Continuing Medical Education

Extracorporeal Membrane Oxygenation

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Summary

Background: Veno-venous extracorporeal membrane oxygenation (VV-ECMO) and veno-arterial extracorporeal membrane oxygenation (VA-ECMO), also known as extracorporeal life support (ECLS), can both be used to treat patients with acute pulmonary or cardiovascular failure.

Methods: This review is based on publications retrieved by a selective search in PubMed on the topics of cardiogenic shock and acute pulmonary failure, also known as the acute respiratory distress syndrome (ARDS), as well as on ECMO. Attention was given chiefly to randomized, controlled trials and guidelines.

Results: Initial findings from prospective, randomized trials of VV-ECMO are now available. Trials of ECLS therapy are now in progress or planned. A meta-analysis of two randomized, controlled trials of VV-ECMO for ARDS revealed more frequent survival 90 days after randomization among patients treated with VV-ECMO, compared to the control groups (36% vs. 48%; RR = 0.75 [95% confidence interval 0.6; 0.94]). For selected patients, after evaluation of the benefit–risk profile, VV-ECMO is a good treatment method for severe pulmonary failure, and ECLS for cardiogenic shock and resuscitation. The goal is to secure the circulation so that native heart function can be stabilized in the patient's further course or a permanent left-heart support system can be implanted, or else to support lung function until recovery.

Conclusion: ECMO is a valid option in selected patients when conservative treatment has failed.

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Extracorporeal membrane oxygenation (ECMO) is a means of treating patients with severe pulmonary and/or cardiac failure by temporarily bypassing the functions of these organs.

ECMO generally involves the removal of blood from the venous system, which is then oxygenated, decarboxylated, and returned to the body via either a vein or an artery, depending on the indication.

In primary, isolated and refractory pulmonary failure, the removed blood is returned into a vein (veno-venous ECMO, VV-ECMO). In primary cardiac failure, the blood is returned into an artery in order to sustain the circulation (veno-arterial ECMO, VA-ECMO, also called "extracorporeal life support" [ECLS]). ECLS replaces the deficient function of both the lungs and the heart.

In this review, we give a detailed description of the common indications, the techniques used, patient monitoring, and weaning from ECMO. The information presented here is derived from publications that were retrieved by a selective literature search in PubMed on the topics of cardiogenic shock, ARDS, and ECMO.

Learning objectives

This article is intended to enable readers to:

- know the main indications, treatment goals, and basic mechanisms of action of VV-ECMO and ECLS
- be familiar with the different types of cannulation for VV-ECMO and ECLS
- be aware of the more common complications of

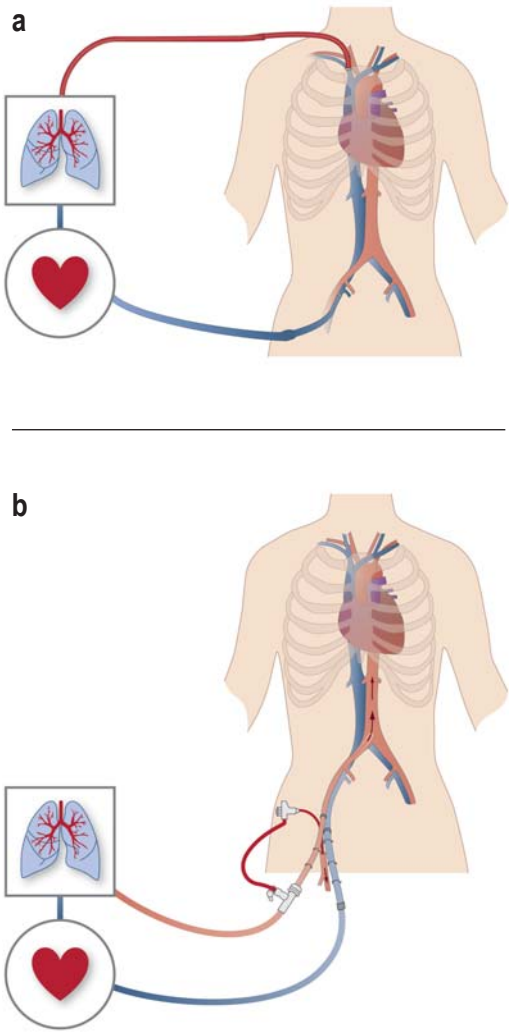
Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation is a means of treating patients with severe pulmonary and/or cardiac failure by temporarily bypassing the functions of these organs.

Mechanism of action of ECMO

In primary, isolated and refractory pulmonary failure, the removed blood is returned into a vein. In primary cardiac failure, the blood is returned into an artery in order to sustain the circulation.

FIGURE 1



Different cannulations for VV-ECMO and ECLS

a) Veno-venous ECMO. A cannula is usually inserted via the femoral vein so that its tip lies at the level of the renal veins or the inferior vena cava near the right atrium. The drained blood is oxygenated, decarboxylated, and returned to the venous system through a cannula located in the jugular vein an adequate distance away from the draining cannula.

b) Femoral veno-arterial ECMO/ECLS. A cannula is inserted via the femoral vein so that its tip lies at the level of the right atrium. The drained blood is subsequently oxygenated and decarboxylated and returned to the arterial system via a cannula in the femoral artery. An antegrade leg perfusion cannula has also been inserted to prevent limb ischemia.

VV-ECMO, veno-venous extracorporeal membrane oxygenation; ECLS, extracorporeal life support

these treatments and the challenges associated with them.

Severe pulmonary failure

VV-ECMO can be implanted in patients suffering from severe pulmonary failure. This usually involves the insertion of two venous cannulae: a long femoral cannula that drains venous, deoxygenated blood proximal to the right atrium, and a short jugular cannula that returns blood that has been oxygenated and decarboxylated by ECMO to the superior vena cava *(Figure 1a)*.

Two randomized trials were carried out to determine whether VV-ECMO improves the outcome of patients with severe respiratory failure ([ARDS], "acute respiratory distress syndrome"). In the CESAR trial, VV-ECMO yielded a survival benefit (1), but the informative value of this finding is limited because 24% of the patients who were randomized to the intervention group and transferred to an ECMO center ultimately were not treated with ECMO. The CESAR trial, therefore, is perhaps best understood as documenting the benefit of treating patients with severe respiratory failure in a specialized center. In 2018, Combes and colleagues published the EOLIA trial, which is the largest trial to date of VV-ECMO for severe lung failure (2). The patients were randomized to receive either VV-ECMO therapy or invasive ventilation alone. A nonsignificant reduction in 60-day mortality was found in the ECMO group: 35%, compared with 46% in the control group, corresponding to a relative risk of 0.76 (95% confidence interval: [0.55; 1.04]). This methodologically excellent but statistically underpowered study was stopped early because of the low expectation of achieving statistical significance. There were, however, clear indications of the benefit of ECMO therapy with respect to the secondary endpoints. The reduction of ventilator-associated lung injury by less invasive ventilation is considered to be a possible pathophysiological explanation (3). A meta-analysis and post-hoc Bayesian analysis of the combined data from the EOLIA and CESAR trials revealed a survival benefit from VV-ECMO therapy in severe lung failure (4, 5). By day 90 after randomization, 77 of 214 patients (36%) in the ECMO group and 103 of 215 patients (48%) in the control group had died (relative risk [RR] 0.75, 95% CI: [0.6; 0.94]; p = 0.013; I2 = 0%). In the "per-protocol" and "as-treated" analyses, the relative risk of dying in the intervention group was 0.75 (95% CI: [0.6; 0.94]) and 0.86 (95% CI: [0.68; 1.09]), respectively. VV-ECMO should be

Veno-venous ECMO

A cannula is inserted via the femoral vein so that its tip lies at the level of the renal veins or the inferior vena cava near the right atrium. The drained blood is oxygenated, decarboxylated, and returned to the venous system through a cannula located in the jugular vein.

Femoral veno-arterial ECMO/ECLS

A cannula is inserted via the femoral vein so that its tip lies at the level of the right atrium. The drained blood is subsequently oxygenated and decarboxylated and returned to the arterial system via a cannula in the femoral artery.

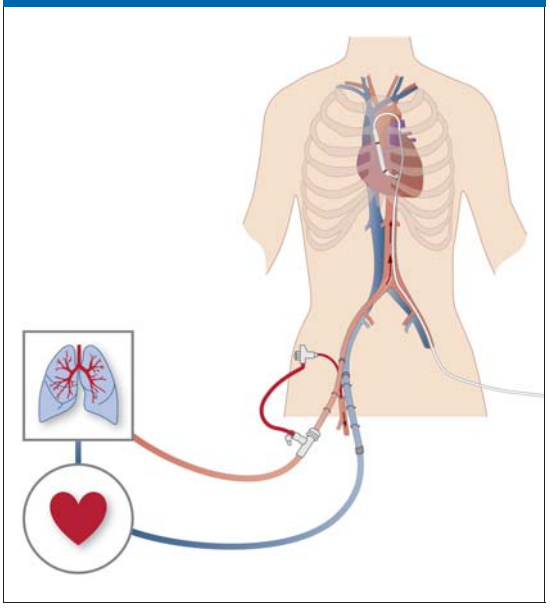
performed in a center for severe respiratory failure (ARDS center) with adequate and trained staff; it may lessen mortality in severe cases. Most centers use the EOLIA indication criteria, which specify that at least one of the following must be the case for a patient with ARDS: oxygenation index (paO_2/FiO_2) < 50 mmHg for > 3 hours or < 80 mmHg for > 6 hours, or an arterial pH < 7.25 with an arterial partial pressure of CO_2 greater than 60 mmHg for > 6 hours. The S3 guideline on invasive ventilation, in which VV-ECMO is recommended in severe ARDS only as rescue therapy, was written in 2017, before the EOLIA trial was published (6). These more recent findings imply that ECMO may be useful in situations beyond rescue therapy, but its potential complications must be considered as well ([e1] and *eTable*). Treatment in a specialized center with appropriately qualified and available nursing staff is essential. Moreover, patients should receive high-quality basic therapy, especially lung-protective ventilation and prone positioning therapy, before VV-ECMO is implanted.

Cardiogenic shock and resuscitation

In recent years, ECLS has become an increasingly common treatment for patients in cardiogenic shock and those with sustained cardiac arrest (7).

In cardiogenic shock, which is characterized by severe hypoperfusion of the body due to cardiac dysfunction, the immediate goal of therapy is to secure adequate organ perfusion as rapidly as possible (8, 9). This should prevent, or at least mitigate, further worsening of the condition by interrupting the so-called shock cascade (8, 9); it should also enable recovery of the myocardium, with the aid of further measures such as early revascularization, if needed. Once the myocardium has recovered sufficiently to keep the organs perfused without additional help, weaning from ECLS can be begun (8, 9). The use of ECLS for this indication has been based only on retrospective data until now. The reported survival and recovery rates of patients who have undergone ECLS vary widely, depending on the cause of cardiogenic shock and the occurrence of complications (9, 10). In a recent meta-analysis of 17 000 patients with ECLS implantation for refractory cardiogenic shock, survival at 1 and 5 years was 36.7% and 29.9%, respectively (10). Two randomized trials (ECLS-SHOCK and EURO-SHOCK) are now in progress that should yield important new information about the safety and efficacy of ECLS in the near future (11,12).

FIGURE 2



Femoral veno-arterial ECMO/ECLS and additional femoral transaortic microaxial pump: A cannula is inserted via the femoral vein so that its tip lies at the level of the right atrium. The drained blood is oxygenated, decarboxylated, and returned to the arterial system via a cannula in the femoral artery. A microaxial pump, inserted via the femoral artery and through the aortic valve into the heart, pumps blood from the left ventricle into the aortic root.
ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation

Similarly, in patients with sustained cardiac arrest, if conventional resuscitation does not succeed in reestablishing spontaneous circulation, ECLS-assisted resuscitation (eCPR) is a valid option in selected cases (13). The ARREST trial, whose results were published in late 2020, was the first randomized trial to document the superior efficacy of this approach compared to conventional resuscitation (14), albeit in a small group of patients (N = 30) *(Figure 3a)*. Survival to hospital discharge was 7% in the control group (95% confidence interval: [1.6; 30.2]) versus 43% [21.3; 67.7] in the ECLS group (risk reduction 36.2%, 95% CI: [3.7; 59.2]).

A femoral percutaneous access route is usually chosen for ECLS of either indication *(Figure 1b)*, as it enables perfusion to be established quickly and safely. Unfortunately, however, this also leads to retrograde

The implementation of VV-ECMO

VV-ECMO should be performed in a center for severe pulmonary failure (an ARDS center) with adequate staffing and trained personnel. It can lower mortality in severe cases.

Cardiogenic shock

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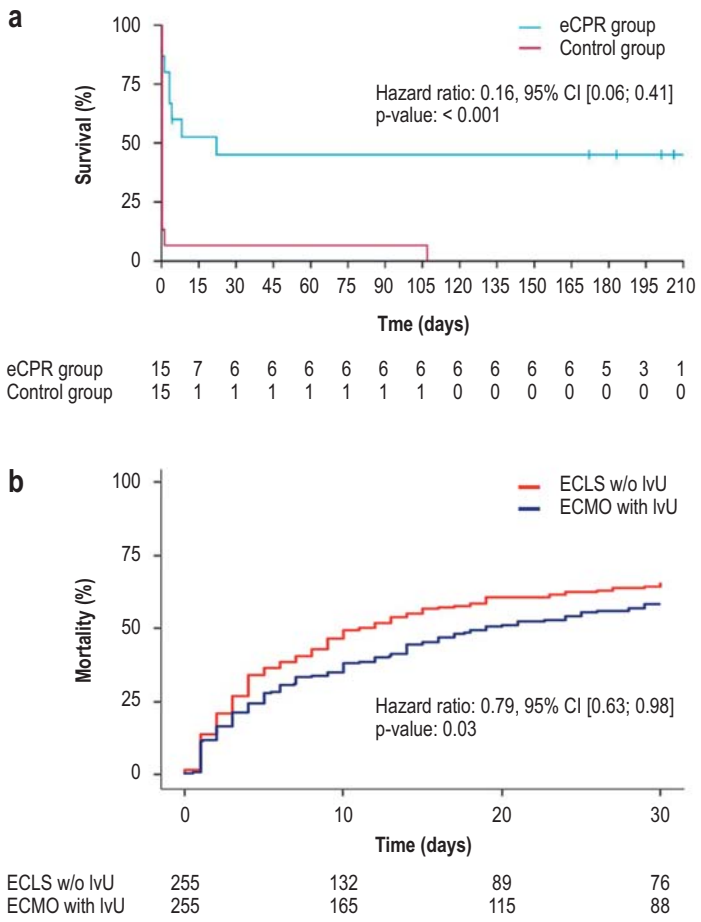
FIGURE 3



Kaplan-Meier curves from recently published ECLS trials, modified from Yannopoulos et al. and Schrage et al. (14, 16).

(a) Survival after ECLS-assisted versus conventional resuscitation: data from the prospective, randomized ARREST trial.

(b) Mortality after left ventricular unloading during ECLS: data from a retrospective registry study.

CI, confidence interval; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; eCPR, ECLS-supported cardiopulmonary resuscitation; lvU, left ventricular unloading

flow in the aorta, which increases left ventricular afterload (15). This can impair the recovery of myocardial function and even cause life-threatening complications such as left ventricular thrombosis or fulminant pulmonary edema (8). The risk of afterload increase must therefore be considered in all potential recipients of ECLS. In recent years, the additional implantation of a microaxial cardiac pump that pumps blood from the left ventricle into the aorta has been used to combat this problem by lessening left ventricular wall tension and preventing back-up of blood into the pulmonary circulation *(Figure 2)*. Preliminary data from a large retrospective study suggest that this approach lessens mortality but may lead to more complications *(Figure 3b)* (16).

The benefits of ECLS for both indications must be weighed against its risks: in particular, bleeding and ischemic complications are common (8, 15, 16) *(Table)*. This underscores the importance of careful patient selection, even if it has been shown that the complication rate falls with increasing experience and case numbers *(Box)* (17).

It should be noted that ECLS is primarily a temporary support device (18). The time gained can be used to treat the cause of the disease (e.g., with early revascularization, in cases where cardiogenic shock has been caused by myocardial infarction) (18). The selection criteria for ECLS are thus designed to identify patients with treatable underlying conditions. They are also intended to exclude those who probably will not benefit from ECLS or are at excessive risk (e.g., those with severe concomitant illnesses). This was already reflected in the indications for eCPR in a consensus statement published in 2018 (13), presented in modified form in the *Box* for cardiogenic shock. These criteria are useful for guidance in clinical decision-making; yet, ultimately, decisions on treatment must still be made case by case.

Use during high-risk coronary interventions

A rare indication for ECLS is the potential bridging of circulatory instability during high-risk percutaneous coronary interventions (PCI). These are defined as complex interventions in patients with a high-risk constellation, such as PCI in the setting of a very low left-ventricular ejection fraction or main-stem PCI for an occluded right coronary vessel. This should only be attempted if a multidisciplinary heart team has determined that surgical revascularization is not possible.

ECLS implantation in such a situation is prophylactic, and the need for it must be weighed against risk of cannulation-associated complications (e.g. bleeding and ischemia). No prospective studies of high-risk PCI under ECLS have been published to date; the available literature consists only of case series. These suggest an acceptable safety profile (because of the elective cannula

Benefits and risks

The benefits of ECLS must always be weighed against its risks: in particular, bleeding and ischemic complications are common.

The therapeutic goal of ECLS

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placement) and adequate circulatory support during the intervention, but they are, of course, subject to selection bias.

Circulatory failure after cardiac surgery

An ECLS system can also be implanted in patients with persistent circulatory failure after cardiac surgery. In this condition, called postcardiotomy shock or postcardiotomy syndrome, the heart does not function well enough for the patient to be weaned off the heart-lung machine. Prolonged connection to the machine is associated with the activation of multiple physiological cascades leading to negative outcomes, and thus the use of the heart-lung machine itself should be limited (19). ECLS can be used to help the patient get through the acute perioperative and early postoperative phases of postcardiotomy shock. This can involve either the central cannulation of thoracic vessels with provisional chest closure *(eFigure 1),* or else the percutaneous cannulation of peripheral vessels (e.g., the femoral artery and femoral vein). The putative advantage of central over peripheral cannulation is debated (19,20), as both techniques have advantages and disadvantages. Central cannulation allows insertion of a larger cannula directly into the ascending aorta, as well as central flow. This lessens the burden on left ventricle while enabling better oxygenation of the ascending aorta and the cranial vessels (preventing the harlequin phenomenon). The peripheral implantation technique enables definitive sternal closure, does not require a second procedure, and may lessen bleeding into the chest as well as infectious complications (20). Alternatively, axillary implantation of the arterial ECLS cannula can be performed. In this case, venous cannulation is usually performed via the femoral vein *(eFigure 2)*. Here, too, the advantages of central cannulation are antegrade flow and avoidance of the harlequin phenomenon.

Implantation strategies and ECLS transport

ECLS can serve a variety of goals, which may also change during the course of treatment and are subject to interdisciplinary reevaluation. ECMO can be used for bridging until the recovery of native cardiac function ("bridge to recovery"), bridging until another type of treatment is decided upon ("bridge to decision"), or bridging until another type of cardiac support system is implemented ("bridge to bridge").

The type and location of cannulation depend on the staffing, spatial, and logistical resources of the treating institution. Central thoracic or axillary arterial cannulation usually requires surgery for access, but peripheral implantation can be performed anywhere. Imaging with fluoroscopy or sonography makes vascular puncture safer and helps prevent access-related complications. For the most part, ECLS cannulae are inserted percutaneously with the Seldinger technique, but the vessels can also be surgically exposed and the cannulae directly inserted. For peripheral cannulation, it is recommended that a further arterial cannula be inserted into the femoral artery distally in addition to the two ECLS cannulae. This ensures perfusion of the leg on the side of the insertion, as the main ECLS arterial cannula impairs distal perfusion by compromising the lumen, potentially causing leg ischemia. An alternative to surgical or percutaneous insertion of the cannulae with the Seldinger technique is end-to-side anastomosis of a prosthesis onto the femoral artery.

Now that this form of treatment has become safer and more widespread and miniaturized ECMO systems have come into use, some specialized centers have

BOX

Criteria for and against ECLS to treat cardiogenic shock

- **For**
  - a treatable or reversible cause (e.g., acute myocardial infarction, pulmonary artery embolism)
  - short "no flow" (≤ 5 minutes) or "low flow" time (≤ 60 minutes) with continuous, sufficient resuscitation measures
  - young patients (≤ 65 years) without relevant comorbidities
  - low lactate concentration (≤ 10 mmol/L) or balanced pH
- **Against**
  - non-treatable cause with no other treatment option (e.g., end-stage heart failure with no option for heart transplantation or LVAD implantation)
  - ECLS as a "bridge to decision" where applicable
  - unobserved cardiac arrest, prolonged "no flow" (≥ 10 minutes) or "low flow" time (≥ 90 minutes), inadequate resuscitation measures
  - very frail elderly patients (≥ 75 years)
  - signs of persistent, insufficient tissue perfusion, independently of the duration of resuscitation (lactate ≥ 20 mmol/L, pH < 6.8)
  - signs of irreversible brain damage
  - significantly lowered life expectancy because of other diseases, e.g., cancer
  - excessive risk of bleeding or contraindication for anticoagulation
  - refusal by the patient

ECLS, extracorporeal life support; LVAD, left ventricular assist device

Circulatory failure after cardiac surgery

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Criteria for ECLS in cardiogenic shock

- a treatable or reversible cause
- short "no flow" or "low flow" time with continuous, sufficient resuscitation measures
- young patients without relevant comorbidities
- low lactate concentration or balanced pH

TABLE

Complications of ECLS, modified from Cheng et al. (40)

Complication	Number of studies	Pooled rate (%)	Published rate (minimum and maximum in %)	95% CI
Acute renal failure	6	55.6	29.9–86.7	[35.5; 74.0]
Renal replacement therapy	15	46	7.84–86.7	[36.7; 55.5]
Bleeding complications	5	40.8	14.8–63.6	[26.8; 56.6]
Significant infections	10	30.4	13.7–64.5	[19.5; 44.0]
Limb ischemia	13	16.9	3.7–37.5	[12.5; 22.6]
Neurologic complications	9	13.3	5.9–22.1	[9.9; 17.7]
Fasciotomy or compartment splitting of the limbs	5	10.3	5.4–20.7	[7.3; 14.5]
Stroke	3	5.9	3.9–9.7	[4.2; 8.3]
Limb amputation	5	4.7	0–8.1	[2.3; 9.3]

CI, confidence interval; ECLS, extracorporeal life support

developed programs for the implantation of ECMO systems in the referring hospitals or even outside the hospital, both for severe lung failure and for cardiogenic shock, and even for resuscitation (21). For this purpose, a 24-hour on-call service with appropriate logistics is available to bring the implanting team and equipment to the patient as quickly as possible. The patient, after having been stabilized by ECMO or ECLS implantation, is then transported to the appropriate center for the evaluation and provision of further treatment.

Staffing requirements

In view of the complexity of this form of treatment, we believe < should be available in every ECMO center, especially for ECLS, even if the current S3 guideline does not require this (22). Aside from perfusionist support, the care of the patient essentially lies in the hands of teams of intensive care physicians, intensive care nurses, cardiologists, and cardiac surgeons specially qualified for this purpose, as well as accompanying teams of physiotherapists and psychologists. Full staffing of this type is not now mandatory for the establishment of an ECMO program, and a wide variety concepts can be seen implemented across different regions and hospitals. Nonetheless, many specialty societies support this approach in their consensus papers on eCPR and on the training of ECLS centers (13, 23). It should also be mentioned that a relatively large number of ECMOs are carried out in Germany (VV-ECMO 2012: 3.0 : 100 000; VA-ECMO/ECLS 2014: 3.5 : 100 000) compared to the rest of Europe as a whole, yet with a markedly higher mortality than in other countries (24). In the 2009 influenza pandemic, the in-hospital survival rate of ECMO-treated patients was 68% in Italy, 47% in Australia and New Zealand, and 46% to 30% in Germany (24–26). Because of differences in data collection across the individual studies from different countries, selection effects cannot be excluded, and survival rates should be compared with caution. The S3 guideline specifies structural requirements with respect to minimum case numbers and staffing levels. The nursing staff is very important as well (27).

Monitoring

Baseline monitoring of ventilation parameters and regular blood gas analyses are recommended for all patients on ECMO (6). In patients with ECLS, monitoring of perfusion, hemodynamics, and cardiac unloading is also required. Knowledge of the effect of ECMO/ECLS on hemodynamic parameters is important for the critical interpretation of monitoring (28).

Upper-body hypoxia in peripherally cannulated ECLS (harlequin syndrome, also called north-south syndrome) may occur if lung function is poor (e.g., because of pulmonary edema) but there is still some residual cardiac contractility. As a result, insufficiently oxygenated blood is pumped into the aortic

ECLS for bridging

- until the recovery of native cardiac function
- until another type of treatment is decided upon
- until another type of cardiac support system is implemented

Staffing requirements

In view of the complexity of this form of treatment, we believe perfusionists should be available in every ECMO center, especially for extracorporeal life support (ECLS), even if the current S3 guideline does not require this

root and arch. In particular, in femorally cannulated ECLS, the oxygenated blood enters the aortic arch in retrograde fashion from the descending aorta, and a watershed arises between adequately oxygenated blood distally and insufficiently oxygenated blood proximally. To ensure an adequate supply of oxygenated blood to the brain and central nervous system, arterial oxygen saturation is measured in the right arm. In addition to blood sampling from the radial or brachial artery, near-infrared spectroscopy (NIRS) is also useful for this purpose (29). Ultrasonography, too, is critically important in ECLS, as it provides valuable information on cardiac function, left ventricular filling status, volume status, leg perfusion, and cannula position. In particular, the assessment of left ventricular ejection fraction and the detection of left ventricular distention are essential for assessing potential indications for left ventricular unloading. We advocate daily ultrasonographic examinations.

Laboratory monitoring includes parameters of end-organ function, hemolytic parameters, and differential coagulation parameters. Anticoagulation is classically performed with heparin and correspondingly monitored with the activated partial thromboplastin time. The clinical examination must include neurological checks, leg perfusion checks, and clinical indicators of hemolysis. Device checks should also be performed regularly, including audiovisual control of the system and checking of the insertion sites. There should be regular monitoring of RPM, blood flow, transmembrane pressure gradient, and blood gas analyses proximal and distal to the oxygenator.

Weaning from VV-ECMO

Evidence for weaning strategies from VV-ECMO is lacking, and thus center- and patient-specific weaning algorithms are needed (30). The weaning process should begin when pulmonary gas exchange and compliance have improved. Lung-protective ventilation is maintained while blood and gas flow in the ECMO system are reduced to a level where adequate gas exchange can still be ensured. It must be borne in mind that every centrifugal pump is designed for an optimal blood flow range, below which hemolysis may occur (31). Unlike in ECLS, where this should never be done, the oxygenating effect of the VV-ECMO system can be reversibly eliminated during weaning by turning off the gas flow to the oxygenator for a few hours, or, ideally, days. If adequate gas exchange is maintained under these conditions while lung-protective ventilation continues to be given, this is a good predictor of successful weaning. The strategy of extubation before decannulation should be considered in particular patient groups (e.g., in patients with chronic obstructive pulmonary disease, "bridging to lung transplantation") but has not become part of routine clinical practice (32).

Bridging to lung transplantation

VV-ECMO is also used as a bridge to lung transplantation in patients with end-stage pulmonary failure, who have generally already been evaluated for transplantation and placed on the waiting list. The long-term survival of these lung transplant recipients has improved in recent years, approaching that of patients bridged to transplantation without ECMO (33). Strict patient selection is essential. Bridging to transplantation with ECMO via jugular double-lumen cannulae may be advantageous, as this enables patients to be extubated and mobilized. Both of these things improve the outcome after lung transplantation (34,35).

Weaning from ECLS

Circulatory support with ECLS is usually provided for three to ten days, which is enough time for the treating team to evaluate the three key therapeutic options in this situation:

- recovery from circulatory failure and weaning from ECLS;
- provision of a permanent ventricular assist device;
- or transition to palliative care.

Multiple factors enter into this decision, including the underlying diagnosis and the patient's age and intercurrent illnesses.

In patients undergoing ECLS, the circulatory failure for which they are being treated is often of primary cardiac origin. Its cause must be identified and treated as rapidly as possible. At the same time, the accompanying goals for intensive care include the optimization of pulmonary, renal, and coagulation values and functions, as well as the comprehensive prevention and treatment (if needed) of infection. Echocardiographic monitoring at close intervals and a tailored regimen of circulatory drugs and fluid administration are of great help in achieving the objective of timely weaning (36). By using this strategy, a German ECLS center was able to raise the rate of successful weaning from 56.6% to 74.1%, and 30-day survival from 34.0% to 50.0% (36).

Bridging to a left ventricular assist device

Patients who cannot be weaned off of ECLS because of persistent left heart failure may have a left ventricular

Upper-body hypoxia

Upper-body hypoxia in peripherally cannulated ECLS (harlequin syndrome, also called north-south syndrome) may occur if lung function is poor (e.g., because of pulmonary edema) but there is still some residual cardiac contractility.

The ECMO weaning process

The ECMO weaning process should begin when pulmonary gas exchange and compliance have improved. Lung-protective ventilation is maintained while blood and gas flow in the ECMO system are reduced to a level where adequate gas exchange can still be ensured.

assist device implanted for permanent left ventricular support (37). Patients are usually kept on ECLS until the prospect of left ventricular recovery in a reasonable time is no longer realistic and there are no contraindications to the insertion of a left ventricular assist device, such as neurological impairment or infection. The evaluation of right ventricular function can be difficult in patients under ECLS, but it is nonetheless very important for ensuring successful therapy after a left ventricular assist device is implanted. Thus, some centers have reported success with a switch from ECLS to a microaxial pump at an axillary implant site (38). This allows patient optimization, including mobilization and evaluation of the right heart under sole support of the left ventricle (38, 39).

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Conflict of interest statement
PD Bernhardt has served as a paid consultant for Abbott, Abiomed, Berlin-Heart, and Medtronic, companies that are active in the field with which this review is concerned. He has received lecture honoraria from Abbott, Abiomed, AstraZeneca, BerlinHeart, Medtronic, and Novartis.

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Weaning from ECLS

Circulatory support with ECLS is usually provided for three to ten days.

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► **Supplementary material**

eReferences, eCaseReports, eTables, eFigures, eMethods: www.aerzteblatt-international.de/m2022.0068

Further information on CME

- Participation in the CME certification program is possible only via the Internet: cme.aerzteblatt.de. This unit can be accessed until 31 March 2023. Submissions by letter, e-mail, or fax cannot be considered.
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- This article has been certified by the North Rhine Academy for Continuing Medical Education. CME points can be managed using the "uniform CME number" (einheitliche Fortbildungsnummer, EFN). The EFN must be stated during registration on www.aerzteblatt.de ("Mein DÄ") or entered in "Meine Daten", and consent must be given for results to be communicated. The 15-digit EFN can be found on the CME card (8027XXXXXXXXXX).

CME credit for this unit can be obtained via cme.aerzteblatt.de until 31 March 2023.

Only one answer is possible per question. Please select the answer that is most appropriate.

Question 1

What is the main goal of extracorporeal membrane oxygenation?

a) supportive therapy of severe chronic obstructive lung disease
b) temporary treatment of pneumothorax
c) treatment of isolated pulmonary failure
d) long-term support of the pumping function of the heart
e) temporary bridging of severe lung and/or heart failure

Question 2

What is the goal of treatment with ECLS?

a) the temporary securing of organ and tissue perfusion
b) myocardial unloading
c) maintenance of the shock cascade
d) isolated assumption of the oxygenating function of the lungs
e) permanent support of circulatory function

Question 3

A 55-year-old woman is brought to the shock room by the emergency rescue service. She has refractory ventricular fibrillation. An interdisciplinary decision is made to insert an ECLS system. What approach should be preferred in this situation?

a) central, thoracic insertion of the arterial cannula into the left atrium and of the venous cannula into the right atrium
b) central thoracic insertion of the arterial cannula into the ascending aorta and of the venous cannula into the right atrium
c) percutaneous cannulation of the axillary artery for arterial access and of the axillary vein for venous access
d) percutaneous cannulation of the femoral artery for arterial access and of the femoral vein for venous access
e) percutaneous cannulation of the femoral vein with a double-lumen catheter

Question 4

Which of the following criteria favors the use of ECLS in the treatment of cardiogenic shock?

a) limited life expectancy
b) excessive risk of bleeding
c) evidence of irreversible brain damage
d) a young patient (under age 65) without relevant comorbidities
e) untreatable causes with no other therapeutic options

Question 5

Which of the following therapeutic uses of ECLS is obsolete?

a) circulatory support until native heart function recovers ("bridge to recovery")
b) circulatory support until a decision is made about further treatment ("bridge to decision")
c) permanent circulatory support ("destination therapy")
d) circulatory support until the implantation of a permanent support system ("bridge to bridge")
e) circulatory support until heart transplantation ("bridge to transplantation")

Question 6

What cannulations are usually used for veno-venous extracorporeal membrane oxygenation?

a) drainage via femoral vein, return via femoral artery
b) drainage via femoral vein, return via jugular vein
c) drainage via superior vena cava, return via pulmonary artery
d) drainage via femoral vein, return via pulmonary artery
e) drainage via pulmonary artery, return via jugular vein

Question 7

Which of the following findings constitutes an indication for ECMO according to the EOLIA criteria?

a) arterial pH 7.3 with arterial CO_2 partial pressure of 50 mmHg for at least 6 hr
b) oxygenation index < 50 mmHg for at least 1 h
c) oxygenation index < 70 mmHg for at least 5 hr
(d) arterial pH < 7.25 with arterial partial pressure of CO_2 higher than 60 mmHg for longer than 6 hr
e) oxygenation index < 40 mmHg for at least 2 hr

Question 8

A meta-analysis was performed that included 2 RCTs concerning the use of VV-ECMO in patients with severe pulmonary failure. What was the relative risk of death in the intervention arms compared to the control arms of these two studies?

a) 1.5
b) 1.25
c) 1.0
d) 0.75
e) 0.5

Question 9

According to a meta-analysis, what is the most common complication of ECLS?

a) acute renal failure
b) lower limb amputation
c) hemorrhagic stroke
d) ischemic stroke
e) liver failure

Question 10

A small-scale randomized trial was conducted to determine whether patients with cardiac arrest benefit from ECLS-assisted resuscitation. What percentage of patients survived at least until hospital discharge?

a) 27% in the intervention group vs. 1% in the control group
b) 35% in the intervention group vs. 4% in the control group
c) 43% in the intervention group vs. 7% in the control group
d) 48% in the intervention group vs. 11% in the control group
e) 52% in the intervention group vs. 14% in the control group

►► Participation is possible only via the Internet: cme.aerzteblatt.de

Supplementary material to:

Extracorporeal Membrane Oxygenation

by Alexander M. Bernhardt*, Benedikt Schrage*, Ines Schroeder, Georg Trummer, Dirk Westermann, and Hermann Reichenspurner

Dtsch Arztebl Int 2022; 119: 235–44. DOI: 10.3238/arztebl.m2022.0068

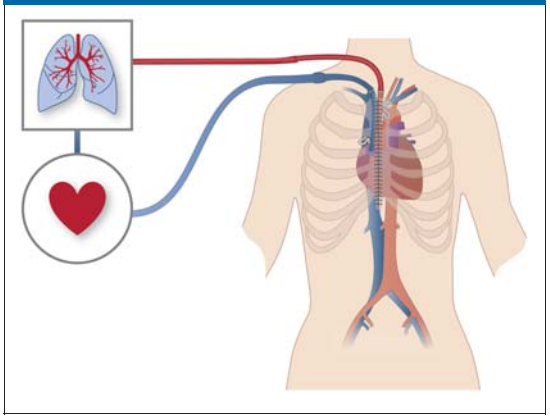
eReferences

e1. Vaquer S, De Haro C, Peruga P, Oliva JC, Artigas A: Systematic review and meta-analysis of complications and mortality of veno-venous extracorporeal membrane oxygenation for refractory acute respiratory distress syndrome. Ann Intensive Care 2017; 7: 51.

CASE ILLUSTRATION

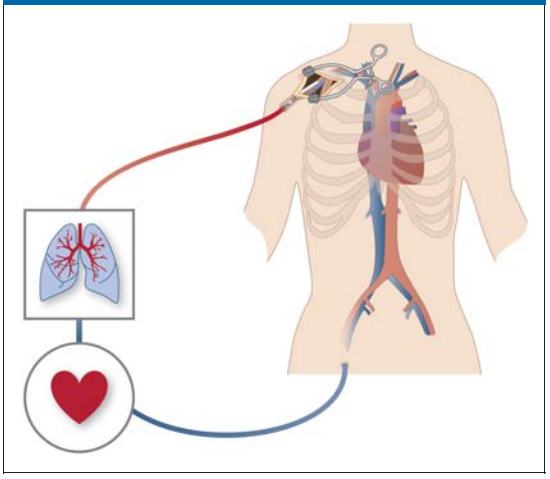
A 60-year-old man, in good health except for arterial hypertension and type 2 diabetes mellitus under dietary control, was transported to the hospital emergency department by the rescue service with symptoms of angina pectoris and an EKG showing ST-segment elevation over the anterior surface of the heart. Shortly after arrival, he went into cardiac arrest with ventricular tachycardia. Cardiopulmonary resuscitation was instituted according to the relevant guidelines but did not succeed in restabilizing the circulation. The interdisciplinary shock team decided to implant an extracorporeal life support (ECLS) device. The patient was taken to the neighboring cardiac catheterization laboratory and an ECLS device with an antegrade femoral perfusion cannula was implanted under ultrasonographic and fluoroscopic control. The total duration of a resuscitative measures until ECLS implantation was 25 minutes. The patient was defibrillated and coronary angiography was performed, revealing an occluded left anterior descending artery, into which a drug-eluting stent (DES) was then inserted. To unload the left ventricle, a transaortic microaxial pump was implanted into the contralateral femoral artery. The patient was transported to the intensive care unit. After initial therapeutic hypothermia and rewarming, he was extubated four days after arrival. Flow of the ECLS was slowly reduced until the device could be removed five days later. The transaortic microaxial pump was left in place for two further days as a temporary left-heart support system, then removed. Secondary prophylaxis for coronary heart disease and drug treatment for heart failure were initiated. At the end of the patient's hospital stay, his left ventricular function was only mildly impaired. He was discharged to cardiac rehabilitation without any neurologic deficit.

eFIGURE 1



Thoracic veno-arterial ECMO/ECLS. A cannula is inserted via the right atrial appendage into the right atrium. Blood is drained, oxygenated and decarboxylated, and then returned to the arterial system through a cannula in the ascending aorta. The cannulae are led out of the chest and the chest is provisionally closed. Definitive chest closure is performed after weaning from ECLS and decannulation. ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation

eFIGURE 2



Axillary veno-arterial ECMO/ECLS. A cannula is inserted via the femoral vein so that its tip lies in the right atrium. The drained blood is oxygenated, decarboxylated, and returned to the arterial system via a prosthesis anastomosed to the axillary artery.
ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation.

eTABLE

Complications of VV-ECMO, modified from Vaquer et al. (e1)

Complication	Number of studies	Published rate and 95% CI
Hospital mortality	12	37.7% [31.8; 44.1]
Mortality due to complications	8	6.9% [4.1; 11.2]
Mortality due to bleeding	7	3.3% [2; 5.4]
Medical complications	12	40.2% [25.8; 56.5]
Bleeding	12	29.3% [20.8; 39.6]
Significant bleeding	9	10.4% [5.6; 18.7]
Cannula bleeding	8	9.3% [5.3; 15.6]
Intracerebral hemorrhage	5	5.4% [2.7; 10.3]
Pulmonary bleeding	5	6.4% [3.2; 12.4]
Other bleeding	6	9.3% [4.9; 16.9]
Deep venous thrombosis of lower limbs/ pulmonary arterial embolism	3	4.6% [2.2; 9.2]
Pneumothorax	3	5.7% [1.1; 24.2]
Cannula infections	3	9.9% [4.2; 21.5]
Mechanical complications	4	10.9% [4.7; 23.5]
Oxygenator failure	2	12.8% [7.1; 21.7]
Cannula failure	3	4.5% [2.5; 8.1]

CI, confidence interval; ECMO, extracorporeal membrane oxygenation; vv, veno-venous