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ECHO EDUCATION

CRITICAL CARE ECHO ROUNDS

Extracorporeal membrane oxygenation

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Abstract

Extracorporeal membrane oxygenation (ECMO) is an advanced form of organ support indicated in selected cases of severe cardiovascular and respiratory failure. Echocardiography is an invaluable diagnostic and monitoring tool in all aspects of ECMO support. The unique nature of ECMO, and its distinct effects upon cardio-respiratory physiology, requires the echocardiographer to have a sound understanding of the technology and its interaction with the patient. In this article, we introduce the key concepts underpinning commonly used modes of ECMO and discuss the role of echocardiography.

Case:
A 38-year-old lady, with no significant past medical history, was admitted to her local hospital with group A Streptococcal pneumonia. Rapidly progressive respiratory failure ensued and, despite intubation and maximal ventilatory support, adequate oxygenation proved impossible. She was attended by the regional severe respiratory failure service who established her on veno-venous (VV)-ECMO for respiratory support. Systemic oxygenation improved; however, significant cardiovascular compromise was encountered and echocardiography demonstrated a severe septic cardiomyopathy (ejection fraction $<15\%$, aortic velocity time integral 5.9 cm and mitral regurgitation dP/dt 672 mmHg/s). Her ECMO support was consequently converted to a veno-veno-arterial configuration, thus providing additional haemodynamic support. As the sepsis resolved, arterial ECMO support was weaned under echocardiographic guidance; subsequent resolution of intrinsic respiratory function allowed the weaning of VV-ECMO support. The patient was liberated from ECMO 7 days after hospital admission.

Introduction

Extracorporeal membrane oxygenation (ECMO) is an advanced form of cardiac and/or respiratory support that may be indicated in patients with respiratory or cardiac failure refractory to conventional intensive care therapies (1, 2). Utilising similar technology to the cardiopulmonary bypass machine found in cardiac theatres, ECMO can support the failing respiratory system by oxygenating and removing carbon dioxide from blood, and support haemodynamics by providing mechanical circulatory assistance.

Typical ECMO circuit configurations in adults are outlined in Fig. 1. An access cannula – which is typically inserted percutaneously via the femoral vein – draws blood from the proximal inferior vena cava (IVC). The internal jugular vein provides an alternative means of accessing the vena cava. Blood flow through the circuit is driven by a centrifugal, vortex pump. Venous blood passes from the pump to an 'oxygenator' in which oxygen diffuses from a flow of fresh gas across a specialised, semi-permeable membrane into blood and carbon dioxide diffuses in the

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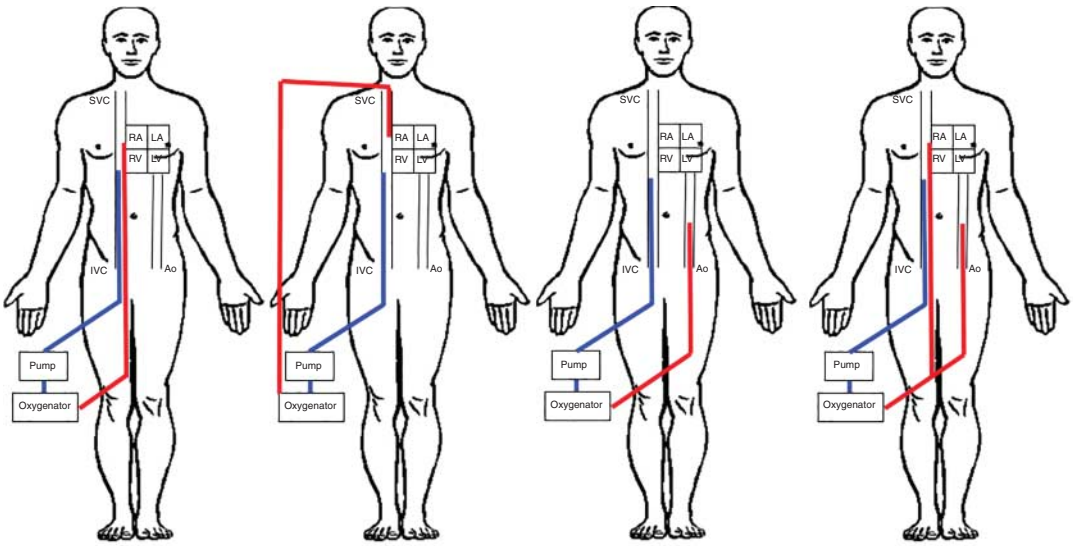


Figure 1

Typical ECMO configurations in adults. Blood is drawn from the vena cava by an access cannula; a centrifugal pump drives blood around the circuit; blood passes through an oxygenator where gas exchange occurs; a return cannula then returns blood to the right atrium or the aorta or is split between the two (in respective VV- (both femoral and internal jugular return shown); VA- or V-VA-configurations) depending upon the support required. Ao, aorta.

opposite direction. The oxygenated and decarboxylated blood is then returned to the patient via a return cannula.

The location of the return cannula depends upon the organ support required. In patients with isolated respiratory failure, the oxygenated blood is returned to the right side of the circulation: both access and return cannulae are located in the venous system, and hence this mode is described as veno-venous (VV)-ECMO. In VV-ECMO, the return cannula can be inserted via the contralateral femoral vein and the tip advanced to the mid-right atrium (RA) or IVC/RA junction. Alternatively, the internal jugular vein is accessed and the tip of the return cannula is placed in the mid-RA or at the superior vena cava (SVC)/RA junction. In the majority of adults on VV-ECMO, separate access and return cannulae are used (3). However, dual-lumen, single cannulae are also available with access ports that lie in the SVC and IVC and a single return port that lies in the RA.

VV-ECMO relies upon adequate intrinsic cardiac function to distribute the externally oxygenated blood around the circulation. The extent to which VV-ECMO improves systemic oxygenation, in the absence of pulmonary gas exchange, will depend upon the flow of blood through the circuit relative to the intrinsic cardiac output; the greater the ECMO blood flow relative to cardiac output, the greater the proportion of venous blood that is oxygenated resulting in increased mixed venous saturation of pulmonary arterial blood. Oxygenation is thus primarily manipulated by the flow of blood through the circuit. Clearance of carbon dioxide is largely independent of blood flow and is instead determined by the rate of 'sweep' fresh gas flow through the membrane oxygenator.

If cardiac support is required, blood is returned to the left side of the circulation – veno-arterial (VA)-ECMO – the circuit thus supporting oxygenation and decarboxylation via the membrane oxygenator and circulatory flow by pumping blood directly into the systemic arterial circulation.

If cardiac and respiratory failure co-exist, it may be desirable to return blood to both the venous and arterial systems; a V-VA-ECMO configuration provides the operator with the ability to alter the relative flow to the venous and arterial returns using 'gate clamps'. This is important if cardiac dysfunction resolves more quickly than respiratory failure; gradual transition from primarily VA support to VV support reduces the risk of the ECMO support competing with the recovering intrinsic cardiac function.

While the peripheral approach for VA-ECMO (with the arterial return cannula inserted via the femoral artery either percutaneously or using a surgical cut down approach) is the most common configuration (3), access

may also be obtained centrally whereby access and return cannulae are inserted directly through the open chest into the RA and aorta respectively. This approach is commonly used via the open sternotomy after cardiac surgery if the patient cannot be weaned from intra-operative cardiopulmonary bypass and in paediatric patients in whom the small calibre of peripheral vessels may preclude the percutaneous passage of sufficiently sized cannulae.

Cardiorespiratory physiology and ECMO

In VV-ECMO, the volume of blood removed and that returned to the circulation are equal; therefore, there should be minimal impact upon preload. Patients selected for VV-ECMO will, by definition, be hypoxaemic and/or hypercapnic, with resultant pulmonary vasoconstriction and increased right ventricular (RV) afterload. The improvement in oxygenation and carbon dioxide clearance on ECMO will theoretically reduce pulmonary vasoconstriction, thus reducing RV work and improving performance (4). Furthermore, as extracorporeal gas exchange reduces the reliance on intrinsic pulmonary function, the pressures delivered to the lungs by mechanical ventilation can be significantly reduced: this too reduces RV afterload. VV-ECMO has no direct effect on left ventricular (LV) function; however, improved oxygenation and resolution of respiratory acidosis may improve global myocardial performance (5). Furthermore, improved LV performance may also be observed, as a result of improved RV performance, due to ventricular interdependence.

VA-ECMO has more profound effects on physiology (4). Native cardiac function is, by definition, severely impaired in this patient group. Oxygenated blood from the ECMO circuit is returned to the aorta rather than to the right side of the heart, significantly reducing preload. The goal of VA-ECMO should be to provide partial cardiac support (70–80% of predicted cardiac output) to allow for some cardiac ejection (pulse pressure of 10–20 mmHg) and for some intrinsic venous return to continue to enter the right heart and pass through the pulmonary circulation. However, cardiac function may be reduced to such a degree that the forward flow of blood through the pulmonary vasculature and heart is negligible. Consequences include LV distension (potentially resulting in permanent ventricular damage if untreated) and pulmonary oedema, as blood accumulates within the left ventricle, and thrombus formation around valve apparatus or within the chambers. Recognition of inadequate LV ejection and stasis of blood may be addressed by the addition of inotropic drugs, insertion of an intra-aortic balloon pump, insertion of an Impella percutaneous LV assist device, or the creation of intra-cardiac shunts (6, 7, 8). Conversion of peripheral cannulae to surgically inserted central cannulae has also been described as a means of ventricular decompression (9).

The physiological implications of VA-ECMO alter as the heart recovers. In peripherally placed VA-ECMO, returned blood flows from the distal to the proximal aorta, round the aortic arch, finally reach the aortic root and coronary arteries. This retrograde return flow is in direct competition with blood ejected from the left ventricle by the native heart. At the onset of ECMO, when the function of the failing heart is negligible, there is minimal resistance to retrograde ECMO return flow: perfusion of the coronaries and vessels arising from the aortic arch with oxygenated blood from the ECMO circuit is typically adequate. As the heart recovers, however, and intrinsic contribution to the circulation increases, native anterograde aortic flow will prevent oxygenated ECMO return blood from traversing the arch. This is particularly problematic if cardiac function improves before pulmonary function. The recovering left ventricle will, under such circumstances, be ejecting poorly oxygenated, 'shunted' blood from the pulmonary circulation into the ascending aorta and arch of the aorta. This situation may result in coronary and cerebral hypoxaemia and is known as the Harlequin syndrome: arteries arising from the ascending aorta and proximal arch are supplied by deoxygenated blood ejected from the heart; more distally arising arteries

Table 1 Echocardiography in ECMO: at commencement, during monitoring and for weaning.

At commencement:
Guide insertion and confirm correct cannula position
During monitoring:
General:
LV size and function
RV size and function
Pericardial collection
sPAP
Complications:
Cannula displacement
Cannula or vessel thrombosis
Obstruction of veins or arteries
LV thrombus
Pericardial collection/tamponade
Pulmonary embolism
Weaning from VA-ECMO: (during trial of reduced blood flow of 1.0 l/min for 30 min)
LVEF $\geq$20–25%
Aortic VTI $\geq$12 cm
TDI lat S' $\geq$6 cm/s

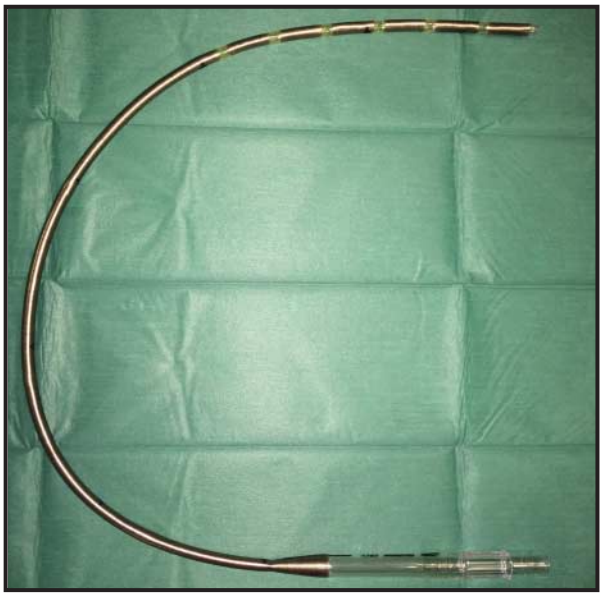


Figure 2
Multi-stage access cannula.

are supplied by oxygenated blood from the ECMO return (10). This problem may be overcome to some extent by the use of V-VA-ECMO to allow relative adjustment of venous and arterial ECMO return blood flow.

Echocardiography

Echocardiography (transthoracic (TTE) or transoesophageal (TOE)) can be used to make decisions regarding appropriateness of ECMO support, to guide cannula insertion and confirm position, to manipulate cannulae once support is established and, finally, to assess clinical progress and suitability for weaning (Table 1) (11).

Role of echocardiography in establishing a patient on ECMO

Correct positioning of access and return cannulae is vital for safe and effective ECMO support. Percutaneous insertion of cannulae can be achieved utilising a Seldinger technique: the target vessel is accessed with a needle using ultrasound guidance, a guidewire is then inserted into the vessel via the needle and, subsequently, serial dilators are passed over the wire to create a tract through the soft tissues. Finally, the cannula is passed over the guidewire. It is essential to confirm that the guidewire (and subsequently the cannula) follow the intended path into the target vessel. For example, during placement into the vena cava, it is important to ensure that the guidewire and cannula pass towards the RA and do not deviate into a tributary vessel. Echocardiography and/or fluoroscopy provide a means of monitoring guidewire and cannula insertion.

The use of echocardiography during cannulation has been demonstrated to reduce the need for subsequent cannula repositioning in the paediatric population (12) and, in one study, echocardiography was reported to be superior to the use of plain chest radiographs alone (13).

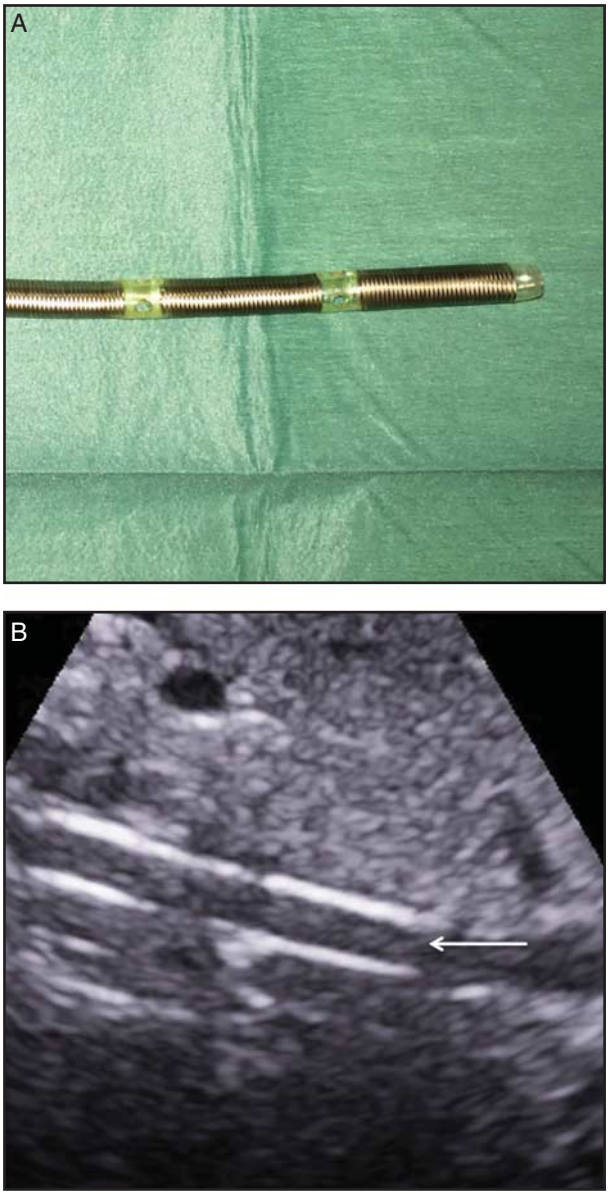


Figure 3
(A) Multi-stage access cannula – detail of intake ports. (B) Two-dimensional image of the access cannula (arrow) positioned within the proximal IVC, above the level of hepatic venous drainage.



Figure 4
Single-stage return cannula (venous).

Furthermore, echocardiography carries the advantages of being more portable than X-ray equipment and avoids exposure of patients and staff to ionising radiation. Studies comparing the efficacy of echocardiography and fluoroscopy during ECMO cannulation are likely to be conducted in centres with significant expertise and enthusiasm in echocardiography and should be interpreted with this in mind. In practical terms, the modality chosen will be dependent upon local preference and resource availability.

Following insertion, the position of the cannulae should be assessed echocardiographically. The desired position is dependent upon the type of cannula being used and the location of its access and/or return ports. Therefore, it is important to have an understanding of the 'anatomy' of the cannula being assessed.

A multi-stage venous access cannula typically has an inlet port at its distal end and further blood intake ports located at regular intervals along its length (Fig. 2); the distal end should lie in the proximal IVC, commonly above the level of hepatic venous drainage. The intake ports along the length of the cannula can be identified echocardiographically, thus allowing identification of this type of cannula (Fig. 3). A single-stage return cannula has a flexible distal tip with multiple outflow ports (Fig. 4). This distal portion of the cannula has a characteristic 'speckled' appearance on echocardiography (Fig. 5). The tip of the return cannula is typically positioned in the mid-RA or at the IVC/RA (femoral access), or at the SVC/RA (internal jugular access) junction. Furthermore, colour flow Doppler imaging can be used to identify evidence of flow at the tip of the return cannula and through the side holes of the access cannula (10). It is important to ensure that a degree of separation between the access and return cannulae ports is maintained; inadequate separation risks the recirculation of oxygenated return blood directly back into the ECMO circuit rather than into the patient circulation, with the resultant decreased efficiency of systemic oxygenation. Unsatisfactory positioning of ECMO cannulae may require subsequent manipulation in order to improve systemic oxygenation and this may be performed under direct echocardiographic guidance. Finally, it is essential to ensure that the return cannula is clear of both the inter-atrial septum and the tricuspid valve to minimise the risk of mechanical trauma and arrhythmias.

A dual-lumen single cannula – in which blood is accessed from the SVC and IVC and returned to the RA using the same cannula – requires a different approach to positioning. This cannula is inserted via the internal jugular vein and it is important to ensure that the tip of the cannula is correctly positioned within the IVC and that the return port is positioned within the RA so that blood flow is directed towards the tricuspid valve (14) (Fig. 6A). This is best confirmed on colour flow Doppler imaging and will require careful manipulation under echocardiographic guidance to achieve optimal positioning (Fig. 6B). Figure 7 demonstrates the manipulation of a dual-lumen, single cannula: the tip of the cannula initially lies within a hepatic vein (Fig. 7A); the cannula is withdrawn under echocardiographic guidance and

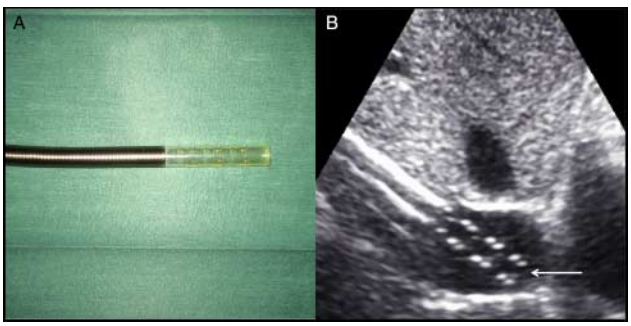


Figure 5
(A) Single-stage return cannula (venous) – detail of flexible distal tip. (B) Two-dimensional image of the return cannula (arrow) at the IVC/RA junction. The distal portion of the cannula has a characteristic 'speckled' appearance.

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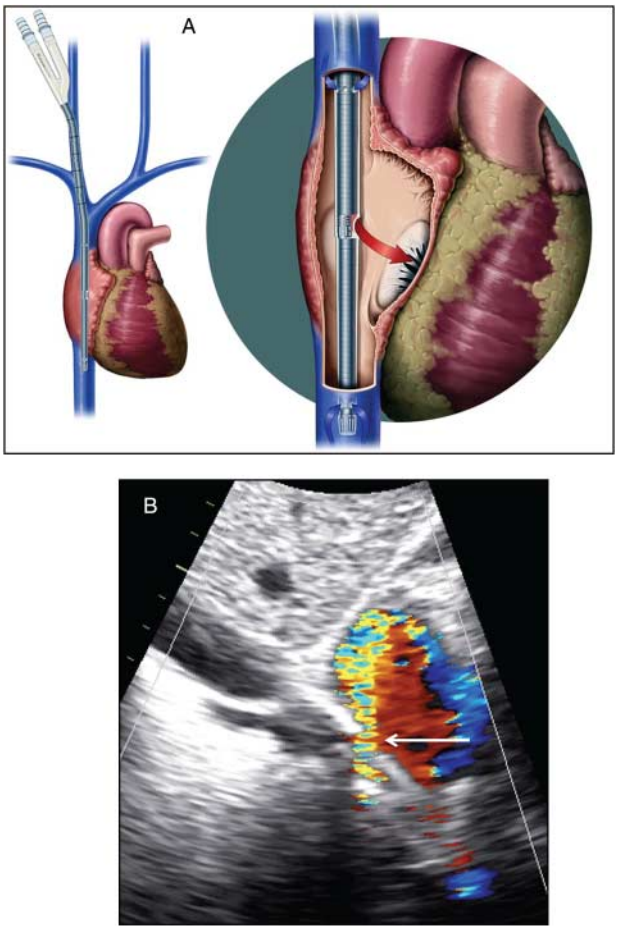


Figure 6
(A) Dual-lumen, single cannula; insertion via internal jugular vein and correct positioning in SVC/RA/IVC. (B) Dual-lumen, single cannula with colour flow Doppler imaging demonstrating flow into the RA (arrow).

re-advanced until the tip lies correctly within the IVC (Fig. 7B).

In peripheral VA-ECMO, the return cannula, inserted via the femoral artery, is typically located in the common iliac artery or at the bifurcation of the abdominal aorta. This area is not well visualised on TTE or TOE imaging alone. As such, a combination of abdominal ultrasound (to confirm the guidewire in the abdominal aorta) and TOE (to confirm passage of the guidewire into the descending thoracic aorta) may be necessary. Other imaging modalities, such as fluoroscopy, provide an alternative option.

In most cases, TTE provides images of sufficient quality for patients on ECMO. In instances when image quality is suboptimal or non-diagnostic, TOE may offer superior spatial resolution. Although the use of TOE is a common practice in critical care, use within the ECMO patient cohort should be considered with caution. Patients receiving ECMO routinely receive anticoagulation in the form of heparin, are commonly thrombocytopaenic and have an acquired von Willebrand factor deficiency (15, 16); the risk of complications, particularly significant haemorrhage, is therefore increased (17). It has been suggested that contrast-enhanced TTE may prove a useful tool to alleviate some of the risks associated with TOE while maintaining improved endocardial definition and

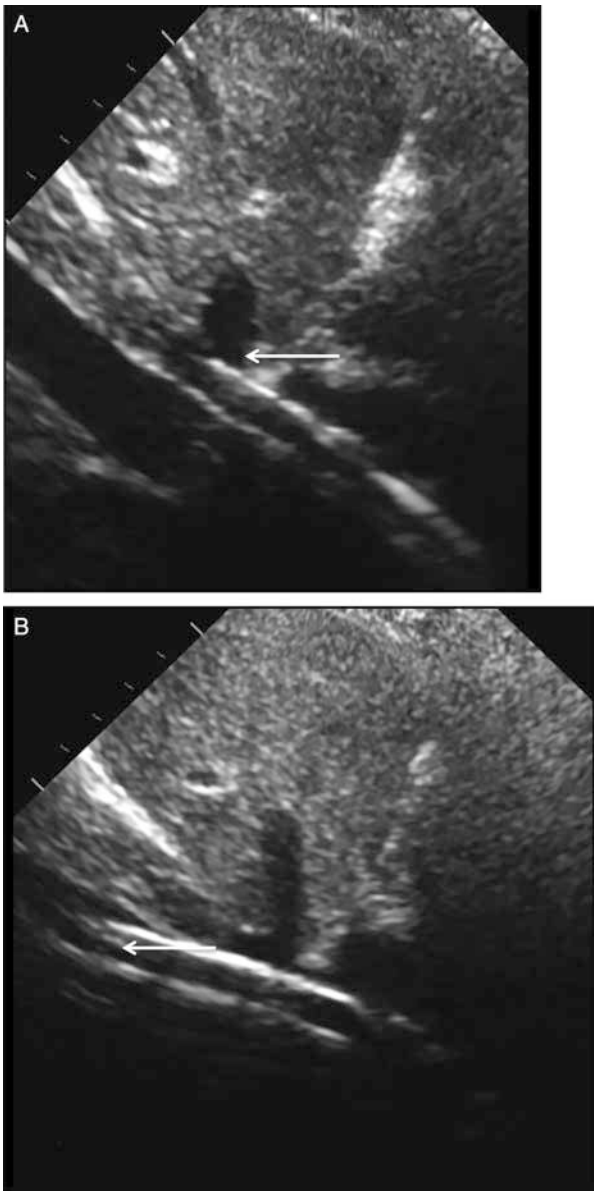


Figure 7
Manipulation of a dual-lumen, single cannula: (A) the tip of the cannula initially lies within a hepatic vein (arrow) and (B) the cannula is withdrawn under echocardiographic guidance and re-advanced until the tip lies correctly within the IVC (arrow).

border delineation when compared with TTE alone (18). The use of contrast has been shown to be feasible within the ECMO population and is recommended by the American Society of Echocardiography (ASE) (19).

Role of echocardiography during monitoring

During VV-ECMO, echocardiographic assessment is focused primarily on the assessment of RV size and systolic function. ASE recommendations emphasise a thorough and comprehensive assessment of the RV based on a combination of imaging modalities and multiple acoustic windows (20). RV size is best estimated at end diastole, in a focused apical four-chamber view, using a measurement of the maximal short-axis dimension at the basal level. Tricuspid annular plane systolic excursion (TAPSE) should be assessed to measure RV longitudinal function using M-Mode at the tricuspid annulus level in an apical four-chamber view. Measurement should be based on the distance between the nadir and the systolic peak. The peak systolic integral of the tricuspid lateral annular plane should also be obtained and measured using tissue Doppler imaging (RV TDI S'). Peak tricuspid regurgitation velocity, as a surrogate for estimating systolic pulmonary artery pressure (sPAP) in the absence of pulmonary stenosis, should also be measured routinely. Furthermore, RV fractional area change and RV dP/dt can also be measured in the assessment of RV systolic function. However, the significance of these measurements in this patient cohort is uncertain due to scarcity of evidence. Additionally, for all patients on VV-ECMO, it is important to ensure that the position of the ECMO cannulae remains unchanged compared with initial placement and that there is no evidence of a developing pericardial collection that may indicate a cannula-related cardiac injury.

Owing to constant variability in preload, filling pressures and IVC flow, the interpretation of absolute echocardiographic parameters in patients on VV-ECMO is challenging. There is little evidence regarding the interpretation of absolute echocardiographic values and ranges within this patient cohort. For this reason, serial echocardiographic studies to monitor changes in RV size, RV function, and estimated sPAP are more useful than values from a single study.

During VA-ECMO, it is imperative to assess the size and function of both the LV and the RV. LV cavity size is an important consideration as increasing dimensions may suggest the stasis of intra-cardiac blood flow and need for inotropic support or an additional mechanical device to promote forward flow. A comprehensive assessment of systolic function should be undertaken using standard parameters: visual estimation of LV size and ejection fraction (EF), Simpson's biplane EF, TDI to measure lateral mitral annular peak systolic velocity (TDI lat S'), and mitral regurgitation (MR) dP/dt (21, 22). The LV end diastolic dimension, performed in the parasternal long-axis view, should be estimated perpendicular to the major axis of the LV just distal to the tips of the mitral valve at the blood–tissue interface. Simpson's biplane EF estimations should be made from on-axis images aimed at maximal LV areas, while avoiding foreshortening and suboptimal endocardial borders. Measurements should be obtained from apical four- and two-chamber views with careful tracings at the blood–tissue interfaces. TDI lat S' should be obtained with the cursor aligned perpendicular to the MV annulus and the sample volume at the level of the annulus; the modal signal systolic peak should be measured. MR dP/dt measures the rate of rise of ventricular pressure during isovolumetric contraction and can be estimated from the spectral Doppler trace of the MR by measuring the time interval between 1 and 3 m/s. MR dP/dt serves as a surrogate for LV systolic function.

Other utilised markers of LV systolic function in VA-ECMO include the aortic velocity–time integral (VTI) and LV outflow tract VTI (23). The methods incorporate continuous and pulse wave (PW) Doppler, respectively, and are obtained from either an apical five-chamber view or long-axis view. It is important to ensure an optimal alignment with the direction of blood flow, as this guarantees the most accurate echocardiographic estimate of flow. Furthermore, the position of the sample volume for the PW Doppler trace needs to be accurately located. There is some debate regarding the precise sampling point (0.5 or 1 cm from the insertion of the aortic valve leaflets); however, consistency in sampling location is the key consideration when performing serial echocardiographic studies on an individual patient.

Assessment of the RV in patients on VA-ECMO is also vital and should be carried out in the same way as for patients on VV-ECMO (described earlier).

Assessment of systolic function should be undertaken frequently; if evidence of cardiac recovery is apparent, then VA-ECMO support can be weaned, typically to a minimum blood flow of 2–2.5 l/min during general care. Further assessment can be performed by transiently reducing support to lower blood flow rates (see role of echocardiography in weaning from ECMO).

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Complications of ECMO detected by echocardiography

Up to 5.3% of adult ECMO patients may develop cardiac complications while on ECMO (3) support, and echocardiography can be an indispensable (24) tool in detecting potentially life-threatening problems. The occurrence of complications will be governed by patient factors, cannula type and position, and the mode of ECMO support.

Passage of guidewires or cannulae through the myocardium may result in significant pericardial collections, for which echocardiography is the diagnostic modality of choice. However, traditional markers of tamponade physiology may be of limited use in the ECMO patient (25). Dynamic changes in preload, afterload, ECMO blood flow, and ventilatory settings may profoundly alter the underlying cardiac pathophysiology. Consequently, the interpretation of routinely used echocardiographic markers of haemodynamic compromise can often be challenging, and further evaluation is required to validate their value in the setting of ECMO (26). Furthermore, the absence of evidence of haemodynamic compromise should be interpreted with caution. A pericardial collection, which appears benign while on VA-ECMO support, may prove to be haemodynamically significant when extracorporeal support is weaned and should therefore be monitored closely.

Malposition or migration of ECMO cannulae through the inter-atrial septum has also been described (27) and this complication can be reliably detected echocardiographically (Fig. 8).

Outside the heart, malposition of cannulae may obstruct venous drainage, in the IVC resulting in liver and splanchnic organ congestion (24, 28) (Fig. 9A), and in the SVC causing SVC syndrome and reduced cerebral perfusion, particularly in children (29).

The passage of blood through an extra-corporeal circuit activates the clotting cascade; therefore, patients on ECMO support are at an increased risk of intravascular thrombus formation (15). This risk may be compounded by obstruction to flow by intravascular cannulae and by the low flow state through the heart in patients with severe cardiac dysfunction. Anti-coagulation with heparin is typically administered to reduce the risk of thrombus formation; however, the incidence of intravascular and intracardiac thrombus remains significant, particularly at low ECMO blood flow rates, and evidence of thrombus should therefore be sought in echocardiographic studies (Fig. 9B). Thrombus within the ECMO circuit (often within the oxygenator) may also result in significant consumption of clotting factors and platelets, in turn resulting in a circuit-related coagulopathy; in the context of anticoagulation with heparin, this may result in significant bleeding.

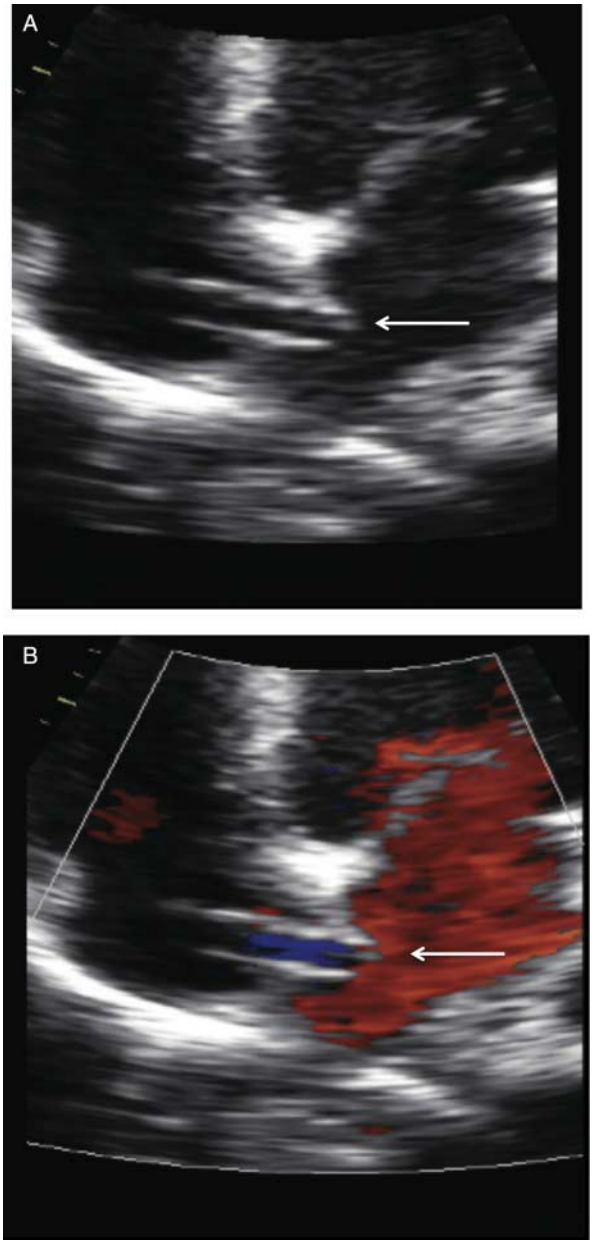


Figure 8
Zoomed apical four-chamber image focusing on the inter-atrial septum on (A) two-dimensional imaging and (B) with colour flow Doppler imaging. The ECMO cannula can be visualised crossing the septum (arrow) with colour flow suggestive of right to left shunting.

The presence of 'spontaneous echo contrast' within the cardiac chambers has been associated with blood stasis and the subsequent increased risk of thrombus formation among the general cardiology population (30). It is therefore assumed to represent an increased likelihood of thrombosis within the ascending aorta, LV cavity and

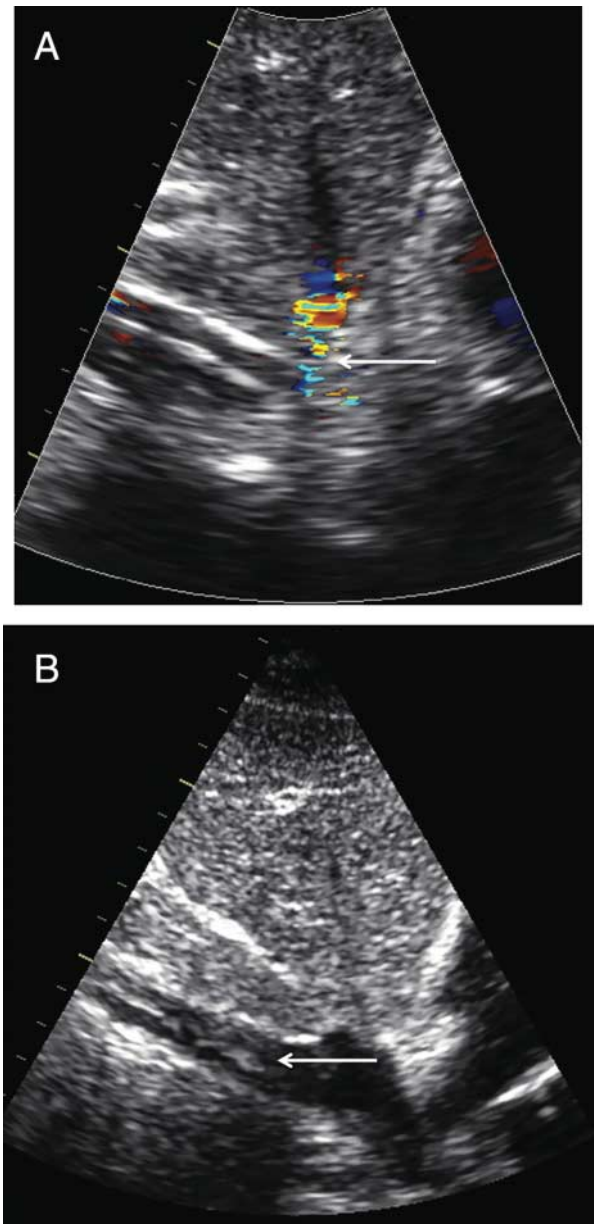


Figure 9
(A) Obstruction of hepatic vein outflow due to ECMO cannula position demonstrated using colour flow Doppler imaging (arrow). (B) Thrombus visualised within the IVC (arrow) post ECMO cannula removal.

pulmonary veins in the ECMO patient (25); a further indication for promoting forward flow by pharmacological or mechanical means.

Role of echocardiography in weaning from ECMO

Weaning from VA-ECMO requires meticulous clinical and biochemical assessment, which can be supported by serial echocardiography. The concomitant use of inotropic support and its effects on cardiac contractility should be taken into consideration when assessing suitability for weaning. Echocardiographic parameters have been shown to be useful predictors of readiness for liberation from VA-ECMO. A trial of reduced VA-ECMO support involves transiently weaning the blood flow to a minimum of 1 l/min for up to a maximum of 30 min (to minimise the risk of thrombus formation), while clinical, haemodynamic and echocardiographic parameters are assessed (23). Currently, there are no internationally recognised echocardiographic protocols to guide weaning from VA-ECMO and approaches to weaning may vary between centres. Parameters that may predict successful weaning from VA-ECMO support include: LVEF $\geq$20–25%, aortic VTI $\geq$12 cm and TDI lat S' $\geq$6 cm/s (11, 31). Furthermore, the absence of LV dilation or a significant pericardial collection should also be sought before weaning (23, 32). TAPSE and RV TDI S' can be used to monitor recovery of the RV; however, serial measurements are more useful than solitary values, as mentioned previously (see 'Role of echocardiography during monitoring' section).

Weaning from VV-ECMO relies primarily on the assessment of intrinsic pulmonary gas exchange and lung compliance, associated with reducing ECMO support. Consequently, echocardiography is not routinely required for weaning from VV-ECMO. However, monitoring of RV size and function in conjunction with serial estimates of sPAP during the weaning period will provide valuable insight into the cardiac response to changing respiratory physiology.

Conclusion

ECMO is becoming an increasingly utilised supportive therapy for severe cardio-respiratory failure in the critical care setting. An integrated echocardiography service is indispensable in all aspects of the ECMO pathway, from assessing suitability and facilitating cannulation, to monitoring and detecting complications, and for weaning. Echocardiography will provide the most benefit when the operator has an appreciation of the technology being used at the bedside, a good understanding of the often unique pathophysiology of patients requiring ECMO support and when there is a close working relationship with members of the multidisciplinary critical care team.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this article.

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