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Distal Perfusion Cannulation and Limb Complications in Venoarterial Extracorporeal Membrane Oxygenation

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Abstract: The utility of distal perfusion cannula (DPC) placement for the prevention of limb complications in patients undergoing femoral venoarterial (VA) extracorporeal membrane oxygenation (ECMO) is poorly characterized. Patients undergoing femoral VA ECMO cannulation at two institutions were retrospectively assessed. Patients were grouped into those who did and those who did not receive a DPC at the time of primary cannulation. The primary outcome was any limb complication. Secondary outcomes included successfully weaning ECMO and in-hospital mortality. A total of 75 patients underwent femoral cannulation between December 2010 and December 2017. Of those, 65 patients (86.7%) had a DPC placed during primary cannulation and 10 patients (13.3%) did not. Baseline demographics, indications for ECMO, and hemodynamic perturbations were well matched between groups. The rate of limb complications was 14.7% (11/75) for the overall cohort and did not differ between groups ($p = .6$). Three patients (4%) required a four-compartment fasciotomy for compartment syndrome in the DPC group; no patients without a DPC required fasciotomy. Of the three patients who required a thrombectomy for distal ischemia, two were in the DPC group and one was in the no-DPC group ($p = .3$). Two patients (2.7%) underwent delayed DPC placement for limb ischemia with resolution of symptoms. The in-hospital morality rate was 59.5% and did not differ between groups ($p = .5$). Patients in the present study, undergoing femoral VA ECMO without preemptive DPC placement did not experience a higher rate of limb complications. However, the two patients who underwent delayed DPC placement for post-cannulation ischemia experienced resolution of symptoms, suggesting that a DPC may be used as an effective limb salvage intervention. **Keywords:** extracorporeal membrane oxygenation, distal perfusion catheter, femoral cannulation, limb ischemia. *J Extra Corpor Technol. 2018;50:155–60*

Venoarterial (VA) extracorporeal membrane oxygenation (ECMO) is a valuable salvage therapy in patients with cardiopulmonary failure from a variety of causes including post-cardiotomy shock, ischemic, and non-ischemic cardiomyopathy, and out-of-hospital cardiac arrest (1–4). However, ECMO support continues to be associated with several serious complications including a high mortality rate, neurologic events, bleeding, and infection (5–8).

A persistent issue with regard to ECMO remains the high rate of cannulation-related limb complications. Owing to ease of access, peripheral femoral cannulation for arterial inflow via a percutaneous technique is typical in patients requiring rapid mechanical support. However, the rate of limb complications associated with lower extremity cannulation ranges from 10 to 70% (9,10), with a recent meta-analysis of vascular complications demonstrating a 17% incidence of ischemia, with 10% progressing to compartment syndrome or requiring fasciotomy, and 4.7% requiring limb amputation (11). Although controversial, some literature has suggested a strong relationship between leg ischemia and in-hospital mortality (12). Potential sources of limb complications in this setting include arterial inflow occlusion due to the use of large cannulas, venous outflow obstruction secondary to large venous cannulae, arterial dissection, or global systemic vasoconstriction as a result of shock state.

A number of techniques have been proposed to attempt to prevent or manage cannulation-related limb complications,

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most importantly, the placement of an ipsilateral antegrade distal perfusion cannula (DPC) in the femoral artery at the time of primary ECMO cannulation. Although a DPC is widely used, its utility in preventing limb complications is debated, with some data advocating its use with impunity, some data showing benefit to its use in selected patients, and others demonstrating no benefit to its use (13–17). In line with this, the most recent Extracorporeal Life Support Organization guidelines do not provide consensus recommendations to reduce limb complications in patients undergoing femoral VA ECMO (18). The aim of the present bi-institutional study was to evaluate the efficacy of preemptive DPC placement in reducing limb complications for patients undergoing femoral VA ECMO cannulation.

METHODS

From December 2010 to December 2017, 85 patients underwent VA ECMO cannulation at two separate institutions. Of those, 75 patients underwent femoral VA ECMO and comprised the study cohort. Patients were separated into two distinct groups: those who underwent DPC placement at the time of primary cannulation and those who did not. Data pertaining to baseline characteristics, hemodynamic perturbations, procedural technique, and clinical events were retrospectively entered into institutional ECMO databases. The primary outcome was the incidence of limb complications related to femoral VA ECMO cannulation, defined as clinical evidence of limb ischemia, the need for fasciotomy, the need for thrombectomy, or the need for delayed DPC placement. Patients who underwent delayed DPC placement were analyzed as part of the no-DPC cohort. These patients were included in the complication rate analysis between the primary DPC group and no-DPC group. Hemorrhagic complications and routine Fogarty catheter embolectomy or femoral endarterectomy at the time of ECMO explantation were not considered to be limb complications. Secondary outcomes included in-hospital mortality, hospital length of stay, and successfully weaning off ECMO support.

Statistical Analysis

Statistical analysis was performed using Stata 15 (StataCorp LLC, College Station, TX). Continuous variables are described as mean ± SD or median with interquartile range (IQR). Categorical variables are described as percentages and were analyzed using the Chi-squared test. Continuous variables were assessed for normality using the Shapiro–Wilk test; Student's t test was used to compare the means of parametric variables and the Wilcoxon rank sum was calculated to compare non-parametric continuous variables. All of the analyses were considered statistically significant at a two-tailed p value of $<.05$.

Femoral ECMO Cannulation Technique and Management

All femoral cannulations were performed by a cardiothoracic surgeon percutaneously. After intravenous heparin administration, using the Seldinger technique, a cannula ranging in diameter from 14 to 24F depending on the patient's body surface area (BSA) was inserted into the femoral artery. The contralateral femoral vein was similarly cannulated using a 20–24F cannula.

DPC placement was performed via a percutaneous Seldinger technique, with open technique used when attempts at percutaneous access failed. All DPC cannulas were 5–8F in diameter and were placed into the ipsilateral femoral artery in an antegrade fashion, using a side port on the main femoral arterial cannula for distal arterial inflow. All patients undergoing femoral VA ECMO cannulation were considered for primary DPC insertion; however, the ultimate decision was left to the discretion of the surgeon. Factors influencing the decision to place a DPC included a known history of peripheral vascular disease, the absence of dopplerable pedal signals after cannula placement, or severely deranged hemodynamics causing global hypoperfusion. Patients who did not meet these general criteria or in whom DPC placement was not technically feasible did not receive a DPC during primary cannulation. Wire access for DPC placement may be obtained before the placement of the main arterial cannula while a palpable pulse is present or after arterial cannulation with or without ultrasound guidance.

Subsequent to successful ECMO cannulation, patients underwent hourly neurovascular assessments in the intensive care unit, with special attention to the cannulated limb. On an hourly basis, trained nursing staff evaluated the limb for temperature, color, skin changes, sensorimotor function, as well as dorsalis pedis and posterior tibial artery Doppler signals. Any documented changes in the clinical picture were immediately confirmed by the cardiothoracic surgical team and the decision to intervene was at the discretion of the surgeon. The appropriate intervention was based on the clinical findings, the time course of the event, as well as the patient's ability to tolerate a procedure. Interventions included four-compartment fasciotomy for compartment syndrome, embolectomy/thrombectomy, conversion to axillary cannulation, or the placement of a salvage DPC. Decannulation was completed in the operating room via an open cut-down technique with patch arteriorrhaphy or Fogarty embolectomy performed if indicated.

RESULTS

During the study period, a total of 75 patients underwent femoral VA ECMO cannulation at two institutions. Patients were excluded if they received venovenous ECMO or underwent primary central or subclavian/axillary artery cannulation. Of these 75 patients, 65 (86.7%) received a DPC at the time of primary ECMO cannulation and 10 (13.7%) did not.

Baseline Characteristics

Measured baseline demographics, including comorbidities as well as hemodynamic and metabolic disturbances did not differ between groups (Table 1). Most patients (74.7%) experienced cardiac arrest before cannulation with a median downtime of 25 minutes before return of spontaneous circulation. The most common indications for ECMO cannulation were ischemic cardiomyopathy (41.3%) and non-ischemic cardiomyopathy (45.3%), which included patients with cardiomyopathy secondary to chemotherapy/immunotherapy, viral myocarditis, and mediastinal lymphoma. Patients had severe hemodynamic disturbances ($p > .05$ between groups) (Table 1). Procedural characteristics with the exception of primary DPC placement also did not differ between groups (Table 2). Twenty-six patients (35.6%) underwent ECMO cannulation during a cardiac arrest (emergency cardiopulmonary resuscitation [ECPR]) ($p = .8$ between groups). The mean cannula diameter was 17.2F ± 2 for the entire cohort and cannulae sizes did not differ between groups ($p = .07$). In the case of difficulties encountered during attempted percutaneous DPC placement, operators used an open technique in six patients (8%).

Limb Complications

In this cohort of patients with well-matched measured baseline and procedural characteristics, patients without a DPC did not experience a higher rate of limb complications; however, 2/10 patients developed limb ischemia that resolved after salvage DPC placement (Table 3). Clinical manifestations of limb ischemia included the loss of pedal doppler signals, skin changes, temperature changes, and compartment syndrome. The overall rate of limb ischemia was 14.7% and did not differ between groups (9/65 patients in the DPC group and 2/10 patients in the no-DPC group, $p = .6$). Of those 11 total patients with clinical evidence of limb ischemia, nine patients underwent an intervention and two patients were not offered an intervention because of their moribund status and impending mortality. Four-compartment fasciotomy was necessary in three patients (4.6%) in the DPC group. In the first patient, the DPC was inadvertently placed in the deep femoral artery, and placement of another DPC in the superficial femoral artery under ultrasound guidance and subsequent fasciotomy resulted in limb salvage. In the second patient, the DPC was inadvertently placed in the femoral vein, with signs of lower extremity ischemia, salvaged by a cut down and placement in the femoral artery and subsequent fasciotomy. In another patient, contralateral venous obstruction related to the venous cannula was the culprit. No patient in the no-DPC group required a fasciotomy ($p = .5$). Three patients from the entire cohort required a thrombectomy for acute limb ischemia. Two of these (3.1%) were in the DPC group and one (10%) was in the no-DPC group ($p = .3$). As a salvage maneuver in patients with limb ischemia who did not undergo primary DPC placement, two patients underwent successful delayed DPC placement with resolution of ischemia while one patient underwent a failed attempt at DPC placement and subsequent conversion to axillary arterial access for ECMO also with resolution of ischemia. There were no lower extremity amputations. Red blood cell transfusion was used as a surrogate for evaluating bleeding risk in the setting of ECMO cannulation; this endpoint did not suggest that DPC insertion increased bleeding complications (median 13 units in both the DPC and the no-DPC groups, $p = .7$).

Table 1. Baseline demographics before VA ECMO.

Baseline Characteristics	Overall Cohort (n = 75)	DPC (n = 65)	No DPC (n = 10)	*p* Value
Age, years	56.3 ± 3	55.4 ± 17.3	62.1 ± 14.4	.3
Female, gender	33 (44)	28 (43.1)	5 (50)	.7
BMI	28.1 ± 4.5	27.8 ± 4.3	29.7 ± 5.7	.2
BSA	1.9 ± 0.2	1.9 ± 0.2	1.9 ± 0.2	.8
ESRD on HD	3 (4)	3 (4.6)	0 (0)	.5
Acute CRRT	12 (16)	10 (15.4)	2 (20)	.7
Cardiac arrest	56 (74.7)	49 (75.4)	7 (70)	.7
Downtime, minutes	25 (IQR 10–50)	20 (IQR 10–48)	41.5 (IQR 15–56)	.3
Indication for ECMO	–	–	–	.6
Post-cardiotomy	10 (13.3)	8 (12.3)	2 (20)	–
Ischemic cardiomyopathy	31 (41.3)	26 (40)	5 (50)	–
Non-ischemic cardiomyopathy	34 (45.3)	31 (47.7)	3 (30)	–
Hemodynamic perturbations	–	–	–	–
pH	7.2 31 ± .2	7.2 ± .2	7.2 ± .1	.9
Lactate, mmol/L	8.9 (IQR 3.9–12.3)	9.2 (5.1–12.4)	3.6 (2.0–11.1)	.2
PaO2:FiO2 ratio	94 (73–177)	94 (IQR 73–165)	137 (IQR 59–398)	.6

BMI, body mass index; ESRD, end stage renal disease; HD, hemodialysis; CRRT, continuous renal replacement therapy.

Table 2. VA ECMO technical characteristics.

Operative Characteristics	Overall Cohort (n = 75)	DPC (n = 65)	No DPC (n = 10)	*p* Value
ECPR	26 (35.6)	22 (34.9)	4 (40)	.8
Femoral arterial cannula (Fr)	–	–	–	.07
14	1 (1.4)	0 (0)	1 (4.2)	–
15	7 (9.7)	6 (12.5)	1 (4.2)	–
16	30 (41.7)	25 (50)	6 (25)	–
17	10 (13.9)	5 (10.4)	5 (20.8)	–
18	5 (6.9)	3 (6.3)	2 (8.3)	–
19	5 (6.9)	1 (2.1)	4 (16.7)	–
20	6 (8.3)	5 (10.4)	1 (4.2)	–
21	7 (9.7)	4 (8.3)	3 (12.5)	–
24	1 (1.4)	0 (0)	1 (4.2)	–
DPC technique	–	–	–	.3
Percutaneous	69 (92)	59 (90.8)	10 (100)	–
Open	6 (8)	6 (9.2)	0 (0)	–

Secondary Outcomes

In-hospital mortality after the initiation of femoral VA ECMO was 58.1% (43 of 75 patients) and did not differ between groups ($p = .6$). Most patients died from multisystem organ failure. Other secondary endpoints, listed in (Table 4), such as median hospital length of stay (18 days) and successful weaning from ECMO support (59.5%) also did not differ between groups ($p = .4$ and $p = .9$, respectively).

DISCUSSION

In patients undergoing peripheral ECMO cannulation, the incidence of limb ischemia has been linked to unsuccessful weaning of ECMO and has been shown to be an independent predictor of in-hospital mortality (12,19). DPC placement for all patients at the time of ECMO cannulation has been adopted by many centers in an attempt to decrease limb complications; however, this practice has yielded controversial results (13,16,17,20–22). In the present series, patients undergoing femoral VA ECMO cannulation who did not receive a preemptive DPC did not have a significantly higher rate of limb complications. Patients without a DPC also achieved equivalent secondary endpoints compared with patients who did receive a DPC including successfully weaning ECMO, mortality, and hospital length of stay. However, once there was clear clinical evidence of limb ischemia in patients without a DPC, our data suggest that reflexive DPC placement may be an adequate limb salvage therapy.

The incidence of vascular and limb complications associated with peripheral VA ECMO is variable but ranges from 10 to 70% (9,10). In the present study, 11 of 75 (14.7%) patients experienced a limb complication, a figure lower than most historical cohorts. Although most patients in this study underwent primary DPC insertion, this relatively low rate of limb complications should not be attributed merely to frequent DPC placement (13.9% limb ischemia in the DPC group and 20% limb ischemia in the no-DPC group, $p = .6$). Previous studies commenting on the incidence of complications and DPC placement are sparse and divided. Lamb et al. (20) reported a series of 91 patients supported with femoral VA ECMO; a DPC was placed in 62 patients with no subsequent limb ischemia in these patients. Of the 29 patients without a DPC in that study, 41% developed limb ischemia. On the other hand, Ranney et al. (17) demonstrated no statistically significant difference in overall vascular complication rate (28.7%) in a study comparing 14 patients with a DPC and 66 patients without a DPC; however, the authors of the study advocated for primary DPC placement because of a trend in decreased complications. In line with this, Ma et al. demonstrated no relationship between limb complications and DPC placement in a cohort of 70 patients. The present study, although similarly limited by sample size, demonstrates similar results.

Table 3. Limb complications.

Limb Complication	Overall Cohort (n = 75)	DPC (n = 65)	No DPC (n = 10)	*p* Value
Limb ischemia	11 (14.7)	9 (13.9)	2 (20)	.6
Fasciotomy	3 (4)	3 (4.6)	0 (0)	.5
Thrombectomy	3 (4)	2 (3.1)	1 (10)	.3
Conversion to axillary ECMO	1 (1.3)	0 (0)	1 (10)	–
Delayed DPC placement for ischemia	2 (2.7)	0 (0)	2 (20)	.3
Packed red cell transfusion, units	13 (IQR 7–25)	13 (IQR 7.5–2.4)	19.6 (IQR 6–34)	.7

Table 4. Patient outcomes.

Outcome	Overall Cohort (n = 75)	DPC (n = 65)	No DPC (n = 10)	*p* Value
ECMO successfully weaned	44 (59.5)	38 (59.8)	6 (60)	.9
ECMO duration, days	5 (IQR 4–8)	5 (IQR 4–8)	4 (IQR 1–4)	.1
Length of stay, days	18 (IQR 9–27)	18 (IQR 9–28)	17 (IQR 9–19)	.4
In-hospital stroke	11 (14.7)	10 (15.4)	1 (10)	.7
In-hospital mortality	43 (58.1)	38 (59.4)	5 (50)	.6

It is noteworthy that the placement of a DPC is subject to selection bias. It is the practice of one institution in this study to place a DPC during primary ECMO cannulation in every patient, whereas the other institution in the study has a more heterogeneous practice. Patients who did not receive a DPC may have had other predisposing factors to warrant this. In addition, it is essential to take into account the pathophysiology of the ischemic complications that occur in patients that have undergone ECMO cannulation to decipher the utility of a DPC. For example, in this cohort of patients, three patients (4%) required a fasciotomy, with all of them being in the DPC group and none in the no-DPC group ($p = .5$). Although this lack of significance ($p = .5$) may be because of small sample size, it highlights the variability of the pathophysiologic basis for these complications. Although two of the three patients had compartment syndrome due to arterial thrombosis despite a DPC, one of these patients developed compartment syndrome due to a venous outflow obstruction from the venous cannula on the contralateral limb, unrelated to the arterial inflow.

As there are currently no consensus guidelines for the preemptive use of DPCs, several other strategies have been developed to attempt to minimize limb complication in peripheral VA ECMO patients. By contrast, with antegrade DPC placement, retrograde distal limb perfusion via a posterior tibial artery cut down in 20 patients undergoing femoral VA ECMO was associated with no episodes of limb ischemia in one study (23). Intra-arterial pressure monitoring distal to the femoral artery cannulation site has been used to guide the decision of placing a DPC cannula, with a value of <50 mm Hg set as the cutoff for DPC placement in a small cohort of patients (24). Other techniques including end-to-side chimney graft (25,26) or T graft (27,28) attempt to decrease limb ischemia by avoiding the insertion of the arterial cannula directly into the lumen. More recently, near-infrared spectroscopy has been used in an attempt to objectively identify cerebral and limb ischemia, or patients at risk for limb ischemia who are undergoing peripheral ECMO cannulation, and although not yet clinically validated, has demonstrated promising preliminary results (20,29).

In this study, DPC placement was used twice as a salvage therapy in patients without a primary DPC who later developed clinical evidence of ischemia; both patients recovered completely from their limb ischemia after secondary DPC placement. In addition, in two patients in the DPC group the DPC was not correctly placed in the common/superficial femoral artery resulting in limb ischemia salvaged by DPC replacement and fasciotomy. Recent studies mirror our experience with these two patients and demonstrate a high rate of success of DPC placement as a salvage therapy for limb ischemia, albeit in very small cohorts of patients (2–6 patients) with an associated increased risk of bleeding in some patients (15,17). However, in our series—in which we used red blood cell transfusion rate as a surrogate for bleeding—we did not demonstrate an increased bleeding risk with DPC placement.

Limitations

Our study has a number of important limitations. Our study is a bi-institutional series i.e., limited by its retrospective nature and small sample size. Patients who did not undergo DPC placement are subject to selection bias, as it is generally the practice of both institutions to place a preemptive DPC at the time of primary ECMO cannulation, so patients without a DPC either had excellent clinical evidence of limb perfusion or other non-quantifiable factors that contributed to them evading a DPC. Although our patients were well matched in all measured baseline demographics, indications for ECMO, and procedural characteristics, we were unable to meaningfully and objectively evaluate the presence of peripheral vascular disease in these patients, owing to the presence or absence of vascular disease not being reliably recorded in the medical record. In addition, the specific causes of limb ischemia such as decreased perfusion pressure due to cardiogenic shock or sepsis vs. vasoconstriction due to pressors or hypercoagulability due to prothrombotic states—all of which have different underlying pathophysiologies and only some of which may benefit from DPC—were not elucidated.

Conclusions

Limb complications are common in patients undergoing femoral VA ECMO. In the present study, limb complications did not occur more frequently in the absence of DPC placement; however, delayed DPC placement appears to be an appropriate salvage strategy for patients with evidence of limb ischemia. That being said, we cannot advocate against early DPC placement and clinicians should evaluate candidates on an individual basis. Larger, prospective, randomized investigations are necessary to evaluate the utility of primary DPC placement and to identify objective measures to aid in clinical decision-making.

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