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# Treatment of Bronchopleural and Alveolopleural Fistulas in Acute Respiratory Distress Syndrome With Extracorporeal Membrane Oxygenation, a Case Series and Literature Review

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**OBJECTIVES:** To describe a ventilator and extracorporeal membrane oxygenation management strategy for patients with acute respiratory distress syndrome complicated by bronchopleural and alveolopleural fistula with air leaks.

**DESIGN, SETTING, AND PARTICIPANTS:** Case series from 2019 to 2020. Single tertiary referral center–University of California, San Diego. Four patients with various etiologies of acute respiratory distress syndrome, including influenza, methicillin-resistant *Staphylococcus aureus* pneumonia, e-cigarette or vaping product use-associated lung injury, and coronavirus disease 2019, complicated by bronchopleural and alveolopleural fistula and chest tubes with air leaks.

**MEASUREMENTS AND MAIN RESULTS:** Bronchopleural and alveolopleural fistula closure and survival to discharge. All four patients were placed on extracorporeal membrane oxygenation with ventilator settings even lower than Extracorporeal Life Support Organization guideline recommended ultraprotective lung ventilation. The patients bronchopleural and alveolopleural fistulas closed during extracorporeal membrane oxygenation and minimal ventilatory support. All four patients survived to discharge.

**CONCLUSIONS:** In patients with acute respiratory distress syndrome and bronchopleural and alveolopleural fistula with persistent air leaks, the use of extracorporeal membrane oxygenation to allow for even lower ventilator settings than ultraprotective lung ventilation is safe and feasible to mediate bronchopleural and alveolopleural fistula healing.

**KEY WORDS:** acute respiratory distress syndrome; barotrauma; extracorporeal membrane oxygenation; pneumothorax; thoracostomy

Bronchopleural and alveolopleural fistulas (BAPFs) are exceedingly difficult to treat in patients with acute respiratory distress syndrome (ARDS) on ventilatory support. Approximately 10–30% of ARDS cases are complicated by a BAPF, with 2% having a persistent air leak (PAL) (1, 2). Despite conventional ventilator strategies for ARDS (i.e., low tidal volume [TV] ventilation), increased transpulmonary pressures (TPPs) and high respiratory rates (RRs) may impede closure of a BAPF (2, 3). We describe patients with ARDS and BAPF who were placed on extracorporeal membrane oxygenation (ECMO) to allow for low ventilator pressures that promote BAPF closure.

BAPF are pathologic connections between either the bronchi or alveoli to the pleural space. Differentiating between them can be difficult and both can have a prolonged or PAL defined as an air leak greater than 5 to 7 days (4). PALs

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are associated with longer hospital stays and increased mortality. Bronchopleural fistulas can occur in trauma, post-radiation or microwave ablation, pulmonary infections, or iatrogenic due to pulmonary resections or airway procedures (5). Alveolopleural fistulas etiologies include spontaneous pneumothorax, pulmonary infections such as necrotizing pneumonias, malignancies, iatrogenic after thoracentesis or chest tube placement, and barotrauma from mechanical ventilation. There is considerable overlap in the etiologies of BAPFs and differentiating the cause may be important for therapeutic options. Traditionally bronchopleural fistulas are treated surgically, while alveolopleural fistulas are managed nonoperatively, that is, tube thoracostomy. When positive pressure ventilation is required, the goal is to minimize airway pressures to facilitate BAPF closure (6). Other therapies for refractory BAPF have included surgical repair, endobronchial procedures (endobronchial valves, etc.), and pleurodesis (7). There is considerable variability in the management of BAPFs, depending on the etiology and local expertise.

Conventional ventilator management in ARDS relies on low TV ventilation and plateau pressure goals, which are defined as 6 mL/kg of ideal body weight (IBW) and less than 30 cm $H_2O$, respectively. However, this level of ventilatory support may impede BAPF healing due to high TPP. TPP is the distending pressure across the lung (pressure difference from airway opening to pleural space) (8). In the setting of BAPFs, high TPP promotes PALs (9). Thus, decreasing the TPP may help facilitate closure of BAPF.

ECMO is a type of mechanical life support for refractory cardiac and/or respiratory failure (10). This technology has been increasingly used for severe ARDS in the United States since the 2009 H1N1 influenza pandemic and again in 2020 due to the coronavirus disease 2019 (COVID-19) pandemic (11). There is controversy surrounding ventilator management while on ECMO for ARDS. While on ECMO, the Extracorporeal Life Support Organization (ELSO) recommends ultra-protective lung ventilation (UPLV), which is used at the majority of ECMO centers (12). UPLV is defined as positive end-expiratory pressure (PEEP) of 10–15 cm $H_2O$, a driving pressure (DP) of 10 cm $H_2O$, and RR of 5–10 breaths per minute (13). Depending on the respiratory system compliance, the lower DP results in lower TVs of ~2–4 mL/kg of IBW. Thus, the goal of UPLV supported by ECMO is to lower the TPP further than low TV ventilation, which will facilitate BAPF closure by decreasing stress across the lung.

We describe our experience in using even lower than UPLV settings in four patients with ARDS and BAPF to allow for further decreases in TPP to promote BAPF closure.

## PATIENTS AND METHODS

This is a retrospective case series from a single tertiary care academic hospital system. Patient records for study inclusion were identified in a previously existing ECMO database from January 1, 2017, to September 30, 2020. Our ECMO database contains data required by the ELSO and is maintained by a group of physician and nurse leaders as part of an institutional quality improvement database. The Institutional Review Board waived the need for informed consent. All patients over the age of 18 years with ARDS who had a BAPF prior to ECMO initiation were included. The primary outcomes were BAPF closure and survival to discharge. Excel 365 (Microsoft, Redmond, WA) was used for data collection and analysis.

## RESULTS

These four patients' demographics, etiology of ARDS and BAPF, and ventilator settings can be seen in **Table 1**. The ventilator settings throughout the patient's hospitalization are found in **Figure 1**. Patient outcomes can be seen in **Table 2**.

### Patient 1

A woman in her late 20s with a history of IV drug abuse presented with fevers and altered mental status and was found to have right internal jugular vein septic thrombophlebitis complicated by methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia, MRSA pneumonia, and ARDS. She was intubated for hypoxic respiratory failure and developed bilateral pneumothoraces for which chest tubes were placed. She also had pneumomediastinum and subcutaneous emphysema with air leaks noted in both chest tubes. The patient was then transferred to our institution with severe ARDS (ratio of $Pa{O_2}$ to $F{IO_2}$ of 96) with a PAL noted from both chest tubes for the preceding 6 days and anuric renal failure. Continuous renal replacement therapy was started using a right femoral dialysis catheter upon arrival. She was also placed on venovenous ECMO with a left femoral

**TABLE 1.**
**Baseline Characteristics, Illness Etiology and Severity, and Ventilator Settings**

| Case | Patient 1 | | Patient 2 | | Patient 3 | | Patient 4 | |
|---|---|---|---|---|---|---|---|---|
| Age range | Late 20s | | Early 20s | | Early 30s | | Early 50s | |
| Sex | Female | | Male | | Female | | Male | |
| Medical history | Illicit drug abuse (methamphetamine and narcotics) | | Asthma, vaping | | Obesity | | Hypertension, polycythemia | |
| Etiology of bronchopleural and alveolopleural fistula | MRSA pneumonia | | E-cigarette or vaping product use-associated lung injury | | Influenza, MRSA pneumonia | | Coronavirus disease 2019 pneumonia | |
| Hospital course, complications, and organ dysfunction | Acute renal failure requiring continuous renal replacement therapy | | *Clostridium difficile* colitis, dysphagia | | Acute renal failure, MRSA bacteremia, *Aspergillus pneumonia* | | None | |
| Sequential Organ Failure Assessment score at ICU admission | 14 | | 8 | | 9 | | 8 | |
| $Pa_{O_2}/F_{IO_2}$ ratio pre-ECMO | 96 | | 115 | | 88 | | 64 | |
| Pre-/Post-ECMO[a] | Pre | Post | Pre | Post | Pre | Post | Pre | Post |
| $Pa_{O_2}$ | 87 | 63 | 66 | 58 | 87 | 97 | 55 | 88 |
| $Pa_{CO_2}$ | 102 | 43 | 44 | 83 | 55 | 38 | 34 | 41 |
| Respiratory rate | 30 | 12 | 32 | 10 | 30 | 19 | 24 | 10 |
| Tidal volume, mL (mL per kg of ideal body weight) | 277 (4.8) | 86 (1.5) | 300 (3.8) | 124 (1.6) | 330 (5) | 78 (1.2) | 370 (6) | 70 (1.1) |
| Positive end-expiratory pressure, cm $H_2O$ | 16 | 14[b] | 12 | 5 | 2 | 2 | 6 | 0 |
| Mean airway pressure, cm $H_2O$ | 23 | 15 | 18 | 7.5 | 15 | 5.2 | 12 | 1.2 |
| Driving pressure, cm $H_2O$ | 20 | 8[b] | 13 | 10 | 36 | 10[b] | 21 | 10[b] |

ECMO = extracorporeal membrane oxygenation, MRSA, methicillin-resistant *Staphylococcus aureus*.
[a]Values pre-ECMO (immediately prior to cannulation); post-ECMO (24 hr postcannulation).
[b]Patient's positive end-expiratory pressure and driving pressure were adjusted while on ECMO, see Figure 1 for day-to-day changes.

21F drainage and left internal jugular 18F reinfusion cannula. Immediate post-ECMO, UPLV was initiated which consisted of: RR from 30 to 12 breaths per minute, DP 20 to 8 cm $H_2O$ resulting in TV from 277 mL (4.8 mL/kg of IBW) to 87 mL (1.5 mL/kg of IBW), and PEEP from 16 to 14 cm $H_2O$. Her PAL resolved after 3 days on ECMO, however, due to intermittent recurrence of air leak, the PEEP was further decreased to 5 and then 0 cm $H_2O$ on ECMO days 12 and 17, respectively. Concurrently, DP was decreased to 5 and then 1 cm $H_2O$ on ECMO days 16 and 17, respectively. With these ventilator settings, which were lower than UPLV (i.e., essentially on T-piece), she required full ECMO support. Three days after these changes, even the intermittent air leak was no longer present. Ventilatory support was gradually increased without recurrent air leak, see Figure 1 for

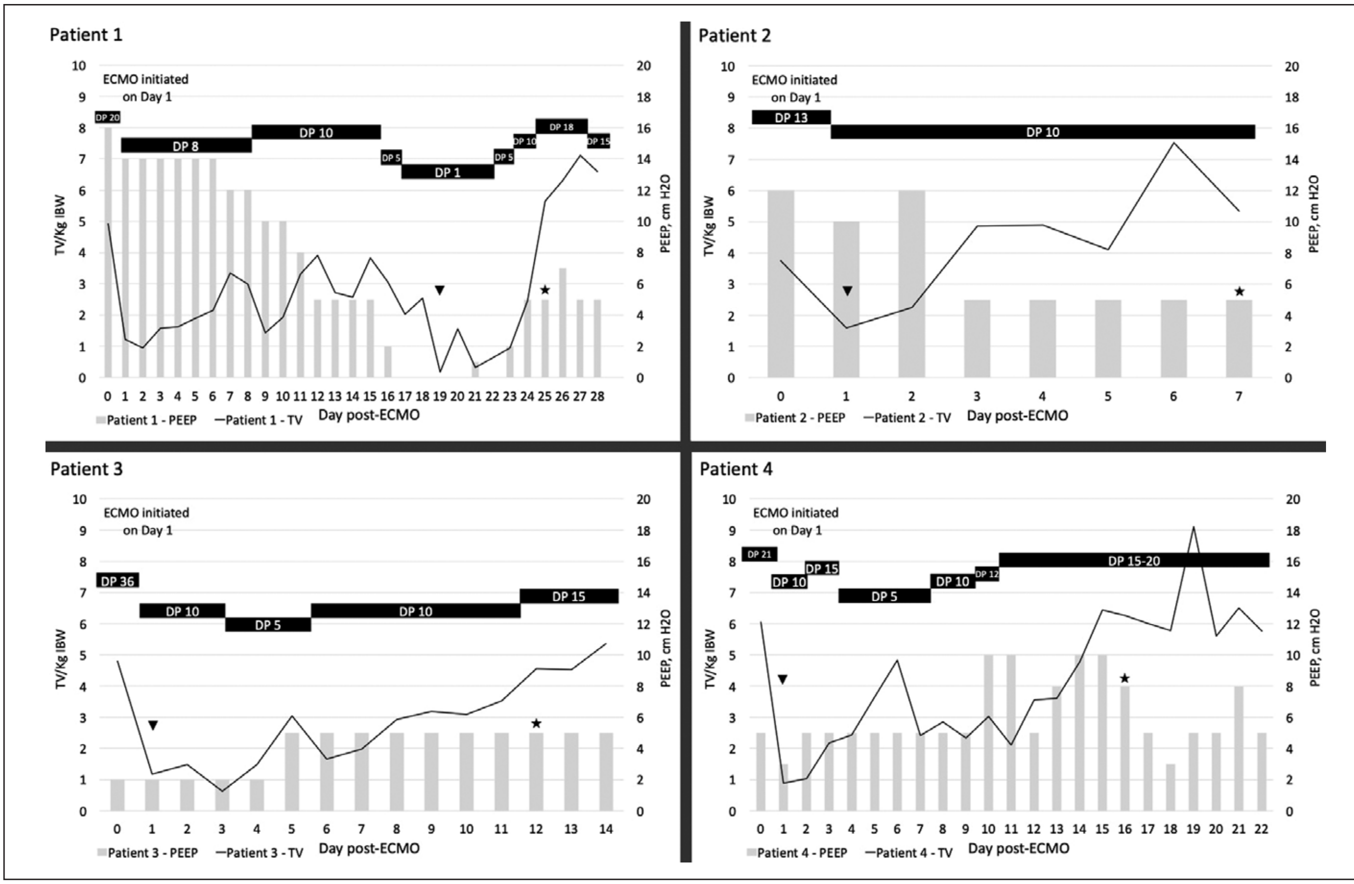


**Figure 1.** The patient's ventilator settings pre- and post-extracorporeal membrane oxygenation (ECMO). *Bar graphs* and *lines* represent the patient's positive end-expiratory pressure (PEEP) and tidal volumes (TVs), respectively, during hospitalization. The *horizontal black bars* represent driving pressure (DP). Day 0 represents the PEEP and TV 24 hr pre-ECMO cannulation. Day 1 represents the ventilator settings immediately post-ECMO cannulation. While on volume cycled ventilation, DP was calculated as end-expiratory plateau pressure minus PEEP. *Star*, date of ECMO decannulation. *Triangle*, last day of chest tube persistent air leak. IBW = ideal body weight.

ventilator management on ECMO. She was weaned off ECMO on day 25 and liberated from the ventilator on day 27. Chest tubes were removed after 35 days, and she was discharged to a long-term acute care (LTAC) facility. Four months later, she returned to visit our ICU and was on room air with no dyspnea.

## Patient 2

A man in his early 20s with a history of asthma who was actively vaping presented with acute dyspnea and developed respiratory failure requiring mechanical ventilation, with course complicated by right-sided pneumothorax requiring a chest tube that had a continuous air leak. An extensive workup for etiology of his respiratory failure, including infectious, medication-induced, and rheumatologic causes, was negative, so he was diagnosed with e-cigarette, or vaping, product use-associated lung injury (EVALI) (14). The patient was placed on venovenous ECMO for moderate ARDS ($Pao_2/Fio_2$ 115) with barotrauma. He had a 28F bicaval dual-lumen ECMO cannula placed in his left subclavian vein under fluoroscopy guidance. Ventilator changes immediately post-ECMO consisted of: RR from 32 to 10 breaths per minute, DP of 13 to 10 cm $H_2O$ resulting in TV from 300 mL (3.8 mL/kg of IBW) to 124 mL (1.6 mL/kg of IBW), and PEEP from 12 to 5 cm $H_2O$. The pre-ECMO PEEP was already in the UPLV desired range of 10–15 cm $H_2O$, thus post-ECMO, the PEEP was specifically titrated even lower to mediate BAPF closure. The patient had a chest tube for 2 days prior to ECMO with a continuous air leak, which resolved immediately upon initiation of ECMO and implementation of UPLV. His pulmonary compliance improved without recurrent air leak, see Figure 1. He tolerated endotracheal intubated and was able to walk around the unit with assistance. After 7 days on ECMO, the patient was decannulated and successfully

**TABLE 2.**
**Case Series Outcomes**

| Case | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| Total CT days/CT days pre-ECMO/ CT days post-ECMO initiation | 35/6/29 | 11/2/9 | 9/3/6 | 28/13/15 |
| Time to resolution of air leak | Three d post-ECMO initiation and minimization of ventilator RR, driving pressure, and PEEP[a] | Same day as ECMO initiation and minimization of ventilator RR, TV, and PEEP | Same day as ECMO initiation and minimization of ventilator RR, TV, and PEEP | Same day as ECMO initiation and minimization of ventilator RR, TV, and PEEP |
| Ventilator days | 27 | 8 | 20 | 27[b] |
| Tracheostomy (intubation day) | Yes (24) | None | Yes (8) | Yes (24) |
| ECMO days | 25 | 7 | 12 | 16 |
| ECMO complications | None | None | None | None |
| Length of hospitalization, d[c] | 35 | 12 | 24 | 42 |
| Survival to hospital discharge | Yes | Yes | Yes | Yes |

CT = chest tube, ECMO = extracorporeal membrane oxygenation, PEEP = positive end-expiratory pressure, RR = respiratory rate, TV = tidal volume.

[a]Patient had a recurrent persistent air leak requiring further decreases in PEEP and TV.

[b]Ventilator days were longer than recorded due to patient being transferred to an long-term acute care while still requiring partial ventilatory support.

[c]Length of hospitalization at our institution; total hospitalization may be longer due to transfer.

extubated the same day, after 8 days on the ventilator. Chest tube was removed after 11 days, and he was discharged home after a 12-day hospitalization.

### Patient 3

An obese woman in her early 30s presented with hypoxic respiratory failure due to influenza with MRSA pneumonia superinfection. Her hospital course was complicated by a right-sided pneumothorax 3 days postintubation requiring a chest tube. Subsequently, a continuous air leak was noted for 3 days prior to transfer to our center, where she was placed on venovenous ECMO (right femoral 25F drainage and right internal jugular 21F reinfusion cannula) for severe ARDS ($Pao_2/Fio_2$ 88) and barotrauma. Ventilator changes post-ECMO consisted of: RR from 30 to 19 breaths per minute, DP from 36 to 10 cm $H_2O$ resulting in TV from 330 mL (5 mL/kg of IBW) to 78 mL (1.2 mL/kg of IBW), and PEEP was maintained at 2 cm $H_2O$. The continuous air leak immediately resolved with ECMO and lower than UPLV settings (specifically the PEEP). There was gradual improvement of pulmonary compliance without recurrent air leak, see Figure 1, and the chest tube was removed after 11 days. The patient was weaned off ECMO after a total of 12 days and extubated after 20 days, and she was discharged home after a 24-day hospitalization.

### Patient 4

A man in his early 50s with hypertension and polycythemia presented with fevers and cough, and he was found to have COVID-19 pneumonia. He was intubated for hypoxic respiratory failure and subsequently developed a right-sided pneumothorax with PAL. He was transferred to our center and placed on venovenous ECMO (right femoral 25F drainage and right internal jugular 21F reinfusion cannula) for severe ARDS ($PaO_2/FIO_2$ 64) and barotrauma. Ventilator changes post-ECMO consisted of: RR from 24 to 10 breaths per minute, DP from 21 to 7 cm $H_2O$ resulting in TV from 370 mL (6 mL/kg of IBW) to 70 mL (1.1 mL/kg of IBW), and PEEP from 6 to 2 cm $H_2O$. With these lower than UPLV settings (DP and PEEP) on ECMO, the patient's PAL, which had been present for 13 days, immediately resolved. Ventilatory support was gradually increased without recurrent air leak, see Figure 1. He was decannulated from ECMO after 16 days, and the chest tube was removed the same day. After 27 days on the ventilator, he was able to tolerate intermittent trach collar and was discharged to an LTAC after his 42-day hospitalization.

## DISCUSSION

We present a case series and literature review of patients who have BAPF with ARDS. There are multiple observations: 1) ECMO should be considered in patients with ARDS complicated by BAPF and PALs; 2) a ventilation strategy with even lower PEEP and DP than UPLV (ELSO guidelines) may be used while on ECMO to further decrease TPP and RR to mediate BAPF closure with air leaks (patients 2 and 3), or PALs (patients 1 and 4); and 3) this strategy may apply to multiple etiologies of ARDS and BAPF including EVALI, influenza, COVID-19, and MRSA pneumonia.

ECMO may be considered in patients with severe ARDS and BAPF (15, 16). ECMO support maintains oxygenation and ventilation, allowing clinicians to minimize ventilatory support, which, in addition to tube thoracostomy, can promote healing of BAPFs. While ECMO cannulation strategies are beyond the scope of this case series, we recommend a cannulation strategy that offers maximal flows with minimal recirculation. This strategy usually requires a two-catheter approach—three patients described in our series had a femoral drainage and internal jugular return cannula. Only case 2 had a single site, dual-lumen ECMO cannula (e.g., Crescent [Medtronic, Minneapolis, MN] or Avalon Elite [Getinge Maquet, Rastatt, Germany]) (17, 18). Single site catheters may be limited due to lower ECMO flows and the need for transesophageal echocardiography or fluoroscopy for cannula placement.

In patients with ARDS and BAPF, ECMO may facilitate closure if used with the appropriate ventilator management that minimizes TPP (i.e., UPLV or lower). This strategy decreases the patient's mean airway pressure and RR. Many ECMO centers use UPLV, similar to the landmark ECMO to Rescue Lung Injury in Severe ARDS study, in an effort to minimize ventilator-induced lung injury (VILI) in ARDS patients (12, 15, 19). Furthermore, decreasing the TPP by reducing the DP may have a mortality benefit in patients with ARDS (9). UPLV can mediate BAPF closure by minimizing air leak that promotes pleural apposition. In three cases (patients 2–4), the air leaks resolved immediately with ventilator settings lower than UPLV as seen in Table 2 and Figure 1. The ventilator settings in these cases were not slowly titrated down but immediately changed post-ECMO cannulation, resulting in the resolution of the air leaks.

However, even with UPLV while on ECMO, some patients may continue to have PAL. This occurred in case 1, who had ongoing air leak while on UPLV. Therefore, we further minimized TPP with a DP of 1 cm $H_2O$ and PEEP of 0 cm $H_2O$, which led to resolution of the air leak. After 3 days, we then challenged the lung with increasing PEEP to see if the air leak would reoccur. In these scenarios, the further decrease in the TPP likely promoted BAPF healing. Additionally, due to the efficiency of ECMO to remove carbon dioxide, the RR can be decreased to 5–10 breaths per minute to further facilitate BAPF closure. This strategy may also further minimize VILI through the decrease in cyclical lung strain with each ventilated breath (19). We acknowledge that some levels of PEEP may be protective against VILI in patients with ARDS by preventing atelectatic trauma and thus superinfections (20, 21). Although there is a paucity of data on long-term outcomes, we believe our strategy offers a pragmatic approach to BAPF treatment.

In some centers, after ECMO initiation, an early tracheostomy is performed, or the patient is extubated, so that they may be quickly weaned off sedation and mechanical ventilation. This strategy minimizes or eliminates the need for positive pressure ventilation that will decrease TPP. Our center does not routinely perform early tracheostomies for ARDS and the decision is made on a case-by-case basis. For example, case 2 did not undergo tracheostomy as it was believed he might recover quickly, and he was still able to participate in physical therapy and other care even with an endotracheal tube in place. However, we note that TPP might still be high (even off of positive pressure ventilation) depending on respiratory drive and the patient's negative intrathoracic pressure during inspiration. Those who are delirious or have ARDS with very poor lung compliance may have persistently high RR/drive. For example, Crotti et al (22) showed that increases in ECMO gas sweep could effectively reduce RR and drive in those ECMO patients with chronic obstructive pulmonary disease or bridge to transplant, but not uniformly in those with ARDS. Thus, we believe minimizing time on positive pressure ventilation (with or without tracheostomy) may help mediate BAPF closure in select patients if their respiratory patterns (as a surrogate for TPP) and BAPF are closely monitored.

To our knowledge, there are no prior reports utilizing our ventilator strategy in medical (i.e., nonsurgical) patients with ARDS and BAPF. There is limited literature utilizing ECMO for patients with traumatic or surgical bronchopleural fistulas, which are summarized in **Table 3** (23–27). Similar to our cohort, ventilator settings were minimized post-ECMO to promote bronchopleural fistula closure. However, these studies have three notable differences. First, our population consists of patients with ARDS, while these studies only included patients with surgical complications resulting in bronchopleural fistulas. Second, the patients in these surgical case series required interventions to repair their BAPFs. Finally, we used venovenous ECMO

**TABLE 3.**
**Previous Case Reports and Series With Bronchopleural Fistulas Treated With Extracorporeal Life Support**

| References | Etiology of Bronchopleural Fistulas | Ventilator Strategies Post-Extracorporeal Life Support | Survival to Discharge/ Total (%) | Other Notes |
|---|---|---|---|---|
| Grant et al (23) | Gunshot wounds, motor vehicle accident | RR 6–7 beats/min, TV ≤ 4 mL/kg of IBW, PEEP ≤ 10 cm $H_2O$, goal PIP 30 cm $H_2O$, and plateau pressure < 25 cm $H_2O$ | 3/3 (100) | ICU days: 84, 175, and 80 d<br>ECMO days: 24, 20, and 16 |
| Khan et al (24) | Lung transplant in cystic fibrosis patient | RR 12 beats/min, driving pressure 18 mm Hg, and PEEP 2 mm Hg | 1/1 (100) | Two cm fistula in donor right main stem bronchus closed with a pericardial and intercostal pedicle flap |
| Daoud et al (26) | Lung transplant, lobectomies, and esophagectomies | RR ≤ 10 beats/min, TV ≤ 4 mL/kg of IBW, PEEP ≤ 5 cm $H_2O$, goal PIP 30 cm $H_2O$, and $FIO_2$ ≤ 0.6 | 2/5 (40) | All were placed on venoarterial ECMO |
| Hommel et al (25) | Pneumonectomy, lobectomy, trauma, and esophageal resection | TV ≤ 4 mL/kg of IBW and PEEP not titrated | 4/4 (100) | Treated with pumpless extracorporeal carbon dioxide removal. Two were treated with surgical repair and the other two with fibrin |
| Dünser et al (27) | Pneumonectomy | Airway pressure release ventilation, peak pressure 25 mbar, PEEP 12 mbar, inspiratory time 1.7 s, expiratory time 0.5 seconds, and $FIO_2$ 1.0 | 1/1 (100) | Surgical repair with ECMO support |

beats/min = breaths per minute, ECMO = extracorporeal membrane oxygenation, IBW = ideal body weight, PEEP = positive end-expiratory pressure, PIP = peak inspiratory pressure, RR = respiratory rate, TV = tidal volume.

for all our patients, while some patients in these series were placed on extracorporeal carbon dioxide removal or venoarterial ECMO.

The standard therapy for BAPF with air leaks may not apply in patients with ARDS; thus, we have recommended the following algorithm in **Figure 2**. Therapies for PALs such as endobronchial valves, stents, and surgical repair may not be tolerated in patients with ARDS due to their high oxygenation and ventilation requirements. Endobronchial valve placement may not be feasible as multiple lobes may be affected by BAPFs since ARDS causes diffuse lung injury. Furthermore, these patients may not tolerate neither the sequential balloon occlusion necessary to determine optimal endobronchial valve location nor having a lung segment unable to participate in gas exchange postvalve placement (28). However, during ECMO support, these therapies may be better tolerated. Only in case 1 were endobronchial valves considered; however, we decided to pursue a trial of very low TPP before attempting placement of a valve. Cases 2–4 did not have endobronchial valves considered due to the quick resolution of the BAPF post-ECMO and implementation of UPLV or lower. Case 4 was also not considered a candidate due to the concerns for staff exposure to COVID-19 during the procedure. Finally, use of blood patches for BAPF in patients with ARDS may not be feasible or safe since these critically ill patients often have a baseline low hemoglobin and would poorly tolerate infectious complications.

There are many unanswered questions. Importantly, the optimal PEEP, DP, and resulting TPP in patients with ARDS on ECMO is currently unknown. Because TPP includes spontaneous respiratory efforts, it may

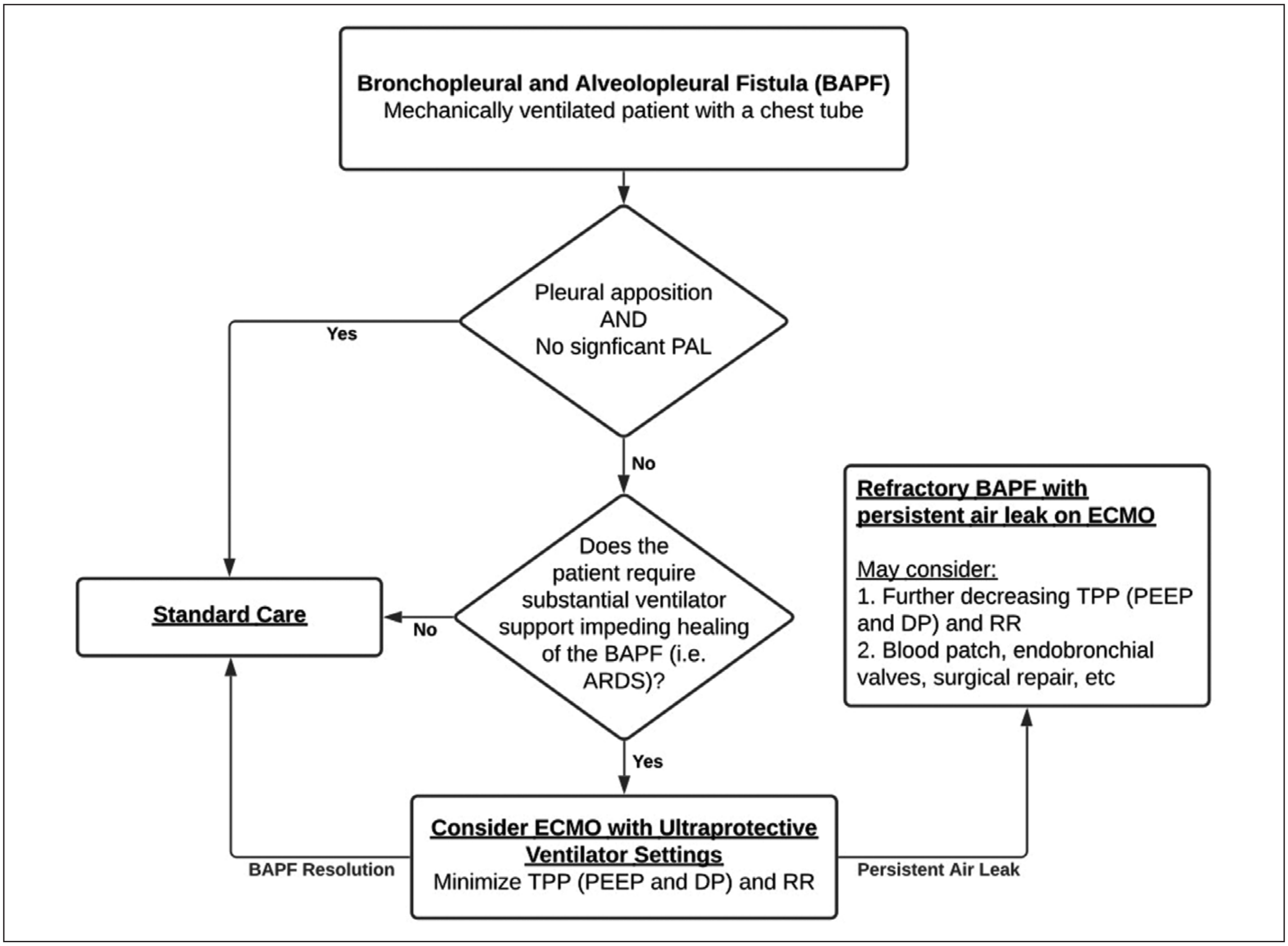


**Figure 2.** Algorithm for treatment of mechanically ventilated patients with acute respiratory distress syndrome (ARDS) and bronchopleural and alveolopleural fistulas (BAPFs). DP = driving pressure, ECMO = extracorporeal membrane oxygenation, PAL = persistent air leak, PEEP = positive end-expiratory pressure, RR = respiratory rate, TPP = transpulmonary pressure.

be important to also reduce spontaneous respiratory drive with sedation or even neuromuscular blockade while providing full ECMO support. Substantial respiratory drive that increases TPP may be a limiting factor to early extubation (with or without tracheostomy) while on ECMO support. We further have little evidence to guide our duration of UPLV (or even lower ventilator settings as in our cases) with low TPP, when to rechallenge the lung with higher TPP, and the long-term outcomes in these patients. Longer courses of UPLV increase the inherent risks associated with mechanical ventilation and ECMO support, such as ventilator-associated pneumonia and bleeding. Importantly, in our series, the decision to place patients on ECMO were based not solely on presence of BAPF but also the severity of ARDS. Again, the risks and benefits of this approach have not been delineated. Further rigorous research in this area is needed, both small physiologic studies carefully measuring TPP as well as larger multicenter studies of ventilator management comparing hard outcomes.

## CONCLUSIONS

In patients with ARDS, ECMO and standard UPLV can be used to promote closure of BAPF. However, even with UPLV, there are select cases with refractory PALs in which further decreases in TPP (DP and PEEP) and RR could be considered.

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