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LETTER

Extremely high transpulmonary pressure in a spontaneously breathing patient with early severe ARDS on ECMO

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Dear Editor,

Early switch of patients with severe acute respiratory distress syndrome (ARDS) from controlled to spontaneous ventilation (i.e. after the first 48 h) might prevent decline of muscle function, improve haemodynamics and decrease sedation needs [1]. On the other hand, high spontaneous inspiratory efforts might aggravate lung injury by generating elevated transpulmonary pressure (P_L) [2]. We previously observed that extracorporeal carbon dioxide (CO_2) removal through extracorporeal membrane oxygenation (ECMO) might control the respiratory drive and effort of spontaneously breathing patients recovering from severe ARDS [3]. Assisted mechanical ventilation coupled with ECMO might be viewed as a promising alternative to controlled ventilation for severe ARDS patients. On the other hand, a recent experimental study suggested that control of breathing might be more challenging in the early phases of severe ARDS [4]. We present here data from a patient with early severe ARDS switched to spontaneous breathing and assisted ventilation while on ECMO.

The mobile ECMO team of the Maggiore Policlinico Milan Hospital was contacted by the intensive care unit (ICU) of a peripheral hospital for evaluation of a 54-year-old diabetic male patient intubated and mechanically ventilated for ARDS due to *Pneumocystis jirovecii* lung infection as first outset of acquired immunodeficiency syndrome. Onsite evaluation of the patient's respiratory condition [i.e., PaO_2/FiO_2 55 mmHg with FiO_2 100 % and positive end-expiratory pressure (PEEP) 15 cmH_2O] and the need to transport the patient to the ICU of the Maggiore Policlinico Milan Hospital (distance 142 km) prompted the decision to start veno-venous femoro-femoral ECMO with blood flow of 3.5 l/min and gas flow 3 l/min. After ECMO institution, respiratory rate (RR) was set at 8 breath/min, Vt at 4 ml/kg PBW while PEEP was maintained at 15 cmH_2O: in this way, PaO_2 increased to 90 mmHg with ventilator FiO_2 decreased to 80 % and the patient could be safely transported by ambulance. Bronchial bleeding and haemodynamic instability requiring vasoactive support characterized the first days following ECMO institution. On ECMO day 7, haemodynamics became more stable and bleeding was well controlled. The patient's respiratory function was still severely impaired with intrapulmonary shunt of 66 % and respiratory system compliance of 15 ml/cmH_2O. Nonetheless, sedation and paralysis were interrupted to switch the patient to protective assisted ventilation. After 20 min, the patient kept his eyes open, contact could be established and spontaneous inspiratory triggering appeared evident on the airways tracings. Pressure support was set to obtain Vt around 6 ml/kg PBW, PEEP level (15 cmH_2O) and ECMO BF (3.3 l/min) were left unchanged, while sweep gas flow was increased to the maximum technically allowed by the ECMO machine (11 l/min) with FiO_2 of 100 %, both at the ventilator and ECMO. Then, continuous recording of airway pressure, flow, Vt, oesophageal and transpulmonary pressure tracings was performed; arterial blood gas analysis and CO_2 elimination through the native, diseased lung (VCO_2-NL) and through the membrane lung (VCO_2-ML) were measured (Fig. 1). With the aforementioned settings, apparently, protective assisted ventilation could be established

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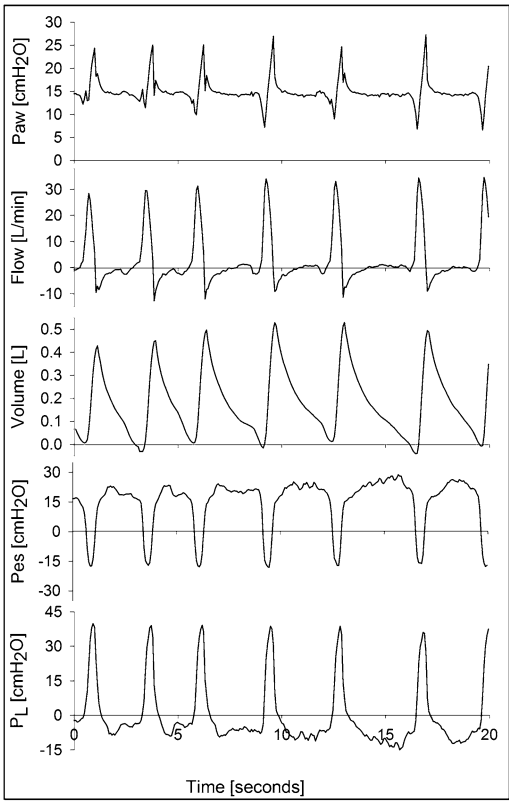

	Volume controlled	Pressure support
PEEP (cmH_2O)	15	15
Vt (ml/kg PBW)	4	6.5
RR (bpm)	10	21
Ppeak (cmH_2O)	37	24
ECMO GF (l/min)	6.5	11.0
VCO_2-NL (ml/min)	n.a.	74
VCO_2-ML (ml/min)	n.a.	253
VCO_2-ML/VCO_2-TOT (%)	n.a.	77
ΔPes (cmH_2O)	+2	-35
P_L (cmH_2O)	12	38
pH	7.42	7.47
PaO_2 (mmHg)	63	63
$PaCO_2$ (mmHg)	45	37

Fig. 1 Ventilation waveforms and relevant physiologic parameters of a spontaneously breathing patient with early severe acute respiratory distress syndrome (ARDS) on extracorporeal membrane oxygenation (ECMO). Pressure support ventilation was set at 10 cmH_2O to obtain tidal volume around 6 ml/kg while ECMO removed 77 % of the patient's CO_2 production. In this way, respiratory rate and minute ventilation were reasonably controlled. However, oesophageal pressure swings averaged −35 cmH_2O, yielding extremely elevated absolute values of dynamic transpulmonary pressure (around 38 cmH_2O). *Paw* airway pressure, *Pes* oesophageal pressure, P_L transpulmonary pressure, *PEEP,* positive end-expiratory pressure, *Vt* tidal volume, *PBW* predicted body weight, *RR* respiratory rate, *Ppeak* peak inspiratory pressure, *ECMO* extracorporeal membrane oxygenation, *BF* blood flow, *GF* sweep gas flow, VCO_2 CO_2 production/extraction, *NL* natural lung, *ML* membrane lung, VCO_2-*TOT* VCO_2-NL + VCO_2-ML, PaO_2 partial arterial O_2 tension, $PaCO_2$ partial arterial CO_2 tension

with peak airways pressure of 24 cmH_2O, Vt 6.5 ml/kg, RR 21 and VCO_2-ML/(VCO_2-NL + VCO_2-ML) 77 %. Nonetheless, despite the elevated extracorporeal respiratory support, oesophageal pressure swings averaged 35 cmH_2O yielding extremely high absolute values of dynamic P_L (38 cmH_2O) (Fig. 1). Controlled mechanical ventilation, sedation and paralysis were therefore re-established, given the non-protective respiratory pattern of the patient. On ECMO day 45, the patient eventually died while still on controlled ventilation as a result of non-resolving multidrug-resistant bacterial infection.

These observations suggest that, in early severe ARDS, mechanisms other than arterial and cerebrospinal fluid O_2, CO_2 and pH levels might influence the respiratory neural centres. In particular, stimuli arising from pulmonary receptors sensing oedema, inflammation and lung microembolism might influence the control of breathing inducing dyspnea and strenuous inspiratory efforts [5]. The present case and sound physiologic background generate the hypothesis that, in the early phases of severe ARDS, extracorporeal CO_2 removal through full ECMO support might not suffice to control spontaneous respiratory effort and to keep transpulmonary pressure within safe limits.

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Compliance with ethical standards

Conflicts of interest
On behalf of all authors, the corresponding author states that there is no conflict of interest.

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