Dear ladies and gentlemen, dear ADVOS users and interested parties,
we are pleased to present you another issue of our ADVOS Literature Service. We regularly select one or more papers from international journals which might be of interest to you in connection with our ADVOS procedure. This month we have selected the following:

OPTIONS IN EXTRACORPOREAL SUPPORT OF MULTIPLE ORGAN FAILURE.

Huber et al.

Obituary Prof. Wolfgang Huber

The author of this article, Prof. Wolfgang Huber, unfortunately passed away in May. Throughout the past decades he was a reference in critical care medicine and clinical development. As this review shows, he was a true expert in extracorporeal organ support. During his career, he has followed innovation and excellence in the treatment of his patients and was a great teacher for his students, his staff and partners.

In fact, he was one of the pioneers in the clinical ADVOS therapy application. He contributed a lot in the development of ADVOS as a sound believer in its therapy concept and potential benefit for critically ill patients. The ADVITOS family loses a great partner, but above all, we lose a friend. Thank you, Wolfgang! Rest in Peace.

Key message

This review describes different options for extracorporeal organ support (ECOS). Multiorgan support can be provided by sequential and/or intermittent therapy with single-organ support systems. Considering the additive treatment of blood in several devices, integrated multiorgan support using one multifunctional device might be the most intriguing approach in patients with multiple organ failure.

Background

Multiorgan dysfunction syndrome (MODS) or multiorgan failure (MOF) was first described 50 years ago and is the most frequent cause of mortality in critically ill patients. The concept of extracorporeal organ support was introduced about 100 years ago, when the first devices for renal replacement therapy (RRT) were investigated. In parallel, extracorporeal support for other organs was developed.

Renal Replacement Therapy

- Severe acute kidney injury (AKI) occurs in up to 25% in the intensive care unit (ICU), with a mortality rate >50% if accompanied by multiorgan failure.
- RRT can be applied with continuous or intermittent modalities, including slow continuous ultrafiltration (SCUF), continuous veno-venous hemofiltration (CVVH), continuous veno-venous hemodialysis (CVVHD), intermittent hemodialysis (IHD), continuous veno-venous hemodiafiltration (CVVHDF), intermittent hemodiafiltration (IHDF), continuous veno-venous high-flux hemodialysis (CVVHFD), or intermittent high-flux dialysis (IHFD).

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Extracorporeal lung support: oxygenation

- Acute respiratory distress syndrome (ARDS) still has a mortality > 40% and affects about 10% of ICU patients.
- Extracorporeal lung support was introduced more than 80 years ago with Gibbon's heart–lung machine.
- The CESAR and EOLIA trials gave hints on a reduction of mortality by ECMO in selected patients with ARDS.
- The outcome of patients with ECMO therapy is strongly predicted by concomitant non-pulmonary organ failure.

Extracorporeal lung support: CO_2 removal

- Considering the invasiveness and risks of high-flow ECMO, Gattinoni and coworkers introduced the concept of less invasive extracorporeal lung support restricted to CO_2 removal (ECCO2R).
- At least five studies reported on the feasibility of low-flow ECCO2R combined with an ultraprotective ventilation aimed at tidal volumes of 4 instead of 6 ml/kg predicted bodyweight.
- ECCO2R technologies have been applied in combination with other ECOS devices, in particular with RRT.

Extracorporeal liver support

- Albumin dialysis was introduced in the 1990s as an extracorporeal method to eliminate protein-bound toxins.
- Single pass albumin dialysis (SPAD), molecular adsorbent recirculating system (MARS), fractionized plasma separation and adsorption system (FPSA), high-volume plasma exchange (HVP), bioartificial liver (BAL) support, and hemadsorption are some of the modalities employed.
- Table 1 summarizes the features of clinically available devices for extracorporeal liver support.

Liver support system	Renal support	ECCO2R	Acid–base modulation	Improved coagulation	Resources required	Availability	Financial burden
SPAD	+	+	–	–	+++	++	+++
MARS	+	+	–	–	+++	+	+++
PROMETHEUS	+	+	–	–	+++	+	+++
ADVOS	+	+	+	–	++	+	+++
ELAD	+	+	–	–	++++	–	++++
Plasma separation	+	–	–	+	++	++	++
CytoSorb	+	–	–	–	++	+++	++

Table 1: SPAD: Single Pass Albumin Dialysis; MARS: Molecular Adsorbent Recirculating System; ADVOS: Advanced Organ Support, ELAD: Extracorporeal Liver Assist Device (adapted from Huber et al. 2020)

Advanced Organ Support (ADVOS)

- The advanced organ support (ADVOS) multi therapy device is based on the principle of albumin dialysis.
- Overall, the ADVOS therapy intends to provide a multiple organ (i.e. liver, lungs, kidney) support by means of water-soluble, protein-bound toxins elimination, direct H^+ removal (i.e. acid–base balance) and CO_2 elimination.
- The most differentiating factor of the ADVOS therapy in comparison to other apparently similar medical devices is the possibility to adjust the pH of the dialysate before and during treatment.

- Consequently, excess H^+ can diffuse from blood into the dialysate producing blood HCO_3^- and providing an acidosis correction.
- The capacity of the ADVOS system to remove CO_2 depends on blood flow, dialysate pH and the bicarbonate concentration.
- It takes 2 to 4 hours for ADVOS multi running at 100–200 ml/min blood flows to normalize blood pH.

Detoxification in sepsis

Several options are available with conflicting results from clinical trials:

- Hemoperfusion using fiber columns containing polymyxin B (an antibiotic with high affinity to endotoxins) has been used in several studies.
- CytoSorb provides hemoadsorption of cytokines and other mid-molecular weight toxins by multiple porous polymeric beads.
- The HA 330 and HA 380 cartridges contain neutro-macroporous resin adsorbing beads with a pore size of 500 D–60 kD.

The authors conclude:

- All types of ECOS share the challenges of vascular access, treatment of vlood in a device, induction of extracorporeal blood flow, anticoagulation with potential bleeding or clotting complications and other technology related side effects.
- Depending on the individual organ failures, in some patients, multiorgan support can be provided by sequential and/or intermittent therapy with single-organ support systems. Another option is combined organ support (normally two organ support) using serially connected devices driven by one blood pump.
- Considering the additive treatment of blood in several devices, integrated multiorgan support using one multifunctional device might be the most intriguing approach.

If you have further questions or suggestions - please contact us at marketing@advitos.com.