Extracorporeal Membrane Oxygenation in Adults – Variants, Complications during Therapy, and the Role of Radiological Imaging

Extrakorporale Membranoxygenierung bei Erwachsenen – Varianten, Komplikationen unter Therapie und die Rolle der radiologischen Diagnostik

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ABSTRACT

Background Extracorporeal membrane oxygenation (ECMO) and extracorporeal life support (ECLS) as respiratory and circulatory assist therapies are gaining in importance in the treatment of critically ill patients. Depending on the place of cannulation – veno-venous for ECMO and veno-arterial for ECLS – distinct changes in hemodynamics will occur. In this review we describe the different types of ECMO and ECLS systems, the typical cannula placement and frequent complications under therapy. The most suitable imaging modalities will be presented and typical hemodynamic pitfalls in contrast-enhanced computed tomography or angiography will be elucidated.

Methods The review is based on a literature search in PubMed with the terms "ECMO" and/or "ECLS" and/or "extracorporeal life support" and/or "imaging" and/or "complications". Statistical data was taken from the ECMO register of the "Extracorporeal Life Support Organization (ELSO)".

Results Critical illness- and therapy-associated complications are common so that imaging, particularly computed tomography, becomes increasingly important. Following veno-venous cannulation in ECMO, the normal sequential blood flow is preserved, so that no contrast enhancement irregularities should be expected when the right timing and an adequate amount of contrast agent are selected. After veno-arterial cannulation in ECLS, different artifacts like pseudo-filling defects, pseudomembranes and irregular/low contrast enhancement of heart and pulmonary vessels can be found, depending on the site of cannulation and the residual cardiac function.

Key points
- Cannula placement is usually documented by radiography.
- Computed tomography is appropriate in the face of inconclusive cannula placement and probable complications.
- In veno-venous ECMO, no contrast enhancement artifacts are to be expected.
- Veno-arterial ECLS leads to pseudo-filling defects, pseudomembranes and irregular contrast enhancement of heart and pulmonary vessels.

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ZUSAMMENFASSUNG

Hintergrund Die extrakorporale Membranoxygenierung etabliert sich zunehmend in der Intensivmedizin zur Behandlung von Patienten mit pulmonalem und/oder kardialem Versagen. Prinzipbasiert wird zwischen pulmonal-unterstützenden, venovenösen Systemen (Extracorporeal Membrane Oxygenation, ECMO) und kardiozirkulatorisch-unterstützenden, venoarteriellen Systemen (Extracorporeal Life Support, ECLS) unterschieden, die je nach Ort der Kanülierung zu Veränderungen der Hämodynamik führen. In dieser Arbeit wird auf die verschiedenen Varianten der ECMO- und ECLS-Systeme, deren typische Lage und häufige Komplikationen unter Therapie eingegangen. Die bildgebenden Modalitäten, die zur Abklärung geeignet sind, werden vorgestellt und hämodynamische Fallstricke im Rahmen der kontrastmittelgestützten computertomografischen und angiografischen Diagnostik beleuchtet.

Methode Dieser Artikel beruht auf einer Literaturrecherche in PubMed mit den Stichwörtern „ECMO" und/oder „extracorporeal life support" und/oder „imaging" und/oder „complications". Statistische Daten wurden dem ECMO-Register der „Extracorporeal Life Support Organization (ELSO)" entnommen.

Ergebnisse und Schlussfolgerung Erkrankungs- und therapieassoziierte Komplikationen sind aufgrund der kritischen Gesamtkonstellation der Patienten häufig, sodass die bildgebende Diagnostik mittels Computertomografie und ggf. Angiografie zunehmend an Bedeutung gewinnt. Bei der venovenösen ECMO wird der antegrade Blutfluss beibehalten, sodass bei Wahl des richtigen Untersuchungszeitpunkts und eines adäquaten Kontrastmittelvolumens keine Kontrastierungsphänomene auftreten. Unter venoarterieller ECLS kann es in Abhängigkeit der Kanülierung, des extrakorporalen Flusses und der linksventrikulären Restfunktion zu Kontrastierungsphänomenen mit einem arteriellen Pseudofüllungsdefekt, einer arteriellen Pseudomembran oder einem Kontrastierungsdefekt des Herzens und der Pulmonalstrombahn kommen, welche bei der Bildinterpretation berücksichtigt werden müssen.

Introduction

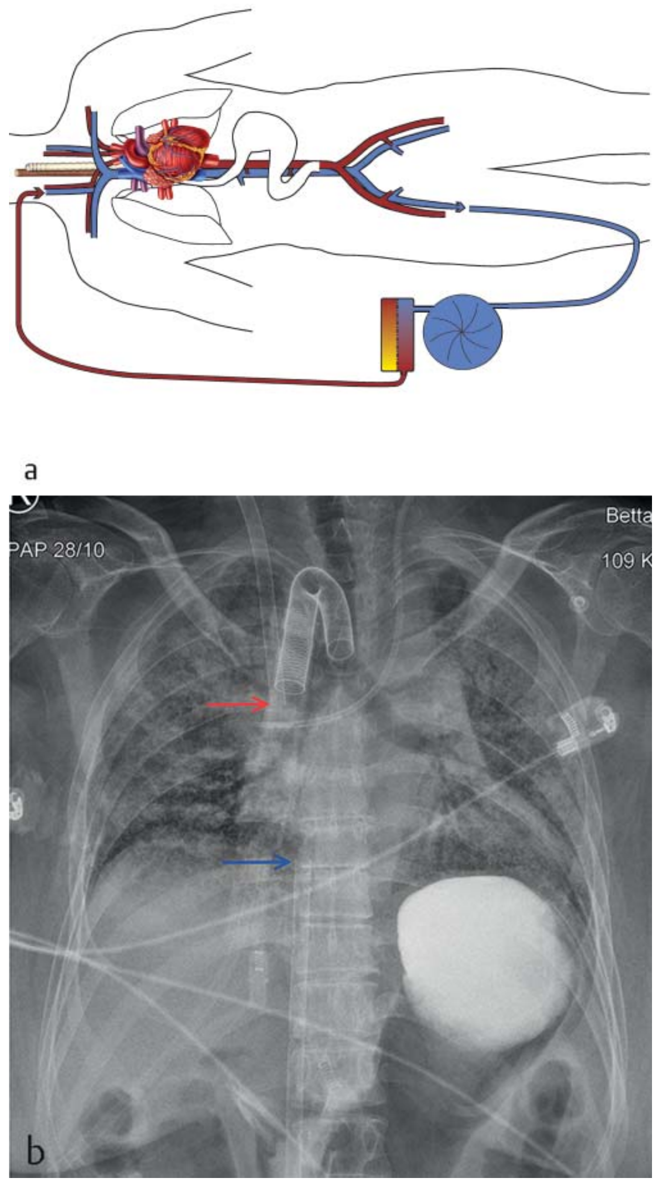
Extracorporeal membrane oxygenation is becoming increasingly established as an emergency treatment in patients with acute respiratory distress syndrome (ARDS) and/or cardiovascular failure. Depending on the type of cannulation, the support of gas exchange and thus pulmonary function (ECMO = extracorporeal membrane oxygenation) or cardiac function for circulatory support (ECLS = extracorporeal life support) is partially or completely taken over.

Extracorporeal membrane oxygenation was developed in the 1970 s [1]. A significant increase in ECMO treatment was triggered by confirmation of a survival advantage in the CESAR study (conventional ventilatory support versus ECMO for severe adult respiratory failure) [2] and by the H1N1 virus pandemic in 2009 [3]. In 2014, over 14,000 adult patients at 251 centers worldwide were registered at the extracorporeal life support organization (ELSO) for ECLS therapy. The number has more than doubled in the last 10 years. The survival rates were 65 % in the case of solitary respiratory failure, 56 % in the case of cardiac failure and 39 % after reanimation [4].

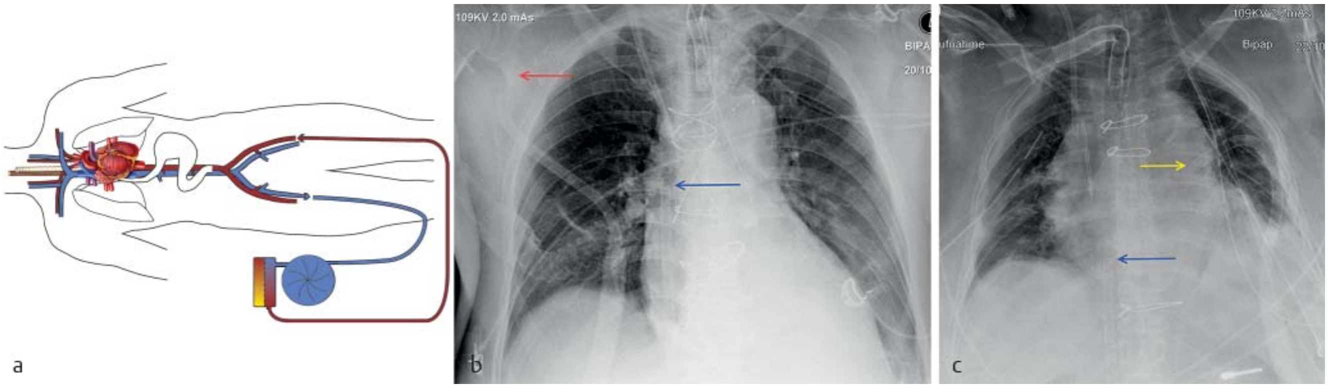
Since ECMO/ECLS therapy and also the primary diseases requiring therapy have a high complication rate, patients often undergo diagnostic imaging during their intensive care stay. Radiologists can be confronted with this issue bedside in the intensive care unit in the case of ultrasound and projection radiography as well as in the case of computed tomography (CT) and, less frequently, angiography. Knowledge of the ECMO/ECLS systems being used and the hemodynamic changes due to the extracorporeal circulation and of possible artificial contrast enhancement phenomena is therefore essential for examination planning and image interpretation.

ECMO and ECLS systems: Design and variants

An ECMO or ECLS system generally includes an extracorporeal blood circuit with a venous outflow cannula and a venous or arterial inflow cannula. The deoxygenated blood is pumped by a centrifugal pump through a membrane oxygenator and is enriched with oxygen while carbon dioxide is removed. The oxygenated blood is returned to the systemic circulation via the inflow cannula [5 – 9]. There are two different methods depending on the type of cannulation [10, 11]:



▶ **Fig. 1** ECMO venous outflow cannula in the inferior vena cava and inflow cannula placement through the superior vena cava in the right atrium, illustration **A** and radiographic correlation **B**. Positive enteric contrast after use as prokinetic agent. Pneumonia.



▸ **Fig. 2** Schematic representation of the femorofemoral peripheral ECLS **A**. Peripheral ECLS with arterial cannula in the axillary artery (red arrow) and venous drainage cannula in the superior vena cava (blue arrow) **B.** Central ECLS with venous cannula in the right atrium (blue arrow) and arterial cannula in the ascending aorta (yellow arrow); the part of the arterial tract proximal to the aorta is made of Dacron and is not radiopaque **C**.

▸ **Table 1** Summary of clinically relevant information on ECMO- and ECLS-Systems.

	outflow cannula		**inflow cannula**		**function**
	cannulation site	**tip position**	**cannulation site**	**tip position**	
ECMO (syn. VV-ECMO)	femoral vein	inferior vena cava	cervical vein femoral vein	superior vena cava right atrium	gas exchange
ECLS (syn. VA-ECMO)	femoral vein	inferior vena cava superior vena cava	axillary/subclavian artery carotid artery femoral artery thoracic bypass	thoracic aorta	gas exchange circulatory support

Extracorporeal membrane oxygenation (ECMO)

The veno-venous support system serves in the case of isolated severe hypoxemic respiratory distress to ensure vital gas exchange and is referred to as "classic" ECMO therapy (syn.: vv-ECMO) [12, 13]. The blood that is removed venously and is oxygenated and decarboxylated extracorporeally is returned to the venous system or the right atrium. Systemic blood flow and blood pressure are ensured by heart function regardless of the extracorporeal flow so that sufficient cardiac pump function is a requirement [5 – 8, 14, 15].

In femoroatrial ECMO, the venous outflow cannula is placed transfemorally in the inferior vena cava ideally below the branches of the hepatic veins. The diameter – usually between 21 and 29 French in adults – determines the maximum achievable flow rate that is usually 60 ml/kg KG/min (80 ml/kg KG/min in children, and 100 ml/kg KG/min in newborns). The blood is returned through the superior vena cava into the right atrium. In the femorofemoral variant, the outflow cannula is positioned in the distal inferior vena cava. The blood is returned through the ipsilateral or contralateral femoral vein into the right atrium. In both variants, it must be ensured that the tip of the inflow cannula is pointing in the direction of the tricuspid valve so that recirculation of the blood through the extracorporeal circuit is minimized (▸ **Fig. 1**). Alternatively, it is possible to use a double lumen cannula (13 – 31 Fr) that is positioned through the internal jugular vein and the right atrium with the tip in the inferior vena cava [6, 12, 13, 16, 17].

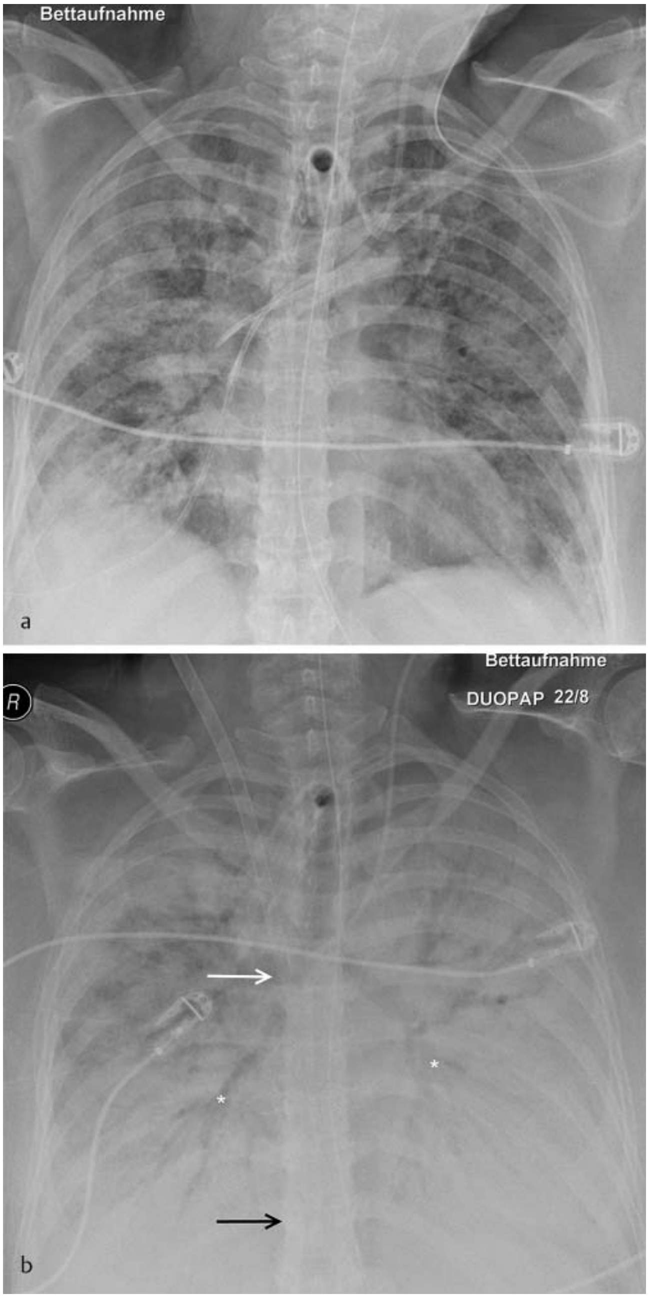
Extracorporeal life support (ECLS)

In the case of treatment-refractory cardiac failure or combined heart-lung failure, veno-arterial support is used to maintain systemic perfusion. This is referred to as ECLS therapy [10, 12, 13]. The term veno-arterial ECMO therapy (va-ECMO) is often used as a synonym in the clinical routine as well as the literature.

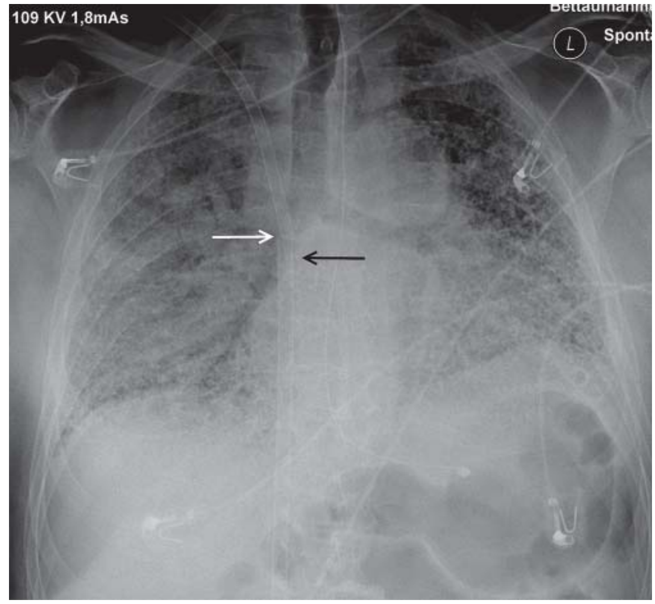
The venously drained, extracorporeally oxygenated blood is returned to the aorta while avoiding the pulmonary circulation. The systemic blood flow is thus comprised of the extracorporeal ECLS volume and the ejection fraction of the left ventricle [5, 6]. In the case of poor pulmonary and cardiac function, the oxygen supply in the aortic arch, the coronary arteries, and the supraaortic vessel branches is limited and can be optimized by an increase in the ECLS flow rate. However, based on the increased aortic resistance, this can result in increased impairment of left ventricular function [1, 14].

ECLS can be connected peripherally as well as centrally [7, 10, 12, 13, 16]:

In the case of peripheral ECLS, venous drainage is performed via the inferior vena cava or the superior vena cava. The blood is returned to the aorta typically in a retrograde manner via the femoral artery with the cannula positioned in the descending thoracic



► **Fig. 3** Initial worsening of pulmonary function ("white lung") during ECMO therapy **B**; inflow cannula – white arrow, outflow cannula – black arrow.



► **Fig. 4** Femoroatrial ECMO with possible recirculation due to close proximity of the inflow and outflow cannulas in the right atrium; inflow cannula – white arrow, outflow cannula – black arrow.

aorta. Alternatively the subclavian artery or the axillary artery can also be used. The diameters of commonly used inflow cannulas are between 18 and 24 French.

In the case of central ECLS, the cannula is positioned in the right atrium and the aorta after thoracotomy. It is accordingly full of complications but provide maximum cardiac support (► **Fig. 2**).

► **Table 1** summarizes the clinically relevant information on ECMO– and ECLS–Systems.

Complications

ECMO/ECLS therapy is associated with a high mortality rate specified as being between 47 % and 61 % in a metaanalysis [18]. Whether and to what extent this is to be attributed to the general condition of the patient and the patient's comorbidities or to technical and therapy-associated procedures remains unclear.

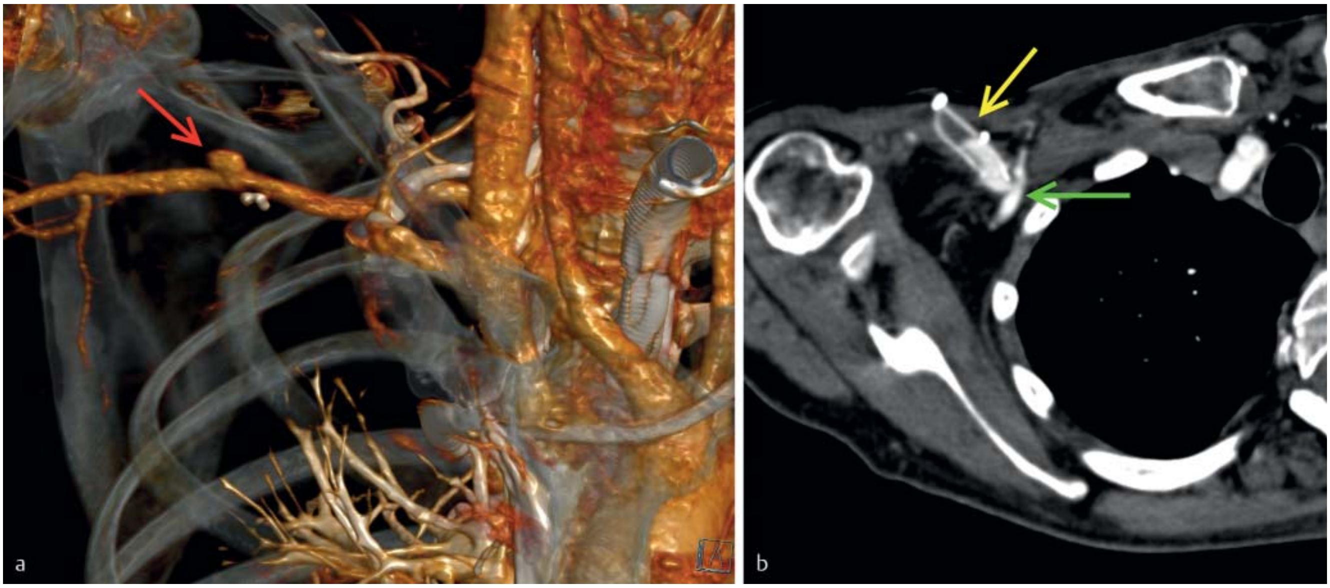
Systemic reaction to extracorporeal surfaces

In the initial days after connection of the ECMO/ECLS, the critical disease of the patient and the contact of the blood with the large, non-endothelial foreign surfaces of the extracorporeal system result in a systemic, complement-mediated, inflammatory reaction and activation of coagulation and fibrinolysis [6, 7]. This can be expressed in the form of increased vasodilation with pleural effusion, ascites, and anasarca as well as worsening of acute pulmonary failure. Restrictive fluid therapy in the initial days improves pulmonary function. Plain radiographs of the thorax show initial worsening of pulmonary function with increasing interstitial-alveolar pulmonary edema to the complete presentation of "white lung" (► **Fig. 3**). Clinical examination and an ultrasound of the abdomen confirm anasarca and ascites [9, 19].

A differentiation is made between technical and patient-related systemic complications in the case of the following additional risks [9, 20].

Cannula positioning

When positioning the ECMO/ECLS cannulas, vessel injury with dissection or bleeding can occur. Local puncture-related complications can typically be diagnosed bedside via ultrasound.



▶ **Fig. 5** Postoperative complications after removal of ECLS: Pseudoaneurysm of the subclavian artery (red arrow) **A**; retained arterial cannula fragment (yellow arrow) with a persisting arterial fistula to the subclavian artery (green arrow) **B**.

Cannula position

Projection radiography is used to ensure that the cannulas are in the correct position. Therefore, depending on the cannulation site, both chest X-rays and plain films of the abdomen are necessary [16, 19].

If the tips of the two cannulas are too close together in veno-venous ECMO, the blood primarily flows through the extracorporeal circuit from one cannula to the next so that the pulmonary circulation and thus also the systemic circulation primarily receive insufficiently oxygenated blood due to the recirculation [5, 13, 16, 17] (▶ **Fig. 4**).

If the arterial cannula in ECLS is positioned in the ascending aorta, the afterload is increased so that left ventricular pump failure can occur. If the position of the arterial cannula is too distal in the descending aorta, the oxygen supply of the coronary arteries and the extra- and intracranial arteries can be reduced [5]. Every change in the position of cutaneously fixed cannulas in projection radiography is suspicious for the complication of cannula dislocation [11, 16].

After successful therapy and removal of ECLS systems, a pseudoaneurysm can form as a complication in the region of the previous arterial puncture site. As an extremely rare complication, torn off hose segments can remain in situ (▶ **Fig. 5**).

Thrombus formation in the extracorporeal system

The most common mechanical complication is thrombus formation in the extracorporeal circuit. Thrombi form primarily at the oxygenator or at the hose connection points, particularly in the case of contraindicated systemic anticoagulation [5]. Thrombi can result in dysfunction of the oxygenator. However, they can also be rinsed into the systemic or pulmonary circulation.

Rare technical complications

Technical failure of the membrane oxygenator in the case of an increase in thrombus formation or failure of the pump can occur in the case of a long treatment duration so that component replacement must be performed on an emergency basis [5, 20].

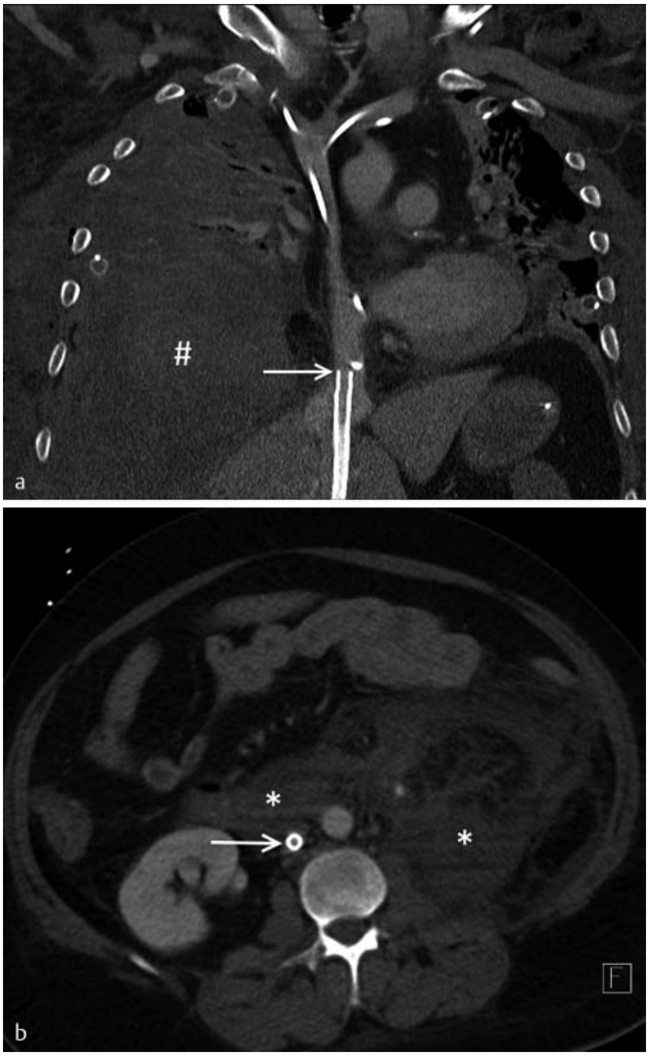
Extremity ischemia

Depending on the diameter of the implanted arterial cannula, ischemia of the dependent extremity segments can occur. An additional arterial cannula can be inserted on a prophylactic basis for perfusion of the distal segments [5, 19]. In addition, the risk of an arterial vascular occlusion with an increase in appositional thrombus formation, particularly arising from existing arteriosclerosis, is increased. In a metaanalysis, vascular complications with extremity ischemia are described in up to 17 % of patients [21].

Bleeding

Bleeding complications are the most common complications during ECMO/ECLS therapy [9, 11, 15]. The causes have a multifactorial genesis. Intensive care patients have an imbalance between pro- and anticoagulatory factors, resulting in the presence of thrombocytopenia, for example. The connected extracorporeal circuit results in thrombocyte activation, an inflammatory reaction, and consumption of coagulation factors and can ultimately result in disseminated intravascular coagulation (DIC). Hemolysis is also a possible complication. To prevent embolisms, systemic anticoagulation is necessary. The implanted venous and/or arterial vascular accesses also have a large diameter [7]. Cannula-associated bleeding can be an indication of loosening or dislocation of the cannulas. Oozing hemorrhage from the cutaneous or subcutaneous vessels often occurs [15].

Primary sonographic diagnosis is performed in the intensive care unit. Fatal bleeding can be ubiquitous. A greater occurrence

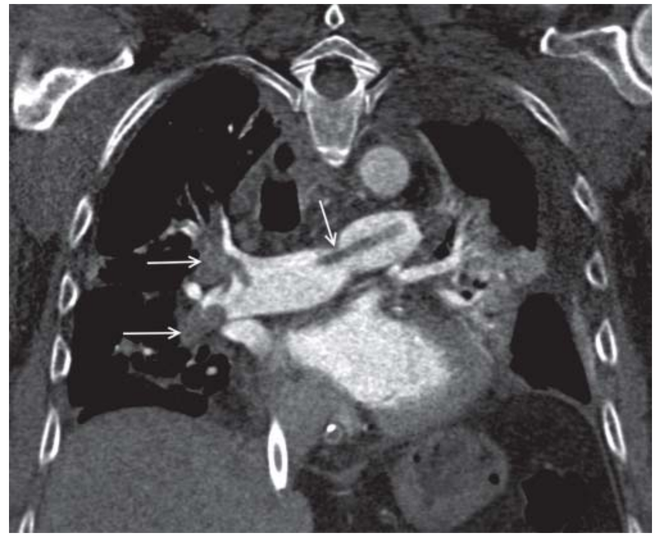


► **Fig. 6** Bleeding complications like hematothorax (#) **A** or retroperitoneal hematoma (*) during ECMO/ECLS therapy **B**; outflow cannula – white arrow.

of postoperative bleeding, particularly after thoracotomy, has been observed [15]. Intracerebral bleeding is typically extensive and necessitates emergency neurosurgery. Spontaneous bleeding into the parenchymal organs, thorax or peritoneum has been observed (► **Fig. 6**). Gastrointestinal bleeding occurs in the case of esophagitis, gastritis, or gastroduodenal ulcers. Therefore, stress prophylaxis in the intensive care unit is important. Damage to the mucosa during intensive care treatment, e. g. during placement of a feeding tube or tracheal cannula, can cause bleeding. Computed tomography and an absolute emergency indication are often necessary to diagnose bleeding complications [7].

Venous thromboembolisms

The risk of thrombus formation is increased during ECMO/ECLS therapy due to the above-described inflammatory reaction with activation of the coagulation cascade [7]. Thrombi can form in the extracorporeal circuit (see above). Thrombus formation in the venous vascular system is described in up to 10 % of patients



► **Fig. 7** Bilateral pulmonary artery embolisms (white arrows) secondary to ECMO therapy.

[18]. The rinsing of thrombi into the systemic circulation can result in pulmonary artery embolisms or stroke (► **Fig. 7**). Peripheral thrombus formation is primarily diagnosed with ultrasound. Computed tomography is needed to diagnose thrombi that have been carried to the periphery or into the supraaortic vessels. An ischemic stroke can be treated, for example, primarily with interventional neuroradiology via thrombectomy depending on the affected vascular segment.

Left heart insufficiency and aortic stasis

In the case of limited left heart function, stasis of the arterial blood in the left ventricle, the left ventricular outflow tract, and the ascending aorta can occur [22]. Echocardiographic exclusion of thrombi is complicated by the often postoperatively limited acoustic window so that computed tomography is needed for further diagnosis. However, detection of thrombi with computed tomography can also be complicated by a possible lack of contrast enhancement of the left heart.

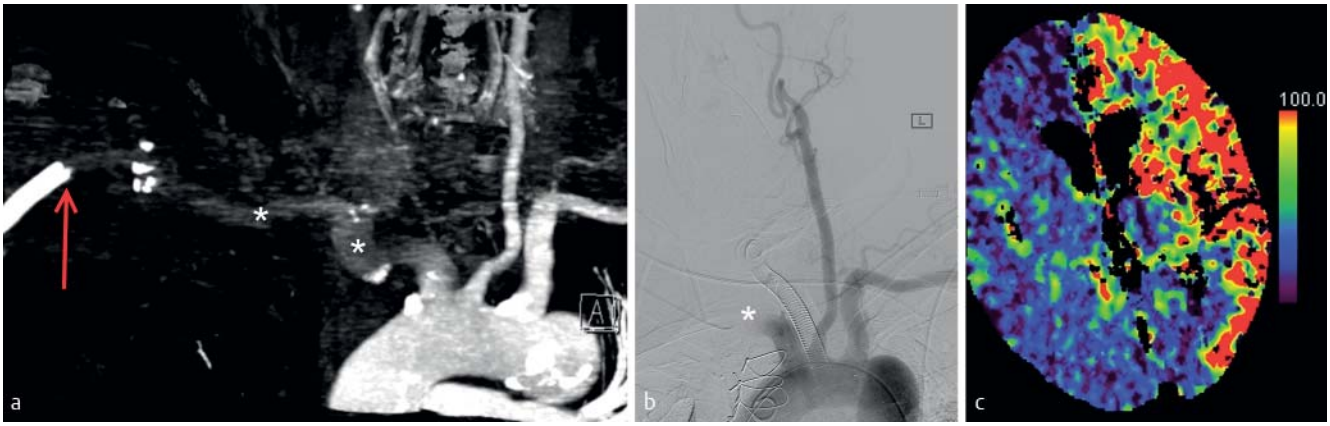
Neurological complications

Neurological complications frequently occur during ECMO/ECLS therapy with the incidence in the literature fluctuating greatly (8 – 50 %) [18, 23]. The long-term result for patients is limited by the neurological consequences [23].

Due to the systemic anticoagulation, there is an increased risk of cerebral hemorrhage during ECMO/ECLS therapy. Cerebral infarcts arise from thrombotic or air microembolisms or occur on a territorial basis due to large thrombi. As a result of a poor cardiac ejection fraction or therapy-associated acidosis, the development of hypoxic brain damage is possible. Further diagnosis via CT angiography and CT perfusion can be complicated by the position of the cannula in ECLS.

Organ failure

With a rate of 52 %, kidney failure that requires dialysis is a common complication [18]. This must be taken into consideration in



▶ **Fig. 8** Pseudo-filling defect of the right subclavian (*) and carotid arteries caused by ECLS inflow in the right subclavian artery (red arrow) (**A** – CT angiography, **B** – conventional angiography). Consecutive right hemispheric perfusion deficiency marked by reduced CBF **C**.

the case of intravenous contrast agent application during CT. Liver failure is seen as a complication in up to 16 % of patients.

Infections

The risk of infection with bacterial pneumonia (33 %) or sepsis (26 %) is often higher due to the condition of the often critically ill patients undergoing respiratory therapy [18].

Imaging

Initial venous cannulation is typically performed interventionally under ultrasound guidance, while peripheral arterial cannulation can be performed interventionally as well as surgically. The central ECLS is connected surgically during thoracotomy. In the further course, echocardiography/ultrasound and projection radiography are the methods of choice for determining cannula position and cannula-associated complications in the intensive care unit.

In the case of computed tomography, attention must be paid to hemodynamic changes caused by the extracorporeal circuit. Peripheral-venous contrast agent administration in the drainage area of the venous outflow cannula should be avoided to reduce dilution effects as a result of passage through the ECMO or ECLS system. Therefore, contrast agent injection is typically performed via a central venous access in intensive care patients.

In the case of veno-venous ECMO, the oxygenated blood is conducted through the extracorporeal circuit in an antegrade manner into the right atrium and mixes there with the central-venously injected contrast agent. This non-contrast-enhanced "competitive flow" can be compensated by increasing the contrast agent volume and the contrast agent flow rate or by temporarily reducing the ECMO flow rate. To avoid the uncertainties of contrast agent timing, additional use of a bolus tracking mechanism in the body region to be examined is possible. However, the start of a possibly necessary manual examination in the event that the previously defined threshold value is not reached must be factored in [11, 14, 25, 26].

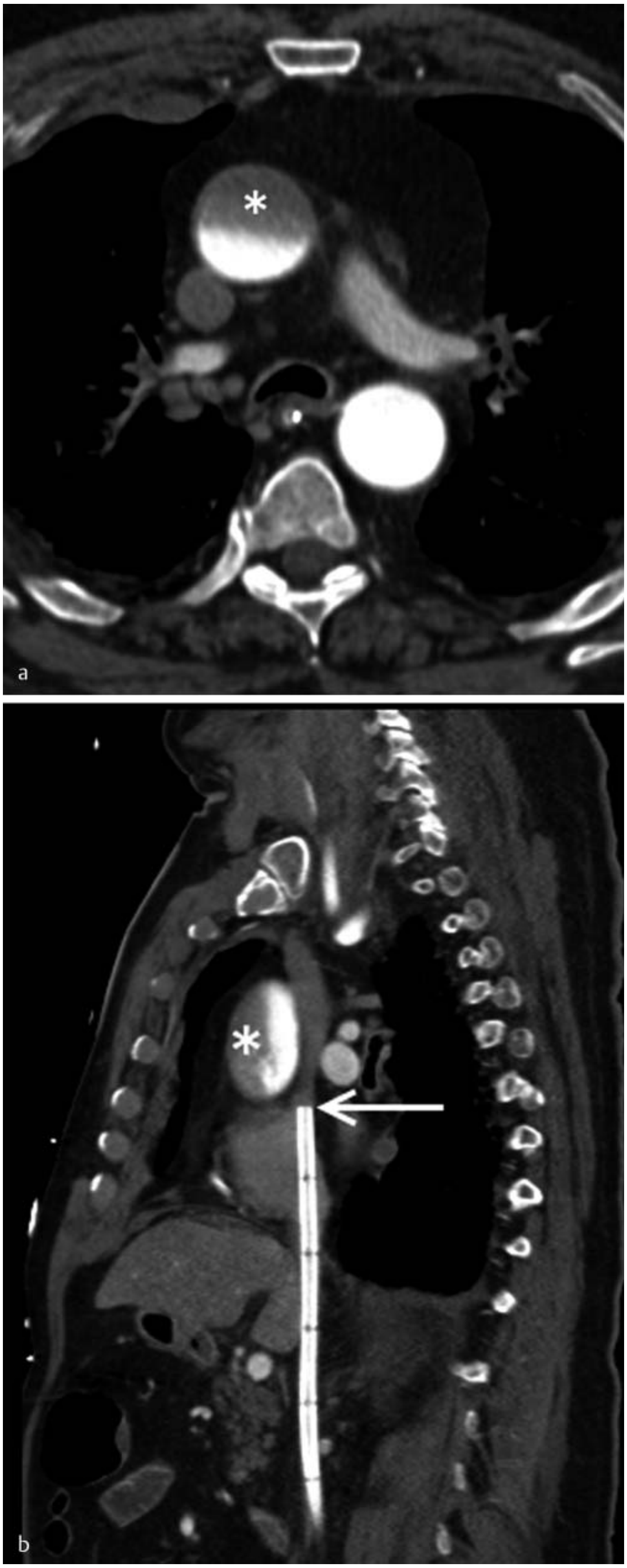
When using veno-arterial ECLS, the contrast enhancement of vessels depends on the preserved cardiac pump function [25 – 27]. The oxygenated blood from the extracorporeal circuit flows back into the aorta. The contrast agent injected in central venous manner passes the pulmonary circulation in the case of still (partially) maintained cardiac pump function and flows in an antegrade manner into the aorta so that mixing of contrast-enhanced "venous" antegrade blood and non-contrast-enhanced extracorporeal arterial blood occurs. However, if cardiac pump performance is so limited that the contrast agent is already being conducted in a retrograde manner through the venous drainage cannula into the extracorporeal circuit, there is a lack of contrast enhancement of the distal pulmonary vascular system and the left heart. The contrast agent is then conducted through the extracorporeal circuit directly into the arterial system. In the arterial CT phase, the following contrast enhancement phenomena can thus occur:

Arterial pseudo-filling defect

In the case of preserved cardiac pump function, the corresponding artery appears completely hypodense due to the retrograde return of the non-contrast-enhanced arterial blood from the extracorporeal circuit so that the impression of a vascular occlusion can be given. This must be taken into account in particular in the case of suspicion of a stroke since, for example, in the case of inflow into the right axillary artery, the impression of a vascular occlusion of the common carotid artery and the vertebral artery as well as a perfusion deficit in CT perfusion can be given (▶ **Fig. 8**).

Arterial pseudomembrane

If the CT scan is started during peripheral ECLS before complete contrast enhancement of the left heart chambers has occurred, the different densities between the non-contrast-enhanced blood and the contrast-enhanced blood can result in a sedimentation phenomenon in the aorta so that the impression of a dissection membrane or an intramural hematoma can be given [27]. This phenomenon occurs in particular during inflow of the blood into the descending aorta with consecutive retrograde flow into the ascending aorta (▶ **Fig. 9**). This is thus to be taken into consideration in particular in the case of limited cardiac pump function and bolus tracking with the region of interest (ROI) in the descending thoracic aorta. In the venous or "late" phase, this phenomenon is



▶ **Fig. 9** Contrast-enhanced CT with pseudo-layering (*) in the ascending aorta during arterial phase imaging under transfemoral ECLS (white arrow) **A**, **B**.

eliminated as a result of the recirculation and homogenization of the contrast enhancement [11, 14, 27].

Contrast enhancement defect of the left heart and the pulmonary vascular system

In the case of severely compromised heart function, a high extracorporeal veno-arterial flow must maintain systemic perfusion. Due to the high (retrograde) aortic resistance, contrast enhancement of the left heart and possibly also of the pulmonary vascular system does not occur (▶ **Fig. 10**). Contrast agent is drained with the venous blood through the vena cava and is returned directly to the aorta so that it is difficult to rule out a pulmonary artery embolism [11, 24 – 26].

A reduction of the ECLS flow of the pump or a complete pause by the cardiac technician can help to prevent arterial contrast enhancement phenomena [9, 18, 25] provided that the clinical condition of the patient will allow this for the duration of the examination. Alternatively, it is possible to inject the intravascular contrast agent directly into the arterial ECLS cannula connected to the membrane oxygenator. However, due to potential risks, such as air embolisms, this should be viewed critically [11, 19]. A supplementary late phase with weaker but homogeneous contrast enhancement can often prove the above-mentioned phenomena to be artificial. The higher radiation exposure is usually of secondary importance compared to the risk of the acute situation [14]. Moreover, an additional ultrasound examination can help to differentiate between an artifact and a thrombus.

In rare cases, diagnostic and therapeutic angiography can be indicated for further diagnosis and treatment, for example in the case of stroke diagnosis and therapy. Depending on the cannulation, flow artifacts can also occur so that an arterial pseudo-filling defect can also be observed and should not be misinterpreted as vascular occlusion. In the case of therapeutic interventions, the insertion of stents against the arterial flow through the extracorporeal system is complicated by the counter-current. Unintentional displacement of the device must be avoided.

Summary

As a result of the rise in ECMO/ECLS treatment and the associated complications, radiological diagnosis with ultrasound, projection radiography and computed tomography has become increasingly important. Knowledge of the different types of cannulation and hemodynamic changes is essential for intensive care physicians, cardiac technicians and radiologists for optimal interdisciplinary planning and interpretation of examinations.

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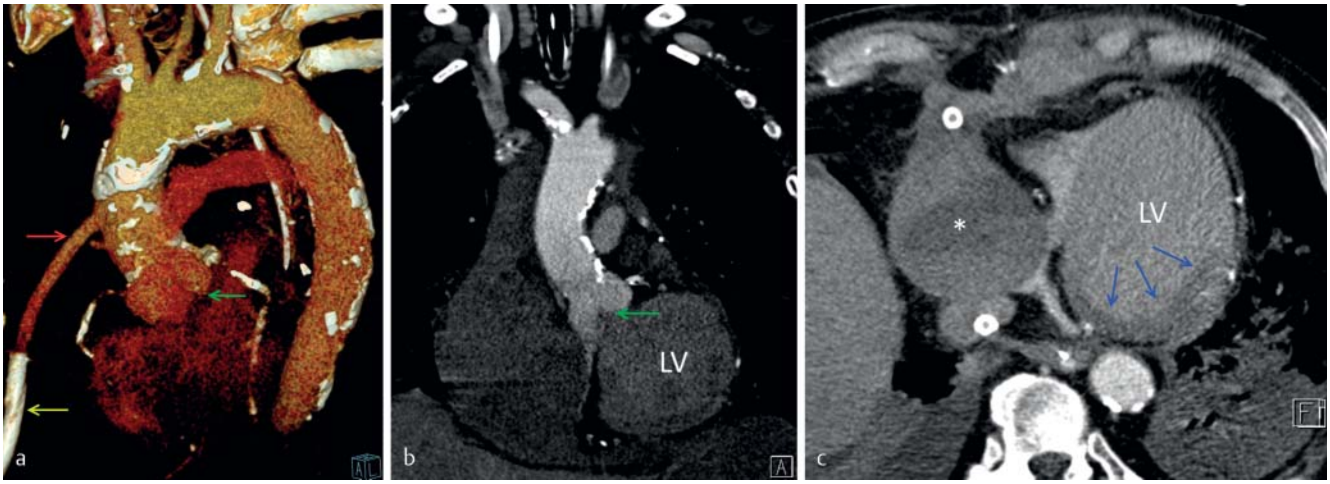

▸ **Fig. 10** Filling defect of the left heart (green arrow) caused by retrograde contrast enhancement of the ascending aorta during ECLS therapy **A**, **B** with high extracorporeal flow rate. Pericardial hematoma compressing the right atrium and ventricle (*) and myocardial infarction (blue arrows) **C**; inflow cannula – red and yellow arrows.

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