Ankle-brachial index to monitor limb perfusion in patients with femoral venoarterial extracorporeal membrane oxygenation

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Abstract:

Background: Limb ischemia is a major complication of femoral venoarterial extracorporeal membrane oxygenation (VA-ECMO). Use of ankle-brachial index (ABI) to monitor limb perfusion in VA-ECMO has not been described. We report our experience monitoring femoral VA-ECMO patients with serial ABI and the relationships between ABI and near infrared spectroscopy (NIRS).

Methods: This is a retrospective single-center review of consecutive adult patients placed on femoral VA-ECMO between January 2019 and October 2019. Data were collected on patients with paired ABI and NIRS values. Relationships between NIRS and ABI of the cannulated (E-NIRS and E-ABI) and non-cannulated legs (N-NIRS and N-ABI) along with the difference between legs (D-NIRS and D-ABI) were determined using Pearson correlation.

Results: Overall, 22 patients (mean age 56.5±14.0 years, 72.7% male) were assessed with 295 E-ABI and E-NIRS measurements, and 273 N-ABI and N-NIRS measurements. Mean duration of ECMO support was 129.8±78.3 hours. ECMO-mortality was 13.6% and in-hospital mortality was 45.5%. N-ABI and N-NIRS were significantly higher than their ECMO counterparts (ABI mean difference 0.16, 95%CI 0.13-0.19, $p<0.0001$; NIRS mean difference 2.51, 95%CI 1.48-3.54, $p<0.0001$). There was no correlation between E-ABI vs. E-NIRS ($r=0.032$, $p=0.59$), N-ABI vs. N-NIRS ($r=0.097$, $p=0.11$), or D-NIRS vs. D-ABI ($r=0.11$, $p=0.069$).

Conclusions: ABI is a quantitative metric that may be used to monitor limb perfusion and supplement clinical exams to identify limb ischemia in femorally cannulated VA-ECMO patients. More studies are needed to characterize the significance of ABI in femoral VA-ECMO and its value in identifying limb ischemia in this patient population.

Introduction

Peripheral venoarterial extracorporeal membrane oxygenation (VA-ECMO) is associated with acute limb ischemia (ALI) with rates ranging between 10-70%.[1–3] ALI is a difficult diagnosis to make in patients supported by VA-ECMO as they are generally critically ill, sedated, on ventilatory support, and overall physiologically deranged (non-pulsatile flow). The diagnosis of ALI is typically dependent on laboratory tests such as lactic acid and creatinine kinase and subjective clinical assessments of skin appearance, temperature, compartment tension, and bedside Doppler tone checks. However, by the time detectable changes are manifested, ischemia may be irreversible.

Near infrared spectroscopy (NIRS) oximetry, used to monitor cerebral perfusion during cardiopulmonary bypass, has recently been applied to monitor the perfusion of lower extremities in VA-ECMO patients.[4–7] Its greatest appeal is that it provides continuous quantitative data in a non-invasive manner. However, there are several issues with its application to VA-ECMO patients. There is a poor understanding of what an absolute NIRS value means; equipment is not widely available, and values are dependent on dynamic factors such as patient temperature, sensor positioning, exposure to light, and adhesive integrity; use requires reliable monitoring and documentation; and it is costly.

While NIRS has been a helpful adjunctive tool for identifying limb ischemia, there is still a need for objective strategies to identify limb malperfusion. Ankle brachial index (ABI) has long been used to diagnose and quantify peripheral artery disease (PAD), but it has not been described in VA-ECMO patients. We report our experience performing serial ABI assessments in femoral VA-ECMO patients, the correlation between ABI and NIRS, and present a series of patients who developed ABI changes, without changes in NIRS, leading to identification of a clinically significant event.

Materials and Methods

Patients and Methods:

Consecutive patients placed on femoral VA-ECMO were retrospectively reviewed between January 2019 and October 2019 after a quality improvement initiative was started to incorporate serial ABI assessments to monitor limb perfusion. Approval was obtained by our Institutional Review Board (IRB: STU00211826). Patient and clinical variables were collected from the electronic medical record.

VA-ECMO Cannulation Techniques and Management:

All patients were cannulated by cardiac surgery fellows or attendings using ultrasound. Outflow cannula was placed in the common femoral artery (CFA) (Edwards Lifesciences Femflex II) and inflow cannula was placed in the ipsilateral or contralateral common femoral vein (CFV) (Medtronic Bio-Medicus Multi-stage). Cannula size was chosen based on patient weight (16 French (Fr) arterial and 21 Fr venous for less than 70kg and 18-Fr arterial and 25-Fr venous for greater than 70kg). Antegrade perfusion of the cannulated leg was obtained by placement of a distal perfusion catheter (DPC) (Arrow- Super Arrow-Flex PSI) in the ipsilateral superficial femoral artery (SFA) (usually a 6 Fr cannula placed at the time of ECMO cannulation or within 4 hours of cannulation).

The ECMO system was a polymethylpentene fiber oxygenator system (Quadrox-iD Adult: Maquet Getinge group) with Bioline-coated circuits (Maquet Getinge group). All patients were supported using centrifugal pumps (Rotaflow Centrifugal pump; Maquet Getinge group). Managing protocol for ECMO was directed in accordance with Extracorporeal Life Support Organization (ELSO) guidelines.[8] Patients were cared for by ECMO-specialized nursing staff, anesthesia intensive care, and cardiac surgery.

NIRS Oximetry

ForeSight Elite oximeter sensors (Edwards Lifesciences, Irvine, CA) were placed on both legs lateral to tibia approximately midway between the knee and ankle to monitor the anterior compartment. NIRS values were recorded hourly by nursing staff. Sensors were changed per our institution standard protocol (i.e. daily or when functional integrity is questioned).

ABI Assessment:

ABI were assessed on both the cannulated and non-cannulated legs by either cardiac surgery fellows or ECMO specialized nursing staff. ABIs were performed using the Doppler method to measure the systolic blood pressure (SBP) of the dorsalis pedis (DP) and posterior tibialis (PT) arteries and dividing it by the SBP of the upper extremity to generate a ratio.[9] A modification was made from the conventional method due to presence of invasive arterial monitoring in all ECMO patients. The brachial systolic pressure was derived from invasive hemodynamic pressure measurements from the existing radial arterial line rather than using a cuff and Doppler. A clinically relevant decrease in ABI was defined as a decrease by 0.15 from initial baseline ABI on isolated measurements or a decrease between 0.10 and 0.15 with associated clinically change.[10] Skeletal muscle can tolerate approximately 4-6 hours of ischemia.[11] Therefore, ABI were recorded every 4 hours by nursing staff and isolated decreases in ABI$\geq$0.15, or between 0.10-0.15 with associated changes in NIRS or clinical limb examination prompted further study or intervention.

Statistical Methods:

Descriptive statistics were expressed as mean ± standard deviation. Relationships between NIRS (E-NIRS) and ABI (E-ABI) of the cannulated leg, NIRS (N-NIRS) and ABI (N-ABI) of the non-cannulated leg, as well as the difference between the legs (D-NIRS and D-ABI), were described using Pearson correlation. Means were compared by independent T-tests. A p-value <0.05 was considered statistically significant for all comparisons. All statistical analysis was done using SPSS version 24 (IBM, Armonk, NY).

Results

There were 22 patients who had paired measurements of ABI and NIRS. Of these, mean age was 56.5 ± 14.0 years and 72.7% were male. All patients were cannulated via femoral artery and vein. Only one patient did not receive a DPC at the time of cannulation as she was emergently taken to the operating

room after cannulation for limb ischemia. Ten patients (45.5%) had in-hospital mortality, 3 of whom (13.6%) died while on ECMO support. Additional cohort characteristics are shown in Table 1.

There were 295 paired recordings of ABI and NIRS of the cannulated leg and 273 pairs of ABI and NIRS of the non-cannulated leg. ECMO flow and limb perfusion data are shown in Table 2. Using both ABI and NIRS, non-cannulated limbs had greater perfusion than cannulated limbs. N-ABI was greater than E-ABI (mean difference 0.16, 95% CI 0.13-0.19, $p<0.0001$) and N-NIRS was greater than E-NIRS (mean difference 2.51%, 95% CI 1.48-3.54%, $p<0.0001$).

Pearson correlation was performed between perfusion variables that demonstrated no correlation between E-ABI vs. E-NIRS ($r=0.032$, $p=0.59$), N-ABI vs. N-NIRS ($r=0.097$, $p=0.11$), or D-ABI vs. D-NIRS ($r=0.11$, $p=0.069$) (Figures 1A-C). Comparing within subjects, E-ABI had a moderate and significant positive correlation with N-ABI ($r=0.31$, $p<0.0001$) (Figure 2A). E-NIRS had a strong and significant positive correlation with N-NIRS ($r=0.67$, $p<0.0001$) (Figure 2B). The NIRS and ABI of both cannulated and non-cannulated legs shared mild-to-moderate but statistically significant negative correlations with ECMO flow (Figure 3A-D). We describe 4 patients who had clinically significant events identified by clinical exam and ABI without correlated changes in NIRS.

Patient 1

A 35-year-old female with previously implanted continuous flow left ventricular assist device (LVAD) acutely presented in cardiogenic shock, low LVAD flows (0.2 L/min), and suspected LVAD thrombus. Despite aggressive resuscitation, she developed cardiac arrest, requiring emergent femoral VA-ECMO. Cannulation was performed using an 18-Fr arterial cannula in the right CFA and a 25-Fr venous cannula in the right CFV. She was then taken emergently taken to the operating room for LVAD exchange for pump thrombosis and ECMO decannulation with primary repair of the femoral vessels. Given the immediacy of operating room transfer, a DPC was not placed. Throughout the operation, the patient's

legs were warm and E-NIRS ranged from 78 to 82% and N-NIRS ranged from 81-84%; ABI assessments were not performed intraoperatively. When the patient returned to the ICU, her E-NIRS and N-NIRS remained stable, but the previously cannulated leg was noted to be cool with an ABI of 0.2 before losing Doppler tones in the next hour. The non-cannulated leg had an ABI of 1.0, raising concern for acute limb ischemia of the previously cannulated limb. Vascular surgery was urgently consulted, and the patient was taken back to the operating room emergently for leg thrombectomy and prophylactic calf fasciotomy. Following revascularization, the E-ABI and N-ABI were 0.7 and 1.0, respectively. Bilateral NIRS values, however, remained unchanged from pre-operative values. The patient made a full recovery and was discharged with preserved limb function.

Patient 2

A 71-year-old female presented to the Emergency Department with saddle pulmonary embolus and witnessed PEA-arrest. Left femoral VA-ECMO was emergently established during resuscitation with an 18-Fr arterial cannula in the left CFA, a 25-Fr venous cannula in the right CFV, and a 6-Fr DPC in the left SFA. Initially, E-ABI and N-ABI were 0.91 and 0.98, respectively. E-NIRS and N-NIRS were 67% and 87%, respectively. Two hours later, the patient's E-ABI became 0.0 (N-ABI was not recorded) while E-NIRS remained largely unchanged (64%) and N-NIRS dropped to 63%. The patient was taken to the operating room for cannula revision. The contra-lateral (right) leg was cannulated for ECMO using a 16-Fr arterial cannula in the right CFA and a 6-Fr DPC in the right SFA. The left femoral artery was repaired with a venous interposition graft and prophylactic calf fasciotomy was also performed. Post-operatively, left leg ABI improved progressively from 0.44 to 0.95 and left leg NIRS increased from 68% to 93%. Unfortunately, the patient developed anoxic brain injury and expired on hospital day 6.

Patient 3

A 37-year-old male with heart failure due to suspected viral myocarditis was placed on femoral VA-ECMO with a 20 Fr arterial cannula in the left CFA, a 25-Fr venous cannula in the right CFV, and an 8-Fr

DPC for progressive cardiogenic shock at a referring hospital and transferred to our institution. At presentation, the E-ABI was 0.42 (N-ABI assessments were not recorded), E-NIRS was 79% and N-NIRS was 86%. Over the next several assessments, E-ABI remained approximately 0.4 while the NIRS of both legs fluctuated between 65-82%. This prompted examination of the DPC, which was found to be thrombosed. Despite numerous attempts at aspirating and flushing, flow was not returned via DC and the DPC was replaced. Following replacement, E-ABI increased to 0.8, but the NIRS of both legs remained in the 74-84% range. In the ensuing days, E-ABI was stable between 0.8 and 0.9 while both E-NIRS and N-NIRS oscillated between 75 and 85%. The patient was bridged to recovery, decannulated on hospital day 5 and discharged home on hospital day 15.

Patient 4

A 61-year-old male with ischemic cardiomyopathy developed hypoxemic arrest 5 days after coronary artery bypass surgery. He was emergently placed on femoral VA-ECMO with an 18 Fr arterial cannula in the right CFA and a 25 Fr venous cannula in the right CFV with a 5 Fr DPC. Initially, E-ABI ranged between 0.65-0.8 and N-ABI ranged between 1.0-1.2 while E-NIRS was 60-80% and N-NIRS was 80-90%. Three days after ECMO initiation, E-ABI acutely dropped to 0.42 while N-ABI, E-NIRS and N-NIRS remained unchanged. This prompted investigation and identification of DPC thrombosis, which was cleared with aspiration and flushing of the DPC. E-ABI subsequently increased to 0.71 and E-NIRS to 88%. The patient recovered and was discharged.

Conclusions

Our series demonstrates the utility of performing ABI assessments on patients supported with femoral VA-ECMO. Overall, ABI and NIRS values were significantly lower in the cannulated leg compared to non-cannulated leg. However, the described clinical events occurred only in the setting of decreased ABI values, without a decrease in NIRS. There was no statistically significant correlation between ABI and NIRS for either leg, nor was there a correlation in D-NIRS vs. D-ABI. However, the described patients

highlight the utility of ABI on identifying complications. Patients 1 and 2 developed decreased ABI and ultimately loss of Doppler tones in the absence of oximetry changes and underwent leg revascularization while patients 3 and 4 had DPC thrombosis discovered only after decreased ABI, again in the absence of oximetry changes.

Wong et al. and Kim et al. monitored cannulated extremities with NIRS and defined "significant events" as StO2 <40% or >25% drop from baseline and intervened with placement or replacement of a DPC.[4,5] These criteria were derived from cerebral oximetry studies and have not been validated for skeletal muscle perfusion. Patton-Rivera et al. used NIRS StO2 differential between cannulated and non-cannulated legs of >15% as criterion for ischemia and reported that 3 patients with suspected cannula-related ischemic events had differentials >15% that resolved with placement of DPC.[6] In our series, only patient 4 had an StO2 differential >15% that preceded the loss of Doppler tones. However, there was no differential in NIRS StO2 at the time of loss of Doppler tones. Other patients who had an intervention, even the patient who developed CFA thrombosis, did not demonstrate an StO2 differential >15%. NIRS oximetry is easy to use and provides convenient continuous monitoring if providers reliably monitor and record values. However, absolute oximetry StO2 values can be falsely reassuring and not sensitive enough to ischemic events with one group raising caution on the overreliance on NIRS oximetry by demonstrating comparable StO2 values between humans and select vegetables.[12]

ABI is an accepted and reliable measure of PAD.[13] NIRS has also been used in PAD and while NIRS StO2 recovery following exercise (PAD patients had a drop in StO2 during exercise with a return to baseline at rest) has demonstrated good correlation with ABI,[14–16] the absolute values of NIRS have shown poor correlation with ABI.[17] Thus, it is not surprising that the NIRS StO2 values did not correlate with ABI in our patients. Our findings suggest that down-trending ABI may precede StO2 depression on NIRS oximetry, which may be due to vascular collateralization and compensatory mechanisms. Determining a clinically significant cutoff using ABI can lead to earlier interventions to prevent limb malperfusion.

There are several limitations to our study. This was a retrospective study with a small patient sample size. Patients placed on VA-ECMO, especially in an emergent setting, do not always have fully available medical histories so prevalence of pre-existing PAD is not known. Neither NIRS oximetry nor ABI has been validated nor physiologically studied in VA-ECMO patients, a population with severe physiological alterations. Therefore, it is difficult to define clinically significant cutoff values for either NIRS StO2 or ABI necessary for adequate limb perfusion in supported patients. However, our study does show that regular ABI assessments in conjunction with NIRS oximetry could serve as a good combination to monitor limb perfusion. Moreover, patients often suffer from microvascular disease and high doses of pressor support, which can affect tissue perfusion and it is unclear how those factors affect ABI and NIRS in VA-ECMO. Another limitation is potential variability in how ABI is performed; however, this was addressed by holding numerous training sessions with intensive care nursing staff with accessible resources on all ECMO circuits for review.

In conclusion, ABI could provide quantitative data on patients placed on femoral VA-ECMO to assist in the diagnosis of acute limb ischemia. Further studies are needed to better understand their role in VA-ECMO patients.

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Disclosures

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Author Contributions

Concept/design: AYS, DP

Data analysis/interpretation: AYS, RHJ, TU, AA

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Critical revision: ASK, RHJ, RM, AP, KJH, DP

Approval of article: DP

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Table 1. Patient characteristics.

Variable	**N=22**
Male	16 (72.7)
Age, years	56.5 ± 14.0
Race	
White/Caucasian	15 (68.2)
Black/African American	6 (27.3)
Other	1 (4.5)
BSA, kg/m^2	2.13 ± 0.27
ECMO indication	
Cardiac arrest or cardiogenic shock	18 (81.8)
Decompensating heart failure	4 (18.2)
ECLS	7 (31.8)
Hours on ECMO	129.8 ± 78.3
Arterial Cannula Size, French	17.3 ± 1.1
Venous Cannula Size, French	24.4 ± 1.4
Ipsilateral cannulation	17 (77.3)
Distal Perfusion Cannula Size, French	5.4 ± 0.8
Mortality on ECMO	3 (13.6)
In-hospital mortality	10 (45.5)
Continuous data expressed as mean ± standard deviation and categorical data as number (%). ECLS, extracorporeal life support; BSA, body surface area; ECMO, extracorporeal membrane oxygenation	

Table 2. Perfusion assessments.

Variable	**Mean ± Standard Deviation**
Flow, L/min (n=295)	3.91 ± 0.96
E-NIRS, % (n=295)	75.14 ± 10.47
E-ABI (n=295)	0.79 ± 0.23
N-NIRS, % (n=273)	77.34 ± 10.71
N-ABI (n=273)	0.97 ± 0.19
D-NIRS, % (n=273)	2.51 ± 8.65
D-ABI (n=273)	0.16 ± 0.25
Continuous data expressed as mean ± standard deviation. E-, ECMO; N-, non-ECMO; NIRS, near infrared spectroscopy; ABI, ankle brachial index; D-, delta	

Table 3. Difference in ABI and NIRS between cannulated and non-cannulated leg.

	Mean difference	95% CI	P-Value
N-ABI – E-ABI (N=273 pairs)	0.16	0.13-0.19	<0.0001
N-NIRS – E-NIRS (N=273 pairs)	2.51	1.48-3.54	<0.0001
CI, confidence interval; N-, non-ECMO; E-, ECMO; ABI, ankle brachial index; NIRS, near infrared spectroscopy.			

Figure Legend

Figure 1. Pearson correlations of ABI and NIRS between cannulated (E-) or non-cannulated (N-) extremities at all time points (N=22 patients). (A) Correlation between E-ABI and E-NIRS (N=295 pairs); (B) Correlation between N-ABI and N-NIRS (N=273 pairs); (C) Correlation between D-ABI and D-NIRS (N=273 pairs).

Figure 2. Pearson correlations between ABI and NIRS of cannulated (E-) and non-cannulated (N-) extremities at all time points (N=22 patients). (A) Correlation between E-ABI and N-ABI (N=273 pairs); (B) Correlation between E-NIRS and N-NIRS (N=273 pairs).

Figure 3. Pearson correlations between ECMO flow and ABI or NIRS at all time points (N=22 patients). (A) Correlation between E-ABI and flow (N=295 pairs); (B) Correlation between E-NIRS and flow (N=295 pairs); (C) Correlation between N-ABI and flow (N=273 pairs); (D) Correlation between N-NIRS and flow (N=273 pairs).