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Introduction to multiple organ support

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There is a renewed interest in novel extracorporeal technologies as a means of supporting individual organ failures. An emphasis should be placed on characterising the spectrum of extracorporeal devices for various organs and understanding how devices intended for support of one organ can have an indirect or direct impact on other organs, which is particularly relevant as different extracorporeal platforms may become integrated.

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Multisystem organ failure is commonly encountered in the intensive care setting, often requiring a multi-disciplinary approach to management. It is increasingly being recognised that organ failures do not exist in isolation, but rather result from and have an impact on the dysfunction of other organs, mediated by haemodynamic, neurohormonal and cell signalling feedback mechanisms, an interplay that has been termed organ crosstalk (Husain-Syed et al. 2015; Husain-Syed et al. 2016; Pelosi and Rocco 2011). Common examples of this relationship between organ systems include the cardiorenal, hepatorenal and pulmonary-renal syndromes, each of which has a significant impact on the likelihood of recovery of individual organs and overall prognosis (Davenport et al. 2017; Husain-Syed et al. 2016; Malbrain et al. 2014; Nadim et al.
2012; Ronco et al. 2012; Ronco et al. 2008).

Likewise, the treatment of one organ failure often directly impacts and may adversely affect another, as has been demonstrated with the direct effects of invasive mechanical ventilation on haemodynamics and the downstream effects of ventilator-induced lung injury on kidney function (Goligher et al. 2016; Husain-Syed et al. 2016; Luecke and Pelosi 2005).

The concept of extracorporeal support of organ failure is not new, with mechanical ventilation and renal replacement therapy (RRT) having been available for decades as a means of artificially supporting lung and kidney function, respectively (Bellomo et al. 2017; Neri et al. 2016). However, in light of recent technological advances, there has been a renewed interest in novel extracorporeal technologies as a means of supporting individual organ failures, such as venovenous extracorporeal membrane oxygenation (ECMO) and extracorporeal carbon dioxide removal (ECCO2R) for respiratory failure, venoarterial ECMO, ventricular assist devices (VAD) and total artificial heart for cardiac failure, and artificial liver detoxification systems for hepatic failure (Abrams et al. 2014; Aissaoui et al. 2018; Brodie and Bacchetta 2011; Chiumello et al. 2017; Thompson et al. 2017; Trudzinski et al. 2016). As a result, an emphasis has been placed on characterising the spectrum of extracorporeal devices for various organs, collectively termed extracorporeal organ support (ECOS) (**Figure**) (Ranieri et al. 2017).

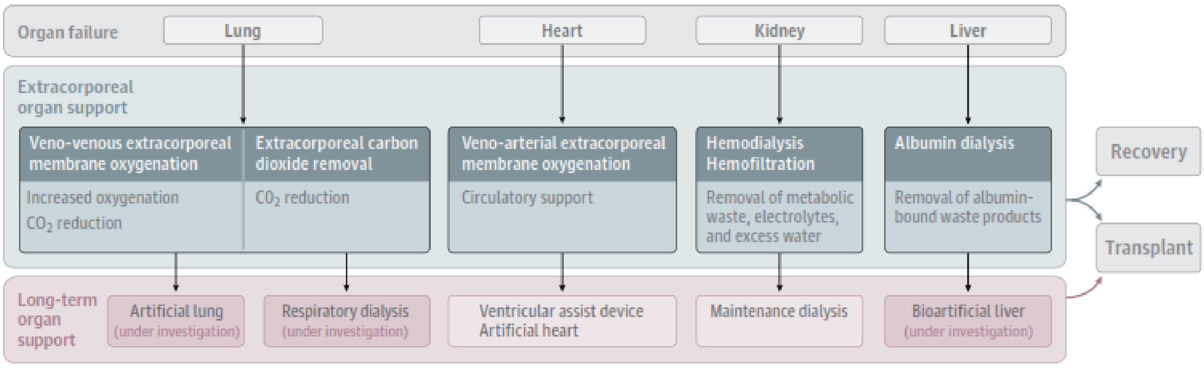

Figure.

Phases of extracorporeal organ support for the lung, heart, kidney, and liver (Ranieri et al. 2017)

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It will be important with time to better understand how devices intended for support of one organ can have an indirect or direct impact on another organ. This becomes particularly relevant as different extracorporeal platforms may become integrated, as has already been shown to be feasible with ECMO and RRT (Fleming et al. 2012). As these devices evolve to offer simultaneous support for multiorgan failure (Ronco et al. 2015), it will be important to emphasise a multidisciplinary approach at centres with capabilities of performing both extracorporeal and advanced non-extracorporeal management strategies, which in turn may warrant particular organisational and regionalisation considerations (Abrams et al. 2018; Combes et al. 2014).

The potential for development of integrated extracorporeal platforms has significant implications for clinical outcomes. Traditionally, patients who might benefit from one form of ECOS, such as venovenous ECMO for acute respiratory distress syndrome, are often deemed to be ineligible due to severe extra- pulmonary organ dysfunction (e.g. hepatic failure). However, with multiorgan ECOS availability, such patients might be considered preferred candidates for an integrated extracorporeal approach.

Importantly, the discussion of ECOS often focuses on the management of acute organ failure within an intensive care setting. However, as these devices become more efficient, portable, and durable (Cheung et al. 2015; Kischkel et al. 2017; Ronco et al. 2014; Seiler et al. 2017), the conversation must also address the potential future role of ECOS in the management of chronic organ failure, both as novel single-organ devices and applications (e.g. artificial lung, chronic respiratory dialysis) and as integrated destination device systems (e.g.VAD plus artificial lung, RRT plus extracorporeal liver assist device, etc). In both the acute and chronic setting, advances in extracorporeal technology hold the promise of these integrated systems being able to engage in artificial organ crosstalk and auto-regulation, much in the way native organs currently behave (Vincent et al. 2017).

In this issue of *ICU Management & Practice*, the authors will address the role of various ECOS systems as they currently exist, the potential for these single organ-focused systems to be integrated into multiorgan platforms, and future directions of ECOS toward long-term, multiorgan support systems, all of which will help to reframe the concept of ECOS in a new paradigm for the management of severe organ failure.

Conflict of interest

Daniel Brodie is currently the co-chair of the Trial Steering Committee for the VENT- AVOID trial sponsored by ALung Technologies. He was previously on the medical advisory board of ALung Technologies and Kadence.

Abbreviations

ECCO2R extracorporeal carbon dioxide removal

ECMO extracorporeal membrane oxygenation

ECOS extracorporeal organ support

RRT renal replacement therapy

VAD ventricular assist devices

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