airway driving pressure of 16 cm H_2O on day 1 of mechanical ventilation; both of these values are associated directly with increased risk for alveolar stress and mortality. When comparing day 1 and day 2 of mechanical ventilation, the authors reported a V_T decrease from $>$ 8 mL/kg PBW (53%) to V_T of 6–8 mL/kg PBW (49%). Median V_T among our subjects did not change significantly when comparing V_T values before P_L guided LPV (6.0 mL/kg PBW [IQR 5.6–6.0]) with V_T values after P_L-guided LPV (6.0 mL/kg PBW [IQR 6.0–7.0], $P = .17$). Three of our subjects had a V_T increase to $>$ 8.0 mL/kg PBW to optimize ventilation. They had a plateau pressure $>$ 30 cm H_2O prior to increasing V_T, and plateau pressure did not change significantly after V_T and PEEP increase. However, P_L driving pressure did decrease significantly from 10 cm H_2O (IQR 7–12) to 6 cm H_2O (IQR 4–8). Having P_L driving pressure measurements available for these subjects allowed our clinicians to comfortably customize mechanical ventilator settings by increasing V_T while objectively assessing for risk of alveolar stress when confronted with clinically important acute respiratory acidosis.

Direct and elastance ratio-based methods are used to obtain P_L measurements, but these methods yield different results. When the esophageal catheter balloon is properly placed in the retrocardiac position, a reasonable estimate of plateau pressure in the chest can be obtained with either method. Yoshida et al[33] conducted an animal and cadaver study that compared esophageal pressure at the mid-thoracic region and direct pleural pressure measured from sensors placed in the pleura space. The authors reported that the direct method reasonably estimated P_L in the dependent lung region (ie, the region most prone to atelectasis), whereas the elastance ratio-based method estimated P_L better in the nondependent lung region (ie, the region most at risk for overdistention). While the elastance ratio-based method may provide a more accurate estimate of P_L in the nondependent lung compared to the direct method, there is controversy surrounding this method because of assumptions that must be made to obtain valid measurements. For example, one assumption is that plateau pressure and P_L are equal at end-inspiration and end-expiration. However, extrathoracic pressure resulting from obesity increases plateau pressure, thus causing a negative P_L, which challenges this assumption. These changes lead us to use the direct method described by Talmor et al[8] to measure both inspiratory and expiratory P_L.

There is a long-standing concern that higher airway pressures result in hemodynamic instability and negatively affect right-ventricular function. Twelve of our 20 subjects were on a vasoactive drug prior to P_L-guided ventilator management. Nine subjects remained on vasoactive drugs after the study, and 1 subject was started on a vasoactive drug after set PEEP increase. We can also report that there were no pneumothorax events with significant ventilator setting adjustments. The ART trial[34] reported an increased need for vasoactive drug administration and increased incidence of pneumothorax when comparing lung recruitment maneuver with set PEEP titration to low set PEEP groups. In contrast, Florio et al[22] reported that lung rescue with lung recruitment and set PEEP titration resulted in a decrease in the need for vasoactive drugs. This was explained by the decrease in pulmonary vascular resistance and reduced right-ventricular workload when atelectatic lungs are recruited. The decrease in P_L driving pressure after P_L-guided set PEEP increase suggests lung tissue recruitment in our cohort of subjects. This may partially explain the decrease in vasoactive drug administration experienced by some of our patients after they received P_L-guided LPV.

A multinational ARDS workgroup[7] conducted a large observational study to better understand the impact of ARDS globally. Importantly, it was found that clinicians underrecognized ARDS when it was present. Our licensed independent practitioners requested a P_L manometry consult within 16 h of initiating mechanical ventilation. When considering ARDS pathogenesis and its typical clinical presentation time of 24–48 h after exposure to a risk factor,[35] we believe that clinicians caring for patients in our analysis recognized unresolving hypoxemia early and subsequently recommended P_L manometry to optimize mechanical ventilator settings. Our data suggest that obese subjects who received P_L-guided LPV experienced ventilator setting adjustment that may have mitigated progression of hypoxemia severity and risk of atelectrauma.

Limitations

This study has several limitations, the first being the study design. Quality improvement data analysis and not having a control group for comparison limits the generalization of our findings. It is possible that the use of a high PEEP/F_{IO_2} table or electrical impedance tomography to guide LPV may yield similar findings. Second, our sample size was relatively small due to being a single-center retrospective analysis. Third, we used 2 methods to obtain P_L measurements. However, the respiratory therapists who performed the P_L measurements received procedure training and followed a standard of practice clinical practice guideline that includes validated methods for obtaining P_L measurements using esophageal pressure manometry as described previously. Fourth, cardiac function and volume status evaluation with bedside echocardiography were not available for comparison of findings before and after P_L-guided LPV ventilator setting adjustments. Fifth, it has been reported that obese patients with ARDS have a high prevalence of complete airway closure at end-expiration during passive ventilation, which lends itself to the possibility of overestimating set PEEP requirement when targeting a PEEP. A calculation to correct for this possibility has been proposed[13]; however, we did not adjust our measured expiratory P_L measurements to correct for this possibility. While it is possible that an adjusted expiratory P_L may have resulted in a lower set PEEP requirement, our set PEEP finding is similar to what other investigators have reported for this patient population.

Conclusions

The use of esophageal pressure manometry to determine P_L measurements could potentially help clinicians optimize LPV ventilator settings, improve pulmonary mechanics, and improve oxygenation among morbidly obese patients. Future studies should compare the early use of P_L-guided LPV to a control group treated with a strategy that consists of a high PEEP/F_{IO_2} table or electrical impedance tomography to determine if there is a difference in LPV ventilator settings and important clinical outcomes for obese mechanically ventilated patients.

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