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Individualized Multimodal Physiologic Approach to Mechanical Ventilation in Patients With Obesity and Severe Acute Respiratory Distress Syndrome Reduced Venovenous Extracorporeal Membrane Oxygenation Utilization

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OBJECTIVE: To investigate whether individualized optimization of mechanical ventilation through the implementation of a lung rescue team could reduce the need for venovenous extracorporeal membrane oxygenation in patients with obesity and acute respiratory distress syndrome and decrease ICU and hospital length of stay and mortality.

DESIGN: Single-center, retrospective study at the Massachusetts General Hospital from June 2015 to June 2019.

PATIENTS: All patients with obesity and acute respiratory distress syndrome who were referred for venovenous extracorporeal membrane oxygenation evaluation due to hypoxemic respiratory failure.

INTERVENTION: Evaluation and individualized optimization of mechanical ventilation by the lung rescue team before the decision to proceed with venovenous extracorporeal membrane oxygenation. The control group was those patients managed according to hospital standard of care without lung rescue team evaluation.

MEASUREMENT AND MAIN RESULTS: All 20 patients (100%) allocated in the control group received venovenous extracorporeal membrane oxygenation, whereas 10 of 13 patients (77%) evaluated by the lung rescue team did not receive venovenous extracorporeal membrane oxygenation. Patients who underwent lung rescue team evaluation had a shorter duration of mechanical ventilation ($p = 0.03$) and shorter ICU length of stay ($p = 0.03$). There were no differences between groups in in-hospital, 30-day, or 1–year mortality.

CONCLUSIONS: In this hypothesis-generating study, individualized optimization of mechanical ventilation of patients with acute respiratory distress syndrome and obesity by a lung rescue team was associated with a decrease in the utilization of venovenous extracorporeal membrane oxygenation, duration of mechanical ventilation, and ICU length of stay. Mortality was not modified by the lung rescue team intervention.

KEY WORDS: acute respiratory distress syndrome; mechanical power; mechanical ventilation; obesity; recruitment maneuver; venovenous extracorporeal membrane oxygenation

The worldwide prevalence of obesity is rising. In the United States, nearly one in two adults are predicted to be obese by 2030 (1). Historically, obesity was a contraindication to using venovenous extracorporeal membrane oxygenation (VV ECMO) given the potential for increased difficulties in obtaining vascular access and the challenges with repositioning

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and transporting the patient (2). Additionally, it can be more challenging to match extracorporeal membrane oxygenation (ECMO) flow to the higher cardiac output associated with obesity and maintain oxygenation. Recent advances in VV ECMO use in patients with obesity have led many centers to adopt its use in this patient population (3–5).

In the United States, the respiratory therapist is the healthcare provider responsible for managing ventilation of patients in the ICU. The respiratory therapist follows the best ventilation protocols ($Pa{O_2}/F{I}{O_2}$ acute respiratory distress syndrome network [ARDSnet] tables) and local guidelines (tidal compliance). At the Massachusetts General Hospital (MGH), patients with obesity and acute respiratory failure are managed using the ARDSnet protocol (6, 7).

Mechanical ventilation is based on either the low positive end-expiratory pressure (PEEP)/high $F{I}{O_2}$ ARDSnet table or the best tidal compliance and driving pressure. Since 2015, VV ECMO was introduced at our institution as rescue therapy for refractory respiratory failure in patients with obesity.

In 2014, the Respiratory Care service at MGH developed a lung rescue team (LRT). The LRT is formed by a critical care physician experienced in cardiopulmonary physiology, the ICU respiratory therapist, the ICU nurse, and two critical care fellows (8). The role of LRT is to assist clinicians in managing patients with obesity and severe acute respiratory distress syndrome (ARDS) by individualizing titration of PEEP and lung recruitment maneuvers while maintaining lung-protective ventilation (8–11). This approach reduced mortality of patients with body mass index (BMI) above 40 and ARDS by nearly 50% compared with the standard-of-care (SOC) PEEP titration approach (12). Since June 2015, the LRT has offered its services to teams managing patients with refractory respiratory failure who have consulted the ECMO team for planned VV ECMO cannulation.

We performed a retrospective evaluation of patients with obesity and ARDS who were evaluated for VV ECMO cannulation and were either evaluated by the LRT or received SOC without LRT consultation. We hypothesized that the individualized approach compared with a protocol-based approach to mechanical ventilation would improve lung mechanics and oxygenation in patients who had failed SOC ventilator management and would reduce the need for VV ECMO.

MATERIAL AND METHODS

Population Selection

This is a single-center retrospective study conducted at MGH, approved by the ethics committee (Partners Healthcare Institutional Review Board number 2019P001995).

Patients with obesity (BMI ≥ 30 kg/m^2) and severe ARDS (13) for whom the ECMO team had planned for VV ECMO cannulation between June 2015 and June 2019 were included in this study. Patients enrolled in an interventional clinical trial or candidates for venoarterial ECMO were excluded. Patients were stratified by those who were evaluated by the LRT ("LRT" cohort) and those who were not ("SOC" cohort).

Data Collection

Data were extracted from the electronic medical record, Heart ECMO Center database, and LRT database. Since the cohorts were not randomized, we compared the likelihood of mortality in each group during the first 48 hours from ICU admission. Simplified Acute Physiology Score (SAPS) II (14), Acute Physiology and Chronic Health Evaluation (APACHE) II (15), and Sequential Organ Failure Assessment (SOFA) (16) scores were recorded. Hospital and ICU length of stay and duration of mechanical ventilation were calculated from the day of hospital admission (at MGH or referring center) and from the day of ECMO team activation. Cessation of mechanical ventilation was defined as spontaneous breathing without any ventilatory support other than oxygen supplementation. Hospital outcomes were recorded until time of death or discharge from MGH. Mortality was assessed at hospital discharge, 30-day, and 1-year after ECMO team activation.

Hemodynamic data, ECMO variables, ventilator settings, drug dosages, and arterial blood gases were recorded. Baseline measurements were collected from within 4 hours before ECMO team evaluation. Follow-up data were collected after ECMO initiation or after LRT consultation if the patient did not undergo ECMO and every 24 hours for 5 days.

Driving pressure, respiratory system compliance, airway resistance, transpulmonary pressure, and mechanical power were calculated as previously described (7, 16). Tidal volume and mechanical power were indexed to predicted body weight. Duration of neuromuscular blockade was calculated from the time of intubation along the first 5 days. The Vasoactive Inotropic Score (17, 18) was calculated and indexed to adjusted body weight to account for the increase of lean body mass in patients with obesity (19).

Mechanical Ventilation

During the study period, patients with obesity were routinely ventilated with PEEP adjusted according to the low PEEP/high FIO_2 ARDSnet table or the best tidal compliance (5, 6, 19). Standard ventilation protocols carried by respiratory therapists did not include the use of spontaneous breathing trials in the early management of ARDS patients. Furthermore, esophageal manometry or CT scan to define lung recruitability was not clinical standards of our center. ECMO patients were ventilated in pressure control mode at a respiratory rate of 10–12 breaths per minute, with 5–10 cm H_2O of PEEP depending on their hemodynamic status. Driving pressure was kept between 10 and 12 cm H_2O. As a result, tidal volume varied depending on lung compliance and patient effort (if not paralyzed) but was never allowed to exceed 8 mL/kg of ideal body weight. The FIO_2 of the sweep gas was always set at 100%. The ventilator FIO_2 was set to achieve an oxygen saturation of at least 88%. Ventilator and ECMO settings were monitored and adjusted as needed by a respiratory therapist.

In the LRT cohort, ventilator settings were adjusted after a multimodal physiologic assessment to optimize medications, ventilator settings, and hemodynamics (8), as summarized in **Figure 1**. The PEEP was tailored following the “Best PEEP” approach previously described by our group (11) and summarized in **Figure 2**. The LRT titrated ventilation after assessing lung mechanics and hemodynamics by using a combination of advanced lung mechanic measurements including, esophageal manometry, transthoracic heart ultrasound, and electrical impedance tomography.

If the ICU and ECMO teams were not satisfied with the patient’s vitals and lung mechanics after the LRT consultation, VV ECMO was initiated, and the ventilator settings were set following the standard practice. The final decision whether proceed to or abort VV ECMO cannulation was independently taken by the ECMO team together with the clinicians responsible for the patient. The LRT had no role in this process.

Patients were weaned from mechanical ventilation following the recommendations of the 2005 International Consensus Conference (21).

Statistical Analysis

All comparative tests were performed according to the initial group assignment. A p value of less than 0.05 was defined as statistically significant. Further details about the statistical analyses performed are reported in the **Supplemental Materials** (see Statistical analysis section, http://links.lww.com/CCX/A668).

RESULTS

Patient Characteristics

From June 2015 to June 2019, VV ECMO cannulation was considered for 33 patients with both severe ARDS and obesity. The LRT consult was requested in all the cases. Thirteen patients received LRT evaluation prior to the final cannulation decision, whereas 20 were treated according to SOC practices. We successfully collected all necessary data for this analysis, except for the ventilator settings of one patient in the SOC group. This patient was included in all other analyses.

There were no differences between the SOC and LRT groups in age, gender, APACHE II, SAPS, and SOFA scores at admission to the ICU. Across both groups, baseline PaO_2/FIO_2 ratio was 82 (68–100), and $PaCO_2$ was 57 mm Hg (42–70 mm Hg). The time spent on mechanical ventilation before the LRT consultation or the start of VV ECMO was below 1 week and similar in both groups (**Table S1**, http://links.lww.com/CCX/A669).

Prone position was not attempted in any patient. Sixty-two percent of patients were on vasoactive medications at the time of ECMO team activation. Median weight was significantly greater in the LRT group (122 vs 103 kg; $p = 0.04$), but there was no difference between groups in BMI or any other anthropometric data (**Table 1**) (Table S1, http://links.lww.com/CCX/A669).

Impact of a Personalized Approach on Clinical Outcomes

The clinical team always implemented the suggestions of the LRT staff. The individualized approach followed by the LRT led to a change in the setting of the ventilator in all patients assessed. Of

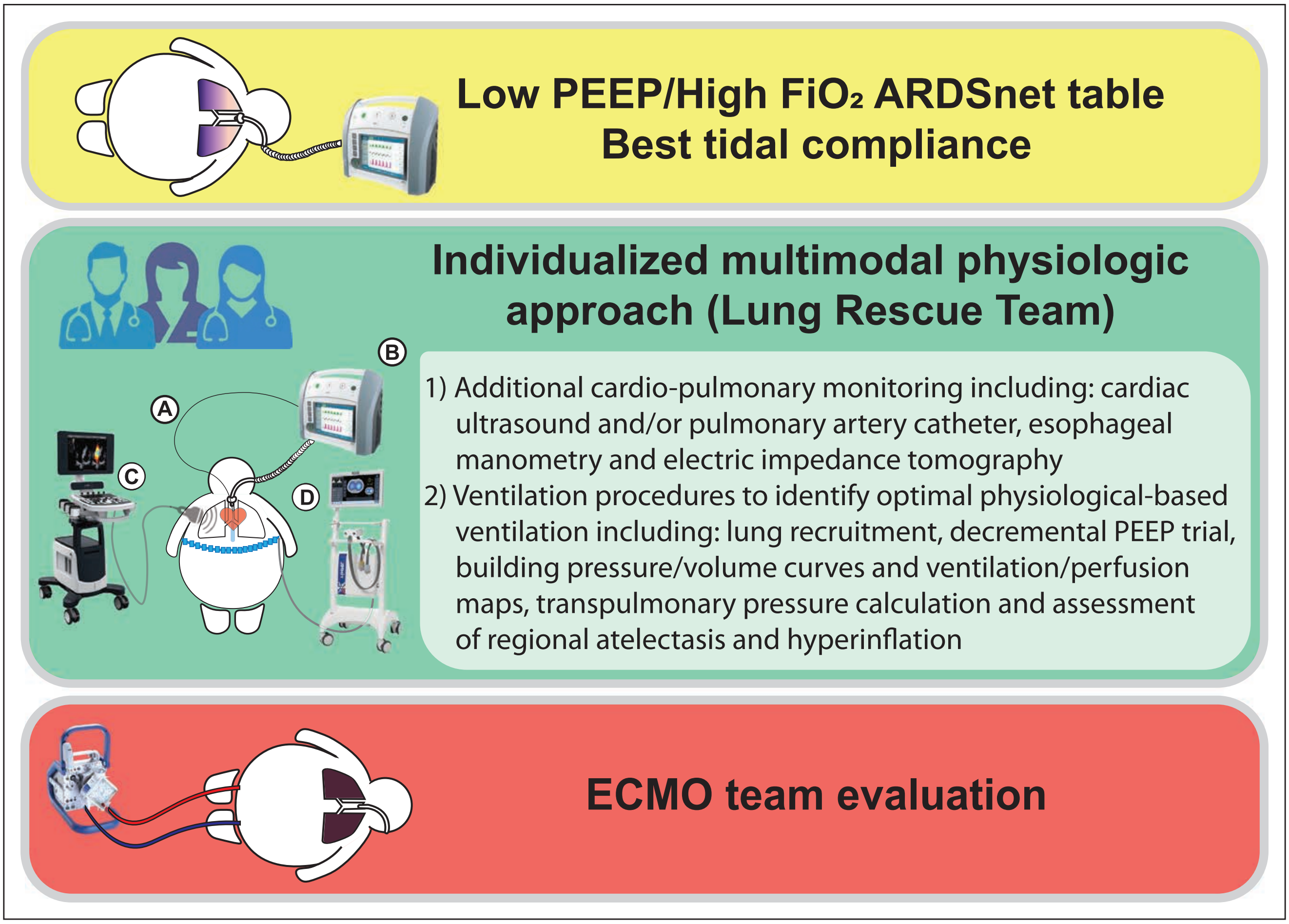

Figure 1. The flow chart shows the clinical pathways of a patient with obesity affected by severe acute respiratory disease. Standard-of-care cohort: patients with obesity and acute respiratory distress syndrome (ARDS) were ventilated according to a protocol-based approach (i.e., ARDS network [ARDSnet] protocol and best tidal compliance). When the patient's lung function deteriorated and the extracorporeal membrane oxygenation (ECMO) Extracorporeal Life Support Organization criteria (20) for VV ECMO were met, the ECMO team started venovenous ECMO. Lung rescue team (LRT) cohort: the LRT was activated together with the ECMO team when a patient with obesity and severe acute respiratory distress syndrome (ARDS) was a candidate for ECMO. Additional criteria to request the LRT consult included the following: 1) patients with class III obesity (i.e., body mass index > 40 kg/m^2) and progressive acute respiratory failure not improving in the first 24 hr of ventilation despite strict compliance to best-practice ventilation protocols; 2) patients with severe ARDS and refractory hypoxemia (i.e., $Pao_2 < 60$ mm Hg, Fio_2 0.8–1.0, and a positive end-expiratory pressure [PEEP] > 10 cm H_2O for > 12–24 hr). Unlike the standard practice, the LRT followed an individualized multimodal physiologic approach to guide ventilation of the patients. At the end of the consultation, the clinical team decided whether to proceed or to hold ECMO cannulation. (A) esophageal manometry, (B) advanced lung mechanics measurements, (C) transthoracic heart ultrasound, (D) electrical impedance tomography.

the 13 patients evaluated by the LRT, the plan for ECMO was aborted in 10 (77%; $p < 0.001$). ECMO was initiated in the remaining three patients because lung compliance did not improve and driving pressure remained elevated (above 15 cm H_2O) regardless of PEEP titration. A description of these three patients' clinical conditions is summarized in (**Table S2**, http://links.lww.com/CCX/A670). The LRT cohort had a significantly shorter duration of mechanical ventilation (median 9 vs 20 d; p = 0.03) and ICU length of stay (median 13 vs 21 d; p = 0.03) and a trend toward less frequent need for tracheostomy (31% vs 65%; p = 0.08).

Last, there were no differences between groups in hospital length of stay, medication use, incidence of acute kidney injury, initiation of renal replacement therapy, intrahospital mortality, or 30-day and 1-year mortality (**Table 2**) (Table S1, http://links.lww.com/CCX/A669). Notably, the only three deaths in the LRT cohort were those same three patients who required VV ECMO.

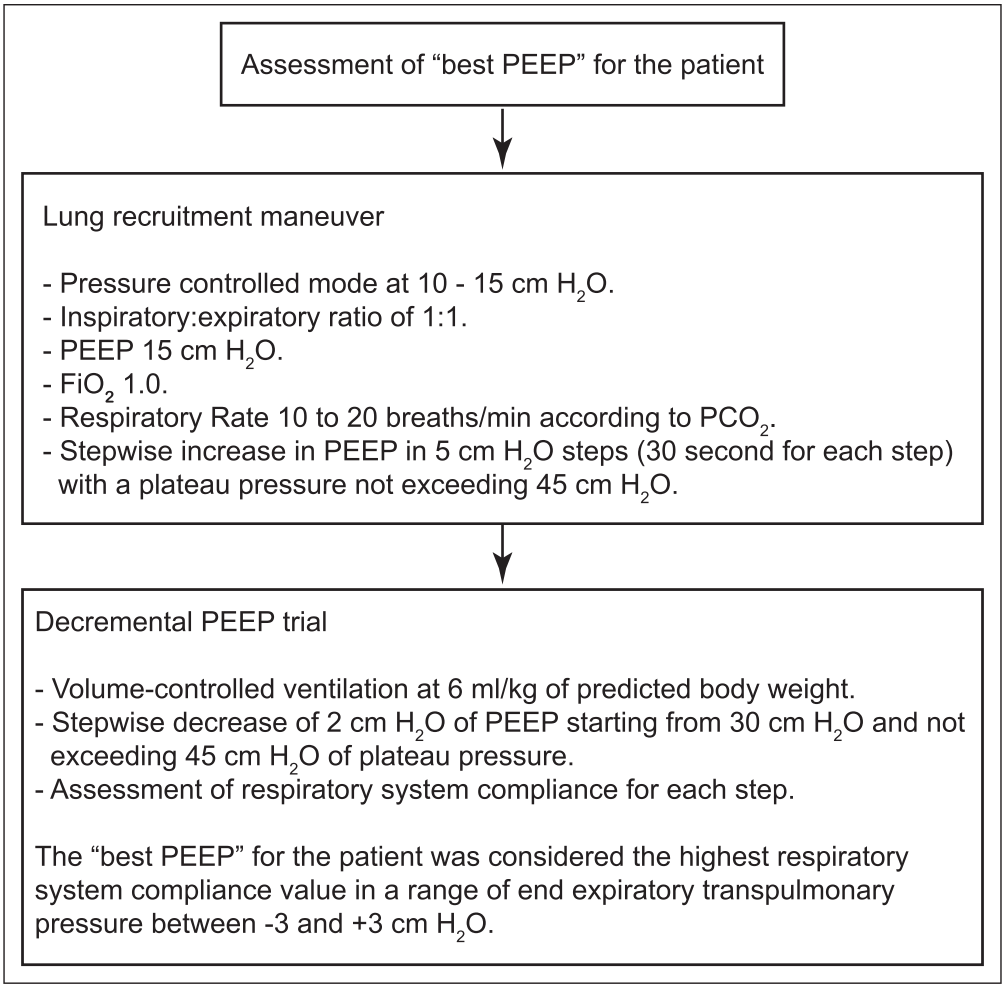

Figure 2. The flow chart summarizes the main procedure for positive end-expiratory pressure (PEEP) titration. End-expiratory transpulmonary pressure was calculated as the difference between total PEEP (PEEP set on ventilator + auto-PEEP) and end-expiratory esophageal pressure.

Ventilation Management and Respiratory System Function

The baseline PEEP and end-expiratory esophageal pressure of LRT cohort recorded during the consultation were 14 cm H_2O (10–16 cm H_2O) and 18 cm H_2O (17–27 cm H_2O) ($p = 0.02$), respectively. The end-expiratory transpulmonary pressure was measured in 11 patients and was −8 cm H_2O (−9 to 0 cm H_2O) (please note changes of transpulmonary pressure trace in a patient before and after LRT assessment) (**Fig. S1**, http://links.lww.com/CCX/A668). Ventilation was titrated to best lung mechanics in the LRT cohort of patients (**Fig. 3**). As expected, the LRT cohort had an improvement in respiratory system compliance and oxygenation following the LRT intervention. Driving pressure was overall reduced below 15 cm H_2O, whereas tidal volume and mechanical power remained unchanged (Fig. 3, *B* and *F*, respectively). Oxygenation (Pao_2/Fio_2 median 146 [121–258]) and respiratory acidosis (mean pH 7.31 ± 0.09) improved (**Table S3**, http://links.lww.com/CCX/A671), eliminating the need for VV ECMO in 10 patients.

In the SOC cohort, VV ECMO allowed an ultra-protective mechanical ventilation strategy with tidal volumes well below 6 mL/kg of ideal body weight (22–24). PEEP and overall respiratory system compliance remained unchanged during the first 5 days after the intervention (**Fig. 3, *A*** and ***C***, respectively).

Safety of Procedures

One patient in the LRT cohort experienced a transient increase in the need for inotropic-vasoactive IV medication (norepinephrine) after recruitment maneuver was performed, and 20 cm H_2O of PEEP was set on the ventilator. The highest dose used to counterbalance the hypotension was 0.05 μg/kg/min. No additional adverse events (e.g., pneumothorax or hypotension) were noted with LRT interventions.

DISCUSSION

The present hypothesis-generating study investigates whether the introduction of an individualized multimodal physiologic-based titration of mechanical ventilation through an LRT in addition to ARDSnet protocols was associated with reduced need for VV ECMO in patients with severe ARDS and obesity. We found that individualized titration of mechanical ventilation was associated with avoidance of VV ECMO in 77% of ARDS patients with obesity, compared with the protocol-based approach. The multimodal

TABLE 1.
Baseline Patient Characteristics

Characteristics	Total, *n* = 33	Standard-of-Care Cohort, *n* = 20	Lung Rescue Team Cohort, *n* = 13	*p*
Age, yr, mean ± sd	47 ± 14	46 ± 15	49 ± 14	0.56
Female sex, *n* (%)	15 (45)	10 (50)	5 (38)	0.52
Body mass index kg/m^2, median (interquartile range)	37 (32–45)	34 (32–41)	43 (35–48)	0.10
Obesity, *n* (%)				0.30
Class 1, BMI 30–34.9	16 (49)	11 (55)	5 (38)	
Class 2, BMI 35–39.9	5 (15)	4 (20)	1 (8)	
Class 3, BMI ≥ 40	12 (36)	5 (25)	7 (54)	
Acute Physiology and Chronic Health Evaluation II, mean ± sd	19 ± 5	18 ± 5	21 ± 5	0.11
Sequential Organ Failure Assessment, median (interquartile range)	9 (7–11)	9 (5.5–11)	9 (8–11)	0.97
pH, mean ± sd	7.28 ± 0.12	7.29 ± 0.14	7.27 ± 0.10	0.75
Paco$_2$ mm Hg, median (interquartile range)	57 (42–70)	56 (40–70)	62 (52–68)	0.41
Pao$_2$ mm Hg, median (interquartile range)	82 (64–93)	84 (68–93)	80 (64–85)	0.52
Pao$_2$/Fio$_2$, median (interquartile range)	84 (68–100)	85 (69–93)	84 (66–105)	0.97
Vasoactive drug use, *n* (%)	20 (62)	11 (56)	9 (69)	0.47
Vasoactive Inotropic Score/adjusted body weight, median (interquartile range)	4.2 (0–8.2)	2.9 (0–6.8)	4.2 (0–19.0)	0.44
Outside hospital transfer, *n* (%)	28 (85)	18 (90)	10 (77)	0.36
Cause of acute respiratory distress syndrome, *n* (%)				0.75
Pneumonia	21 (64)	12 (60)	9 (69)	
Sepsis	5 (15)	2 (10)	3 (23)	
Trauma	1 (3)	1 (5)	0 (0)	
Autoimmune	1 (3)	1 (5)	0 (0)	
Others	5 (15)	4 (20)	1 (8)	

BMI = body mass index.

physiologic approach was also associated with an improvement in respiratory system mechanics and gas exchange. The duration of mechanical ventilation and ICU length of stay were significantly reduced in the LRT cohort, but there was no difference in in-hospital, 30-day, or 1-year mortality between the two cohorts.

Patients with obesity typically have increased pleural pressure, atelectasis, and airways closure (8, 24–26). Obstructive sleep apnea (27) and obesity hypoventilation syndrome (28) are common comorbidities and are also associated with impaired gas exchange (28, 29). Acute respiratory diseases like ARDS or pneumonia can easily destabilize this precarious physiologic state, as can sedation and placement in the supine position, further reducing lung volumes, worsening atelectasis, and impairing gas exchange.

Patients with ARDS (6) are typically managed with lung-protective ventilation, using low tidal volumes, low mean airway pressure, and permissive hypercapnia. A recent trial (30) found that recruitment maneuvers and decremental PEEP trials, compared with low PEEP strategies, increased all-cause mortality in patients with moderate to severe ARDS. However, this study did not report patients' BMI. Physiologic studies in patients with class III obesity demonstrate a baseline elevation in pleural pressure that necessitates a higher than normally used PEEP in order to achieve a positive transpulmonary pressure (8, 10, 24–26).

TABLE 2.
Clinical Outcomes in Those Evaluated for Venovenous Extracorporeal Membrane Oxygenation

Outcomes	Total, *n* = 33	Standard-of-Care Cohort, *n* = 20	Lung Rescue Team Cohort, *n* = 13	*p*
ECMO utilization, *n* (%)	23 (70)	20 (100)	3 (23)	< 0.001
ECMO duration, d, median (interquartile range)	8 (5–14)	2 (1–14)	9 (6–18)	0.22
Neuromuscular blockade duration, hr mean ± sd	45 ± 27	50 ± 35	41 ± 20	0.38
Pulmonary vasodilator use, *n* (%)	24 (73)	14 (70)	10 (75)	1.0
Occurence of reintubation, *n* (%)	9 (27)	7 (35)	2 (15)	0.26
Acute kidney injury, *n* (%)	27 (82)	15 (75)	12 (92)	0.36
Of which required renal replacement therapy	16 (59)	9 (60)	7 (58)	0.93
Duration of mechanical ventilation, d, median (interquartile range)	16 (8–22)	20 (12.5–29.5)	9 (5–16)	0.03
ICU LOS after consult, d, median (interquartile range)	17 (11–27)	21 (13–35)	13 (11–16)	0.03
Hospital LOS after consult, d, median (interquartile range)	26 (14–44)	32 (14.5–57)	21 (14–27)	0.19
ICU mortality, *n* (%)	10 (30)	7 (35)	3 (23)	0.70
In-hospital mortality, *n* (%)	10 (27)	7 (35)	3 (23)	0.70

ECMO = extracorporeal membrane oxygenation, LOS = length of stay.

In a 2012 case series of 14 patients, most of whom had obesity and severe ARDS, Grasso et al (31) advocated for the use of lung recruitment maneuvers guided by transpulmonary pressure prior to proceeding with the initiation of ECMO. In a 2016 prospective crossover study of 14 patients with BMI greater than or equal to 35 kg/m^2 and acute respiratory failure, Pirrone et al (9) demonstrated that clinicians often apply inadequate PEEP in obese patients. These patients were found to have highly recruitable lungs, and physiologically guided recruitment maneuvers safely improved oxygenation and respiratory system compliance. Fumagalli et al (11) found that patients with obesity and ARDS also have highly recruitable lungs and require high PEEP to allow for adequate ventilation. Our study similarly showed that these patients with ARDS and obesity responded favorably to higher PEEP. When measured, esophageal pressures were elevated, leading to negative end-expiratory transpulmonary pressure. Hypotension and hemodynamic stability have been a major clinical concern when high airway pressures are applied. In a recent study, De Santis Santiago et al (32) showed that levels of airway pressure that oppose high pleural pressure are well-tolerated hemodynamically in patients with class III obesity and recruitable lungs.

Our results confirmed that even in severely hypoxemic ARDS patients with obesity who had failed conventional ventilator management and were being considered for ECMO, many are still highly recruitable. The individualized LRT approach was safe (only one patient experienced a transient increase in the need for vasoactive medication) and was associated with a reduced need for ECMO. Our results suggest that initiation of ECMO without individualized lung optimization may therefore be premature. Last, our results support the use of an individualized multimodal physiologic approach to mechanical ventilation in the obese population.

To study lung stress due to mechanical ventilation, we determined the mechanical power applied in both groups (16, 21, 31, 33). By providing oxygenation to patients in a near-apneic state (i.e., ultraprotective lung ventilation) (34), ECMO instantly reduced mechanical power. Recently, Serpa Neto et al (35) reported a positive association between mechanical power, hospital length of stay, ICU length of stay, ICU mortality, and 30-day mortality and identified an increased risk of death when the absolute mechanical power was higher than 17.0 J/min. In a regression analysis, Dianti et al (36) identified the tidal volume, the driving pressure, and the dynamic component of mechanical power

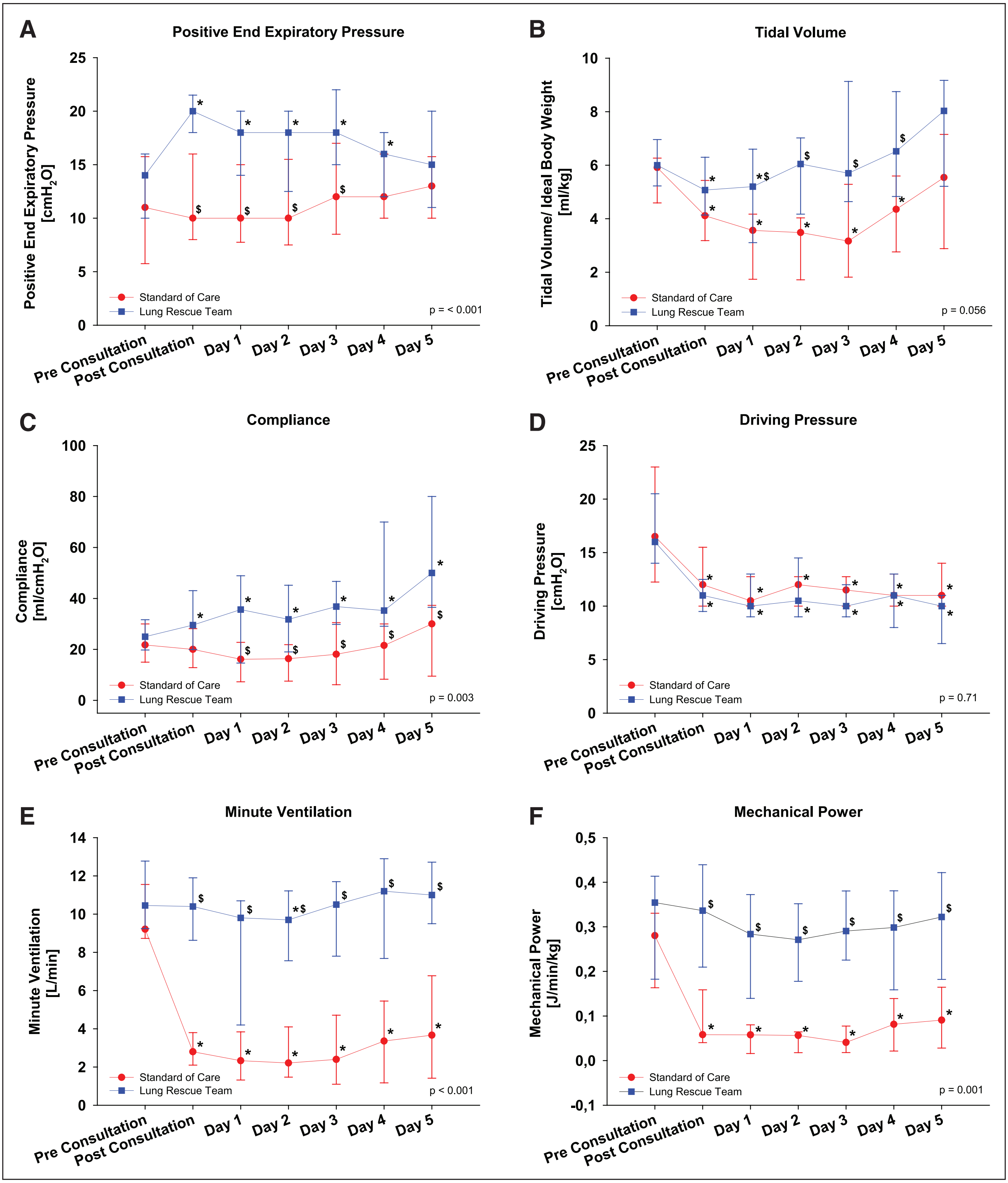

Figure 3. Synoptic panel summarizing the main lung mechanic measurements. **A**, Positive end-expiratory pressure trends along the first 5 d; (**B**) tidal volume trends along the first 5 d; (**C**) compliance trends along the first 5 d; (**D**) driving pressure trends along the first 5 d; (**E**) expired minute ventilation trends along the first 5 d; (**F**) mechanical power trends along the first 5 d. *Within-subjects analysis versus pre consultation $p < 0.05$. $Between-subjects analysis $p < 0.05$.

as major culprits for mortality. However, to date, no human studies have demonstrated the impact of total mechanical power on mortality (31, 36). Furthermore, definitive data are still missing on the use of an ultra-protective lung ventilation strategy during VV ECMO, compared with standard ARDSnet tidal volume calculations. However, recently, Del Sorbo et al (24) demonstrated that there was a linear relationship between tidal volume and plasma biomarkers of ventilator-induced lung injury, whereas Costa et al (37) found that among ventilator variables, only driving pressure and respiratory rate had significant associations with mortality.

In our study, patients in the SOC cohort experienced a significant reduction in applied mechanical power when undergoing VV ECMO due to the adoption of an ultraprotective lung ventilation strategy. In the LRT cohort, mechanical power remained unchanged despite increased PEEP, presumably due to successful recruitment maneuvers with resultant improvement in respiratory system compliance, leading to a reduced driving pressure for the same tidal volume.

Despite LRT evaluation and attempt at respiratory optimization, three patients still received VV ECMO. It is important to remark that we do not believe that an individualized approach is an alternative to VV ECMO, since there are clearly states of lung disease that are not amenable to further ventilator optimization and that will only benefit from lung rest (23, 37, 38). However, we believe that this retrospective study indicates that among patients with ARDS who also have obesity, lung recruitment and mechanics can often be further optimized with methods employed by the LRT. In addition to protocol-based ventilation, a personalized approach such as LRT approach could therefore avoid the need for ECMO support in some patients. Widespread implementation of an LRT-like approach at nontertiary hospitals may obviate the need for hospital transfers from centers without ECMO available (39), eliminating the inherent risks of patient transport and preserving referral center capacity for other cases.

There are several limitations to this study. First, this is a small, retrospective, single-center study that should be limited to describing physiologic patterns and outcomes, and a larger randomized trial would be necessary to demonstrate a benefit. Second, despite the LRT being informed about VV ECMO evaluation, our staff was not always immediately available to gather and support the primary clinical team. Whether the implementation of a 24×7 LRT improves mortality is unknown. Although the baseline characteristics and the pulmonary function in the SOC group are similar to those of the LRT group, there may be unmeasured differences between the groups. In addition, it is not clear which LRT intervention provided the most benefit and whether all elements of the protocol are necessary to see benefit. There are also no data on whether the patients in either group had already received personalized PEEP titration; notably, all but one of the SOC group were enrolled in the medical ICU, where a best tidal compliance approach is standard, and it is not clear the degree to which the LRT would have benefitted these patients. Last, given the unique physiology of patients with obesity, it is not clear whether these results can be generalized to a larger population.

CONCLUSIONS

The implementation of an LRT-like approach can guide the management of patients with obesity and severe ARDS by optimizing ventilator settings and respiratory system compliance. An individualized multimodal physiologic-based mechanical ventilation was associated with a reduced need for ECMO and reduced duration of mechanical ventilation and ICU length of stay.

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REFERENCES

1. Ward ZJ, Bleich SN, Cradock AL, et al: Projected U.S. state-level prevalence of adult obesity and severe obesity. *N Engl J Med* 2019; 381:2440–2450
2. Tulman DB, Stawicki SPA, Whitson BA, et al: Veno-venous ECMO : A synopsis of nine key potential challenges, considerations, and controversies. *BMC Anesthesiology* 2014; 14:65
3. Kon ZN, Dahi S, Evans CF, et al: Class III obesity is not a contraindication to venovenous extracorporeal membrane oxygenation support. *Ann Thorac Surg* 2015; 100:1855–1860
4. Galvagno SM Jr, Pelekhaty S, Cornachione CR, et al: Does weight matter? Outcomes in adult patients on venovenous extracorporeal membrane oxygenation when stratified by obesity class. *Anesth Analg* 2020; 131:754–761
5. Al-Soufi S, Buscher H, Nguyen ND, et al: Lack of association between body weight and mortality in patients on venovenous extracorporeal membrane oxygenation. *Intensive Care Med* 2013; 39:1995–2002
6. Brower RG, Matthay MA, et al; Acute Respiratory Distress Syndrome Network: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000; 342:1301–1308
7. Brower RG, Lanken PN, MacIntyre N, et al; National Heart, Lung, and Blood Institute ARDS Clinical Trials Network: Higher versus lower positive end-expiratory pressures in patients with the acute respiratory distress syndrome. *N Engl J Med* 2004; 351:327–336
8. Spina S, Capriles M, De Santis Santiago R, et al; Lung Rescue Team: Development of a lung rescue team to improve care of subjects with refractory acute respiratory failure. *Respir Care* 2020; 65:420–426
9. Pirrone M, Fisher D, Chipman D, et al: Recruitment maneuvers and positive end-expiratory pressure titration in morbidly obese ICU patients. *Crit Care Med* 2016; 44:300–307
10. Fumagalli J, Berra L, Zhang C, et al: Transpulmonary pressure describes lung morphology during decremental positive end-expiratory pressure trials in obesity. *Crit Care Med* 2017; 45:1374–1381
11. Fumagalli J, Santiago RRS, Teggia Droghi M, et al; Lung Rescue Team Investigators: Lung recruitment in obese patients with acute respiratory distress syndrome. *Anesthesiology* 2019; 130:791–803
12. Florio G, Ferrari M, Bittner EA, et al; investigators of the lung rescue team: A lung rescue team improves survival in obesity with acute respiratory distress syndrome. *Crit Care* 2020; 24:4
13. Ferguson ND, Fan E, Camporota L, et al: The Berlin definition of ARDS: An expanded rationale, justification, and supplementary material. *Intensive Care Med* 2012; 38: 1573–1582
14. Le Gall JR, Lemeshow S, Saulnier F: A new Simplified acute physiology score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993; 270:2957–2963
15. Knaus WA, Draper EA, Wagner DP, et al: APACHE II: A severity of disease classification system. *Crit Care Med* 1985; 13:818–829
16. Vincent JL, Moreno R, Takala J, et al: The SOFA (sepsis-related organ failure assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996; 22:707–710
17. Gattinoni L, Tonetti T, Cressoni M, et al: Ventilator-related causes of lung injury: The mechanical power. *Intensive Care Med* 2016; 42
18. Nguyen HV, Havalad V, Aponte-Patel L, et al: Temporary biventricular pacing decreases the vasoactive-inotropic score after cardiac surgery: A substudy of a randomized clinical trial. *J Thorac Cardiovasc Surg* 2013; 146:296–301
19. Kane-Gill SL, Wytiaz NP, Thompson LM, et al: A real-world, multicenter assessment of drugs requiring weight-based calculations in overweight, adult critically ill patients. *Sci World J* 2013; 2013:909135
20. Extracorporeal Life Support Organization (ELSO): Guidelines for Adult Respiratory Failure. *Extracorpor Life Support Organ* 2017; 1:32
21. Boles JM, Bion J, Connors A, et al: Weaning from mechanical ventilation. *Eur Respir J* 2007; 29:1033–1056
22. Schmidt M, Pham T, Arcadipane A, et al: Mechanical ventilation management during extracorporeal membrane oxygenation for acute respiratory distress syndrome. An international multicenter prospective cohort. *Am J Respir Crit Care Med* 2019; 200:1002–1012
23. Fanelli V, Ranieri MV, Mancebo J, et al: Feasibility and safety of low-flow extracorporeal carbon dioxide removal to facilitate ultra-protective ventilation in patients with moderate acute respiratory distress sindrome. *Crit Care* 2016; 20:36
24. Del Sorbo L, Goffi A, Tomlinson G, et al; International ECMO Network (ECMONet): Effect of driving pressure change during extracorporeal membrane oxygenation in adults with acute respiratory distress syndrome: A randomized crossover physiologic study. *Crit Care Med* 2020; 48:1771–1778
25. Tharp WG, Murphy S, Breidenstein MW, et al: Body habitus and dynamic surgical conditions independently impair pulmonary mechanics during robotic-assisted laparoscopic surgery. *Anesthesiology* 2020; 133:750–763
26. Coudroy R, Vimpere D, Aissaoui N, et al: Prevalence of complete airway closure according to body mass index in acute respiratory distress syndrome. *Anesthesiology* 2020; 133:867–878
27. Wittels EH, Thompson S: Obstructive sleep apnea and obesity. *Otolaryngol Clin North Am* 1990; 23:751–760
28. Olson AL, Zwillich C: The obesity hypoventilation syndrome. *Am J Med* 2005; 118:948–956

29. Pelosi P, Croci M, Ravagnan I, et al: The effects of body mass on lung volumes, respiratory mechanics, and gas exchange during general anesthesia. *Anesth Analg* 1998; 87:654–660
30. Cavalcanti AB, Suzumura ÉA, Laranjeira LN, et al: Effect of lung recruitment and titrated Positive End-Expiratory Pressure (PEEP) vs Low PEEP on mortality in patients with acute pespiratory distress syndrome: A Randomized Clinical Trial. *JAMA* 2017; 318:1335–1345
31. Grasso S, Terragni P, Birocco A, et al: ECMO criteria for influenza A (H1N1)-associated ARDS: Role of transpulmonary pressure. *Intensive Care Med* 2012; 38:395–403
32. De Santis Santiago R, Teggia Droghi M, Fumagalli J, et al: High pleural pressure prevents alveolar overdistension and hemodynamic collapse in ARDS with class III obesity. *Am J Respir Crit Care Med* 2020; 203:575–584
33. Silva PL, Ball L, Rocco PRM, et al: Power to mechanical power to minimize ventilator-induced lung injury? *Intensive Care Med Exp* 2019; 7:38
34. Zietz A, Seiler F, Trudzinski FC, et al: Application of ultra-protective ventilation during extracorporeal membrane oxygenation – feasibility under real-world conditions. *Eur Respir J* 2017; 50:PA2123
35. Serpa Neto A, Deliberato RO, Johnson AEW, et al; PROVE Network Investigators: Mechanical power of ventilation is associated with mortality in critically ill patients: An analysis of patients in two observational cohorts. *Intensive Care Med* 2018; 44:1914–1922
36. Dianti J, Matelski J, Tisminetzky M, et al: Comparing the effects of tidal volume, driving pressure, and mechanical power on mortality in trials of lung-protective mechanical ventilation. *Respir Care* 2020; 66:221–227
37. Costa ELV, Slutsky A, Brochard LJ, et al: Ventilatory variables and mechanical power in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2021Mar 30. [online ahead of print]
38. Vasques F, Duscio E, Pasticci I, et al: Is the mechanical power the final word on ventilator-induced lung injury?-we are not sure. *Ann Transl Med* 2018; 6:395
39. Gutsche J, Vernick W, Miano TA; Penn Lung Rescue: One-year experience with a mobile extracorporeal life support service. *Ann Thorac Surg* 2017; 104:1509–1515