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High-Frequency Percussive Ventilation Facilitates Weaning from Extracorporeal Membrane Oxygenation in Adults

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Abstract: Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is an invaluable rescue therapy for patients suffering from cardiopulmonary arrest, but it is not without its drawbacks. There are cases where patients recover their cardiac function, yet they fail to wean to mechanical conventional ventilation (MCV). The use of high-frequency percussive ventilation (HFPV) has been described in patients with acute respiratory failure (RF) who fail MCV. We describe our experience with five patients who underwent VA-ECMO for cardiopulmonary arrest who were successfully weaned from VA-ECMO with HFPV after failure to wean with MCV. Weaning trials of HFPV a day before decannulation or at the time of separation from VA-ECMO were conducted. Primary endpoint data collected include pre- and post-HFPV partial pressures of oxygen (PaO_2) and PaO_2/FIO_2 (P/F) ratios measured at 2 and 24 hours after institution of HFPV. Additional periprocedural data points were collected including length of time on ECMO, hospital stay, and survival to discharge. Four of five patients were placed on VA-ECMO subsequent to percutaneous coronary intervention. One patient had cardiac arrest secondary to RF. Mean PaO_2 (44 ± 15.9 mmHg vs. 354 ± 149 mmHg, $p < .01$) and mean P/F ratio (44 ± 15.9 vs. 354 ± 149, $p < .01$) increased dramatically at 2 hours after the initiation of HFPV. The improvement in mean PaO_2 and P/F ratio was durable at 24 hours whether or not the patient was returned to MCV (n = 3) or remained on HFPV (n = 2) (44 ± 15.9 mmHg vs. 131 ± 68.7 mmHg, $p = .036$ and 44 ± 15.9 vs. 169 ± 69.9, $p < .01$, respectively). Survival to discharge was 80%. The data presented suggest that HFPV may be used as a strategy to shorten time on ECMO, thereby reducing the negative effects of the ECMO circuit and improving its cost efficacy. **Keywords:** high frequency percussive ventilation (HFPV), extra-corporeal membrane oxygenation (ECMO), volume diffusive respirator (VDR), mechanical conventional ventilation (MCV). *J Extra Corpor Technol. 2018;50:53–57*

Venoarterial extracorporeal membrane oxygenation (VA-ECMO) has been invaluable as a rescue therapy for patients suffering from cardiopulmonary arrest, but it is not without its drawbacks. Because of its serious hemorrhagic, thromboembolic, and infectious complications, the duration of VA-ECMO should be limited in patients as long as their cardiopulmonary status is stable. At our institution from December 2011 to December 2016, we weaned five patients from VA-ECMO to high-frequency percussive ventilation (HFPV), thereby reducing the time spent on VA-ECMO.

HFPV is useful in patients with respiratory failure (RF) who fail mechanical conventional ventilation (MCV) and are being considered for ECMO. However, we have also used HFPV to wean or rescue patients from VA-ECMO, in addition to obviating the need for it. Historically, patients being treated for severe acute respiratory distress syndrome (ARDS) or pulmonary failure with ECMO receive "lung rest" with MCV. Literature on the preferred mode of ventilation in patients being treated for cardiac failure with VA-ECMO, however, is limited. Some reports suggest HFPV may improve oxygenation and ventilation at lower mean and peak airway pressures than MCV with minimal effect on hemodynamics and reduced regional overdistension and associated ventilator-induced lung injury. We report our experience using HFPV to separate five patients from VA-ECMO instituted for cardiopulmonary arrest.

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METHODS

This study was approved by our local institutional review board. Informed consent was waived because of

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the observational retrospective design of the study. Our institution's electronic medical records were queried using the term ECMO, from December 2011 to December 2016. Forty-six patients were identified with 34 of them being VA-ECMO. Of all VA-ECMO cases, five patients were weaned from VA-ECMO to HFPV after they failed to be weaned to MCV. Based on our institution's algorithm for RF treatment, HFPV is used in patients who fail MCV and are being considered for ECMO (1). This algorithm was applied to these five patients who were already on ECMO to facilitate their weaning from ECMO.

Information collected included demographics, data pertaining to ECMO (time from ECMO initiation to HFPV, duration of ECMO), and pre- and post-respiratory parameters such as fraction of inspired oxygen (FiO_2), peak end-expiratory pressure (PEEP), peak inspiratory pressure (PIP), tidal volume, partial pressures of arterial oxygen (PaO_2), and PaO_2 to FiO_2 (P/F) ratios at 2 and 24 hours after initiation of HFPV, duration of HFPV (Tables 1–2). Lung compliance and Murray scores of each patient before HFPV initiation were calculated using their PIP and chest radiographs.

Statistical Analysis

Baseline demographic and clinical data are presented as mean ± SD. Continuous data were analyzed with Student's t test. A p-value of $<.05$ was considered statistically significant. Analysis was performed using Stata 14.1 (StataCorp, College Station, TX).

RESULTS

Five VA-ECMO patients were weaned to HFPV after they failed weaning to MCV. Mean patient age was 54 ± 23 years. All patients underwent ECMO during cardiopulmonary arrest. Four of them had cardiac arrest during percutaneous coronary intervention and one went into cardiopulmonary arrest after being intubated for RF. Pre-HFPV and HFPV data at 2 and 24 hours are listed in Table 2. Mean time on ECMO was 5.8 ± 4.7 days. Arterial blood gas and ventilatory settings just before the institution of HFPV demonstrated severe hypoxemia with a mean P/F ratio of 44 ± 15.9 and a mean PEEP of 7.8 ± 1.8 cm of H_2O. The mean Murray score was 2.7 ± .7, consistent with the presence of severe lung injury. The mean PaO_2 increased significantly from 44 ± 15.9 to 354 ± 149 mmHg ($p < .01$) 2 hours after the initiation of HFPV with corresponding increase in mean P/F ratio from 44 ± 15.9 mmHg to 354 ± 149 mmHg ($p < .01$). The effect of HFPV on oxygenation was durable 24 hours after initiation of HFPV with a mean PaO_2 of 131 ± 68.7 mmHg ($p < .036$) and the mean P/F ratio of 169 ± 149 ($p < .01$) (Table 2). Mean time on HFPV was 2.2 ± 2.2 days and mean time on a ventilator was 18.6 ± 12.4 days. Survival to discharge was 80%, with one patient succumbing to progressive right heart failure after separation from ECMO.

DISCUSSION

In this article, we present our experience with HFPV as a weaning method for VA-ECMO patients who fail weaning from ECMO to MCV. It appears that in these patients, improvement in the respiratory function lags behind improvement of their cardiac function, and therefore, does not allow adequate ventilation and oxygenation on MCV. ECMO has become an essential rescue therapy in the management of our critically ill patients suffering from respiratory or cardiac failure who fail therapy on maximal ventilator settings and pharmacologic support. As our institution has gained considerable experience with the use of ECMO and its complications, we started looking for ways to limit the time our patients spend on ECMO to decrease its associated complications. Some of the more severe causes of morbidity and mortality seen in patients on ECMO include bleeding, thromboembolic events, infection, hypoxemia, and central nervous system events. Bleeding complications, which are very common in patients on ECMO, may be because of the fact that most ECMO patients need anticoagulation. However, apart from systemic anticoagulation, bleeding might also be a result of

Table 1. Individual patient data.

Patient	Etiology of Cardiac Arrest	Etiology of Respiratory Failure	Procedures	Age, Years	Gender	Outcome
1	Cardiac arrest during PCI related aortic dissection	ARDS CPE	PCI, CABG, and aortic repair	61	Male	Died, due to right heart failure
2	Cardiac arrest secondary to anomalous coronary artery	CPE	PCI	16	Female	Survived to discharge
3	Cardiac arrest secondary to hypoxemia from severe pneumonia	Pneumonia CPE	None	75	Male	Survived to discharge
4	Cardiac arrest during PCI	CPE	PCI	52	Female	Survived to discharge
5	Cardiac arrest during PCI	ARDS CPE	PCI	64	Male	Survived to discharge

CABG, coronary artery bypass grafting; CPE, cardiogenic pulmonary edema; PCI, percutaneous coronary intervention.

Table 2. ECMO and ventilatory variables.

Subject	1	2	3	4	5	Mean ± SD
Pre-HFPV ventilatory data						
Ventilatory mode	PRVC	PRVC	CMV	ASV	PRVC	
Murray's score	1.8	3.3	3.3	2.3	2.8	2.7 ± .7
PEEP, cm H_2O	8	8	10	5	8	7.8 ± 1.8
PIP, cm H_2O	14	36	19	18	20	21.4 ± 8.5
Respiratory rate/min	22	25	16	24	12	19.8 ± 5.6
FiO_2, %	100	100	100	100	100	100 ± .0
pH	7.4	7.2	7.7	7.3	7.5	7.40 ± .2
PaO_2, mmHg	28	61	61	32	38	44 ± 15.9
pCO_2, mmHg	36	42	27	38	43	37.2 ± 6.4
O_2 saturation, %	48	84	96	57	76	72.2 ± .2
P/*F* ratio	28	61	61	32	38	44 ± 15.9
2 hour HFPV ventilatory data						
Ventilatory mode	HFPV	HFPV	HFPV	HFPV	HFPV	
FiO_2, %	100	100	100	100	100	100 ± .0
pH	7.4	7.4	7.3	7.5	7.6	7.4 ± .1
PaO_2, mmHg	158	481	230	436	466	354 ± 149
pCO_2, mmHg	30	45	60	31	40	41.2 ± 12.2
O_2 saturation, %	99	100	100	100	100	99.8 ± .0
P/*F* ratio	158	481	230	436	466	354 ± 149
24 hour HFPV ventilatory data						
Ventilatory mode	HFPV	HFPV	PRVC	CMV	PRVC	
FiO_2, %	100	100	50	90	60	80 ± .2
pH	7.4	7.3	7.5	7.4	7.4	7.4 ± .1
PaO_2, mmHg	55	221	108	184	90	131 ± 68.7
pCO_2, mmHg	66	44	35	39	42	45.2 ± 12.1
O_2 saturation, %	88	100	99	100	97	96.8 ± .1
P/*F* ratio	55	221	216	204.4	150	169 ± 69.9
Duration of ECMO, days	14	4	4	2	5	6.0 ± 5.1
Days on ECMO to HFPV	15	1	4	2	5	5.4 ± 5.6
Time on HFPV, days	2	6	1	1	1	2.2 ± 2.2
Tracheostomy	Yes	Yes	No	No	Yes	
Time on ventilator, days	15	29	10	5	34	18.6 ± 12.4
Length of hospital stay, days	17	44	17	12	40	26.0 ± 14.8
Survival to discharge	No	Yes	Yes	Yes	Yes	

FiO_2, fraction of inspired oxygen; PaO_2, partial pressure of oxygen; pCO_2, partial pressure of carbon dioxide; *P*/*F* ratio, PaO_2/FiO_2 ratio.

thrombocytopenia and clotting factor deficiencies, which arise when contact of blood with the foreign surface of the ECMO circuit leads to activations of platelets, leukocytes, and the coagulation cascade (2). In addition, in a retrospective analysis of infections occurring in ECMO patients, Sun et al. (3) found that duration of ECMO therapy was an independent risk factor for developing bloodstream infections. In another study by Hsu et al. (4) the authors found that more than 10 days of ECMO was associated with higher rate of infections, with Gram-negative bacilli accounting from up to 78% of cases. Therefore, strategies to minimize the duration of ECMO therapy must constantly be sought after. We believed HFPV should be considered as a possible means to this goal.

HFPV is a unique form of ventilation delivered only by specially designed ventilator called the volume diffusive respirator (VDR-4; Percussionaire Corp, Sandpoint, ID). HFPV has been used in patients with severe respiratory compromise refractory to MCV. High-frequency ventilation implies that ventilatory modality is capable of delivering 150 cycles per minute or more of sub-physiologic tidal volumes. There are three types of high frequency ventilation: jet, oscillatory, and percussive ventilation. High-frequency oscillatory ventilation (HFOV) oscillates the lung at a constant mean airway pressure allowing for maintenance of alveolar recruitment while avoiding low end-expiratory pressure and high peak pressures (5).

Unlike HFOV, HFPV results in stepwise inflation and deflation of the lung based on lung compliance and airway resistance. HFPV delivers pneumatically powered, time-cycled, pressure-limited, flow-interrupted breaths at lower than normal tidal volumes at rates of 300–1,200 per minute superimposed on a respiratory rate of 10–15 per minute. Compared with MCV, HFPV can achieve equivalent or superior levels of oxygenation and ventilation at lower peak and mean airway pressures, thereby reducing the risk of ventilator-associated lung injury. MCV produces more turbulent gas flow in the lungs as it requires a larger volume of gas being delivered in a shorter duration of time. By contrast, high frequency percussive bursts of gas produced by HFPV results in more laminar gas patterns resulting in more efficient and accelerated oxygen delivery to the

alveoli. This laminar gas flow also pushes trapped gas against the walls and creates a countercurrent backflow of carbon dioxide (CO_2). The end result of this efficient form of gas exchange is enhanced oxygenation, ventilation, alveolar recruitment, and clearance of pulmonary secretions and inflammatory debris (6,7). HFPV is able to offer all of these benefits without contributing to ventilator-associated lung injury, barotrauma, or hemodynamic compromise, and therefore, we believe it should be considered when attempting to wean patients from ECMO.

In addition, although the use of ECMO has increased over the past decade, there is limited evidence available to guide MCV management in patients on ECMO. "Lung rest" is the current recommendation but specific guidelines are absent. The Extracorporeal Life Support Organization's (ELSO) current recommendations for ventilator management of patients on ECMO are "reasonable initial ventilator settings during (ECMO) could be decelerating flow (pressure control), a respiratory frequency of 4–5 per minute, modest PEEP (e.g., 10 cm H_20 above PEEP, or a PIP of 20 cm H_20). Once patients stabilize and sedation can be lightened, spontaneous ventilation with pressure support ventilation can be considered" (8). Whereas other cohorts, including the ELSO registry, REVA trial, and CESAR trial used modes of MCV reflecting the theme of "lung rest," none of these used HFPV (9–11).

Based on our experience with this cohort of patients, we suggest that HFPV may not only be used to obviate the need for ECMO, but may rescue patients who are already on it. Furthermore, there were three recently published reports in which HFPV was used as either a rescue modality or weaning method in patients with ARDS on ECMO. Boscolo et al. (12) described a 48-year-old woman who was placed on ECMO for septic shock and hypoxemic RF developed from pneumonia that was refractory to MCV. Thick bronchial secretions prohibited adequate oxygenation with MCV while on ECMO for 18 days, prompting a trial of HFPV. Within 20 minutes of a 4-hour HFPV trial, there was improvement in *P*/*F* ratio and mobilization of secretions. The patient was separated from ECMO the following day. Blondonnet et al. (13) described a case of a 17-year-old male with severe ARDS from aspiration pneumonia who was placed on ECMO after failure to improve gas exchange with non-ventilatory strategies including paralysis, prone positioning, and recruitment maneuvers. Despite ECMO support, oxygenation did not improve and he was subsequently placed on HFPV. Arterial blood gas performed in the first 30 minutes of HFPV showed a 500% increase in PaO_2. He was weaned from ECMO the next day. A protocolized use of HFPV for adults with RF on ECMO was used by Michaels et al. (14) to facilitate alveolar recruitment and pulmonary recovery, resulting in reduced duration on ECMO support. In that study, 39 patients were supported while on ECMO with HFVP resulting in less time on ECMO, thus avoiding further complications. By initiating HFPV in this cohort of patients with acute RF, there was comparable survival, and the ability to wean from ECMO was two-thirds of the time in comparison with ELSO, REVA, and CESAR trial (9–11,14).

Considering these aforementioned reports and our own institutional experience, we suggest HFPV as a possible weaning or rescue tool for patients on ECMO for ARDS. Although the physiologic causes of cardiogenic shock varied among the five patients being analyzed in this report, they all nonetheless responded favorably to initiation of HFPV, with dramatic improvement in their PaO_2 and *P*/*F* ratios within a matter of 2 hours with durable response at 24 hours. These improvements in respiratory status facilitated weaning and decannulation from ECMO, and four of five of our patients survived to discharge, whereas the fifth died of progressive right heart failure. Our findings are promising, given how quickly pulmonary function improved after initiation of HFPV. Given ECMO is such a limited resource with significant costs and risks, any strategy that may allow for a decrease in the duration of extracorporeal life support should be pursued.

However further studies are certainly necessary; based on our report, HFPV may be considered as a rescue or weaning modality in patients on ECMO for cardiopulmonary arrest who fail MCV.

LIMITATIONS

The small sample size of the study potentially hinders the generalizability of the results, despite achieving statistical significance. Additional limitations include possible incomplete or inaccurate data collection inherent to a retrospective analysis using chart review. Last, as clinical practice naturally varies across medical centers, extrapolation of our methods might be of limited value.

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