Extracorporeal life support systems in adult patients: what all intensivists should know

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Introduction and goals of the article

Advances in Intensive Care Unit (ICU) therapy have come in recent years from replacement of failing organs by complex devices. Replacement of cardiac and pulmonary function for short periods of time has been successfully performed since the early sixties when advances in cardiac surgery in both adults and children were obtained due to improved cardiopulmonary bypass (CPB) technology. Extension of the duration of cardiac and pulmonary support to days and weeks became a clinical reality in the early eighties in many cardiac surgery centres. Recent evolution of cardiac and pulmonary support is the extension of this technology to clinical situations other than cardiac surgery.

The authors of this article believe that in the future, several cardiac and pulmonary support devices will become a routine for (nearly) all ICUs. Therefore, the goals of the present article are to: (i) discuss technical aspects that are for most of them common to many clinical situations where such devices are used; (ii) attempt to define, for selected clinical situations, the indications of such devices; (iii) discuss the associated monitoring and therapeutic strategies; (iv) discuss the main management challenges after implantation; (v) discuss complications; (vi) propose a strategy for implementation of these devices in institutions that do not have previous experience.

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Historical aspects and nomenclature

Replacement of the heart and lung functions has been performed in cardiac surgery due to the development of CPB. Many years of technological refinements and improved knowledge in the pathophysiology of CPB have resulted in the current performance and relative safety of CPB (1). The increase in the number of cardiac surgery procedures rapidly revealed the need for cardiac support devices to replace the failing heart after surgery for more than a few hours. At approximately the same time, improved care of patients with adult respiratory distress syndrome (ARDS) revealed the need for replacement of the failing lung by using extracorporeal membrane oxygenation (ECMO). Because both the cardio-circulatory and respiratory functions are necessary for short term survival, the term "life support" devices has been coined. After nearly three decades of technological improvement, the field of cardiopulmonary support is now providing clinicians with a range of options (Table 1). Each of the devices presented in Table 1 has specific technical and clinical constraints. The most recent evolution is the ability to insert the life support systems percutaneously (extracorporeal, as opposed to the term paracorporeal for ventricular assist devices). Therefore, the term extracorporeal life support systems (ECLS) is nowadays used by most authors. The first use of ECLS is reported as early as 1972 (2). For many years, ECLS were confined to the cardiac surgery teams and to a few highly specialized intensive care units (ICU). The present and probably future evolution is a more widespread use of these devices due to miniaturization, improved biocompatibility and better clinical results.

Table 1. Classification of cardio-pulmonary assist devices

- Duration
  - Short: conventional CPB or ECLS
  - Long (> 6 hours): all the others
- Implantation
  - Outside of the operation roop: Intra-aortic balloon pump (IABP)/ ECLS
  - In the operation room: all the others
- Organs supported/ replaced
  - Heart: IABP and paracorporeal artificial ventricles
  - Heart and lungs: CPB/ ECLS
- Administrative constraints (in France)
  - « constrained » CPB/ paracorporeal ventricles
  - Not « constrained »: ECLS/ IABP

Technical aspects of ECLS

The components of all ECLS are: (i) the inflow and outflow cannulas; (ii) the tubings linking the cannulas to (iii) the pump; (iv) the oxygenator; (v) the heat exchanger; (vi) the monitoring devices; (vii) the control panel.

The time course of any ECLS procedure concerns: (i) insertion; (ii) maintenance: (iii) weaning or switch to another therapeutic strategy.

Insertion of cannulas

The main challenges during insertion are getting vascular access (cannulation). In theory, cannulation can be performed strictly percutaneously using the Seldinger technique. In patients that had ECLS to treat cardiac arrest, strictly percutaneous technique was used in approximately a third of patients (3). For patients with still preserved cardiac activity, palpation of the femoral artery pulse can be useful. In the authors' experience, ultrasound-guided identification of the femoral artery and vein is helpful in that saves time. The use of the percutaneous approach was statistically associated with improved survival (3) but it is unclear whether the percutaneous technique was performed in patients with still perceivable femoral artery pulsations. Nevertheless, even if the metal guidewires are inserted in the femoral vessels, cannulation can be difficult and surgical cut-down is probably necessary in many cases, especially in elderly patients with diffuse atheroma. The circuits for canulation can be either veno-arterial or veno-venous (this is the preferred strategy of cannulation for isolated respiratory failure). The venous cannulation site is mainly the inferior vena cava/ right atrium usually through the femoral vein. It is usually performed with an 24 F cannula. Arterial cannulation is usually performed in the femoral artery with an 18 F cannula. Changes from this initial strategy can be required either by inadequate venous return (in this case either an additional major extrathoracic vein is cannulated or an intrathoracic (right atrium) cannula is placed). Changes from the femoral artery are mainly required by local complications such as dissection upon cannulation or lower limb ischemia. Continuous on-line circuit monitors usually include venous drainage blood oxygen saturation, preoxygenator and postoxygenator pressure, and blood pump flow rate.

Insertion can either be performed in a centre that has all the capabilities for ECLS or mobile teams can insert the ECLS in a distant centre and the patient with the ECLS is transported to the "reference" centre (4). This is probably an intelligent solution, although technically challenging during the transport, because build-up of knowledge and technical skills around ECLS takes several months and there are no more reasons to allow for "learning curves" in all centres in 2009.

Timing of insertion is of course a matter of debate. In the present technological environment, when complications of cannulation and maintenance are under (relative) control, the paradigm should be "the sooner the better" provided that: (i) criteria for ECLS have been defined and (ii) the probability of recovery is reasonable; (iii) there are no contraindication to ECLS. For instance, in patients with ARDS, criteria for initiation of ECLS have been a PaO_2/FiO2 ratio < 100 on FiO_2 of 1.0, alveolar-arterial gradient ($AaDO_2$) >600 mm Hg, or transpulmonary shunt fraction > 30% despite and after optimal treatment (4). A patient having these parameters has a probability of death > 80% (4). Contraindication for ECLS in patients with ARDS are age > 70 years, time on the mechanical ventilator longer than 10 days; severe sepsis is not a contraindication (4). For CPR, the cardiac arrest team has to discuss ECLS probably within the first 30 minutes of resuscitation (5) since survival decreases rapidly with the interval between the onset of cardiac arrest the successful insertion of ECLS; low survival for more than 60 minutes before institution of ECLS for patients with in hospital cardiac arrest has been reported (5). The recent development of organ donation after cardiac arrest has added a new level of technical and ethical complexity that has required the institution of recommendations in countries like France where separation of therapeutic as opposed to organ preservation ECLS has been the object of an algorithm (6).

Initiation of ECLS

During cannulation, the ECLS circuit is primed with an asanguineous solution and is ready for connection. In institutions where ECLS is used for management of cardiac arrest, ECLS devices are already primed and connection to the cannulas is performed instantly (6). Anticoagulation is initiated with a bolus of unfractionated heparin (UFH) to the patient and an UFH dose in the priming volume (2 UI/ ml). The organizational problems, are extremely challenging when ECLS is used for CPR (the term e-CPR has been recently coined to describe the strategy in which ECLS is an integral part of the CPR strategy) (6). During day time, in one team, the interval from call (by the CPR team) to arrival of the ECLS team was below 20 minutes for in-hospital cardiac arrests (IHCA)(6). At night, the interval was slightly longer [6]. Such an interval requires a dedicated team composed of a vascular surgeon and a perfusionnist at the minimum as well as the availability of the device at any time (6).

There are relatively few published articles on the technical aspects of ECLS. A recent survey in the United States reported that 145 institutions perform ECLS the United States and there seem to be 24,000 ECLS cases recorded (2).

In the survey reported by Sievert et al., the pumps were mainly rollerheads (65 %, 122/188). This is probably less the case in Europe where centrifugal pumps are the main type of pumps. Most of the circuits use heparin- coated tubings in recent years (2). In the recent report on the use of ECLS for patients with acute respiratory distress syndrome (ARDS) secondary to the H1N1 flu epidemics in Australia and New Zealand, ECMO was provided with centrifugal blood pump driven circuit flow and polymethylpentene low-resistance oxygenators (7). Adult patients had vascular cannulae inserted through a peripheral approach into the femoral, jugular, or both vessels. In 49% of the patients a second access cannula was needed to augment ECMO support (7).

Therapeutic targets

During maintenance, clinicians have to deal with many different problems that are: (i) the initial disease with its natural history modified by the ECLS; (ii) the associated therapy that may become more difficult to implement due to the presence of ECLS; in many clinical situations ECLS is not the "magic bullet" but part of the therapeutic armamentarium with its own problems and complications. Typical therapies associated with ECLS have been described for a large cohort of adult patients that were treated for ARDS or cardiac causes including after cardio-pulmonary resuscitation (CPR) after cardiac arrest (4) (Table 2).

Table 2. Therapies associated with ECLS

Mechanical ventilator
Pressure mode
Limit peak inspiratory pressure to 35-40 cm H20
Optimal PEEP determined on the SvO2 value
Titrate FiO2 to obtain SaO2 > 90 % and SvO2 > 70 %
Inverse I: E ratio
Pharmacological treatments to improve cardiovascular function
Catecholamines
Levosimendan
Inhaled nitric oxide as required if there is increased systolic pulmonary artery pressure (PAPs > 40 mm Hg) or enlarged right ventricle.
Vasoconstrictors to provide adequate cerebral, coronary and renal perfusion pressure (usually mean arterial pressure > 80 mm Hg)
Pharmacological sedation including opioids, hypnotics and neuromuscular blocking drugs with associated monitoring of the neuromuscular function and depth of sedation using an electroencephalography-derived monitor such as the BIS® monitor

Diuresis or hemofiltration to reach the patient's "dry weight"

Enteral or parenteral nutrition once the shock state has been attenuated

Hypothermia in patient with cardiac arrest must be discussed
Avoidance of hyperthermia upon rewarming and at any time

Low dose corticosteroids (hydrocortisone 200 mg/ day) can be discussed

Transfusion of homologous red blood cells to reach the goals of oxygen delivery (see Table 3)

Management of hemodynamic status during ECLS

Although ECLS has in theory the capability to replace the entire heart and lung functions, clinical experience demonstrates that in many cases the flow of the ECLS device can be insufficient. There are many causes of insufficient flow. These can be: hypovolemia, increased intra-abdominal pressure, tamponnade, severe aortic insufficiency with subsequent dilatation of the left ventricle. Echocardiography, most often through the transoesophageal route should be performed each time the flow of the ECLS device is insufficient or varies instantly and at least once daily even in the absence of problems. Interventricular interactions must be understood such that an increased right ventricular afterload with a dilated right ventricle be easily recognized and treated with inhaled nitric oxide (iNO) as necessary. Tamponnade is a frequent complication after intrathoracic cannulation or after CPR and must always be suspected because it can severely impair venous return, ECLS flow and oxygen delivery. Native myocardial function can be maintained with inotropes or inodilators. Maintenance of adequate perfusion pressure for the brain, the coronary and the renal circulations may require the infusion of vasoconstrictors. A difficult issue is the presence of an intra-abdominal compartment syndrome (ACS) secondary to volume expansion and increased venous pressure. Decrease of the intra-abdominal pressure (IAP) is performed with sedation, neuromuscular blocking drugs, hemofiltration to remove fluid, the therapeutic target being that the patient returns to his pre-critical "dry weight"(4). In many instances, inflammation and increased capillary permeability renders this therapeutic goal un-attainable and many teams use low dose corticosteroids to treat the inflammatory syndrome (4). All of the above-cited therapeutic goals require proper monitoring devices, none of which is specific for the ECLS (except for flow measurements and continuous SvO2 estimations dedicated to the ECLS device). Once the cardiovascular function is considered to be optimized, support of the failing organs is symptomatic. Renal support therapy is required in the majority of cases for metabolic and water balance control; it is performed by continuo-

us hemofiltration with or without countercurrent dialysis fluid (4) by adding a hemmofilter to the ECLS circuit. Hemofiltration is usually performed in the continuous hemodiafiltration mode with a dialysis flow rate of 2 L/min (4); hepatic support has been used in selected cases; brain protection using hypothermia and avoidance of hyperthermia is used by many teams. Therapeutic goals during ECLS are presented in Table 3.

Table 3. Therapeutic goals during ECLS

- Systolic pressure > 90 mm Hg or more,
- Cardiac index > 2.2 l/min/m2 or more,
- Oxygen delivery > 520 ml/min/m2 or more
  Hemoglobin >12 g/dl ou plus,
- Oxygen extraction between 20% and 30%
- ACT between 150 to 200 s
- Sedation with neuromuscular blocking drugs
- Parenteral/ enteral (according to tolerance) nutrition during hypothermia in the absence of shock.
- Maintenance of electrolyte homeostasis using hemodiafiltration
- Volume control using hemofiltration
- Hypothermia (32-34 ° C) and avoidance of hyperthermia during rewarming
- Low intra-abdominal pressure

For ECLS in patient with severe ARDS the goals were 4:

- Arterial oxygen saturation > 90 % for veno-arterial ECLS and > 85 % for veno-venous ECLS
- Protective ventilation (typically FiO_2 0.3–0.5, rate 6–10, pressure control ventilation with PIP 30 cm H2O and positive end-expiratory pressure (PEEP) 10 cm H_2O, inspiratory to expiratory ratio of 2:1).

Anticoagulation is a main challenge in that both hemorrhagic and thrombotic complications are very frequent. Nearly all modern circuits are heparin-coated and this is compatible with lower doses or absence of heparin (8) but bleeding is still a challenge. In a study that reported the experience of one centre with 219 consecutive patients that underwent ECLS after cardiac surgery, 62 % had severe bleeding requiring reintervention with thoracotomy and the average transfusion requirements were 24 + 21 units per patient (9). In the recent report on ECLS used in patients with the H1N1 flu, hemorrhagic complications occurred in 54 % of the patients (7). The most common sources of bleeding were the ECMO cannulation sites in 22%, gastrointestinal tract in 10 %, respiratory tract in 10 %, vaginal bleeding in

9%, and intracranial in 9% of the patients respectively (7). Most centres use unfractionated heparin (UFH) as the main anticoagulant and monitoring is performed in most centres with the activated coagulation time (ACT) with ranges that vary from centre to centre (usually below 200 seconds for a normal ACT value of approximately 120 seconds). The literature on anticoagulation is confusing in that; the coagulation abnormalities prior to ECLS insertion are rarely reported; the devices used to measure ACT are rarely specified; the use of other measurements of UFH effect (such as anti-Xa activity) is rarely reported; algorithms for UFH dose adaptation for a given ACT values go from non existent to complex modelling of both the pharmacodynamic and pharmacokinetic effects (10). Anticoagulation for ECLS, given the reported hemorrhagic and thrombotic complications is probably one of the most important issues facing the medical community in the next few years given the increasing number of ECLS devices that are being implanted worldwide.

Weaning from ECLS is an additional challenge. Criteria for weaning probably depend on the indication for the insertion. Table 4 contains the main information concerning the weaning process.

Table 4. Weaning from ECLS in patients with mainly cardio-vascular failure. Weaning should be discussed after 72 hours of ECLS

- Daily cardiac echocardiography to estimate native myocardial recovery (implies changes of ECLS flow)
- Neurological evaluation consistent with the lack of cognitive dysfunction
- Stable hemodynamic status while on pump
  - dopamine or dobutamine < 10 µg/kg/min
  - Central venous pressure (CVP) < 12 mm Hg
  - Left ventricular ejection fraction > 40 %
  - Right ventricular function not altered
- If the above-cited criteria are present:
  - Decrease of ECLS flow by 0.5 L/min with 10 minutes steps
  - If alteration of the hemodynamic status on each step (decreased arterial blood pressure, decreased SvO_2, increased CVP the process should be stopped and the patient should be put back on full ECLS
- If after 5-7 days the weaning process is not feasible and the reversibility of the cardiac dysfunction is not probable, a long term ventricular assist device should be discussed.

Indications for ECLS are numerous. They concern: post cardiotomy in both adults (11) and pediatric (12;13) patients ; ARDS; drug-induced cardiotoxicity (14-16); after cardiac arrest (eCPR) in adults (5) and in children (17); cardiogenic shock (18); after pulmonary embolism (19,20) including

pregnant women (21); after pulmonary graft dysfunction (22); in severe sepsis (23-25); as a bridge to cardiac transplantation (26); refractory status asthmaticus (27,28); after anaphylactic shock (29); after post-partum hemorrhage (30).

Complications of ECLS are dependent on the underlying disease process but may concern, according to the definitions 100 % of the patients with hemorrhage and thrombosis being probably the most frequent, followed by end organ failure or complications (neurologic, renal, hepatic, digestive etc.).

Organizational problems

Historically, ECLS were first used by cardiac surgery centres with several recent trends that are worth mentioning: their use in ICUs in the absence of cardiac surgery facilities; mobile ECLS units that implant the device in a remote hospital and then transport the patient to the reference centre. Given the relatively low cost of ECLS devices and the apparent facility of use, it could be tempting to use ECLS in nearly all ICUs. The recent H1N1 flu epidemics could have represented a strong incentive to adopt this "widespread ECLS" model. The report published in 2009 that shared the Australian and New Zealand experience for patients with severe ARDS that underwent ECLS (7) showed that only approximately 10 % of the ICUs that received patients with ARDS secondary to the H1N1 flu epidemics, actually had ECLS facilities. We strongly support this "concentrated ECLS" model because of the complexity of the patients and the huge amount of expertise that patients on ECLS require. For ICUs and hospitals that want to implement an ECLS program, the best approach would be to collaborate with a centre that has the expertise and then begin their own program with outside help from the expert centre. The initiating centre, within a region or a country can initially provide a mobile unit that would implant the ECLS device in remote locations and then transport the patient to the reference centre.

In conclusion, ECLS is a promising device although the levels of required expertise, complications and cost will probably, in the next few years, limit its use to a few reference centres. For all other ICUs, it is important to include ECLS in the therapeutic strategy of many clinical situations with the idea that provided that the patient has the right indication and no contraindications, "the sooner the better" for ECLS implantation. Literature is rapidly increasing but major challenges are still in front of us, not the least being anticoagulation.

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