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Evolution of distal limb perfusion management in adult peripheral venoarterial extracorporeal membrane oxygenation with femoral artery cannulation

Jorik Simons,[1,2,3] Barend Mees,[3,4] Graeme MacLaren,[5] John F Fraser,[6] Akram M Zaaqoq,[7] Sung-Min Cho,[8,9] Bhavesh M Patel,[10] Daniel Brodie,[11] Jan Bělohlávek,[12] Mirko Belliato,[13] Jae-Seung Jung,[14] Leonardo Salazar,[15] Paolo Meani,[1] Silvia Mariani,[1,16] Michele Di Mauro,[1,3] Demetris Yannopoulos,[17] Lars Mikael Broman,[18,19] Yih-Sharng Chen,[20] Jordi Riera,[21] Walther NKA van Mook[2,22,23] and Roberto Lorusso[1,3]

Abstract

Limb ischaemia is a clinically relevant complication of venoarterial extracorporeal membrane oxygenation (VA ECMO) with femoral artery cannulation. No selective distal perfusion or other advanced techniques were used in the past to

[1]Department of Cardio-Thoracic Surgery, CARIM School for Cardiovascular Diseases, Heart and Vascular Center, Maastricht University Medical Center, Maastricht, The Netherlands
[2]Department of Intensive Care Medicine, Maastricht University Medical Center, Maastricht, The Netherlands
[3]Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht, The Netherlands
[4]Department of Vascular Surgery, CARIM School for Cardiovascular Diseases, Heart and Vascular Center, Maastricht University Medical Center (MUMC+), Maastricht, The Netherlands
[5]Cardiothoracic Intensive Care Unit, National University Health System, Singapore
[6]Critical Care Research Group, The Prince Charles Hospital, University of Queensland, Brisbane, QLD, Australia
[7]Department of Anesthesiology, Division of Critical Care, University of Virginia, Charlottesville, VA, USA
[8]Division of Neuroscience Critical Care, Department of Neurology, School of Medicine, Johns Hopkins University, Baltimore, MD, USA
[9]Division of Neuroscience Critical Care, Department of Anesthesiology and Critical Care Medicine, School of Medicine, Johns Hopkins University, Baltimore, MD, USA
[10]Department of Critical Care, Mayo Clinic Arizona, Scottsdale, AZ, USA
[11]Division of Pulmonary and Critical Care Medicine, Department of Medicine, School of Medicine, The Johns Hopkins Hospital, Baltimore, MD, USA
[12]2nd Department of Medicine - Department of Cardiovascular Medicine, General University Hospital in Prague, Prague, Czech Republic
[13]SC AR 2 Anestesia e Terapia Intensiva Cardiotoracica, Foundation IRCCS Policlinico San Matteo, Pavia, Italy
[14]Department of Thoracic and Cardiovascular Surgery, Korea University Medicine, Seoul, Republic of Korea
[15]Department of Intensive Care, Fundación Cardiovascular de Colombia, Bucaramanga, Colombia
[16]S. Gerardo Hospital is the hospital of the departmen, Monza, Italy
[17]Center for Resuscitation Medicine, University of Minnesota Medical School, Minneapolis, MN, USA
[18]Department of Pediatric Perioperative Medicine and Intensive Care, ECMO Centre Karolinska, Karolinska University Hospital, Stockholm, Sweden
[19]Department of Physiology and Pharmacology, Karolinska Institutet, Stockholm, Sweden
[20]Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan
[21]Department de Medicina Intensiva, Vall d'Hebron Institut de Recerca, SODIR, Hospital Universitari Vall d'Hebron, Barcelona, Spain
[22]School of Health Professions Education, Maastricht University, Maastricht, The Netherlands
[23]Academy for Postgraduate Medical Training, Maastricht University Medical Center, Maastricht, The Netherlands

Corresponding author:
Jorik Simons, Department of Cardio-Thoracic Surgery, CARIM School for Cardiovascular Diseases, Heart and Vascular Center, Maastricht University Medical Center, P. Debyelaan 25, Maastricht 6229 HX, The Netherlands.
Email: jorik_simons@hotmail.com

maintain adequate distal limb perfusion. A more recent trend is the shift from the reactive or emergency management to the pro-active or prophylactic placement of a distal perfusion cannula to avoid or reduce limb ischaemia-related complications. Multiple alternative cannulation techniques to the distal perfusion cannula have been developed to maintain distal limb perfusion, including end-to-side grafting, external or endovascular femoro-femoral bypass, retrograde limb perfusion (e.g., via the posterior tibial, dorsalis pedis or anterior tibial artery), and, more recently, use of a bidirectional cannula. Venous congestion has also been recognized as a potential contributing factor to limb ischaemia development and specific techniques have been described with facilitated venous drainage or bilateral cannulation being the most recent, to reduce or avoid venous stasis as a contributor to impaired limb perfusion. Advances in monitoring techniques, such as near-infrared spectroscopy and duplex ultrasound analysis, have been applied to improve decision-making regarding both the monitoring and management of limb ischaemia. This narrative review describes the evolution of techniques used for distal limb perfusion during peripheral VA ECMO.

Keywords
distal perfusion, extracorporeal membrane oxygenation, limb perfusion, venoarterial

Background

Since its development in the early 1960s, extracorporeal membrane oxygenation (ECMO) has become increasingly used in the last decades for cardiac and pulmonary support of critically ill patients.[1] Besides neurological, renal, haemorrhagic, thrombotic, and infectious complications, limb ischaemia is a well-recognised and clinically important adverse event during peripheral venoarterial (VA) ECMO with femoral artery cannulation, with a risk of 10–30%.[2] Besides the immediate negative impact on early patient management and outcome, its long-term consequences on quality of life are a major concern, for example, due to the possible need for amputation.[2–6] Limb ischaemia and/or major vascular complications are independently associated with mortality in patients with femoral arterial cannulation,[7–11] although some studies showed no increase in mortality in patients who developed clinically relevant limb ischaemia.[9,12,13]

Minimizing the risk of limb ischaemia is of considerable importance and several techniques have been documented to reduce or even prevent its occurrence. Although these techniques were initially developed in the early 1990s, there has been considerable evolution since then.[14,15]

The aim of this narrative review is to provide an overview of the evolution of distal limb perfusion in peripheral VA ECMO, to describe the efficacy of various techniques, to discuss novel techniques, and elaborate on the current guidelines with regards to the management of distal limb perfusion during peripheral VA ECMO.

Historical evolution

Early days of distal limb perfusion

In the early days of ECMO, no distal perfusion cannulas (DPCs) or other techniques were used to maintain distal limb perfusion. Distal limb perfusion was preserved by selecting an individually tailored cannula size which allowed sufficient arterial flow around the cannula towards the distal limb (Figure 1, panel (a)).[16] Indeed, smaller cannulas (15–17 French (Fr)) were associated with less limb ischaemia and selective distal limb perfusion was thus not always needed.[17,18] However, smaller cannulas have a higher resistance, leading to increased shear stress (e.g., a risk factor for haemolysis and platelet activation), and limiting maximum blood flow.[19,20] Some centres still perform an intervention only in case of distal limb hypoperfusion, which is often delayed either in diagnosis or resolution, leading to major complications, like fasciotomy or even amputation. Besides the use of the smallest cannula possible, due to lack of selective distal limb perfusion, limb ischaemia remained a significant risk during VA ECMO; one of the first articles on the incidence of limb ischaemia during peripheral VA ECMO reported rates of 70% and thus indicated that novel and appropriate preventive techniques were required.[21]

The advent of distal perfusion cannula

Greason et al. first described the use of the contemporary DPC in 1995: an 8.5 Fr Arrow-Flex cordis catheter (Teleflex Incorporated, Wayne, PA, USA), placed in the superficial femoral artery (SFA) and connected to the ECMO circuit (Figure 1, panel (b)).[22] Cannulation was done either percutaneously via Seldinger technique or via direct surgical access. The set-up proposed by Greason et al. accomplished 159 ± 13 mL/min blood flow towards the distal part of the limb which provided the theoretically required distal limb flow of 150 mL/min.[23,24] Some centres used the same principle but with smaller DPCs.[25,26]

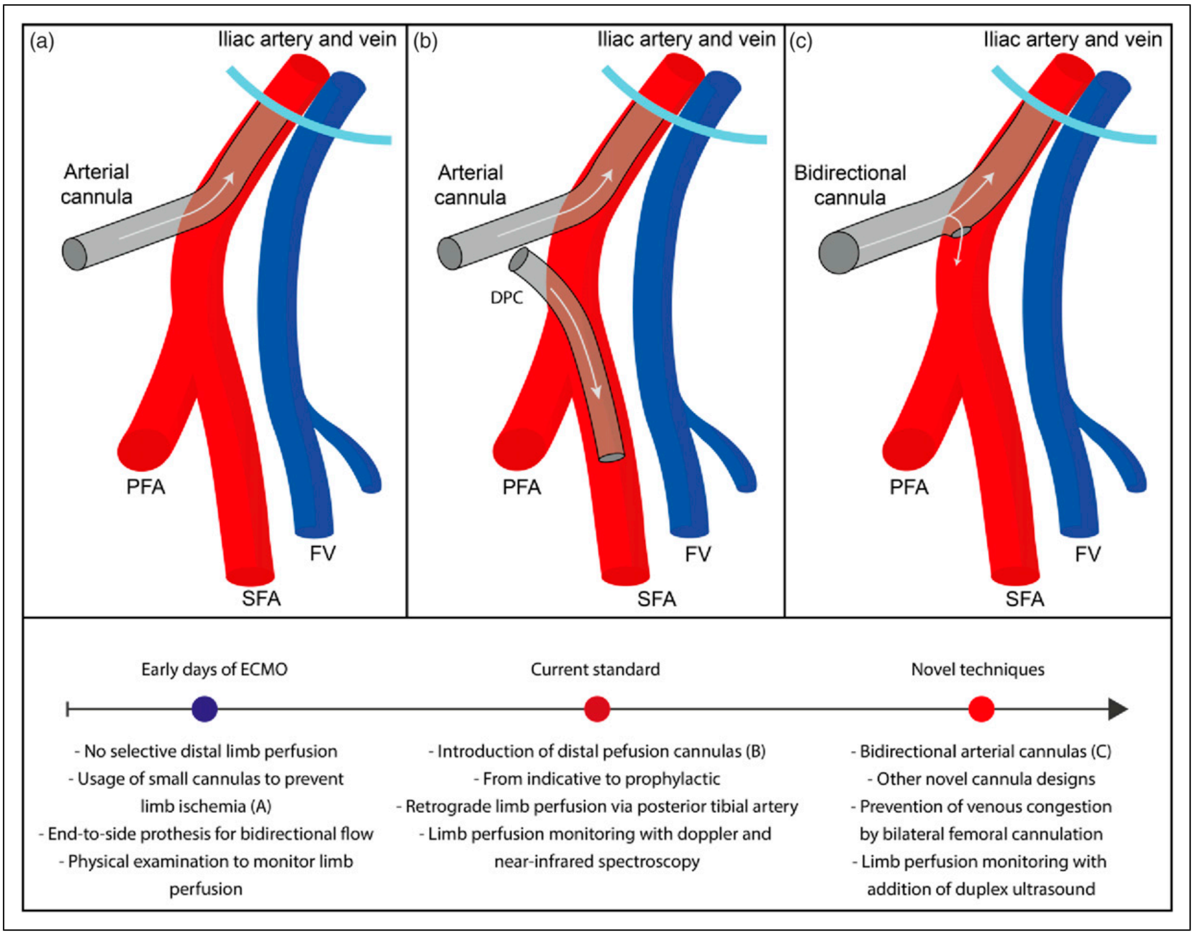

Figure 1. Global overview of the evolution of distal limb perfusion in peripheral VA ECMO. Panel (a): in the early days of peripheral VA ECMO, no selective distal limb perfusion was performed and clinicians relied on blood flow coaxial to the cannula thus cannula sizing was limited. Panel (b): the usage of a DPC to selectively perfuse the superficial femoral artery is current practice in most centres. Panel (c): recent novel cannulas are designed with an integrated distal perfusion 'hole' to provide flow to the distal part of the limb. Note: venous cannulas not displayed. Abbreviations: DPC: distal perfusion cannula; PFA: profunda femoris artery; SFA: superficial femoral artery; FV: femoral vein.

Mohite et al. reported limb ischaemia rates for both the use of 6-8 Fr introducer sheaths as DPCs as 10–12 Fr paediatric cannulas.[27] The risk for limb ischaemia and ischaemia requiring surgical intervention, was significantly higher with the use of the introducer sheaths compared to the cannulas (30.6% vs 15.6% and 15.4% vs 6.25%, respectively). Although these results were based on a retrospective cohort, and thus may be subject to inherent bias. Guidelines from ELSO (the Extracorporeal Life Support Organisation) recommend a short 6–8 Fr armoured DPC in combination with short tubing using a male-to-male connector to the arterial cannula, with a target flow of 100 mL/min.[18] The use of larger and longer DPCs is not recommended since these may be associated with vascular trauma and spasm.[18]

Evolution of DPC

The technique proposed by Greason et al. has several shortcomings. The first relates to the two 90-degree connections (the first from the arterial cannula stopcock, and the second at the introducer). The second connection and the relatively small catheter used may be the source of thrombosis or higher shear stress to blood components. Also, monitoring of blood flow may be more cumbersome due to the small calibre of the tubing, although there are flow measuring probes available. A new method was then proposed by our group using a paediatric aortic cannula (Medtronic Inc, Minneapolis, MN, USA). This configuration allows the use of larger sizes (9 or 11 Fr) which are tailored to patient body size. Furthermore, the second 90-degree connection is avoided providing a fully armed cannula with reduced

Figure 2. Distal perfusion using a paediatric aortic cannula which provides several advantages, including reinforcement, and direct connection to the perfusing tubing, thereby avoiding a 90-degree connection.

risk of kinking (Figure 2). Finally, such a connection allows an easier flowmeter allocation and, therefore, a better distal flow monitoring. However, one participating centre in this work previously reported increased fibrin deposits and clots in coated ¼-inch tubing using paediatric ECMO cannulas as a DPC.[28]

Evidence for the use of DPC

In a meta-analysis evaluating the efficacy of DPCs in adult VA ECMO, the use of a DPC was associated with an absolute risk reduction of 15.7% (9.7 vs 25.4%) and a risk ratio of 0.41 ($p < .01$) for limb ischaemia compared to a no-DPC approach.[29] Notably, the studies included in this meta-analysis had a higher degree of heterogeneity with regards to the selection criteria for DPC placement, which introduces a significant bias since prophylactic and rescue DPC placement are performed in substantially different clinical scenarios.[29] Also, the techniques employed varied among the included studies, although this is likely less important than the bias that resulted from the different timing of DPC placement.

The importance of prophylactic distal limb perfusion

For many years after the introduction of the DPC, definitive placement criteria for DPCs were lacking. Most centres placed a DPC only when a patient developed clinical signs of limb ischaemia (rescue placement), although some centres advocated immediate placement of a DPC in *all* VA ECMO patients, as a 'prophylactic' DPC, trying to limit the risk for reperfusion injury and fasciotomy.[30]

Kaufeld and colleagues reported evidence for the use of a prophylactic DPC in their retrospective cohort study including 307 patients of whom 77% received a DPC during open or percutaneous cannulation or in the first hour after implantation because of clinical signs of limb ischaemia.[31] Approximately one fourth of patients did not receive a DPC during cannulation due to time constraints in case of emergency or due to anatomical reasons. These patients have, of course, a higher risk for hypoperfusion. The group found a significant decrease in need for intervention due to critical limb ischaemia for the distal perfusion group: 3.4% of patients with DPC versus 21.4% of patients without DPC. Other studies, including meta-analysis, also showed evidence for prophylactic placement of a DPC.[17,32–35]

Blood pressure-guided decision-making can also be used to time initiation of DPC placement. Huang et al. measured the immediate blood pressure in the superficial femoral artery during open femoral cannulation via a 23 gauge needle.[30] If below 50 mmHg, an 8.5 Fr DPC was inserted during the same procedure. With this protocol, 34.6% of patients had an indication for distal limb perfusion and no patients developed limb ischaemia. Although the cohort was small (26 patients), the described technique is a feasible tool for decision-making regarding DPC placement. However, this technique is more applicable for open than percutaneous cannulation since an extra puncture is needed in case of percutaneous cannulation.

Although a DPC will initially supply (additional) distal limb perfusion, it can also result in hyperperfusion or venous stasis if too much distal limb flow is provided. This may lead to an increase in compartment pressure and potentially compartment syndrome.[36–38]

Current guidelines recommend distal limb perfusion to be initiated at the time of VA ECMO initiation in all

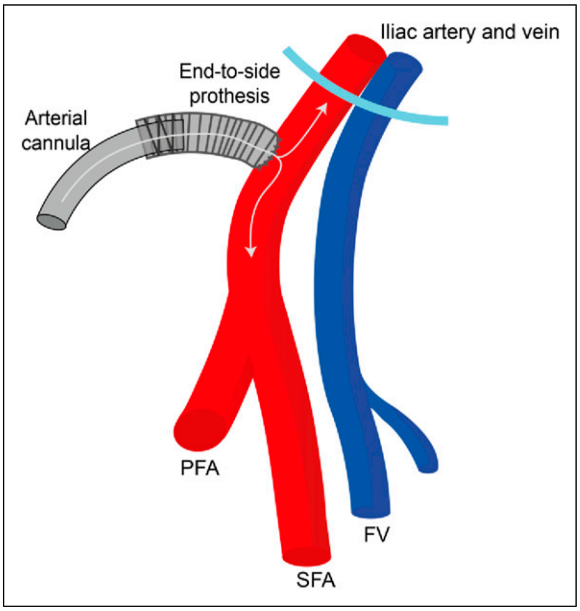

Figure 3. Schematic drawing of the end-to-side 'chimney' prothesis technique proposed by Vander Salm in 1997. The arterial cannula is inserted in the prosthesis instead of the femoral artery to provide bidirectional blood flow. Abbreviations: DPC: distal perfusion cannula; PFA: profunda femoris artery; SFA: superficial femoral artery; FV: femoral vein.

patients, although it might not always be needed with small cannulas (15–17 Fr).[18] If clinicians nevertheless decide to follow a reactive strategy for DPC placement, advanced monitoring techniques should be used to monitor limb perfusion adequacy and help decision making to perform a rescue placement.

Percutaneous versus surgical implantation of DPC

Although randomized controlled trials are not available, the currently available literature shows a trend, although not significant, towards an increased risk for limb ischaemia after percutaneous cannulation compared to surgical cannulation.[39–41] One study comparing percutaneous angiography-guided versus surgical cannulation showed a significant risk reduction in ischaemia-related adverse events for the percutaneously cannulated patients.[42] Also, a large retrospective study based on the ELSO Registry showed that percutaneous cannulation was independently associated with lower in-hospital mortality.[39]

End-to-side graft

Another technique for distal limb perfusion during peripheral VA ECMO, which was translated from its use during intraoperative cardiopulmonary bypass, is the use of an end-to-side graft or "chimney technique" (Figure 3). In 1997, Vander Salm described the use of a 10 mm polytetrafluoroethylene (PTFE) graft as an end-to-side graft after arteriotomy of the common femoral artery, onto a 24 Fr arterial cannula.[43] This method allows flow towards the proximal and distal femoral artery and thus ensures limb perfusion. A disadvantage of this technique is the limited control over the flow ratio between the retrograde flow (via the femoral artery towards the aorta) and the antegrade flow towards the limb; the relative resistance, which alters during ECMO treatment, will determine this ratio. The surgeon might create a slight curve to establish an outflow tract with preferential flow towards the aorta. Unfortunately, this approach is not suitable for emergency situations. However, converting from percutaneous cannulation to an end-to-side graft is possible, as described by Demertzis and Carrel[44] To decrease the risk for infection and bleeding, the graft can be tunnelled in a similar fashion to tunnelled grafts that are created for lower-extremity bypasses.[45] Besides, the wound may be easily oozing because the relative high pressure on the anastomotic site when high flow is required or platelet dysfunction.

Novel techniques

The 'standard' DPC technique is used by many centres around the world and is suitable for the majority of ECMO patients whereas some patients (e.g., severe peripheral artery disease, multiple devices requiring femoral access, lack of axillary artery option, or other factors preventing regular DPC placement in the SFA)[46] require a different, tailored, innovative approach.

Distal superficial femoral artery

In some circumstances, such as bleeding, obstruction/occlusion, and extreme obesity, etc., the SFA may not be accessible close to the retrograde cannula insertion. Alternative approaches might be localization of the same artery more distally. This approach includes the visualization of a functional artery by doppler ultrasound and subsequent percutaneous cannulation using a Seldinger technique (Figure 4). This technique has been utilized in several extremely obese patients (unpublished data) and may also be used as a bailout in case of complications during groin cannulation.

Figure 4. Example of more distal superficial femoral artery cannulation in a patient with persistent bleeding at the groin (transcatheter aortic valve implantation complicated by cardiac arrest and venoarterial extracorporeal membrane implantation at the transcatheter device entry site with subsequent vascular bleeding). The bleeding is controlled with a compression device, preventing insertion of the distal perfusion cannula implantation in the proximal SFA.

Femoro-femoral bypass

One of the first novel techniques described (specifically for VA ECMO) is the external femoro-femoral bypass proposed by Dosluoglu et al. in 2004 (see Figure 5). They reported two patients receiving both intra-aortic balloon pump (IABP) and peripheral VA ECMO treatment, developing limb ischaemia on the side of the ECMO cannulas in whom they accomplished adequate perfusion via a 6 mm by 40 cm PTFE femoro-femoral bypass.[47] The cross-over PTFE bypass was located outside the patient's body and thus vulnerable to infection.

Ghodsizad et al. described an endovascular crossover technique in 2018 which uses a 5 Fr Omni Flush catheter with side holes plus an end-hole that is inserted via the contralateral femoral artery and placed over the aortic bifurcation and distally from the arterial ECMO cannula.[48] This technique can be used if common antegrade selective femoral perfusion or retrograde tibial access is unsuccessful.

In case of concomitant femorally placed left ventricular unloading devices (e.g., IABP or microaxial left ventricular assist devices (MLVAD) like Impella (Abiomed, Danvers, USA)) and VA ECMO placed at the

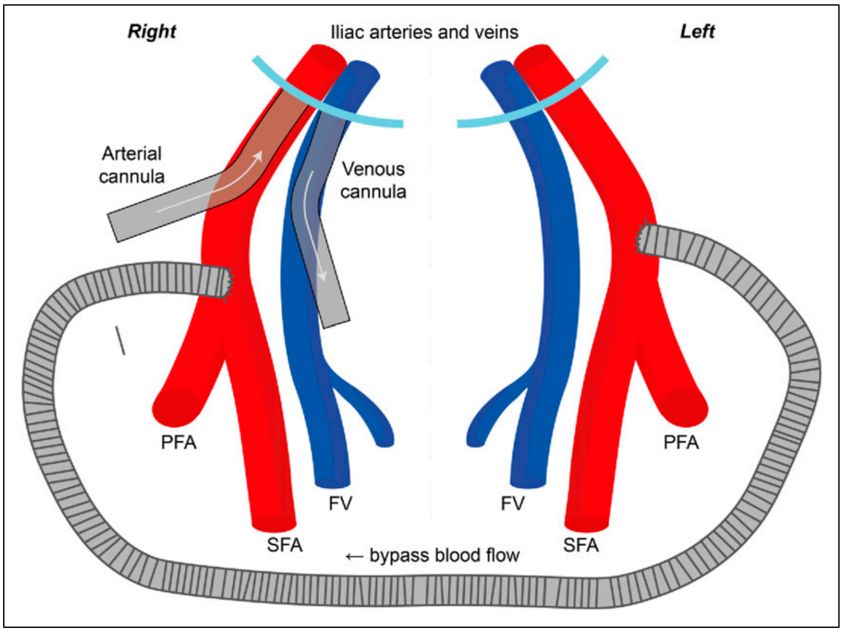

Figure 5. The femoro-femoral bypass. In the right limb the arterial and venous cannula. Abbreviations: PFA: profunda femoris artery; SFA: superficial femoral artery; FV: femoral vein.

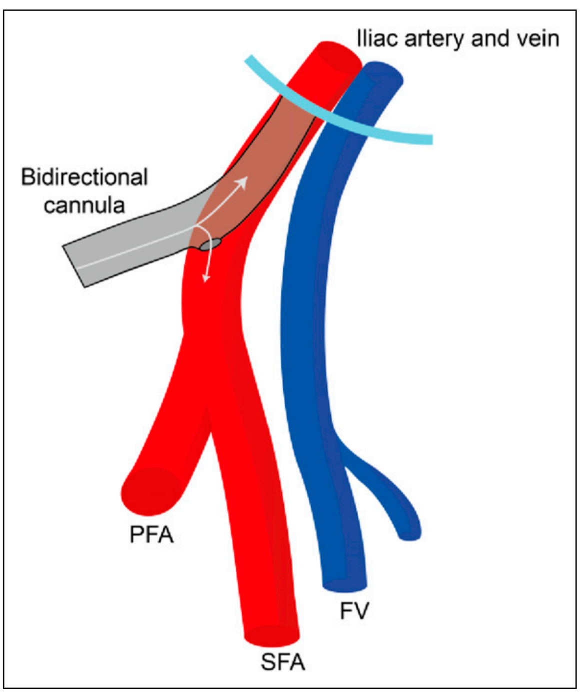

Figure 6. Schematic drawing of a bidirectional cannula in the femoral artery. Abbreviations: PFA: profunda femoris artery; SFA: superficial femoral artery; FV: femoral vein.

femoral site, the ECMO circuit can be used to deliver oxygenated blood via DPC to the side of the unloading device.[49]

Retrograde limb perfusion

Instead of antegrade femoral perfusion, retrograde perfusion of the limb via the posterior tibial artery, dorsal pedis or anterior tibial artery has also been described.[50,51] Spurlock et al. described this technique in 2011: a longitudinal incision of 5 cm posterior to the medial malleolus is made and a 6–8 Fr cannula inserted in the posterior tibial artery after arteriotomy.[51] Spurlock et al. reported 36 patients receiving this distal limb perfusion technique with good results. In only two patients, they were unable to place a posterior tibial catheter because of chronic vessel occlusion. 8.3% (n = 3) of patients developed limb ischaemia (e.g., requiring fasciotomy or amputation) after cannula insertion which was likely due to reperfusion injury since all the cannulas were inserted more than 6 h after ECMO initiation. After retrograde DPC placement, the setup managed to provide 156 ± 82 mL/min of blood flow towards the limb, which was considered adequate. Since collateral arteries were sufficient in most patients,

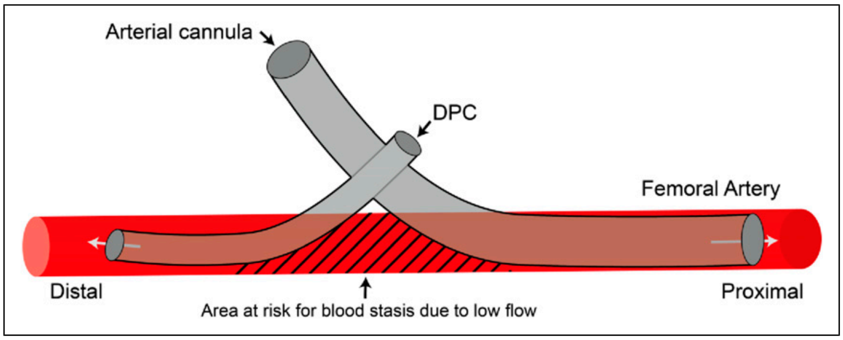

Figure 7. Schematic drawing of the femoral artery cannulated with a DPC and arterial cannula. The hatched area marks the hypercoagulable area due to low flow, caused by both cannulas. Abbreviations: DPC: distal perfusion cannula.

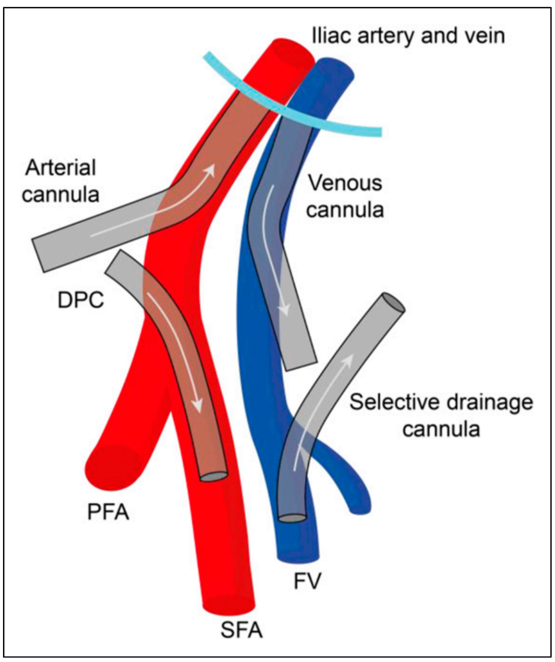

Figure 8. Arterial and venous cannulation with DPC and secondary venous drainage cannula as described by Kasirajan et al. Abbreviations: DPC: distal perfusion cannula; PFA: profunda femoris artery; SFA: superficial femoral artery; FV: femoral vein.

reconstruction of the tibial artery was only necessary in several patients. Since the distal tibial artery was ligated at the time of arteriotomy, ligating the proximal part was often sufficient.

Currently, antegrade DPC in the femoral artery is the predominant approach used worldwide. Retrograde perfusion is an alternative and might be an option if the antegrade approach is not possible.

Bidirectional cannula

In 2018, a novel bidirectional cannula with integrated distal perfusion capabilities was described in a phase 1 study.[52] The cannula incorporates an additional hole at the elbow which allows downstream distal limb perfusion (Figure 6). Although this design would avoid the need of an extra cannula, and limit the risks associated with it (e.g., line infection, bleeding, complications of puncture), there is less control over the blood flow towards the distal limb. The combination of ECMO flow, patient anatomy and haemodynamics determine the resulting distal limb flow, which may not be sufficient. Clinical equipoise is that the bidirectional cannula is associated with a low risk of limb ischaemia-related complications, and represents a safe alternative to a dedicated DPC.[15] However, experience with this cannula during mobilisation have not yet been described.

Another (theoretical) advantage of the bidirectional arterial cannula is the reduced risk for thrombus formation in the femoral artery between the proximal and distal cannula. When using an arterial cannula in combination with a (percutaneously placed) DPC, a low-flow segment at risk of thrombosis formation is created between the cannula and the DPC (see Figures 7).

Vasodilators

Vasodilators are used in cases of suspected arterial vasospasm due to wall shear stress, catecholamine release, and a proinflammatory state by cytokine secretion and platelet activation, for example, due to the cannula placed in the vessel. Arroyo et al. used a combination of 1 mg/mL lidocaine, 0.1 mg/mL nitroglycerin, and 0.25 mg/mL verapamil, based on previous experience with vasospasm in radial arteries during coronary angiography.[53] This multimodal medical approach, particularly calcium blockers and nitrate derivatives, may offer longer and superior vasodilation than single agents or other combinations. The group described using two 5 mL boluses of the aforementioned cocktail, to treat patients with suspected arterial vasospasm, after ruling out any other form of obstructive factors, for example, atherosclerosis, thrombi, dissection, or distal embolization.

Microaxial left ventricular assist devices and ECMO

With the introduction of the MLVAD, a series of trans-aortic left ventricular assist devices became available with large size femoral introducers ranging from 13 to 23 Fr. These introducers obstruct, at least partially, the femoral artery, thus potentially causing limb ischaemia. The reported risk for limb ischaemia during MLVAD is approximately 10%.[54] When using concomitant MLVAD and VA ECMO, the ECMO circuit can be used to vent off a DPC at the side of the MLVAD. In case of MLVAD treatment without this venting option, multiple techniques are described to perfuse the limb at risk of limb ischaemia. Besides venting off the sheath side port in an antegrade direction to the ipsilateral limb, and a femo-femoral crossover technique, the radial artery has also been used as a donor site to supply oxygenated blood to a limb at risk.[55] Richarz et al. published a case series of five patients treated with a femo-femoral crossover technique, consisting of two 7 Fr sheaths connected by regular tubing after development of limb ischaemia (emergency measure) and concluded it was a feasible, safe and effective treatment for limb ischaemia during MLVAD.[54] It is also possible to modify the MLVAD sheath with perfusion orifices to reduce flow resistance along the MLVAD sheath within the femoral artery, and thus optimising distal perfusion. However, this technique is novel and not widely used.[56]

Reducing limb ischaemia during VA ECMO by preventing venous congestion

Limb ischaemia during peripheral VA ECMO predominantly focusses on arterial hypoperfusion of the limb during VA ECMO. However, although less recognized, venous obstruction by the venous cannula, leading to venous stasis, and hence reduced arterial perfusion, may be equally dangerous. In 2002, Kasirajan et al. described a cannulation technique consisting of four cannulas (besides the normal arterial and venous cannula, a DPC in the femoral artery and a selective drainage cannula in the femoral vein), aiming to secure arterial perfusion and avoid venous stasis by reducing venous flow back resistance (Figure 8).[57] Russo et al. described a similar technique.[58] The strategy consisted of a regular extracting (venous) and delivering (arterial) cannula, an additional arterial DPC (10–12 Fr), and a secondary extracting venous cannula (16 Fr) draining from the distal femoral vein. This configuration was able to achieve 4–6 L/min patient flow and 1–2 L/min of distal arterial flow, which is six to 12 times the distal limb flow required for adequate leg perfusion. Providing more blood flow to the distal limb than needed is currently not considered to be a preventive measure for limb ischaemia and rather increases the risk for venous congestion leading to severe tissue damage to the leg.[59]

Bilateral cannulation

Recently, a large retrospective, propensity-matched, cohort study comparing uni-versus bilateral femoral cannulation investigated if bilateral femoral cannulation could reduce the risk for limb ischaemia.[60] The advantage of bilateral femoral cannulation would be the avoidance of the combination of arterial hypoperfusion (due to arterial obstruction by the returning cannula) and venous congestion (due to venous obstruction by the extracting cannula). Although the study showed a decrease in compartment syndrome and lower mortality rates for bilateral cannulation, it did not show an overall reduction of limb ischaemia. Due to the limitations of this study, a randomized controlled trial is needed to confirm these results investigated whether bilateral femoral cannulation ameliorates distal limb perfusion during VA ECMO.

If bilateral femoral cannulation is not feasible, insertion of a venous drainage cannula in the distal part of the femoral vein can be used. Le Guyader et al. used a 11 Fr introducer catheter to successfully treat a patient with limb edema due to venous statis during unilateral peripheral VA ECMO Table 1.[58,61]

Monitoring techniques

Optimization of distal limb perfusion extends beyond applying surgical techniques. Monitoring limb perfusion is essential during peripheral VA ECMO to recognize limb hypoperfusion and ischaemia as early as possible, since delay in treatment could lead to more severe complications. The Rutherford Classification system adopted by the European Society for Vascular Surgery provides a framework for staging and prognosis of acute limb ischemia.[62,63] In addition, in the last two decades, multiple novel monitoring techniques have been introduced in the field of ECMO.

Clinical examination

Regularly assessing distal limb perfusion in all VA ECMO patients with clinical examination is crucial. This involves the six P's: poikilothermia, pallor, pulselessness,

Table 1. Overview of the past, current, and novel preventive techniques for limb perfusion during peripheral venoarterial extracorporeal membrane oxygenation.

Measure	Preventive mechanism	Initiation	Advantages (+)/disadvantages (−)	Recommendations
None	None	− ECMO initiation/ cannula conversion	+ Single cannula use. + Surgical or percutaneous placement. + High availability. + Wide availability of cannula sizes. − No active prevention of limb ischemia. − Requiring intensive limb perfusion monitoring.	− Highly frequent to constant evaluation of limb perfusion. − Prepare strategy in case limb ischemia occurs.
Small cannula size (15 or 17 french)	Antegrade flow around the cannula.	− ECMO initiation/ cannula conversion.	+ Single cannula use. + Surgical or percutaneous placement. + High availability. − No active prevention of limb ischemia. − Requiring intensive limb perfusion monitoring.	− Highly frequent to constant evaluation of limb perfusion. − Prepare strategy in case limb ischemia occurs.
DPC	Antegrade flow via additional cannula.	− ECMO initiation/ cannula conversion. − Emergency.	+ Control over distal limb flow. + Surgical or percutaneous placement. + Wide availability of cannula sizes. + Available sizes of DPC to match patient size. + Distal superficial femoral artery placement possible. − Additional/extension of intervention. − Risk for thrombosis.	− 6–8 french armoured DPC. − Short tubing and a male-to-male connector to ECMO circuit. − Target perfusion of 100 mL/minute.
Bidirectional cannula	Antegrade flow via integrated orifice of arterial cannula.	− ECMO initiation/ cannula conversion.	+ Single cannula use. + Surgical or percutaneous placement. − Less control over distal limb flow. − Limited cannula sizes available. − No reported experiences during patient mobilisation.	− Usage of duplex ultrasound when repositioning. − Extra attention for adequate fixing of cannula. − Distal flow decreases (generally) with lower ECMO flow.

(continued)

Table 1. (continued)

Measure	Preventive mechanism	Initiation	Advantages (+)/disadvantages (−)	Recommendations
End-to-side graft	Bidirectional split of arterial cannula flow.	− ECMO initiation/ cannula conversion.	+ Single cannula use. − Easy oozing due to high pressure on the anastomis site. − No percutaneous placement. − Less control over distal limb flow.	− Hemostasis with sealant if possible.
Bilateral femoral cannulation	Optimizing arterial-venous flow competition. With or without antegrade flow via additional cannula.	− ECMO initiation/ cannula conversion.	+ Using conventional cannulation techniques. + High availability. + Wide availability of cannula sizes. + Control over distal limb flow. + Surgical or percutaneous placement. + No additional cannula required. + Additional prevention to selective arterial perfusion. − Bilateral incision. − Risk for thrombosis (in case of regular DPC). − Additional surgical time/ requirement for two people cannulation.	− Bilateral cannulation in addition to selective arterial perfusion.
DPC (retrograde)	Retrograde flow via additional cannula (in posterior tibial artery).	− ECMO initiation/ cannula conversion. − Emergency.	+ Control over distal limb flow. + Surgical or percutaneous placement. − Center experience might be limited (often not primary choice).	− Recommended in case antegrade DPC is not possible.
Femorofemoral bypass	'Stealing' blood flow originating from contralateral femoral artery.	− ECMO initiation/ cannula conversion. − Emergency.	+ Both external and endovascular approach possible. + Possible if venting of ECMO circuit is not possible. − External approach: risk for infection. − Endovascular approach: requires specialized skills.	− Last reserve technique.

Abbreviations: DPC: distal perfusion cannula; ECMO: extracorporeal membrane oxygenation.

Table 2. Overview of the recommendations by current ELSO guidelines with regards to distal limb perfusion and limb perfusion monitoring.

ELSO guideline recommendations	
Distal limb perfusion	• Short 6–8 Fr reinforced DPC. • Short tubing. • Male-to-male connector to the arterial cannula. • Target flow of 100 mL/min.
Limb perfusion monitoring	• Early detection of limb ischaemia via NIRS. • NIRS values above 50%, preferably 60%. • Constant clinical examination of limb perfusion status.

Abbreviations: DPC: distal perfusion cannula; ELSO: extracorporeal life support organisation; NIRS: near-infrared spectroscopy.

paraesthesia, pain, and paralysis of the limb. However, this examination is challenging when patients are sedated, particularly since paraesthesia, pain, and paralysis - indicators of limb ischaemia are herein not assessable. Therefore, advanced monitoring techniques are needed to evaluate distal limb perfusion.

Near-infrared spectroscopy

In 2008, Schachner et al. reported the use of near-infrared spectroscopy (NIRS) on the lower extremities in 10 patients undergoing assisted endoscopic coronary surgery or atrial septal defect repair on the arrested heart using aortic endo-occlusion catheters.[64] After clamping the femoral artery, the mean NIRS values (regional saturation, rSO_2) dropped from 61% (52–80%) to 38% (18–58%) (p = .001). Following femoral cannula placement and DPC, NIRS values increased to 71% (58–74%), providing initial evidence for NIRS's utility in femoral VA ECMO patients.

Wong et al. provided more evidence, reporting the first adult VA ECMO series with standardized NIRS monitoring of the limb.[65] The cut-off values used for DPC were NIRS values below 40% or >25% from baseline. With their protocol, they reported 35% of VA ECMO patients meeting these criteria, with a 100% restoration of NIRS values after placement or replacement of a DPC; no limb related complications were noted in the patient-group with normal NIRS values.[65] In later correspondence, the group mentioned that they had cannulated more than 160 patients via the femoral vessels and routine distal perfusion catheter placement without any loss of limb and a fasciotomy rate of less than 2%.[66] These outcomes suggest that NIRS may have a role in the routine monitoring of femoral VA ECMO patients.

In 2017, Dong Jung et al. conducted a prospective study comparing NIRS-guided DPC insertion to clinical assessment in combination with serial doppler evaluation of the dorsalis pedis and posterior tibial arteries.[67] While non-randomized, it provided evidence for the use of NIRS during VA ECMO. The study used the same cut-off values for limb ischaemia as Wong et al. NIRS was used to detect ischemia earlier than the combination of clinical assessment and intermittent doppler (mean time to perfusion: 19.6 ± 21.4 vs 42.0 ± 69.0 h). Also, no patients in the NIRS-guided DPC insertion group developed compartment syndrome while 13.9% of the control group did. These results indicate lower reperfusion damage and lower incidence of compartment syndrome due to earlier ischaemia diagnosis and intervention. Other studies' results are in accordance with this conclusion.[37,68] They also reported that only 50% of the patients in the NIRS group with loss of doppler pulse presented with clinical signs of limb ischaemia. This could be due to severe peripheral vasoconstriction and/or low pulse pressures due to non-pulsatile ECMO flow. Doppler pulse monitoring alone may be thus insufficient for VA ECMO distal limb perfusion assessment.

According to ELSO guidelines, NIRS values should be above 50%, preferably 60%, and the difference between bilateral NIRS measurements should be less than 20% to assume adequate limb perfusion.[18] When using smaller arterial cannula sizes, for example, 15–17 Fr, the guideline mentions that distal limb perfusion might not always be needed when using NIRS as a decision-making tool.

In conclusion, to prevent reperfusion damage and compartment syndrome, early NIRS-based limb ischaemia detection may be an important strategy alongside clinical assessment of the legs. This is also recommended by the current ELSO guidelines, particularly during peripheral cannulation. (Table 2).[18,69]

Duplex ultrasound analysis

Duplex ultrasound analysis has potential as an adjunct for limb perfusion monitoring during mechanical circulatory support. Nonetheless, limited research is available with regards to the application of duplex ultrasound analysis in the context of ECMO.[70,71] One study observed major waveform alterations and decreased flow velocities in the superficial femoral arteries on the cannulated side and major waveform alterations in most femoral veins on the cannulated side.[71] The results suggest that continuous flow, with a small difference between the maximum and minimum flow velocity in the femoral vein on the cannulated side, and a large vein diameter ratio, might indicate venous stasis and, thus, the risk of limb ischaemia. However, these observations stem from initial findings in a pilot investigation, which is constrained by a relatively small patient cohort.

Conclusions

Prevention, early detection, and prompt treatment of limb ischaemia is paramount during VA ECMO. Numerous techniques have been developed to ensecure distal limb perfusion with prophylactic antegrade DPC, and novel methods on the horizon. Additional (prophylactic) prevention of limb venous congestion may reduce ischaemia related complications. Monitoring limb perfusion with for example, NIRS, is highly recommended by current guidelines and enables clinicians to limit the risk for additional complications such as compartment syndrome, or amputation.

Declaration of conflicting interests

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ORCID iDs

Jorik Simons https://orcid.org/0000-0003-2037-3907
Akram M Zaaqoq https://orcid.org/0000-0003-3147-5044
Sung-Min Cho https://orcid.org/0000-0002-5132-0958
Paolo Meani https://orcid.org/0000-0001-7356-9036
Yih-Sharng Chen https://orcid.org/0000-0003-3846-8162
Jordi Riera https://orcid.org/0000-0002-1738-4448
Roberto Lorusso https://orcid.org/0000-0002-1777-2045

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Appendix

List of abbreviations

DPC	Distal perfusion cannula
DPCs	Distal perfusion cannulas
ECMO	Extracorporeal membrane oxygenation
ELSO	Extracorporeal life support organisation
Fr	French
FV	Femoral vein
IABP	Intra-aortic balloon pump
MLVAD	Microaxial left ventricular assist devices
NIRS	Near-infrared spectroscopy
PFA	Profunda femoris artery
PTFE	Polytetrafluoroethylene
SFA	Superficial femoral artery
VA	Venoarterial