Percutaneous mechanical circulatory support in cardiogenic shock

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Submitted
ABSTRACT

Extracorporeal membrane oxygenation (ECMO) is an attractive technique for intensivists. The use of veno-venous ECMO (VV-ECMO) is increasing in the most severe forms of acute lung injury. In patients with cardiogenic shock, short-term veno-arterial ECMO (VA-ECMO) provides both pulmonary and circulatory support. Technological improvements and recently published studies suggest that ECMO is able to improve patients’ outcomes. There are however many uncertainties regarding the real benefits of this technique both in hemodynamic and respiratory failure, the territorial organization to deliver ECMO, the indications and the use of concomitant treatments. There is no doubt that ongoing and future studies will be able to resolve these issues.
INTRODUCTION

Extracorporeal membrane oxygenation (ECMO) is an old technique that has benefited from recent technical improvements. Interest for venovenous ECMO (VV-ECMO) for the most severe forms of severe acute lung injury, including acute respiratory distress syndrome (ARDS) has been renewed since the publication of the CESAR study ¹ and its extensive use during the H1N1 pandemic ²⁻⁵. In patients with cardiogenic shock, mortality remains high despite advances in treatment. Short-term percutaneous mechanical circulatory support (MCS) devices can be used for cardiogenic shock patients refractory to conventional therapies. Veno-arterial ECMO (VA-ECMO) provides both pulmonary and circulatory support and can be used as a bridge to myocardial recovery or to other therapies such as transplantation or the implantation of a long-term ventricular assist device (VAD). Even with the many advances in the last decade, a lot of uncertainties remain concerning the use of ECMO during respiratory and/or cardiogenic failure. This review summarizes recent developments and identifies the main areas for future research.

CURRENT STANDARD OF CARE

VV-ECMO for acute respiratory failure

Positive results of the CESAR trial and the successful rescue of the most severe ARDS cases associated with the Influenza A(H1N1) pandemic have led to an exponential use of VV-ECMO for acute respiratory failure in the last decade. ¹⁻⁷ High blood flow through ECMO circuits to provide full blood oxygenation and CO2 elimination is now considered as a reasonable option to support patients with severe acute lung injury refractory to conventional measures. Alternatively, VV-ECMO may be applied in less severe patients in whom it might allow “lung rest” by lowering airway pressures and tidal volume rather than improving oxygenation per se. ⁸ Cannulation strategies for VV-ECMO can either include two single-lumen cannulas or one double-lumen cannula, the latter currently can only be implanted via the right internal jugular vein. ⁹ Most commonly the right femoral vein for outflow and the right internal jugular vein for return flow are used, although the best cannulation configuration has not been tested in randomized trials. Less blood recirculation within the ECMO circuit occurs with double-lumen cannulas. ⁹ They might however be reserved for selected indications (mobilization, groin cannulation impossible), as they are more expensive, flow restricted and potentially more hazardous to implant.
Support of the cardiogenic shock patient

Although there is no strong scientific evidence to support routine MCS therapy in cardiogenic shock patients to date, its use is increasing since that it can provide emergency circulatory support while a definite solution is sought. \(^{10,11}\)

Most of these highly instable patients receive a device as salvage therapy after having already developed signs of multiple organ failure. In these situations, mechanical assistance is frequently used as a bridge to decision, in which cardiogenic shock patients are rescued and optimized until cardiac recovery allowing weaning from MCS or implantation of a surgical solution such as durable VAD or heart transplantation. In the last decade, VA-ECMO has become the first-line therapy in this setting since it provides both respiratory and cardiac support, is easy to insert, even at the bedside, provides stable flow rates, and is associated with less organ failure after implantation compared to large biventricular assist-devices that require open-heart surgery. \(^{12,13}\)

Other short term MCS devices are the Impella\(^{©}\) (ABIOMED Inc., Danvers, MA, USA) that is a catheter-based axial pump positioned retrogradely across the aortic valve into the left ventricle and the TandemHeart\(^{©}\) (TandemLife, Pittsburgh, PA, USA) that is an extracorporeal centrifugal pump that drains blood from the left atrium via a cannula introduced trans-septally through the femoral vein and pumps back blood into the femoral artery. \(^{14-16}\)

Compared to VA-ECMO, these systems are more expensive and are not adapted to patients with severe biventricular failure. The traditional configuration for peripheral VA-ECMO involves femoral venous drainage and femoral arterial reinfusion. ECMO cannulation can also be performed by direct transthoracic access of cardiac cavities following cardiac operations.

Accepted medical indications for MCS may be classified into the following categories: \(^{12,13}\) acute myocardial infarction complicated by cardiogenic shock, \(^{13,17,18}\) acute decompensated heart failure with refractory cardiogenic shock, \(^{12}\) fulminant myocarditis, \(^{19}\) cardiotoxic drug intoxication, \(^{20}\) stress-induced cardiomyopathy, \(^{13}\) post cardiac arrest resuscitation syndrome, \(^{21}\) decompensated pulmonary vascular disease, or massive pulmonary embolism, the highest rate of survival being reported in these case-series for acute myocardial infarction and fulminant myocarditis. \(^{17,19,22}\)

In a single-center, retrospective study, cardiogenic shock post MI patients treated with PCI and adjunctive ECMO had a higher 30 day survival than historical controls without ECMO (60% vs 35%). \(^{18}\)

MCS therapy can be initiated in case of low cardiac output syndrome after heart surgery. \(^{23}\)

A retrospective single-center study of 517 post-heart surgery VA-ECMO patients reported an incidence of 1.28% with hospital survival of only 25%. \(^{24}\)

Successful VA-ECMO therapy in primary graft failure following heart transplantation is encouraging. \(^{25}\)

Earlier initiation of MCS in cardiac surgery, preoperatively or postoperatively, might improve the outcomes of these patients. \(^{26}\)
**ECMO for cardiac arrest resuscitation (ECPR)**

Extracorporeal cardiopulmonary resuscitation with ECMO (ECPR) can give a chance for better neurologic outcome than conventional CPR for in-hospital (IHCA) and out-of-hospital (OHCA) cardiac arrest patients and contribute to organ donation in those who die. A landmark study of 46 IHCA patients demonstrated that ECPR provided significantly higher 1-year survival than conventional CPR. Similar results were reported by Shin et al. in 85 IHCA ECPR patients. Results of ECPR for OHCA patients are more contrasted. Single center studies from Japan in which transport time from scene to ECMO center was around 30 minutes, reported up to 30% survival with good neurological outcome. However, a French series of 51 OHCA ECPR patients for whom mean ischemic time was 120 minutes reported only two survivors. Survival with favorable neurological recovery was low although better than in control patients (11% vs 2%), in the largest (260 VF/VT patients) multi-center (20 hospitals) prospective observation study of ECPR in Japan. Lastly, survival was not improved in ECPR OHCA patients in a large Korean nationwide OHCA database. Data from all these ECPR studies stress that shorter time from collapse to ECMO and then early coronary angioplasty are the most important determinants of outcomes.

**MAJOR RECENT ADVANCES**

**Technical breakthrough in ECMO equipment**

The renaissance of ECMO for severe cardiac and respiratory failures was accelerated by several major technical developments. First, the old silicon membrane oxygenators were replaced by miniaturized, low resistance poly-methyl-pentene oxygenators. These systems offer more effective gas exchange with lower resistance to flow, have smaller priming volumes, are more biocompatible with less platelet and plasma protein consumption and are coated with thrombo-resistant coating allowing less anticoagulation. Second, centrifugal pumps permitted major improvement in efficacy and security over the older roller pumps, with less blood cell trauma, no requirement for venous reservoirs, and very few failure over weeks of support. More recently, the continuing miniaturization of devices permitted the integration of pump and oxygenator within one low weight device and has facilitated transport by mobile ECMO teams. Lastly, sensors without direct blood contact to continuously measure pressures as well as hemoglobin and venous saturation are useful tools for enhanced circuit and patient safety.

**Extracorporeal Life Support Organization and the International ECMO Network**

The Extracorporeal Life Support Organization (ELSO, https://www.elso.org) maintains a large international registry since 1989 and has collected data on over 75000 ECMO
patients. Important data regarding patients’ selection, ECMO results and center organization has been derived from the registry over the last 25 years. This organization also provides valuable resources to clinicians, ECMO center directors and coordinators, hospital directors and health care organizations [9] and organizes regular training activities and meetings. Centers providing ECMO should be encouraged to join ELSO to benchmark their results against other national and international institutions, participate in epidemiologic studies. The recently formed International ECMO Network (ECMOnet http://www.internationalecmonetwork.org) is a growing consortium of ECMO centers and individuals dedicated to conducting high quality, high impact research in the field. By ensuring that expert centers adhere to current best practices for the organization and conduct of ECMO, this group aims to foster the highest quality research.

Regional/National Organization of ECMO support

The soaring growth of centers performing ECMO in adult patients has occurred mostly in the absence of oversight or coordination. However, recent data from the ELSO registry suggested an inverse linear relationship between case volume and mortality, with centers performing more than 30 adult ECMO cases per year having a significantly lower mortality than centers performing fewer than 6 cases per year. Although the minimum acceptable case-volume for an ECMO center remains controversial, many centers conduct few cases annually and outcomes may be suboptimal in this setting. By creating networks of hospitals at the local or regional level (Figure 1), and concentrating case volume in expert centers, using standardized protocols for case selection and management, outcomes would certainly improve. Recent attempts to build regional ECMO networks suggest that some of these goals can be met. However, experience with directing ECMO cases to high-volume centers is limited, and has not been scientifically proven superior as a strategy. A recent study even suggested that low-volume centers have better ECMO in-hospital mortality than high-volume centers, questioning the existence of a positive volume-outcome relationship in this population. Another unresolved issue is the nurse-to-patient ratio for ECMO patients.

ECMO retrieval teams

Since evidence has accumulated that ECMO should be performed in specialized centers to obtain better results, retrieval of patients on ECMO by mobile ECMO teams has become an indispensable precondition for ECMO centers. The mobile team ideally should be available 24 hours a day, 7 days a week and employ experienced personnel trained in the transport of critically ill patients, insertion of ECMO cannulae, and circuit and patient management. Successful transportation of patients on cardiopulmonary support by ambulance, helicopter, and fixed-wing aircraft has been reported. Centers performing ECMO should develop specific guidelines and ensure adequate
staff training to provide uninterrupted availability of transport on ECMO. Development of telemedicine is also important to improve patients selection for ECMO, but also to provide adequate advices regarding alternative strategies to ECMO to less experienced centers.

**Scoring systems to predict the outcomes**

In very recent years, several scoring systems to predict the outcomes of patients after ECMO for cardiac or respiratory indications have been proposed.\(^\text{17,38,49-52}\) Respiratory scores constantly demonstrated the strong negative impact of older age, immunocompromised status, associated extra-pulmonary organ dysfunction, pre-ECMO duration of mechanical ventilation, impaired pulmonary compliance and non influenza-induced ARDS diagnosis. In addition, the RESP and the PRESERVE scores\(^\text{17,52}\) were consistent with recent randomized controlled trials by demonstrating that pre-ECMO prone positioning and neuromuscular blockade were associated with improved survival. Interestingly, no predictive score has shown hypoxemia to be predictive of survival in this setting. The survival after veno-arterial-ECMO (SAVE)-score based on the ELSO registry data from 3846 cardiogenic shock patients showed that preexisting comorbidities, pre-ECMO organ failures and cardiac arrest, lower pulse pressure, and lower serum bicarbonate were risk factors associated with mortality.\(^\text{38}\) The ENCOURAGE score, which was constructed on data from VA-ECMO-treated acute myocardial infarction patients, demonstrated

![Figure 1](image-url)  
*Figure 1* The regional coverage of England by the National Severe Respiratory Failure Service.
the major impact of age, liver and renal failure, coma and serum lactated on patients’ survival.\textsuperscript{17}

These scoring systems should only be considered appropriate for predicting survival in patients for whom ECMO has already been initiated. They might help offering population management information and might facilitate risk-adjusted comparison of outcomes between institutions, regions, and time periods. They have not been validated for prediction of survival in larger populations of patients where ECMO has not yet been instituted and should be used with great caution to select individual patients for cardiac or respiratory ECMO or to decide on futility. These scores have still to be prospectively validated and regularly recalibrated on large populations of patients.

\textbf{CONTRAINDICATIONS IN TRIALS}

What are the common beliefs that have been contradicted by recent trials (Table 1)?

\textbf{Anticoagulation}

Older ECMO circuits using poorly biocompatible materials required major anticoagulation and were associated with substantial bleeding. The advent of coated circuits has permitted a decrease in anticoagulation, small studies reporting that prophylactic systemic anticoagulation was possible in ECMO patients with reduced incidence of complications.\textsuperscript{6} In the setting of severe bleeding the avoidance of anticoagulation for as long as 20 consecutive days has even been reported.\textsuperscript{53} However, proof beyond doubt is missing, that oxygenator clotting or risk of deep vein thrombosis does not increase with less anticoagulation. Anticoagulation targets might also be higher for cardiac patients on VA-ECMO. Rigorous evaluations of anticoagulation use in ECMO patients are needed, since practices vary widely.\textsuperscript{7,54}

\textbf{Transfusion strategies}

The transfusion thresholds for red blood cells and platelets in patients receiving ECMO were traditionally set to maintain values close to the normal range (120-140 g/L and >100 G/L, respectively).\textsuperscript{1} This notion has however been challenged in recent years as transfusions of blood products are costly, induce alloimmunisation in transplant candidates and might cause specific lung injuries.\textsuperscript{8,55} Small observational trials indicated that ECMO can be successfully conducted in patients with a hemoglobin content of less than 80 g/L with consecutive reduced need for red blood cell substitution.\textsuperscript{56} Similarly, platelet transfusion might be discouraged except when severe thrombocytopenia is accompanied by bleeding.\textsuperscript{8,9} More studies are however needed in order to evaluate the short and long-term consequences of lower transfusion thresholds.
<table>
<thead>
<tr>
<th>Organization</th>
<th>Technological improvements</th>
<th>Improve patients selection</th>
<th>Evaluate risk-benefit ratio</th>
<th>Better define the place of associated treatments</th>
<th>Identify criteria for ECMO weaning</th>
<th>Indications of other supportive treatments</th>
</tr>
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<tbody>
<tr>
<td>VV-ECMO</td>
<td>Regionalization, nurse-to-patient ratio, miniaturation, less blood cells injuries, less anticoagulation requirement, better membrane capacities</td>
<td>Non refractory hypoxaemia</td>
<td>Including long-term outcomes</td>
<td>Mechanical ventilation settings, prone positioning</td>
<td>yes</td>
<td>Nutrition, modulation of inflammation, blood cell requirements, anticoagulation</td>
</tr>
<tr>
<td>VA-ECMO</td>
<td></td>
<td>ECPR</td>
<td>IABP, Impella</td>
<td></td>
<td>Inotropes, vasodilators</td>
<td></td>
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Early mobilization and physical therapy on ECMO

Historically ECMO patients have been nursed with full bed rest and managed with high-levels of sedation and minimal interventions because of concerns about short-term safety. However, prolonged immobility exposes to exacerbated muscle weakness and poor long-term outcomes. A recent systematic review of early rehabilitation in adults during mechanical ventilation reported that early rehabilitation may improve strength, functional recovery at hospital discharge and days alive and at home in the six-months after critical illness. Patients receiving ECMO may benefit from less sedation and early rehabilitation, and recent studies found that rehabilitation, including mobilization (Figure 2), during ECMO was feasible and safe.

Fig. 2 Ambulation in an ECMO patient at the Medical ECMO program, Columbia University Medical Center/New York-Presbyterian Hospital. Courtesy of Dr. Daniel Brodie.

ECMO as a bridge to lung transplantation

Due to organ shortage, severe respiratory or circulatory failure develops in many patients on waiting lists for lung transplantation (LTx). Deterioration of waiting list patients commonly triggers to proceed with transplantation to avoid imminent death despite an increased risk of mortality. Therefore, VV- and VA-ECMO have been increasingly used to bridge patients with acute-on-chronic respiratory and/ or circulatory failure to LTx. In an analysis using United Network for Organ Sharing (UNOS) data from 1987 to 2008, patients supported preoperatively by mechanical ventilation or ECMO had markedly worse survival after LTx compared to those transplanted unsupported. More recent analyses using UNOS data from 2010 to 2015, showed that the adverse influence of ECMO was
absent in high-volume lung transplant centers. A systematic review including 14 retrospective studies pointed out that current data do not permit a definitive conclusion on the efficacy of ECMO as a bridge to transplantation. However, these patients may have an acceptable one year survival. These data contradicted the widespread belief that outcome of ECMO patients after lung transplantation is dismal.

Pathophysiological approach and research in cardiogenic shock
From a methodological point of view, the major advance was the proof-of-concept that large randomized trials with mechanical support devices and clinically relevant endpoints (i.e. mortality) are feasible, as shown for the use of IABP in the IABP-SHOCK II trial. Common beliefs in shock research that have been contradicted in recent trials are that: a) devices that increase cardiac output do automatically improve prognosis; b) positive haemodynamic findings seen in healthy laboratory animals without cardiogenic shock can be uncritically translated to the patient with cardiogenic shock; c) what seems reasonable from a pathophysiological point of view does necessarily transforms into clinical benefit; d) cardiogenic shock is a pure hemodynamic problem. Especially the latter view must be disregarded. Cardiogenic shock is a haemodynamic problem only at the very beginning, and soon becomes a very complex disease, with bacterial translocation, overshooting inflammation and the development of multiple organ failure. Indeed, in patients with cardiogenic shock complicating myocardial infarction, APACHE II score is a better predictor of mortality than cardiac output.

AREA OF UNCERTAINTIES
Risk–benefit evaluation of ECMO support
Although ECMO can improve survival of patients with advanced lung and heart disease, there is significant associated morbidity with performance of this intervention. Specifically, the use of ECMO for severe ARDS remains controversial, with conflicting data regarding its impact on survival. Evidence regarding the benefits of temporary MCS in cardiogenic shock not responding to standard therapy, including inotropes, is also still limited. In a meta-analysis of three randomized clinical trials comparing a percutaneous MCS vs. IABP in cardiogenic shock patients, MCS appeared safe and demonstrated better haemodynamics, but did not improve 30-day mortality and was associated with more bleeding complications. Furthermore, a recent randomized controlled trial involving 48 mechanically ventilated cardiogenic shock patients after acute myocardial infarction, the Impella CP was not associated with reduced 30-day mortality compared with IABP. Based on these results, temporary MCS only received a class IIb recommendation from the European Society of Cardiology.
**LV unloading in VA-ECMO**

Peripheral VA-ECMO increases LV afterload that may delay myocardial recovery in case of myocardial infarction or myocarditis. Excessive LV afterload and lack of LV unloading under VA-ECMO might induce serious complications such as LV stasis with thrombus formation, pulmonary edema, myocardial ischaemia caused by ventricular distension and ultimately increase mortality. Current strategies of LV unloading in VA-ECMO patients include atrial septostomy, central percutaneous cannulation of the left atrium or ventricle, combined support with VA-ECMO and Impella, as well as concomitant utilization of an IABP. Adding an IABP to VA-ECMO was shown to improve haemodynamics, to reduce LV dimensions and to decrease pulmonary artery pressures. Furthermore, IABP combined with VA-ECMO was independently associated with improved mortality and successful weaning from ECMO in a Japanese national inpatient database. Alternatively, association of the Impella device to VA-ECMO might provide greater reduction in LV overload while increasing the net forward flow. Indeed, a recent study suggested better outcomes in patients with combined support with VA-ECMO and Impella.

**Mechanical ventilation under VV-ECMO**

The optimal ventilator strategy in VV-ECMO patients is not clear. Tidal volume can be very low, resulting in near-absent tidal stress and strain, and minimal or absent atelectasis. While some experts endorse a higher PEEP strategy (>10 cmH2O) to keep the lung open and prevent atelectasis, some endorse a strategy that includes no external PEEP (i.e., patient extubated). In a recent meta-analysis of 9 VV-ECMO studies, the driving pressure was the only parameter that was independently associated with in-hospital mortality. Avoiding injurious mechanical ventilation should therefore be a principle of lung protection. In general, any mode (e.g., volume/assist-control, APRV, NAVA) that can decrease harmful ventilation might be used. Once patients stabilize transitioning to spontaneous breathing on partial-assist modes (e.g., pressure support ventilation) should be considered.

**Nutrition therapy in ECMO patients**

Nutrition therapy is used in almost all critically ill patients, with no clear evidence about optimal administration. A study of 107 ECMO patients in Australia and New Zealand to determine current nutrition practice showed that enteral nutrition was the most commonly used nutrition-delivery mode during ECMO, but was interrupted on 53% of study days. The authors reported that acceptable amounts of calories and proteins were delivered, although these were less than estimated requirements. The two most commonly reported barriers to the delivery of enteral nutrition included fasting for a therapeutic or diagnostic procedure and high gastric residual volumes.
ECPR
Rescuing cardiac arrest patients with ECMO requires disproportionate human, financial and material resources. However, to date long-term outcomes of the ECPR patients are still poor compared to other groups of ECMO patients.\textsuperscript{32-34} Therefore, what should be patients’ selection criteria for ECPR? To reduce low-flow time, should on field ECPR be preferred to rapid transport of refractory cardiac arrest patients to the closest ECMO center?\textsuperscript{77} Would mechanical chest compression device give better results than long-term conventional CPR awaiting ECMO in this setting? Will additional therapies such as therapeutic hypothermia or other brain protection treatment to attenuate ischemic/reperfusion injuries improve neurological outcome?

TRIALS TO BE DONE IN THE NEXT 10 YEARS
What the international group of experts recommend as the top 10 studies/trials to be done in the next 10 years and what are expected outcomes/results of these trials.

1. Randomized controlled trial (RCT) of VV-ECMO for severe respiratory failure
Beyond rescuing ARDS patients dying of refractory hypoxemia, ECMO may improve the outcomes of less severe ARDS patients by facilitating less damaging ventilation. The ongoing trial international multicenter randomized Extracorporeal Membrane Oxygenation for Severe Acute Respiratory Distress Syndrome (EOLIA, NCT01470703) trial, which tests the efficacy of early VV-ECMO in patients with severe ARDS with tight control of mechanical ventilation in the control group may help to resolve the ongoing controversy in this indication.

2. RCT of VA-ECMO or other MCS devices for severe cardiogenic shock
Although widely used for over 3 decades, the IABP-SHOCK II trial demonstrated that the IABP provided no benefit over medical treatment alone in AMI-related cardiogenic shock. A large randomized trial should now be rapidly conducted to test VA-ECMO, other catheter-based MCS devices or combination MCS support in this setting.

3. RCT of restrictive or very restrictive transfusion policy in ECMO patients
A trial in ECMO patients might demonstrate non-inferiority (or even superiority regarding patients centered outcomes) of transfusion thresholds as low as \(50-60 \text{ g/L}\) or \(20 \text{ G/L}\) for red blood cells and platelets, respectively compared with more liberal strategies.
4. RCT of reduced anticoagulation in VV-ECMO patients
This study might show less bleeding complications and ultimately better short and long-terms outcomes in patients supported by VV-ECMO.

5. RCT testing early mobilization and physical therapy on ECMO
This study might prove that less sedation and early rehabilitation on ECMO is safe and feasible and is associated with improved strength, faster functional recovery and better long-term outcomes.

6. RCT comparing pre-hospital vs. in-hospital ECMO in refractory cardiac arrest
This study is already recruiting cardiac arrest patients in France (ACPAR2, NCT02527031).

7. Studies evaluating pharmacologic strategies on-top-of MCS devices
It could make sense to combine the mechanical circulatory support with some other measures dampening inflammation, autonomous dysfunction, cytopathic hypoxia and MODS. Levosimendan might also accelerate weaning from MCS.

8. Physiologic studies evaluating best ventilation strategies in VV-ECMO patients
These studies should test the effects of MV settings including PEEP, plateau and driving pressures, modes of MV and prone positioning at the different phases of VV-ECMO support.

9. Would regionalization of ECMO with ECMO retrieval teams improve outcomes?
A carefully designed trial comparing a coordinated, regionalized network of ECMO centers and satellite hospitals, with a region hosting a similar population but lacking such coordination, will need to be undertaken. This should demonstrate a cost-effective improvement in outcomes and resource utilization with regionalized care. While ECPR would clearly benefit from concentration of expertise, satellite facilities may not be served rapidly enough by specialized centers. ECPR indications might therefore require a separate study.

10. Retrospective and prospective cohorts to refine indications and to evaluate long-term outcomes after ECMO
Such studies including large cohorts of patients may refine the specific indications and scoring algorithms for patients requiring ECLS support.
**CONCLUSION**

Although there have been considerable advances regarding the use of ECMO in critically ill patients, the risk/benefit ratio remains under-investigated. Organization of ECMO delivery, use of adjuvant therapeutics need also to be explored. Finally, ECMO indications must be carefully identified in order to take into account the costs associated with the use of this unusual salvage therapy.

**REFERENCES**


18. Sheu JJ, Tsai TH, Lee FY, et al. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary interven-


56. Agerstrand CL, Burkart KM, Abrams DC, et al. Blood conservation in extracorporeal membrane oxygenation for acute respira-


