Editorial

Extracorporeal membrane oxygenation for interstitial lung disease: what is on the other side of the bridge?

Sacha Rozencwajg, Matthieu Schmidt

Medical Intensive Care Unit, iCAN, Institute of Cardiometabolism and Nutrition, La Pitié–Salpêtrière Hospital, Assistance Publique–Hôpitaux de Paris, Paris, France

Correspondence to: Dr. Matthieu Schmidt, MD, PhD. Medical Intensive Care Unit, iCAN, Institute of Cardiometabolism and Nutrition, La Pitié–Salpêtrière Hospital, 47, bd de l'Hôpital, 75651 Paris Cedex 13, France. Email: matthieu.schmidt@aphp.fr.

Submitted Jun 09, 2016. Accepted for publication Jun 23, 2016.
doi: 10.21037/jtd.2016.07.50
View this article at: http://dx.doi.org/10.21037/jtd.2016.07.50

Patients suffering from interstitial lung disease (ILD) share a number of similarities with chronic obstructive pulmonary disease (COPD) patients. The natural evolution in both patient groups is a slow deterioration of lung capacity punctuated by exacerbations, and available treatments are mostly aimed at sustaining lung capacity and preventing exacerbations. Additionally, the last treatment option is lung transplantation (LTx), which is usually performed, in chronic, stable patients. However, management discrepancies are noted between the two patient groups regarding intensive care unit (ICU) admission policy. As such, chronic ILD patients are more likely to be denied ICU admission or to be restricted to high-flow oxygen through nasal cannula (HFNC) or non-invasive ventilation (NIV) for respiratory support. This behavior is supported by retrospective studies (1,2) which have highlighted poor prognosis of invasive mechanical ventilation (MV) in the context of ILD.

Use of extracorporeal membrane oxygenation (ECMO) has increased exponentially since the A(H_1N_1) influenza pandemic and results of the CESAR randomized controlled trial (3). Extracorporeal systems provide either pulmonary support by a veno-venous (VV) setting or both cardiac and respiratory support through a veno-arterial (VA) configuration. Consequently, the main indications are, respectively, refractory acute respiratory distress syndrome (ARDS) or refractory cardiogenic shock. However, improvement of ECMO devices has led to expand indications of VV-ECMO.

In a March 2016 issue of the *American Journal of Respiratory and Critical Care Medicine*, Trudzinski *et al.* reported their experience with ILD patients treated with ECMO for acute respiratory failure (ARF) (4). In their study, 21 patients with ILD-related ARF (33% idiopathic ILD and 24% connective tissue disease) received VV-ECMO. Indications of ECMO were refractory hypoxemia or uncompensated hypercapnia during ARDS or refractory hypoxemia despite maximal non-invasive therapies in patients considered "at risk of intubation". In the latter group, ECMO was considered to prevent intubation ("awake-ECMO"). ECMO was only used when patients were considered potential candidates for a lung transplant or when two intensivists agreed on a potentially reversible pulmonary cause (e.g., acute infection on previous chronic ILD). The VV-ECMO setting with percutaneous femoro-jugular cannulation was initially used for all patients. Three patients were secondarily switched to veno-arteriovenous ECMO and 2 were later converted to VA-ECMO for progressive right ventricular dysfunction. Median delay between MV and ECMO cannulation was 7 days (range, 2–15.5 days) for 13 intubated patients, whereas 8 patients were "awake-ECMO". Complications were mainly bleeding (3/21) with a median of 30 units of packed red blood cells and accidents during cannulation procedure (2/21) of which limb ischemia occurred in one case and pericardial effusion in the other. Ultimately, 8 patients were listed for LTx. Four patients were listed prior to ECMO whereas 4 others were already on ECMO (referred to as "salvage transplant" in the study). Of these 8 patients, 6 were transplanted with 5 discharged alive from hospital. Of the 15 patients that were not transplanted, 6 were evaluated for transplant but not listed and consequently had ECMO withdrawn (1

patient improved, 4 died before being fully evaluated and 1 was ineligible because of active smoking). The remaining patients died of septic shock or multi-organ failure.

Although this study is retrospectively issued from a small monocentric cohort, Trudzinski *et al*. are the first to report their experience and the outcome of this very specific ICU population. Their study confirms that ECMO management is changing and new strategies might be proposed for patients with ILD and refractory ARF. As such, two strategies in this study warrant particular attention; the "awake-ECMO" and the "salvage lung transplant".

The term "awake-ECMO" refers not only to non-sedated patients—which we believe should be, when feasible, the standard of care for these patients—but also to non-intubated patients. While the amount of case reports (5-8) and case series (9,10) reporting the feasibility of this strategy is increasing (primarily in patients with chronic pulmonary hypertension on VA-ECMO), Fuehner *et al*. (11) were the first to compare the outcomes of awake-ECMO patients undergoing LTx matched with a historical cohort of mechanically ventilated patients. Results were encouraging with a 6-month survival rate after transplantation of 80% in the "awake-ECMO" group *vs*. 50% in the mechanically ventilated group.

A strategy based on ECMO to avoid using MV might offer numerous benefits. It could prevent ventilator-induced lung injury (VILI) (12), reduce ventilator-associated pneumonia, preserve oral feeding and spontaneous coughing, maintain social interaction and allow early rehabilitation (13). Consequently, ICU length of stay and in-ICU mortality should decrease. However, data to support the use of this strategy is very limited to date. Langer *et al*. (14) performed physiological monitoring on 11 sheep on "awake VV-ECMO" before and after oleic acid-induced ARDS. They concluded that this strategy was safe but emphasized two points which must be taken into account: firstly, the reduction of the tidal volume induced by pulmonary derecruitment/atelectasis increases the pulmonary shunt which might be compensated by application of a high positive end expiratory pressure through intermittent noninvasive ventilation. Secondly, spontaneous breathing and high ventilatory central drive might induce high esophageal pressure swings, which could worsen VILI. As no comparison with intubated sheep on VV-ECMO was performed, these findings remain observational. Thus, "awake ECMO" for ARF is to date limited to highly selected patients (15). Going forward, research should focus on limiting ECMO-related complications and on alleviating the high ventilatory drive of patients with ARDS. If we manage to face these issues, there is no doubt that an "awake-ECMO" strategy might be expanded to severe ARDS.

So far VV-ECMO has been used in two distinct situations: Either as a bridge-to-recovery or as a bridge-to-transplantation for patients already listed. When recovery seems out of reach and when LTx is no longer an option, ECMO is withdrawn once consensus is established between caregivers and next of kin. The lack of lung long-term assistance might lead, more frequently than with refractory cardiogenic shock, to a therapeutic deadlock, referred as "bridge-to-nowhere". In a retrospective study, Hoopes *et al*. recently reported results of 31 transplanted patients with refractory lung disease from mechanical artificial lung support. Of the 31 patients, 19 were ambulatory at transplantation. Patients requiring an ECMO bridge exhibited similar survival compared to patients transplanted without ECMO support. These results challenge current assumptions about the treatment of selected patients with end-stage lung disease and suggest that "salvage lung transplant" is both technically feasible and logistically viable (16). To achieve a complete and fair pre- LTx assessment, blood tests, radiological imaging and medico-psycho-social evaluation are mandatory. In a context of "salvage lung transplant" strategy on ECMO for patients who have not been previously evaluated, this latter is made possible if patient is kept awake. In their study, Trudzinski *et al*. stressed that this strategy was feasible with an acceptable survival rate and long-term outcome. However, clinicians should be aware that such a strategy might lead to ECMO more frequently ending up as a "bridge-to-nowhere" (e.g., when LTx is denied) with an awake patient. In the study of Trudzinski *et al*., one awake patient on ECMO was denied transplantation upon evaluation and was "withdrawn from ECMO and died". These complex ethical situations are challenging as they reinforce the need for a close communication between caregivers, families and patients. To prepare the family for this possible fatal outcome, we strongly encourage clinicians to systematically inform the patient's surrogate decision-maker that ECMO use involves a time-limited trial (e.g., information on the possibility to withdraw ECMO in case of futility).

Overall, this significant study from Trudzinski *et al*. has paved the way for new strategies for patients with ARF in the context of chronic pulmonary disease. The exact role of ECMO and its modalities to improve outcomes in this situation, however, warrant further investigation.

Acknowledgements

None.

Footnote

Provenance: This is an invited Editorial commissioned by Ming Zhong (Associate Professor, Department of Critical Care Medicine, Zhongshan Hospital, Fudan University, Shanghai, China).
Conflicts of Interest: The authors have no conflicts of interest to declare.

Comment on: Trudzinski FC, Kaestner F, Schäfers HJ, *et al*. Outcome of Patients with Interstitial Lung Disease Treated with Extracorporeal Membrane Oxygenation for Acute Respiratory Failure. Am J Respir Crit Care Med 2016;193:527-33.

References

1. Blivet S, Philit F, Sab JM, et al. Outcome of patients with idiopathic pulmonary fibrosis admitted to the ICU for respiratory failure. Chest 2001;120:209-12.
2. Fernández-Pérez ER, Yilmaz M, Jenad H, et al. Ventilator settings and outcome of respiratory failure in chronic interstitial lung disease. Chest 2008;133:1113-9.
3. Peek GJ, Mugford M, Tiruvoipati R, et al. 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;374:1351-63.
4. Trudzinski FC, Kaestner F, Schäfers HJ, et al. Outcome of Patients with Interstitial Lung Disease Treated with Extracorporeal Membrane Oxygenation for Acute Respiratory Failure. Am J Respir Crit Care Med 2016;193:527-33.
5. Garcia JP, Iacono A, Kon ZN, et al. Ambulatory extracorporeal membrane oxygenation: a new approach for bridge-to-lung transplantation. J Thorac Cardiovasc Surg 2010;139:e137-9.
6. Mangi AA, Mason DP, Yun JJ, et al. Bridge to lung transplantation using short-term ambulatory extracorporeal membrane oxygenation. J Thorac Cardiovasc Surg 2010;140:713-5.
7. van Houte J, Donker DW, Wagenaar LJ, et al. Non-intubated recovery from refractory cardiogenic shock on percutaneous VA-extracorporeal membrane oxygenation. Neth Heart J 2015;23:386-8.
8. Wong JY, Buchholz H, Ryerson L, et al. Successful Semi-Ambulatory Veno-Arterial Extracorporeal Membrane Oxygenation Bridge to Heart-Lung Transplantation in a Very Small Child. Am J Transplant 2015;15:2256-60.
9. Olsson KM, Simon A, Strueber M, et al. Extracorporeal membrane oxygenation in nonintubated patients as bridge to lung transplantation. Am J Transplant 2010;10:2173-8.
10. Schmidt F, Sasse M, Boehne M, et al. Concept of "awake venovenous extracorporeal membrane oxygenation" in pediatric patients awaiting lung transplantation. Pediatr Transplant 2013;17:224-30.
11. Fuehner T, Kuehn C, Hadem J, et al. Extracorporeal membrane oxygenation in awake patients as bridge to lung transplantation. Am J Respir Crit Care Med 2012;185:763-8.
12. Slutsky AS, Ranieri VM. Ventilator-induced lung injury. N Engl J Med 2013;369:2126-36.
13. Abrams D, Javidfar J, Farrand E, et al. Early mobilization of patients receiving extracorporeal membrane oxygenation: a retrospective cohort study. Crit Care 2014;18:R38.
14. Langer T, Vecchi V, Belenkiy SM, et al. Extracorporeal gas exchange and spontaneous breathing for the treatment of acute respiratory distress syndrome: an alternative to mechanical ventilation?*. Crit Care Med 2014;42:e211-20.
15. Hoeper MM, Wiesner O, Hadem J, et al. Extracorporeal membrane oxygenation instead of invasive mechanical ventilation in patients with acute respiratory distress syndrome. Intensive Care Med 2013;39:2056-7.
16. Hoopes CW, Kukreja J, Golden J, et al. Extracorporeal membrane oxygenation as a bridge to pulmonary transplantation. J Thorac Cardiovasc Surg 2013;145:862-7; discussion 867-8.

Cite this article as: Rozencwajg S, Schmidt M. Extracorporeal membrane oxygenation for interstitial lung disease: what is on the other side of the bridge? J Thorac Dis 2016;8(8):1918-1920. doi: 10.21037/jtd.2016.07.50

