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Case Report

Severe Acute Respiratory Distress Syndrome Using Electrical Activity of the Diaphragm on Weaning from Extracorporeal Membrane Oxygenation

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The electrical activity of the diaphragm (EAdi) shows global diaphragmatic activation and power output from the central nervous system. We measured the EAdi as an indicator of breathing workload in a 40-year-old man suffering from severe acute respiratory distress syndrome (ARDS) secondary to influenza pneumonia in the process of weaning from extracorporeal membrane oxygenation (ECMO). Turning off the sweep gas flow immediately led to EAdi elevation, followed by hypoxia. The patient was successfully weaned from ECMO by reference to EAdi. This is the first case report to suggest that EAdi monitoring might be useful for ARDS patients during ECMO weaning.

Key words: electrical activity of the diaphragm, breathing workload, respiratory extracorporeal membrane oxygenation, acute respiratory distress syndrome

Extracorporeal membrane oxygenation (ECMO) has recently been used in the wider area of critical care for acute respiratory distress syndrome (ARDS). The introduction of ECMO is almost always an emergency procedure in life-threatening conditions. In contrast, the timing of weaning from ECMO varies depending on the patient's specific conditions. During ECMO treatment for ARDS, the concept of lung rest is also widely appreciated, but there are still many difficulties in assessing respiratory stress and the breathing workload, especially in the process of weaning from ECMO. In this assessment, we conventionally use the parameters of the partial pressure of oxygen in the arterial blood (PaO_2), the partial pressure of carbon dioxide ($PaCO_2$), the respiratory rate (RR) and the tidal volume (TV), but it is difficult to evaluate respiratory reserve in the early stage of ECMO weaning.

The electrical activity of the diaphragm (EAdi) can indicate the global diaphragmatic activation and power output from the central nervous system (CNS), and it is the driving source of neurally adjusted ventilatory assist (NAVA), which is an assisted ventilatory mode that delivers proportional support. Of note, the EAdi is suggested to be an objective indicator of the patient's own breathing effort [1]. The EAdi increases with the worsening of respiratory status, reduced ventilator assist, increased dead space, and other ventilation problems. Conversely, respiratory improvement and adequate ventilator support decrease the EAdi [1]. In individuals without respiratory complications, the normal range of the EAdi is a few μV during resting breathing. An advantage of the EAdi is that it can immediately reflect a patient's breathing workload. We have thus used the EAdi as a potential earlier indicator to evaluate the breathing workload in the process of weaning from ECMO.

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Case Presentation

A 40-year-old Japanese man suffering from respiratory failure with influenza type A was transferred to our ICU for the consideration of ECMO therapy for his refractory hypoxemia. On admission to the ICU, he was already intubated and supported by pressure support ventilation with an inspiratory fraction of oxygen (F_IO_2) of 0.9, positive end-expiratory pressure (PEEP) of 26 cmH_2O, and pressure support (PS) of 4 cmH_2O, because of his strong breathing effort. Arterial blood gas analysis suggested severe hypoxia and metabolic acidosis (pH 7.39; PaO_2, 68 mmHg; SaO_2, 93%; $PaCO_2$, 34 mmHg; HCO_3^-, 20 mmol/L; lactate, 2.9 mmol/L). A chest X-ray and computed tomography showed bilateral diffuse opacities (Fig. 1). Cardiac ultrasound showed that his cardiac function was normal. We made a diagnosis of severe ARDS secondary to influenza viral pneumonia, which was later found to be H1N1 influenza virus by the polymerase chain reaction (PCR) method. Peramivir was administered for 5 days after an attack of fever > 40°C.

Since his PaO_2/F_IO_2 ratio (P/F) was only 75 with the Murray score of 3.7 and his cardiac function was normal with no CNS damage, we established veno-venous ECMO via bilateral femoral veins with 25-Fr cannulas. The ECMO session was initiated with a extracorporeal blood flow of approx. 4 L/min and a sweep gas flow of 4 L/min with 100% oxygen (centrifugal pump, CAPIOX® SP101 PLUS; oxygenator, CAPIOX® LX; Terumo, Tokyo). Anticoagulation therapy with unfractionated heparin was initiated to maintain an activated clotting time > 150 sec.

After the induction of ECMO therapy, we administered sedatives, analgesics and neuromuscular blocking agents (propofol at 4 mg/kg/h, fentanyl at 2 μg/kg/h, and rocuronium at 7 μg/kg/min) and conducted lung rest (F_IO_2 of 0.4, PEEP of 15 cmH_2O, and plateau pressure of 25 cmH_2O). At that time, the patient's TV was around 4 ml/kg of predicted body weight (PBW). On the 4th day of ECMO therapy, his oxygenation had improved to a P/F ratio of 330 under pressure control-synchronized intermittent mandatory ventilation (PC-SIMV) with the PEEP of 15 cmH_2O, plateau pressure of 27 cmH_2O, and PS of 10 cmH_2O above PEEP. We then ceased the administration of the neuromuscular blocking agent and tried to wean the patient from the ECMO. However, the first trial failed because his oxygenation worsened (P/F 60) again with strong spontaneous breathing; the RR was 25 breaths/min and TV was approx. 12 ml/kg of PBW under PC-SIMV with the PEEP of 15 cmH_2O and the plateau pressure of 23 cmH_2O.

We therefore decided to continue the ECMO therapy again and also administered a neuromuscular blocking agent. We performed bronchoalveolar lavage, and there was no detection of influenza virus by PCR and no sign of bacterial infection. We concluded that high transpulmonary pressure due to the patient's increased breathing effort contributed to the lung injury. Nine days later, his oxygenation recovered to a P/F ratio of > 300 under PC-SIMV with the PEEP of 13 cmH_2O and the plateau pressure of 25 cmH_2O, and we decided to attempt a second weaning trial.

In order to deliver proportional support and assess the patient's breathing effort, we applied a NAVA mode with EAdi monitoring (Servo-I; Maquet Critical Care, Solna, Sweden) before the process of weaning from ECMO. A NAVA catheter was inserted nasally to a length of 65 cm guided by an electrocardiogram, and the appropriate position was confirmed by a chest X-ray. The EAdi peak value was approx. 6 μV under ECMO with a sweep gas flow of 3 L/min and PC-SIMV with the PEEP of 13 cmH_2O and the plateau pressure of 25 cmH_2O. At the second weaning trial, turning off the sweep gas flow immediately led to an increase in the EAdi to > 15 μV. After that, we observed that the patient's oxygenation slowly decreased to a P/F ratio of < 150 in 20 min. We therefore stopped this weaning trial.

Following the return to the previous sweep gas flow, the EAdi peak value immediately decreased again to approx. 6 μV (Table 1). As we considered the patient's condition to be premature for weaning, we raised the

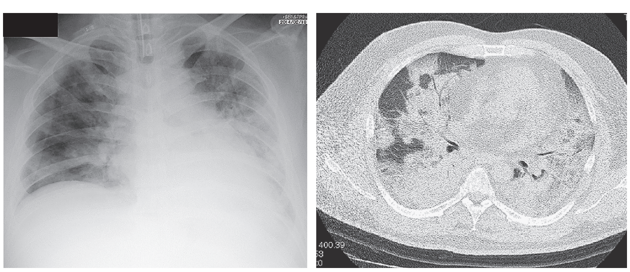

Fig. 1 Chest X-ray and computed tomography scan on admission. The diffuse opacity and nearly complete consolidation of both lungs at the level of the heart are apparent.

Table 1 The changes in the electrical activity of the diaphragm (EAdi), arterial blood gas data and ventilator variables at the 2nd and 3rd ECMO weaning trials

	2nd weaning trial				3rd weaning trial			
	Pre	10 min	20 min	Return to ECMO	Pre	10 min	20 min	Turn off ECMO
ECMO blood flow (L/min)	2.6	2.6	2.6	2.6	1.5	1.5	1.5	0
ECMO sweep gas flow (L/min)	3	0	0	3	3	0	0	0
EAdi peak (μV)	6.2	15.8	14.6	5.8	4.0	6.2	6.8	7.2
pH	7.423		7.441	7.465	7.401		7.419	7.408
PaO_2/F_IO_2 ratio	205		131	255	281		359	322
$PaCO_2$ (mmHg)	46.3		45	44.2	44.2		40.1	39
Tidal Volume (ml)	435	560	535	416	370	451	503	480
Respiratory rate (/min)	12	14	16	10	14	16	18	20
PEEP (cmH_2O)	13	13	13	13	15	15	15	15

At the 2nd weaning trial, turning off the sweep gas flow immediately led to elevation of the EAdi (>15 μV) ahead of a decreased P/F ratio (<150). We therefore stopped the weaning trial. At the 3rd weaning trial, the EAdi could be maintained at <10 μV with enough oxygenation and the elimination of carbon dioxide, and the patient was successfully weaned from ECMO.
ECMO: extracorporeal membrane oxygenation, PEEP: positive end-expiratory pressure.

PEEP to 15 cmH_2O and achieved a negative fluid balance of −2,000 ml for 3 days. Two days later, the patient's EAdi was maintained at < 10 μV at the third weaning trial, and he was successfully weaned from ECMO with enough oxygenation (P/F ratio > 300) and the elimination of carbon dioxide by using the NAVA mode (the PEEP of 15 cmH_2O and NAVA level of 1.0 $cmH_2O/\mu V$) on the 15th day (Table 1). As a result of gradual PEEP titration, the patient was finally extubated on the 19th day and he was discharged from the hospital without any disability on the 42nd day.

Discussion

We treated a patient who suffered from severe ARDS secondary to influenza pneumonia with ECMO and NAVA. We monitored his EAdi under special circumstances that included ECMO weaning, and we observed that the EAdi immediately reacted to the patient's respiratory status ahead of conventional parameters.

ECMO was shown to be an effective treatment for severe ARDS in an earlier study [2] that suggested inception criteria for ECMO therapy and recommended ventilator settings during ECMO. However, there has been no detailed description about ECMO weaning. According to the Extracorporeal Life Support Organization guidelines, the procedure for a trial to wean a patient from veno-venous (VV) ECMO is as follows: "When the sweep gas is stopped and the oxygenator is capped off, we should check SaO_2 and $PaCO_2$ at acceptable ventilator settings for an hour or more and afterwards make sure whether withdrawing from ECMO for patients is possible and adequate or not." Difficulties in assessing respiratory stress and the breathing workload during ECMO weaning are often encountered. Conventional parameters such as arterial blood gas data, RR and measured values on ventilation must be assessed, but they are sometimes insufficient for use as early indicators.

As a new mode of mechanical ventilation, the recent introduction of NAVA has provided us with the opportunity to use the EAdi to evaluate the central respiratory drive. The beneficial point of applying the EAdi is that we can simply confirm a real-time respiratory status without any complicated procedure. Sinderby suggested that the EAdi showed a few μV in patients without respiratory complications during resting breathing and that the EAdi increased with forced breathing [1]. The EAdi has been reported to be a perceptive indicator of breathing workload in not only healthy subjects but also patients with respiratory failure [3, 4]. Several studies reported that the EAdi predicted weaning failure from mechanical ventilation earlier than other parameters [5-7]. The EAdi in patients who were not successfully weaned from the ventilator was significantly higher than that in patients with successful weaning. According to these results, the EAdi could be used as an earlier indicator of breathing workload on weaning from a ventilator.

Our patient's excessive breathing effort induced high transpulmonary pressure, which could have resulted in the respiratory deterioration observed on his first trial of weaning from ECMO. The stronger his breathing workload became, the higher his EAdi value became. Bellani *et al.* reported that the EAdi was closely related to the esophageal pressure, which was suggested to reflect the patient's transpulmonary pressure and could be used to estimate the inspiratory effort [4].

The data regarding the EAdi and NAVA during ECMO therapy are limited. NAVA was reported to reduce asynchrony in ARDS patients with very low compliance during or after ECMO [8,9]. However, there is little informaton about evaluations of the EAdi in the process of weaning from ECMO as in the present patient's case. Karagiannidis *et al.* reported that the combination of extracorporeal lung support and NAVA was a plausible and sensible complementary application of two different techniques in patients with severe lung failure [10]. They showed that the EAdi and NAVA led to better synchrony and autoregulation during ECMO, but they did not describe readiness for weaning from ECMO.

In our patient's case, we used the EAdi in addition to other respiratory parameters such as the PaO_2, $PaCO_2$, RR, TV as indicators of respiratory stress during the weaning trials. At the second failed weaning trial, turning off the sweep gas flow led to the elevation of the EAdi ($>15\ \mu V$), followed by hypoxia. After the modulation of ventilator settings and fluid balance, at the third weaning trial, the EAdi could be maintained at $<10\ \mu V$, which was lower than the previous trial and which had been considered to indicate stable respiratory effort in some reports [1,6]. As a result, the patient was successfully weaned from ECMO with enough oxygenation and the elimination of carbon dioxide. Considering these results, we speculated that the EAdi could be used to assess respiratory reserve earlier than other parameters.

Although there is no definite cutoff point at this time, EAdi monitoring in the process of weaning from ECMO might be useful as in weaning from mechanical ventilation to monitor patients' spontaneous breathing workload. Additional clinical research is needed to confirm the utility of the EAdi as an indicator of breathing workload.

In conclusion, we have reported a case of ARDS treated with ECMO in which EAdi monitoring was used for weaning from ECMO for the first time. In this case, the EAdi reacted to the patient's respiratory status earlier than other respiratory parameters in the process of weaning from ECMO. The EAdi might thus be worthwhile to use for patients during ECMO weaning.

References

1. Sinderby C and Beck J: Neurally adjusted ventilatory assist; in Principles and practice of mechanical ventilation, Tobin MJ eds, 3rd Ed, McGraw-Hill Medical, New York (2013) pp 351–375.
2. Peek GJ, Mugford M, Tiruvoipati R, Wilson A, Allen E, Thalanany MM, Hibbert CL, Truesdale A, Clemens F, Cooper N, Firmin RK and Elbourne D; CESAR trial collaboration: Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial. Lancet (2009) 374: 1351–1363.
3. Beck J, Gottfried SB, Navalesi P, Skrobik Y, Comtois N, Rossini M and Sinderby C: Electrical activity of the diaphragm during pressure support ventilation in acute respiratory failure. Am J Respir Crit Care Med (2001) 164: 419–424.
4. Bellani G, Mauri T, Coppadoro A, Grasselli G, Patroniti N, Spadaro S, Sala V, Foti G and Pesenti A: Estimation of patient's inspiratory effort from the electrical activity of the diaphragm. Crit Care Med (2013) 41: 1483–1491.
5. Dres M, Schmidt M, Ferre A, Mayaux J, Similowski T and Demoule A: Diaphragm electromyographic activity as a predictor of weaning failure. Intensive Care Med (2012) 38: 2017–2025.
6. Barwing J, Pedroni C, Olgemöller U, Quintel M and Moerer O: Electrical activity of the diaphragm (EAdi) as a monitoring parameter in difficult weaning from respirator: a pilot study. Crit Care (2013) 17: R182.
7. Liu L, Liu H, Yang Y, Huang Y, Liu S, Beck J, Slutsky AS, Sinderby C and Qiu H: Neuroventilatory efficiency and extubation readiness in critically ill patients. Crit Care (2012) 16: R143.
8. Mauri T, Bellani G, Grasselli G, Confalonieri A, Rona R, Patroniti N and Pesenti A: Patient-ventilator interaction in ARDS patients with extremely low compliance undergoing ECMO: a novel approach based on diaphragm electrical activity. Intensive Care Med (2013) 39: 282–291.
9. Goto Y, Katayama S, Shono A, Mori Y, Miyazaki Y, Sato Y, Ozaki M and Kotani T: Roles of neurally adjusted ventilatory assist in improving gas exchange in a severe acute respiratory distress syndrome patient after weaning from extracorporeal membrane oxygenation: a case report. J Intensive Care (2016) 4: 26.
10. Karagiannidis C, Lubnow M, Philipp A, Riegger GA, Schmid C, Pfeifer M and Mueller T: Autoregulation of ventilation with neurally adjusted ventilatory assist on extracorporeal lung support. Intensive Care Med (2010) 36: 2038–2044.