Lung-protective ventilation in intensive care unit and operation room

Tidal volume size, level of positive end-expiratory pressure and driving pressure

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Chapter 13

Extracorporeal life support: A “breath-taking” technology?

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Each year, hundreds of thousands of critically ill patients worldwide undergo mechanical ventilation.[1] Ventilation is vital for these patients, but also has strong potential to harm the lungs, a phenomenon frequently referred to as ventilator-induced lung injury.[2] It has been theorized that ventilator-induced lung injury is caused, at least in part, by energy transferred from the ventilator to the lungs. As more energy is transferred with the use of larger tidal volumes and higher respiratory rates, strategies that allow use of lower tidal volumes[3,4] or lower respiratory rates[5,6] could mitigate ventilator-induced lung injury.

Extracorporeal life support (ECLS) is one of several terms used for an extracorporeal circuit that employs a membrane for oxygenation and elimination of carbon dioxide.[7,8] The “veno–venous” approach to ECLS uses a blood pump, in contrast to the “arterio–venous” approach that uses intrinsic arterial blood pressure to drive blood through the extracorporeal circuit. When the primary need is oxygenation (extracorporeal membrane oxygenation or ECMO), larger membranes and a higher blood flow are mandatory. When the goal is primarily or entirely the elimination of carbon dioxide (extracorporeal CO_2 removal or $ECCO_2R$), ECLS can be achieved using smaller membranes and lower blood flow.

ECLS has conventionally been used as a salvage strategy for patients with severe acute respiratory distress syndrome (ARDS). Use of ECLS in these patients may also enhance protective ventilation, by enabling further reduction in tidal volumes delivered by the ventilator. In this issue of *AnnalsATS*, Munshi and coworkers (pp. 802–810) report a systematic review and meta-analysis of four randomized controlled trials and six observational studies comparing a strategy of augmenting mechanical ventilation with ECLS to conventional ventilation alone for patients with ARDS.[9] In the overall analysis, ECLS was not associated with a reduction in in-hospital mortality (relative risk [RR], 1.02; 95% confidence interval [CI], 0.79–1.33; $p > 0.05$). However, ECLS was associated with reduced mortality in studies of veno–venous ECLS (RR, 0.64; 95% CI, 0.51–0.79; $p < 0.05$) and in studies that used lung–protective ventilation with lower tidal volumes (6 ml/kg) (RR, 0.53; 95% CI, 0.53–0.80; $p < 0.05$).

Heterogeneity among the studies included in the meta-analysis may explain, at least in part, why no advantage was found in the overall analysis. Notably, the included randomized controlled trials had important limitations related to quality, with some trials lacking allocation concealment and several not following an intention-to-treat analysis. The finding that ECLS was associated with reduced mortality in studies that used lung-protective ventilation may be explained in part by the lower heterogeneity of these trials. It could also be that use of ECLS was associated with a further reduction of tidal volume size (i.e., below 6 ml/kg), or respiratory rate, or both, thereby improving outcomes. Unfortunately, Munshi and colleagues[9] did not analyze specific ventilator settings.

The meta-analysis by Munshi and coworkers[9] highlights the need for better studies of ECLS. In particular, we need well-powered, high-quality, randomized controlled trials in which ECLS is compared with the current standard of ventilation care (i.e., lung-protective ventilation with lower tidal volumes). We also need a better understanding for why ECLS could benefit patients with ARDS: is it the use of even lower tidal volumes (i.e., lower than 6 ml/kg), or lower respiratory rates, or maybe both? Indeed, the most appropriate ventilator and ECLS settings for patients with severe ARDS who receive ECLS are largely unknown.[7] Large databases like the ELSO registry (www.elsonet.org) may shine additional light on this, but in the end we need randomized controlled trials.

Is there merit for using ECLS in patients without ARDS? Several studies showed that conventional mechanical ventilation is far from a safe strategy for patients without ARDS, and that the lungs of these patients can be protected by using lower tidal volumes.[10] One could thus speculate that there is a role for ECLS in patients without ARDS, and there is some published evidence in support of this hypothesis. Indeed, use of $ECCO_2R$ may avoid intubation and invasive mechanical ventilation in patients with acute on chronic respiratory failure not responding to noninvasive ventilation.[11] $ECCO_2R$ is also successfully used in patients with mild hypoxia and severe hypercapnia awaiting lung transplantation.[12]

Skeptics may argue that the advantages of ECLS over ventilation are far from clear, and that ECLS comes with impediments, including the risks of bleeding under systemic anticoagulation, and limb ischemia, blood stream infections, and other catheter-related complications. But we should not forget that intubation and ventilation comes with complications as well, including the above-mentioned ventilator-induced lung injury, but also ventilator-induced diaphragm dysfunction, ventilator-associated pneumonia, increased needs for sedation, and hemodynamic compromise, to name just a view (Figure 1).

Before we can consider launching randomized controlled trials that test the hypothesis whether ECLS also benefits patients without ARDS, we need to understand better what the best PaO_2 and $PaCO_2$ targets are, and how to wean patients from the ventilator with ECLS. Furthermore, we need answers to questions like which type of ECLS to use for which condition, including type and size of the membrane, and the ideal solution against clotting, and find the best trade-offs.

There is a lot of work to be done, and, as mentioned before: “further development in this direction will occur only with a permanent integration and exchange of knowledge among industry, clinicians, and scientific investigators.

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Figure Legends

Figure 1 – Authors' view of the tradeoffs between ventilation and extracorporeal life support (ECLS) in patients with and without the acute respiratory distress syndrome.

Figure 1 – Authors' view of the tradeoffs between ventilation and extracorporeal life support (ECLS) in patients with and without the acute respiratory distress syndrome.

	ventilation		ECLS	
	ARDS	**non–ARDS**	**ARDS**	**non–ARDS**
efficacy	**oxygenation**, at times requiring higher levels of PEEP and/or proning **decapnezeition**, at times requiring settings known to cause lung injury	**oxygenation**, almost never a problem **decapnezeition**, almost never a problem	**oxygenation**, requiring larger membranes and higher blood flows **decapnezeition**, never a problem	**oxygenation**, never a problem **decapnezeition**, never a problem
safety & easiness	**well–known intervention**, easy to learn **secured airway**	**well–known intervention**, easy to learn **secured airway**	**less well–known intervention**, not so easy in combination with ventilation **airway not protected**, if used without ventilation	**less well–known intervention**, easy when used alone **airway not protected**, if used without ventilation
complications	ventilator–induced **lung injury**, ventilator–induced **diaphragm dysfunction**, ventilator–associated **pneumonia**	ventilator–induced **lung injury**, ventilator–induced **diaphragm dysfunction**, ventilator–associated **pneumonia**	**catheter – associated problems**, limb ischemia, blood stream infections **bleeding**, with systemic anticoagulation	**catheter – associated problems**, limb ischemia, blood stream infections **bleeding**, with systemic anticoagulation
costs	**cheap**, endotracheal tube	**cheap**, endotracheal tube	**high**, disposables, membrane	**high**, disposables, membrane

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