Monitoring during extracorporeal membrane oxygenation

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Purpose of review
Extracorporeal membrane oxygenation (ECMO) offers advanced mechanical support to patients with severe acute respiratory and/or cardiac failure. Ensuring an adequate therapeutic approach as well as prevention of ECMO-associated complications, by means of timely liberation, forms an essential part of standard ECMO care and is only achievable through continuous monitoring and evaluation. This review focus on the cardiorespiratory monitoring tools that can be used to assess and titrate adequacy of ECMO therapy; as well as methods to assess readiness to wean and/or discontinue ECMO support.

Recent findings
Surrogates of tissue perfusion and near infrared spectroscopy are not standards of care but may provide useful information in select patients. Echocardiography allows to determine cannulas position, evaluate cardiac structures, and function, and diagnose complications. Respiratory monitoring is mandatory to achieve lung protective ventilation and identify early lung recovery, surrogate measurements of respiratory effort and ECMO derived parameters are invaluable in optimally managing ECMO patients.

Summary
Novel applications of existing monitoring modalities alongside evolving technological advances enable the advanced monitoring required for safe delivery of ECMO. Liberation trials are necessary to minimize time sensitive ECMO related complications; however, these have yet to be standardized.

Keywords
echocardiography, extracorporeal membrane oxygenation, hemodynamic, monitoring, respiratory

INTRODUCTION

The use of extracorporeal membrane oxygenation (ECMO) for respiratory and/or cardiac failure has grown exponentially over the last decade [1]. ECMO provides mechanical support that allows time for resolution of the primary pathology, organ recovery, or as a bridge to either decision, other mechanical support (including destination therapy), or transplantation. Venoarterial (VA) and venovenous (VV) ECMO are the most common configurations for cardiac and respiratory support, respectively [2▪,3,4]. The clinical use of ECMO requires a thorough understanding and application of cardiorespiratory physiology as well as the interaction between the native and extracorporeal circulations. In addition to assisting in selection of the appropriate extracorporeal support strategy at the outset, monitoring during ECMO is essential for titration of support, timely identification of evolving complications, and determination of sufficient recovery to tolerate discontinuation of extracorporeal support [4]. The aim of this review is to describe commonly used monitoring strategies in patients supported with ECMO, and to summarize the evidence for these where available.

CARDIAC MONITORING

Electrocardiography and Hemodynamics

Electrocardiographic monitoring is of particular importance in the use of VA ECMO where

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Curr Opin Crit Care 2022, 28:000–000
DOI:10.1097/MCC.0000000000000939

KEY POINTS

- Cardiopulmonary function monitoring during extracorporeal membrane oxygenation (ECMO) may lead to earlier liberation and avoidance of complications.
- Novel applications of existing monitoring modalities alongside evolving technological advances enable the advanced monitoring required for safe delivery of ECMO.
- Surrogates of tissue perfusion and organ function are necessary.
- Echocardiography allows to determine cannulas position, evaluate cardiac structures, and function, and diagnose complications.
- Respiratory monitoring is mandatory to achieve lung protective ventilation and identify early lung recovery.

ventricular arrhythmias may be the indication for mechanical support or may alert clinicians to impending ECMO-related complications such as myocardial ischemia from overdistension of the left ventricle (LV), and/or evolving hypoxemic respiratory failure.

Invasive arterial blood pressure monitoring in the presence of VA ECMO can continuously confirm ongoing aortic valve opening and LV ejection by means of pulse pressure (PP) monitoring. This is important in patients who do not have active LV decompression (e.g. through a direct LV vent or microaxial pump) where the risk of LV distension leading to myocardial ischaemia and thrombus formation from stasis are high. Though absolute values of PP are of limited use in formalized assessment of ejection (dependent on monitoring site and subject to the effects of resonance and damping), it provides a continuous trend and may alert clinicians to acute cardiovascular changes (either improvement or decline). Pulsatility has also been shown to be key to maintaining renal cortical blood flow and its absence (despite adequate extracorporeal blood flow) may cause and/or significantly worsen acute kidney injury [5–7].

There is an increasing body of evidence supporting the use of early invasive hemodynamic monitoring with a pulmonary artery catheter (PAC) in patients with cardiogenic shock [8]. Coupled with its frequent use in cardiac surgical patients, a substantial number of patients supported with VA ECMO may already have a PAC in place at the time of cannulation. There are important limitations of thermodilution methods for estimating cardiac output on VA ECMO (exposure of central venous blood to extracorporeal temperatures and in-circuit heater-coolers) and controversy exists around the utility of PAC in this setting [9]. Other means of monitoring cardiac output have similar issues with extracorporeal blood flow (ECBF) impacting transpulmonary thermodilution techniques, and unpredictable and unvalidated effects of changes in arterial resistance and low ejection volumes on arterial pressure waveform analysis monitors [10]. However, the PAC in particular yields other potentially valuable data to include pulmonary artery diastolic pressure and pulmonary capillary wedge pressure measurements which can be useful to identify early patients with increasing LV diastolic pressures at risk of both cardiac (myocardial ischemia and sequelae) and pulmonary (oedema and subsequent respiratory failure) consequences of LV overdistension in VA ECMO. Similarly accurately measured pulmonary artery pressures can assist in continuous monitoring of the right sided circulation in select VV ECMO patients with or at high-risk of right ventricular (RV) dysfunction and/or failure [4].

Tissue perfusion and microcirculatory monitoring

In peripheral VA ECMO, blood from the native circulation (oxygenated via the lungs) does not mix with the ECBF (oxygenated via the membrane) prior to ejection from the LV. This can create a system of parallel circuits, particularly problematic in the presence of mixed cardio-respiratory failure where differential hypoxemia (Harlequin syndrome) can occur. Here, hypoxemic blood ejected from the LV preferentially supplies the coronary and cerebral circulations (proximal branches of the ascending aortic arch) and well oxygenated blood from the ECMO circuit preferentially supplies the lower half the body (distal to the mixing point). Whilst clinical assessment of end-organ function (e.g. capillary refill time, urine output, mentation) and serum biomarkers (SvO_2 and lactate) may assist in monitoring for signs of global perfusion and hypoxia, worsening respiratory failure in a sedated patient on high levels of mechanical support may otherwise mask regional hypoxia as described above. Monitoring pulse oxygen saturations (SpO_2) if sufficient pulsatility, and/or partial pressure of arterial oxygen (PaO_2) as a marker of adequacy of pulmonary gas exchange from a right upper limb sited oximetry probe and/or arterial line is recommended to ensure adequately oxygenated blood from native pulmonary circulation is being supplied to the coronary and cerebral circulations. In the absence of adequate ejection for SpO_2 monitoring, PaO_2 does not provide continuous

monitoring however and thus identification of myocardial and/or cerebral hypoxia may be delayed if used in isolation [11].

Near infrared spectroscopy (NIRS) is a noninvasive modality used to monitor continuous trends in nonpulsatile regional oxygen saturation (SrO_2). It can be used to monitor cerebral oximetry in sedated patients (usually right and left forehead), monitor for differential hypoxia (trends at two sites e.g. forehead and torso) and to detect evolving limb ischemia (placed distal to site of femoral arterial cannulation e.g. in the absence of a reperfusion cannula). Although NIRS for cerebral oximetry has shown good correlation with transcranial Doppler estimates of cerebral blood flow [12], other studies have shown that SrO_2 is significantly influenced by extracranial (scalp) oxygenation [13]. SrO_2 measures mixed arteriovenous oxygenation and although scalp SrO_2 may be proportional to cerebral SrO_2 in many instances, there are some potential confounders. First, the presence of underlying cerebrovascular disease may lead to differential blood flow. For instance, with middle cerebral artery (MCA) stenosis, the risk of MCA territory ischemia may not be well represented by SrO_2 monitored at the frontal lobe location. Second, the effect of treatment response to a falling SrO_2 may be abnormally reflected (e.g., increasing mean arterial pressure using vasopressors may have a differential effect on central versus peripheral blood flow), whereby peripheral vasoconstriction reduces oxygen delivery to scalp vessels (SrO_2 may fall if significant interference from scalp vessels present) despite a net increase in cerebral perfusion pressure and cerebral oxygen delivery overall (would expect SrO_2 to increase if responsive to intervention). Finally, the reliability of SrO_2 at anticipating risk of ischemic cerebral events remains controversial. It is important to note that most studies have focused on early identification of cerebral ischemia, however in differential hypoxemia, myocardial ischemia will occur sooner due to the nature of arterial anatomy (coronaries are proximal to carotid arteries) [14]. Monitoring trends in ECG, cardiac biomarkers, and echocardiography may assist in timely recognition of myocardial ischemia in mixed cardiorespiratory disease.

Whilst much of VA ECMO monitoring centres around adequacy of macrocirculatory hemodynamics, oxygen delivery to tissues is dependent on maintaining adequate microcirculatory flow. There has been increasing interest in more directly monitoring tissue perfusion (most commonly through the sublingual microcirculation) to evaluate prognosis, but this is still mainly experimental and has not been routinely incorporated into clinical practice [15–17].

Echocardiography

Echocardiography is an invaluable tool for the management of patients on ECMO, and it is recommended that an echocardiography-trained physician be part of the ECMO team [18,19]. Precannulation assessment of biventricular function may help determine the best configuration of ECMO support. Echocardiography can identify potential contraindications to VA ECMO (e.g., severe aortic insufficiency or aortic dissection) and potentially reversible causes of hemodynamic deterioration (e.g., cardiac tamponade or valvular pathology) [18,20]. During extracorporeal cardiopulmonary resuscitation (ECPR), echocardiography may also help identify the cause of the cardiac arrest (e.g., massive pulmonary embolism) [21].

During VV ECMO cannulation, cannula malposition may result in blood recirculation, insufficient flow, or injuries of the major vessels and/or cardiac structures. Multiple imaging techniques, including X-ray, fluoroscopy, and echocardiography, can be used to facilitate safe cannulation and mitigate complications (Table 1). However, only echocardiography can determine the exact position of the cannulas' tip in relation to the cardiac chambers [22–24]. Echocardiography can also help to troubleshoot complications during cannulation. Some examples include difficulty advancing the guidewire/cannula when a prominent Chiari network is present; cannulation of the coronary sinus; or pneumothorax [18,25]. Ultrasound-guided cannulation can be performed with either transthoracic (TTE) or transesophageal echocardiography (TEE) [18,22,26–30].

Additional advantages of TEE guidance during VV ECMO cannulation include: visualization of the proximal and distal guidewires in the cardiac chambers (right atrium, inferior [IVC] and superior vena cava [SVC]) (Fig. 1), identification of guidewire migration during staged dilatation, and the positioning of the cannula at the end of the procedure. Final assessment of cannula position should be made with the patient in a semi-recumbent position, and at mechanical ventilation parameters to be used during VV ECMO support (e.g., lung rest settings) [1,8,15]. TEE guidance can also be employed for bedside bicaval dual-lumen cannulation [30,32]. If TEE is contraindicated, a combination of TTE with fluoroscopy can be used [32].

During the ECMO run, echocardiography may address the causes of hemodynamic instability, help assess new or worsening hypoxemia, and rule out ECMO-related complications [4,33▪]. In a hemodynamically unstable patient, volume status and cardiac output can be estimated with echocardiography. Pericardial tamponade, which can occur during

Table 1. Imaging techniques for ECMO cannulation [31,32]

Technique	Advantages	Disadvantages
Fluoroscopy	Noninvasive Visualization of the entire wire without angle dependency Easily available Low cost Minimal training for reliable image interpretation Assess complications like hemo-pneumothorax and mediastinal collections	Need for transport to the interventional room Radiation exposure Limited assessment of ventricular and valvular function Insufficient to locate exact position in relationship to cardiac chambers
TTE (transthoracic echocardiography)	Noninvasive Easily available Low cost No radiation No transport Repeatability Evaluate cardiac structures, ventricular and valvular function Suitable for superficial anatomic structures, especially for IVC	No SVC views Affected by body habitus, lung, and air Visualization of wires can be out of plane Interference with the sterile field Cannot visualize entire wire at any one moment
TEE (transesophageal echocardiography)	Low cost No radiation No transport Evaluate cardiac structures, ventricular and valvular function Good for pericardial assessment No interference with the sterile field	Invasive Risk of bleeding Visualization of wires can be out of plane Cannot visualize entire wire at any one moment May required sedation, but is routine for ECMO cannulation

ECMO, extracorporeal membrane oxygenation; IVC, inferior vena cava; SVC, superior vena cava.

cannulation or at a later stage due to anticoagulation, should always be considered, however, it is essential to remember that this is a clinical diagnosis [4,21].

Hypoxemia during VV ECMO is often multifactorial. For example, collapse of the IVC around the drainage cannula may limit venous drainage, and therefore the ECBF and lead to desaturation. This phenomenon tends to worsen during spontaneous breathing and may lead to inappropriate fluid administration [4]. Evidence shows that up to 38% of ECMO cases will require cannula repositioning during the treatment course [32]. Sonographic guidance during repositioning can also help identify cannula thrombosis [21,32].

For patients on VA ECMO, echocardiography is helpful to document changes in cardiac function, and to diagnose and manage complications like LV distension, blood stasis (seen as spontaneous echocontrast), and intra-cavitary or intra-aortic thromboses (Fig. 2) [20,21,24,26]. If this is the case, reducing both peripheral vascular resistance and ECBF rates may improve ventricular ejection, reduce intra-cavitary stasis, and increase forward blood flow. Other strategies may include PEEP increase to reduce pulmonary arterial flow, inotropic support to improve LV ejection, and diuresis to decrease LV distension. Nevertheless, a LV vent, trans-aortic suction device, or atrial septostomy may be required in some cases [21,34].

Echocardiography-guided weaning trials in patients on VA ECMO can help assess readiness for liberation. One such echocardiography-guided strategy consists of the following sequence: first the biventricular function on full VA ECMO support is evaluated. Second, ECBF is gradually decreased to 50% for 30 min. If the initial ECBF reduction is tolerated, a further reduction to 25% of ECBF for 30 min is attempted. Finally, a successful decrease of ECBF up to 1.2–1.5 l/min defines a liberation attempt. Any hemodynamic instability or sonographic evidence of worsening of LV or RV function at any of these stages should lead to trial cessation [18,20,35,36▪▪]. In addition to clinical and biochemical assessment, echocardiographic parameters that predict successful liberation at minimal ECBF include left ventricular outflow tract velocity time integral (VTI) $\geq$10 cm, LV ejection fraction >20–25%, lateral mitral annulus peak systolic velocity >6 cm/s, 20% increase in strain rate and 3D RV ejection fraction >25% [18,36▪▪,37–39]. Another important role of echocardiography may be during VV ECMO weaning, particularly in patients with RV failure where changes to pulmonary vascular resistance (PVR) secondary to changes in mechanical ventilation and $PaCO_2$ may lead to acute deterioration and weaning failure. It is especially important for patients with a veno-pulmonary artery (VPA) configuration where the ECBF bypasses the RV

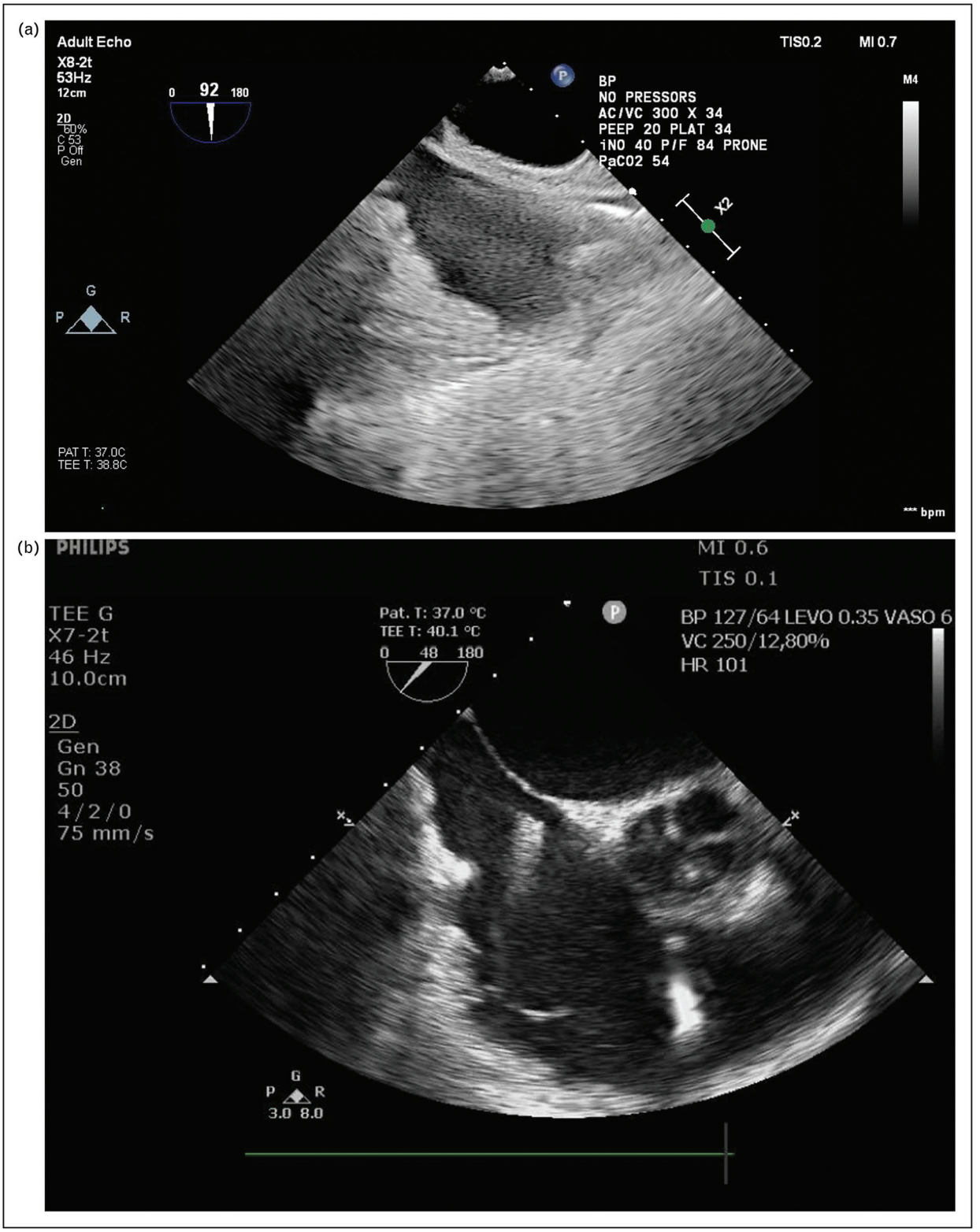

FIGURE 1. Guidewires visualization during VV ECMO cannulation. (a) Mid-esophageal bicaval view with guidewires through both vena cava. (b) Mid-esophageal bicaval view with the guidewire coiled in the right ventricle. ECMO, extracorporeal membrane oxygenation; VV, venovenous.

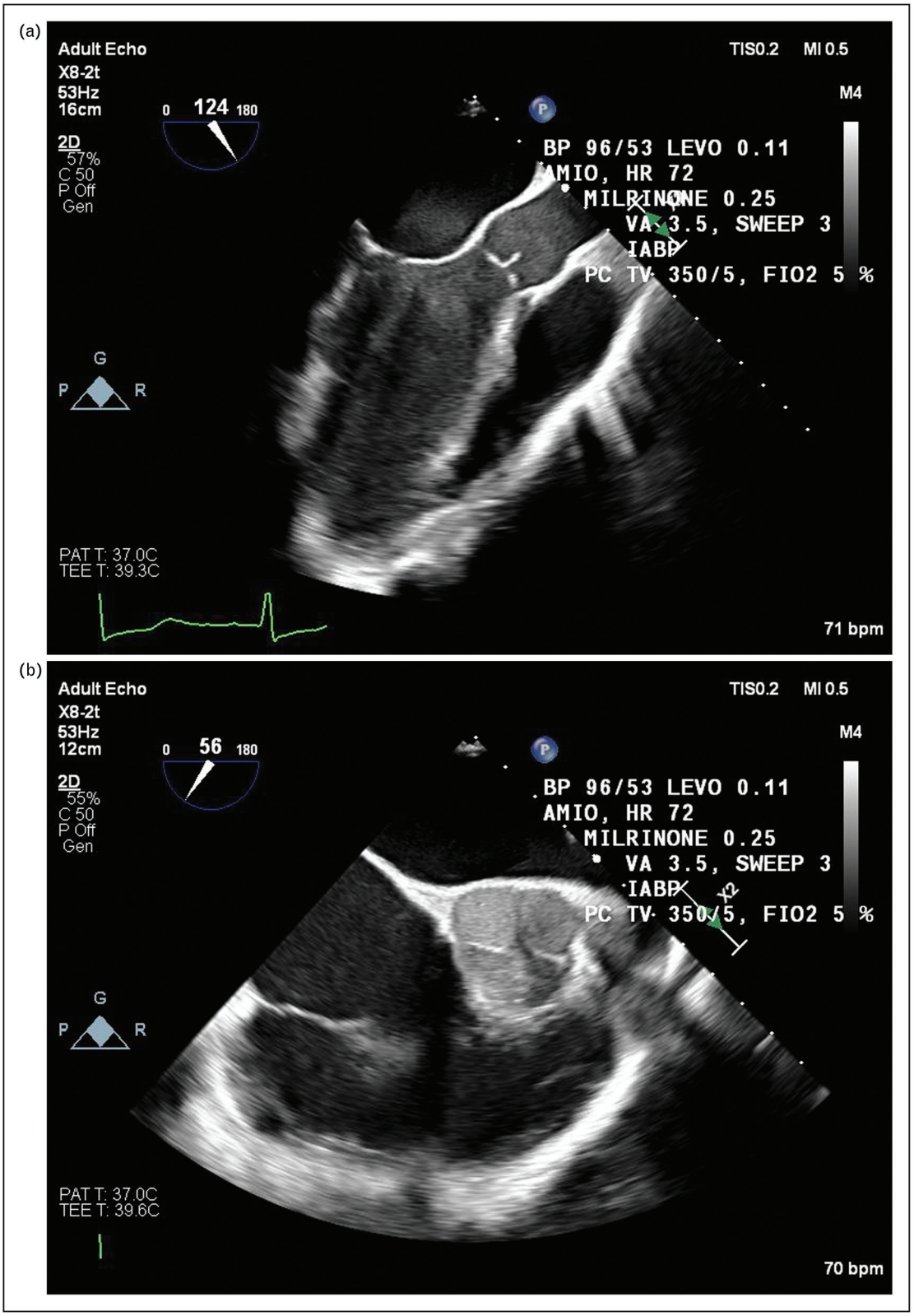

FIGURE 2. Spontaneous echo-contrast. (a) Mid-esophageal AV long axis showing spontaneous echo-contrast in the LV, LVOT and ascending aorta. (b) Mi-esophageal AV short axis showing spontaneous echo-contrast in the AV. AV, aortic valve; LV, left ventricle; LVOT, left ventricular outflow tract.

completely and RV assessment prior to weaning and/or attempts at liberation would otherwise significantly underestimate the degree of RV impairment [18,20].

RESPIRATORY MONITORING

Mechanical ventilation

Mechanical ventilation strategies in patients on VV ECMO are variable [40,41]. The Extracorporeal Life Support Organization (ELSO) guidelines recommend adopting ventilation parameters targeting the lowest achievable driving and plateau pressure, moderate levels of PEEP, low respiratory rates, and low fractions of inspired oxygen (FiO_2) [2▪]. However, the optimal level of respiratory system unloading is unknown. Respiratory system monitoring during ECMO aims to prevent secondary lung injury and promptly identify lung recovery [42▪,43–46].

Patients supported with VV ECMO for respiratory failure will generally have low tidal volumes, low compliance, and low respiratory drive and effort early in the course of extracorporeal support [47▪]. If lung protective parameters are not met, the clinician may opt to further decrease ventilation parameters and/or increase the amount of ECMO support. Alternative strategies to set ventilator parameters during VV ECMO include electrical impedance tomography (EIT) and esophageal manometry in centres experienced in their use [48,49].

As respiratory function improves, ECMO support is weaned, and respiratory system monitoring transitions to identifying readiness for liberation. Evidence on liberation is scarce, and liberation strategies rely on individual practice and clinician judgement [50–54]. Readiness for liberation is considered when a patient is able to sustain sufficient gas exchange off ECMO, with reasonable levels of lung protective ventilation [2▪]. In nonintubated patients, monitoring for readiness is limited to gas exchange adequacy, and unless esophageal manometry is in place, subjective assessment of work of breathing [55]. In intubated patients, respiratory mechanics (driving pressure and tidal volume) at different levels of ECMO support provide an estimate of lung recovery (Fig. 3 – panel a).

Surrogates of respiratory drive ($P_{0.1}$, the pressure generated during the first 100 ms of an inspiratory effort against an occluded airway), respiratory effort (P_{Occ}, the maximum negative pressure deflection during an end expiratory occlusion manoeuvre) (Fig. 3 – panel a) and esophageal manometry, can provide objective evidence of increased work of breathing, and may unmask excessive dynamic transpulmonary pressures during weaning and liberation [56–58]. However, the utility of these surrogates is limited by the lack of widespread adoption and shortage of evidence. Additional signs of lung recovery may be obtained by radiographic resolution of airspace opacities or lung aeration with bedside ultrasound [59].

Evidence from ARDS has shown that ventilator dyssynchrony is frequent and is associated with prolonged ventilation and increased mortality [60,61]. Lung rest parameters, cycles of awakening-sedation-paralysis, and respiratory muscle weakness predispose patients on VV ECMO to ventilator dyssynchronies. Dyssynchronies become particularly relevant during weaning and liberation, and prompt identification and management may accelerate the weaning process (Fig. 3 – panel b).

Readiness for liberation can be tested by performing standardized liberation trials (SLTs), emulating spontaneous breathing trials in ventilated patients (Table 2) [62▪,63▪▪]. Monitoring during these trials include hemodynamic and respiratory parameters, and markers of adequate gas exchange. As no robust evidence to support specific criteria for readiness exists, the decision to proceed with decannulation depends solely on clinical judgement. After decannulation, monitoring of respiratory and hemodynamic parameters can aid in identifying decannulation failure. Any sustained increment in hemodynamic or respiratory support early after decannulation, not attributable to an identifiable cause (mucus plugging, haemorrhage, pneumothorax, etc.), should be considered decannulation failure and approached accordingly [64▪].

Respiratory system monitoring in patients supported with VA ECMO follows the same principles. Unless native lung function is profoundly altered, respiratory system parameters do not play a role in liberation from VA ECMO for isolated hemodynamic support.

Gas exchange

Whilst an improvement in lung elastance may correspond with an improvement in gas exchange during recovery from respiratory failure, this is not always the case and a dissociation in the time course of both onset and recovery of these two elements is not uncommon. Although lung mechanics can be readily assessed at the bedside as outlined above, determining native gas exchange can be challenging for the three reasons. Firstly in VV ECMO extracorporeal and native gas exchange occurs in series and as such where high central venous oxygen saturation ($ScvO_2$) exists, transpulmonary transfer gradients are significantly reduced (and may even be reversed) in well ventilation-

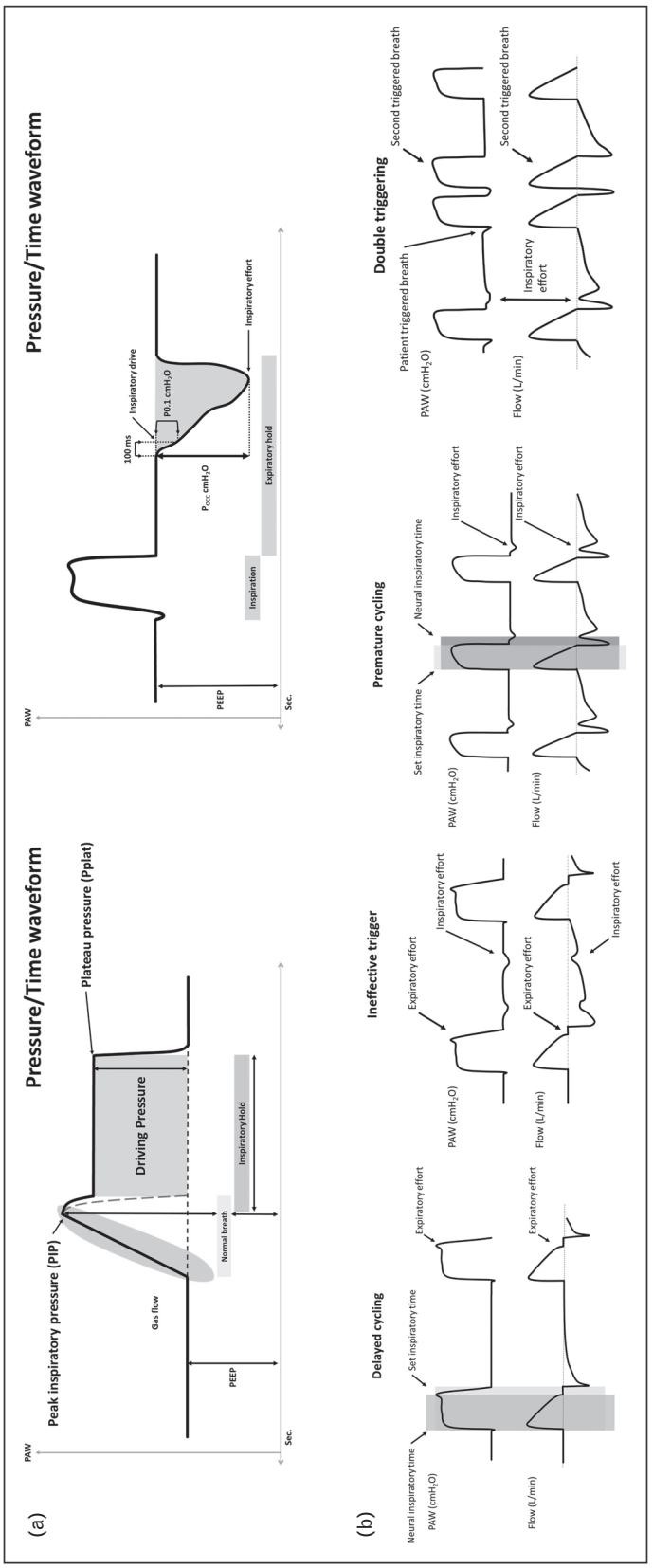

FIGURE 3. (a) Respiratory mechanics and surrogates of respiratory drive and effort. Most ventilators available in the intensive care unit have the capacity to perform inspiratory and expiratory hold maneuvers. Plateau and driving pressures are determined during a 0.5 s inspiratory hold. $P_{0.1}$ is automatically determined from spontaneous breathing efforts in modern ventilators. The occlusion pressure (P_{OCC}) requires an expiratory hold maneuver to determine the maximum negative pressure generated during the occlusion. (b) Common dyssynchronies encountered during weaning from mechanical ventilation and ECMO. Adjustments to the level of support and duration of the set inspiration will solve most common types of dyssynchrony. ECMO, extracorporeal membrane oxygenation.

Table 2. Screening criteria for standardized liberation trials (SLTs) [63▪▪]

Greater than 12 h of treatment for the underlying cause of hypoxemic respiratory failure (antibiotics, bronchodilators, source control, diuresis)
Paralysis has been discontinued for at least 24 h.
Extracorporeal blood flow (ECBF) has been weaned to less than or equal to 5 l/min with: PaO_2 > 60 mmHg and baseline FiO_2 <60% (on the ventilator)
Sweep gas flow has been weaned to less than or equal to 4 l/min with: pH >7.25
Safe mechanical ventilation parameters: Tidal volume <9 ml/kg predicted body weight PEEP <20 cmH_2O FiO_2 <60%
The patient is hemodynamically stable, defined as: Mean arterial pressure >65 mmHg, systolic blood pressure <180 mmHg, heart rate >50 or <140 beats/min Atrial fibrillation with ventricular rates >50 or <140 beats/min No sustained ventricular tachycardia No increase in the vasopressor dose >0.2 μ/kg/min or addition of a second vasopressor agent in the last 2 h prior to the SLT screening
Sedation-Agitation Scale (SAS) 2–4
No interventions to follow in the next 120 min after screening (patient transport, bronchoscopy, tracheostomy, line insertion, etc.)

perfusion matched regions at low ventilator FiO_2. Secondly, the presence of highly oxygenated decarbonated blood through the pulmonary circulation may reverse hypoxic pulmonary vasoconstriction and thereby potentiate blood flow through shunted regions making true assessment of unsupported transfer efficiency difficult [3]. Finally, in the process of 'lung rest' reduced minute ventilation will have implications on both perceived native oxygenation and decarboxylation. Awareness of these confounders, alongside comparison of a postmembrane blood gas with the patient's arterial blood gas, knowing the cardiac output and the specific ECBF, can be used to estimate the contribution of each component [65]. Whilst during severe disease, oxygenation is inherently linked to ECBF rates, randomized controlled trials are needed to assess the role of red blood cell transfusion to augment haemoglobin targets and thereby oxygen content. Currently, there is no agreed upon transfusion threshold in these patients.

The presence of a high premembrane partial pressures of oxygen (PO_2) alerts the clinician to a potential for recirculation (but may also rarely indicate failure in oxygen extraction) and may lead to an overestimate in apparent contribution from ECMO support. Changes in end-expiratory lung volume either due to changes in mechanical ventilation or progression of restrictive disease can lead to cannula migration (particularly in femoral-internal jugular configurations) and thereby an increase in the recirculation fraction. This may be notable by measurement of cannula tip distance on serial chest imaging, but a simple change in the angle of the return jet (rather than position per se) can impact the direction of flow just as significantly and thus echocardiography (using colour Doppler) may provide a more sensitive method for detection. It should be noted that as oxygen extraction is frequently high in these patients as well as significant leftward shift in the oxyhaemoglobin dissociation curve (metabolic alkalosis, low 2,3-DPG from red cell transfusion), the presence of a 'normal' premembrane PO_2 therefore does not exclude the presence of significant recirculation and this needs to be considered in this context.

Whilst pre and postmembrane blood gases provide a method by which to assess the gas exchange function of the ECMO membrane, visual inspection for clot burden and monitoring trends (where available) in transmembrane pressures (relative to ECBF) prove invaluable continuous bedside monitors for evolving issues.

During the weaning phase of VV ECMO, end-tidal CO_2 ($ETCO_2$) can be used as a simple noninvasive method to help assess the dynamic changes in physiological dead space under steady-state conditions by allowing estimation of the proportion of CO_2 elimination occurring through the lungs. In VA ECMO, fluctuations in $ETCO_2$ may be used to predict changes in cardiac output. This can also be useful to predict potential changes in the position of the mixing point which may have important consequences, particularly in the presence of mixed cardiorespiratory failure [65,66].

SEDATION AND PHYSIOTHERAPY

The vast majority of patients supported with ECMO require sedation, with midazolam, propofol, fentanyl and morphine being used most frequently [67]. Although deep sedation has been associated with

increased morbidity and mortality, light sedation allows active mobilization and early mechanical ventilation liberation [68]. As a result, the use of short-acting sedatives, like fentanyl and propofol, may be preferred in ECMO patients [69–71]. Yet, the lipophilic character of these drugs increases the risk of them being adsorbed into the ECMO circuit, requiring higher initial doses to induce sedation or prolonging half-life upon discontinuation of these therapies [69,72,73]. As a solution, some authors have suggested using less lipophilic drugs (i.e., hydromorphone). One small retrospective review of ECMO patients found less requirements of morphine milligram equivalents with hydromorphone than fentanyl [74]. Nevertheless, to this date, the only available pharmacokinetic data of sedatives in ECMO derives from ex-vivo studies, hindering definitive therapeutic recommendations [69,72,73].

Physical therapy for mobilization during VV and VA ECMO is of particular importance in patients being bridged to transplant, for both maintenance of candidacy and potential listing potential [75,76]. The benefits and feasibility of higher levels of physical activity, for example exercise out of bed, have being increasingly recognized across a broad spectrum of ECMO cohorts that includes mobilization of patients with femoral venous and arterial cannulas and those with higher comorbid burden being bridged to recovery [77,78]. During physiotherapy, attention needs to be given to the level of exertion in relation to the degree of mechanical, ventilatory and pharmacological support required, as a transient increase in supports may be required. As an example, in VV ECMO increasing cardiac output will reduce relative percentage of ECBF and therefore the oxygenation support. Unanticipated increased in metabolic work may raise $PaCO_2$ and cause an increase in respiratory drive and RV afterload. Monitoring vital signs, paying meticulous attention to cannula insertion sites to avoid complications related to migration or accidental decannulation, and ensuring circuit functionality (physiological changes in drainage and return pressures may alter ECBF) are essential to make mobilization safe and feasible in well selected patients. However, mobilization requires a skilled and experienced multidisciplinary team [77,78].

CONCLUSION

In summary, the evolution of ECMO as a supportive therapy for cardiorespiratory failure has led to an increased need for careful consideration, selection, and optimization of monitoring strategies. Extended applications of existing monitoring methods as well as advancement in echocardiography, surrogate measurements of respiratory effort and ECMO derived parameters are invaluable in optimally managing these patients. Tissue perfusion and near infrared spectroscopy are not standards of care yet but may provide useful additional information in select patients in centres that are familiar with their use. Finally, liberation trials are necessary to minimize time sensitive ECMO related complications, however these have yet to be standardized.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

Dr Fan reports personal fees from ALung Technologies, Aerogen, Baxter, Boehringer-Ingelheim, GE Healthcare, and Vasomune outside the submitted work.

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