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Capillary refill time and tissue oxygen saturation as factors influencing lower limb ischemia in VA-ECMO: a case-control study

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Abstract

Background and objectives Venous-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) is a pivotal means for rapid cardiopulmonary support, yet it may result in lower limb ischemia. This study aims to explore the high-risk factors for lower limb ischemia following VA-ECMO.

Methods 117 patients who received VA-ECMO treatment at Guangxi Zhuang Autonomous Region People's Hospital from June 2022 to December 2023 were divided into lower limb ischemia group and non ischemia group for case-control analysis.

Results In this case-control study of 117 VA-ECMO patients, 22 (18.80%) experienced lower limb ischemia. Patients with ischemia had significantly lower body surface area (BSA) and lower tissue oxygen saturation (StO_2) levels, but higher capillary refill time (CRT) levels compared to those without ischemia ($P<0.05$). Spearman correlation analysis showed that StO_2 and CRT had strong correlations with ischemia. Binary logistic stepwise regression analysis identified CRT and StO_2 as independent risk factors for lower limb ischemia. Specifically, lower StO_2 levels were associated with an increased risk of ischemia (OR = 0.615, $P<0.05$), while higher CRT levels were also associated with an increased risk (OR = 27.571, $P<0.05$). The Receiver Operating Characteristic (ROC) curve shows that the areas of CRT and StO_2 are 0.924 ($P<0.001$, 95% CI 0.866–0.983) and 0.951 ($P=0.023$, 95% CI 0.906–0.997), respectively.

Conclusions StO_2 reflects real-time tissue perfusion adequacy, whereas CRT serves as a marker of microvascular dysfunction. Lower StO_2 levels (indicating impaired oxygenation) and higher CRT levels (suggesting delayed capillary refilling) were independently associated with an increased risk of lower limb ischemia, suggesting that monitoring these parameters may be useful in identifying patients at higher risk for this complication. These findings provide valuable insights for risk stratification and potential intervention strategies in the management of VA-ECMO patients.

Keywords Veno-arterial extracorporeal membrane oxygenation, Lower limb ischemia, Tissue oxygen saturation, Capillary refill time, Case-control study

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Introduction

Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) represents an advanced therapeutic modality in mechanical circulatory support [1], particularly for patients with refractory circulatory failure due to diverse etiologies that fail to respond adequately to conventional treatments. While VA-ECMO has demonstrated significant efficacy in treating cardiopulmonary failure, it is also associated with high rates of complications and mortality. Lower limb ischemia, a common and severe complication occurring in over 10% of ipsilateral limbs [2–4], poses a particular challenge due to its potential to severely impact patients' quality of life and even lead to fatal outcomes. Despite the existence of various monitoring methods and techniques aimed at preventing lower limb ischemic injury and improving distal limb perfusion, the incidence of this complication remains high [5], the incidence of lower limb ischemia may still exceed 10% [3, 4]. This underscores the urgent need to explore the risk factors for lower limb ischemia after VA-ECMO and to implement effective preventive strategies.

Patients with circulatory failure experience inadequate oxygen supply and fluid accumulation in tissues, often leading to leg edema and exacerbating the risk of lower limb ischemia. Improving fluid circulation and hemodynamics is crucial for these patients, not only to alleviate symptoms but also to enhance the overall success of VA-ECMO treatment, for example, Proper use of cardiac catheterization is one such strategy [6]. Studies have consistently shown that hemodynamic management plays a pivotal role in the management of ECMO patients [7, 8]. This study aims to conduct a retrospective analysis of patients with lower limb ischemic injury following VA-ECMO, identifying potential high-risk factors predictive of severe lower limb ischemia. By providing a basis for clinical prevention and management of lower limb ischemic injury, this research seeks to reduce the incidence of severe limb ischemia complications and ultimately improve the overall success rate of VA-ECMO treatment.

Methods

Patients

A total of 117 patients who underwent VA-ECMO treatment at Guangxi Zhuang Autonomous Region People's Hospital from June 2022 to December 2023 were enrolled in this study. The patients were divided into a non-ischemic group and an ischemic group based on the presence or absence of lower limb ischemia after VA-ECMO.

The inclusion criteria were as follows: (1) patients aged ≥ 18 years, regardless of gender; (2) patients with heart and/or lung failure refractory to conventional treatment (such as conventional drug therapy, mechanical ventilation, intra-aortic balloon pump, etc.) and requiring VA-ECMO; (3) VA-ECMO operation time ≥ 24 h; (4) During the VA-ECMO surgery, patients undergo anticoagulant therapy and other management; (5)no contraindications for VA-ECMO.

The exclusion criteria were: (1) patients with irreversible diseases such as severe cerebral dysfunction, severe central nervous system injury, or advanced malignant tumors; (2) patients with contraindications for anticoagulation, such as liver failure with severe coagulation dysfunction, massive bleeding, recent or expanding intracranial hemorrhage, etc.; (3) patients with severe multiorgan failure; (4) incomplete clinical data. This study was approved by the Medical Ethics Committee of Guangxi Zhuang Autonomous Region People's Hospital (No. KY-ZC-2021-072), and informed consent was obtained from the patients' families.

Method for establishing femoral artery catheterization

The area was routinely and draped, with the disinfection area being sufficiently large. Under bedside B-mode ultrasound guidance, the Seldinger technique was used to place a single-lumen central venous catheter at the intended site for ECMO catheter insertion. After confirming that the single-lumen central venous catheter had smooth blood return within the vessel, it was sealed with heparinized saline. A long guidewire was then inserted through the single-lumen central venous catheter, with the insertion depth exceeding the anticipated length of the indwelling catheter, and properly secured. A dilator was used to gradually dilate the skin and subcutaneous tissue, and after each insertion of the dilator, it was necessary to check that the guidewire moved smoothly and was not kinked. Finally, the ECMO femoral artery catheter with an inner core and a one-way valve was inserted along the guidewire. After withdrawing the guidewire and then the inner core, the catheter was sealed with heparinized saline and clamped with a hemostat. A 6Fr arterial sheath for angiography was placed using the Seldinger technique, and connected to the arterial side branch of the ECMO circuit to improve lower limb perfusion. The ECMO equipment used included a centrifugal pump, oxygenator, extracorporeal circulation catheters, and accessories from Maquet. The arterial catheter was 15 to 19 Fr, the venous catheter was 19 to 21 Fr, and the distal perfusion catheter for the lower limbs was 6Fr. The appropriate catheter size was selected based on the vascular assessment using B-mode ultrasound.

During VC-ECMO, patient management methods

The initial flow rate was set at 60–80 mL/kg/min and adjusted dynamically based on SvO_2 (> 65%) and lactate levels (< 1.5 mmol/L). The MAP target was 65–75 mmHg to avoid excessive left ventricular load, with LVEF, right ventricular function, and thrombi monitored every 4–6 h via TTE. PaO_2 was maintained at 80–120 mmHg,

and SvO_2 >70%. Ultra-protective ventilation was implemented: tidal volume 4–6 mL/kg, PEEP 8–12 cmH_2O, and driving pressure < 15 cmH_2O. Multi-parameter monitoring included: ACT 160–200 s, anti-Xa factor 0.3–0.7 IU/mL, TEG R time 5–8 min, heparin dosage adjusted individually, and ATIII supplementation (> 80%). CVVHDF was initiated early, with an ultrafiltration rate < 25 mL/kg/h, and urinary NGAL was monitored to predict kidney injury. Multimodal monitoring included: rSO_2 >55%, ICP < 20 mmHg, and BIS 40–60. Plasma-free hemoglobin was monitored (< 50 mg/dL), and a centrifugal pump (RPM < 3500) with heparin-coated tubing was used. A DPC was established with a target perfusion pressure > 40 mmHg. NIRS continuously monitored limb oxygen saturation, with a threshold difference < 15%.

The process of weaning off VA-ECMO

Cardiac ultrasound was assessed, confirming an LVEF > 25% and normal left ventricular outflow tract blood flow. Blood pressure was maintained with a MAP > 65 mmHg (with minimal vasopressor use), lactate levels were < 2 mmol/L, and SvO_2 was > 65%. ECMO flow was gradually reduced in stages: from 3.0 L → 2.5 L (over 1 h) → 2.0 L (over 2 h) → 1.5 L. After each reduction, evaluations were performed: ultrasound confirmed no cardiac dilation, blood pressure fluctuations were < 10%, and no new arrhythmias occurred. For cannula removal, the arterial side was closed using a vascular closure device (ProGlide), and ultrasound confirmed patent blood flow (velocity > 40 cm/s). The venous side was closed using a vascular closure device (Angio-Seal), followed by 24 h of compression dressing.

Data collection

The clinical data of VA-ECMO patients were collected, including general information such as gender, age, body surface area (BSA), smoking history, cardiovascular and cerebrovascular diseases, the causes of VA-ECMO implantation and Acute Physiologyand Chronic Health Evaluation (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score.

Operation factors during VA-ECMO included Arterial Cannula Model, Arterial Catheter Diameter/BSA, VA-ECMO Cannulation Time, Placement of Bypass (By-PASS), Intra-aortic balloon pump (IABP), Continuous Renal Replacement Therapy (CRRT), and Extracorporeal Cardiopulmonary Resuscitation (ECPR).

Laboratory examination indicators before the occurrence of lower limb ischemia including lactic acid (LA), ejection fraction (EF), mean arterial pressure (MAP), blood flow, prothrombin time (PT), international normalized ratio (INR) of PT, fibrinogen (Fg), thrombin time (TT), activated partial thromboplastin time (APTT), D-dimer, procalcitonin (PCT), heparin-binding protein (HBP), platelet count (PC), C-reactive protein (CRP), white blood cell count (WBCC), lymphocyte count (LYC), neutrophil count (NEUT), monocyte count (MONO), myoglobin (Mb), creatine kinase (CK), capillary refill time (CRT) and tissue oxygen saturation (StO_2).

Statistical methods

Statistical analysis was performed using SPSS 26.0 software. For continuous variables, the t-test was used if the data followed a normal distribution and was expressed as mean ± standard deviation ($\bar{x} \pm SD$); otherwise, the rank-sum test was used, and the data was expressed as median and quartiles [Q(P25, P75)]. For categorical variables, the chi-square test was used and expressed as [n(%)]. Spearman correlation coefficient analysis was conducted to assess the indicators related to lower limb ischemia. The closer the correlation coefficient is to 1, the stronger the correlation is. Binary Logistic regression analysis was conducted to identify independent factors influencing lower limb ischemia after VA-ECMO. The Receiver Operating Characteristic (ROC) curve was used to analyze the diagnostic performance of clinical indicators for lower limb ischemia after VA-ECMO, where an Area Under Curve (AUC) of 0.5 indicated no predictive value, and an AUC closer to 1 indicated higher accuracy. A P-value < 0.05 was considered statistically significant.

Results

General information of the two patient groups

A total of 117 VA-ECMO patients were collected and grouped based on the presence or absence of lower limb ischemia. Among them, 22 patients (18.80%) belonged to the ischemic group, and 95 patients (81.20%) belonged to the non-ischemic group. Lower limb ischemia occurred after ECMO was performed as shown in Fig. 1.

Comparison between the ischemic and non-ischemic groups revealed no significant differences in gender, age, smoking history, hypertension, chronic kidney disease, cardiovascular and cerebrovascular diseases, and the etiology for VA-ECMO installation ($P > 0.05$). However, the body surface area (BSA) of patients in the ischemic group was significantly lower than that of patients in the non-ischemic group ($P < 0.05$). The diabetes, atherosclerosis of lower limbs and APACHE II score was slightly higher in the ischemic group compared to the non-ischemic group, but the difference was not statistically significant ($P > 0.05$). See Table 1 for details.

VA-ECMO operation factors for lower limb ischemia

During VA-ECMO, compared to the non-ischemic group, patients in the Ischemic group had a larger Artery Catheter Diameter/BSA ratio ($P < 0.05$) and a lower proportion of patients with By-PASS placed ($P < 0.05$). See Table 2 for details.

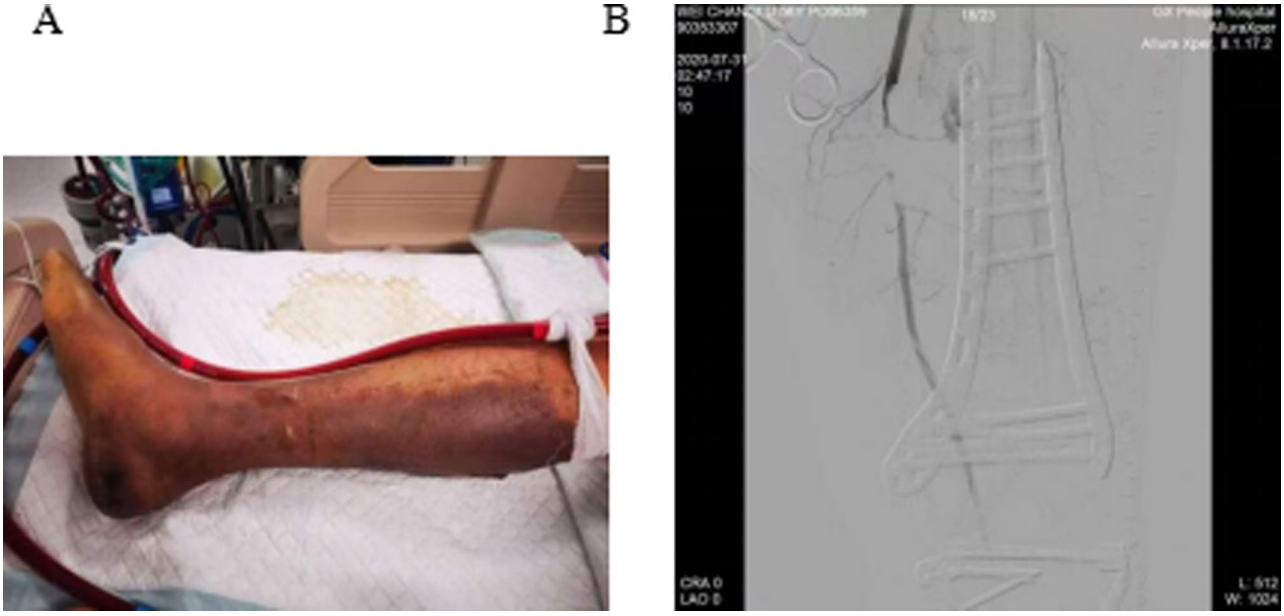

Fig. 1 Lower limb ischemia occurred after ECMO was performed. **A** Manifestations of lower limb ischemia after ECMO was performed. **B** Angiographic manifestations during interventional treatment after lower limb ischemia occurred following ECMO

Table 1 General information of the two patient groups [n(%)]/($\bar{x}\pm s$)/[Q(P25,P75)]

Characteristics		Ischemic($n=22$)	Non-ischemic($n=95$)	*P*
Gender	Male	15(68.18)	69(72.63)	0.676
Age (years)		60.95 ± 13.11	55.25 ± 15.32	0.112
BSA(m^2)		1.36(1.33,1.45)	1.6(1.48,1.68)	< 0.001
Smoking History	Yes	5(22.73)	19(20.00)	1.000
Hypertension	Yes	13(59.09)	39(41.05)	0.125
Diabetes	Yes	9(40.91)	21(22.11)	0.069
Chronic kidney disease	Yes	2(9.09)	11(11.58)	0.738
Atherosclerosis of lower limbs	Yes	7(31.82)	15(15.79)	0.083
Cardiovascular & Cerebrovascular Diseases	Yes	16(72.73)	62(65.26)	0.503
Etiology for VA-ECMO Installation	septic cardiomyopathy	4 (18.18)	38(40.00)	0.135
	Explosive myocarditis	0(0)	5(5.26)	
	Acute myocardial infarction	7(31.82)	19(20.00)	
	Other	11(50.00)	33(34.74)	
APACHE II Score		32.64 ± 5.19	29.96 ± 6.47	0.075
SOFA Score		13.91 ± 2.86	12.77 ± 3.24	0.135

Note: BSA (Body surface area), VA-ECMO (enous-Arterial Extracorporeal Membrane Oxygenationz), APACHE II (Acute Physiologyand Chronic Health Evaluation), SOFA (Sequential Organ Failure Assessment)

Laboratory examination indicators before the occurrence of lower limb ischemia

Upon analyzing the laboratory indicators before the occurrence of ischemia in the two groups, it was found that the plasma Fg, WBCC, MONO, and StO_2 were lower in the Ischemic group compared to the Non-Ischemic group ($P<0.05$), while the levels of D-dimer, HBP, Mb, CK, and CRT were higher in the Ischemic group compared to the Non-ischemic group ($P<0.05$). See Table 3 for details.

Correlation between clinical indicators and lower limb ischemia

A Spearman correlation coefficient analysis was conducted to assess the correlation between the variables with statistical differences from the above univariate analysis and the presence of ischemia. The results indicated that these clinical indicators all had a certain correlation with the presence of lower limb ischemia ($P<0.05$). However, only BSA, Arterial Catheter Diameter/BSA, Fg, D-dimer, CK, CRT, and StO_2 had correlation coefficients above 0.5 with the presence of ischemia. See Table 4 for details.

Table 2 VA-ECMO operation factors for both patient groups [n(%)]/[Q(P25,P75)]

Operation factors		Ischemic($n=22$)	Non-Ischemic($n=95$)	*P*
Arterial Cannula Model	15 F	12 (54.55)	37 (38.95)	0.303
	17 F	10 (45.45)	54 (56.84)	
	19 F	0(0)	4 (4.21)	
Arterial Catheter Diameter/BSA	Yes	11.28 (11.11, 11.72)	10.3 (9.74, 10.75)	< 0.001
VA-ECMO Cannulation Time (min)	Yes	45 (40, 57.5)	44 (38,58)	0.461
VA-ECMO Establishment Method	Partial Incision	1 (4.55)	3 (3.16)	0.571
	puncture	21 (95.45)	92 (96.84)	
By-PAS	Yes	12 (54.55)	79 (83.16)	0.009
IABP	Yes	2 (9.09)	8 (8.42)	1
CRRT	Yes	20 (90.91)	76 (80)	0.372
ECPR	Yes	5(22.73)	16(16.84)	0.517

Note: BSA (Body surface area), VA-ECMO (enous-Arterial Extracorporeal Membrane Oxygenationz), By-PASS (Placement of Bypass), IABP (Intra-aortic balloon pump), CRRT (Continuous Renal Replacement Therapy), and ECPR (Extracorporeal Cardiopulmonary Resuscitation)

Table 3 Laboratory examination indicators before the occurrence of lower limb ischemia [n(%)]/($\bar{x}\pm s$)/Q[(P25,P75)]

	Ischemic($n=22$)	Non-ischemic($n=95$)	*P*
LA	5.20(2.28,11.05)	4.40(2.30,9.50)	0.786
EF	0.53(0.40,0.59)	0.44(0.35,0.58)	0.213
MAP	87.66(78.50,102.91)	91.00(77.66,98.66)	0.813
blood flow	3.00(2.68,3.35)	3.20(2.88,3.62)	0.11
PT (s)	16.85(13.79,18.34)	15.89(13.45,20.45)	0.944
INR	1.74(1.45,2.42)	2.01(1.61,2.56)	0.24
Fg (g/L)	1.50(1.11,1.00)	2.68(2.34,3.32)	< 0.001
TT (s)	16.84(14.38,19.12)	17.46(14.89,22.44)	0.284
APTT (s)	52.28(39.58,66.10)	55.29(44.57,69.34)	0.315
D-dimer (mg/L)	16.32(13.2,19.06)	2.34(0.97,5.45)	< 0.001
PCT (ng/ml)	6.70 (3.06,18.45)	7.25(2.45,15.67)	0.706
HBP (ng/ml)	45.13(34.57,69.64)	33.82(8.96,45.39)	< 0.001
PC (10^9/L)	128.50(73,168.25)	125.00(69,157)	0.772
CRP (mg/L)	67.27(34.14,135.09)	65.43(34.56,124.66)	0.572
WBCC (10^9/L)	10.57 ± 4.98	15.06 ± 7.25	0.007
LYC (10^9/L)	0.56 (0.42,0.74)	0.65(0.45,0.87)	0.32
NEUT (10^9/L)	13.00(11.54,14.71)	14.45(11.34,17.78)	0.103
MONO (10^9/L)	0.44(0.38,0.56)	0.49(0.44,0.59)	0.018
Mb (ng/ml)	1909.85(868.10,2270.98)	1289.50(368.90,1895.80)	0.035
CK (U/L)	459.00(44.50,771.75)	102.00(54.00,151.00)	< 0.001
CRT (s)	4.29 ± 1.04	2.62 ± 0.62	< 0.001
StO_2 (%)	41.14 ± 8.60	59.25 ± 6.71	< 0.001

Note: LA (lactic acid), EF (ejection fraction), MAP (mean arterial pressure), PT (prothrombin time), INR (international normalized ratio), Fg (fibrinogen), TT (thrombin time), APTT (activated partial thromboplastin time), PCT (procalcitonin), HBP (heparin-binding protein), PC (platelet count), CRP (C-reactive protein), WBCC (white blood cell count), LYC (lymphocyte count), NEUT (neutrophil count), MONO (monocyte count), Mb (myoglobin), CK (creatine kinase), CRT (capillary refill time), StO_2 (tissue oxygen saturation)

Binary logistic Stepwise regression analysis of lower limb ischemia

Using the variables with statistical differences from univariate analysis as independent variables and the presence of lower limb ischemia as the dependent variable, a binary logistic stepwise regression analysis was conducted. The resulting risk assessment model included two independent variables: CRT and StO_2. Among them, a lower level of StO_2 was associated with an increased risk of lower limb ischemia (OR = 0.615, $P<0.05$). Conversely, a higher level of CRT was associated with an increased risk of lower limb ischemia (OR = 27.571, $P<0.05$). See Table 5 for details. ROC curves (Fig. 2) were plotted separately for CRT and StO_2 to distinguish whether there was lower limb ischemia. The results showed that the area under the curve for CRT was 0.924 ($P<0.001$, 95% CI 0.866–0.983), and for StO_2 it was 0.951 ($P=0.023$, 95% CI 0.906–0.997).

Table 4 Correlation between clinical indicators and lower limb ischemia

variable	*r*
BSA	0.510**
Arterial Catheter Diameter/BSA	0.534**
By-PASS	0.269**
Fg	-0.605**
D-dimer	0.756**
HBP	0.226*
WBCC	-0.247**
MONO	-0.220*
Mb	0.195*
CK	0.868**
CRT	0.676**
StO_2	-0.710**

Note: BSA (Body surface area), By-PASS (Placement of Bypass), Fg (fibrinogen), HBP (heparin-binding protein), WBCC (white blood cell count), MONO (monocyte count), Mb (myoglobin), CK (creatine kinase), CRT (capillary refill time), StO_2 (tissue oxygen saturation). *$P<0.05$, **$P<0.01$

Discussion

Peripheral VA-ECMO is an imperfect but viable tool in patients with cardiac failure [9]. Study shown that the 10 patients intubated with VA-ECMO were discharged alive [10], which was safe and successful in the early stage of circulatory support. However, ipsilateral lower limb ischemia represents a severe complication with an incidence rate ranging from 10 to 70% [11–13]. This complication may not only necessitate the discontinuation of VA-ECMO treatment but also pose a serious threat to patients, potentially leading to amputation and even death. In the study of Becher et al., all VA-ECMO surgeries performed in Germany from 2013 to 2016 were analyzed, and 30 day in-hospital mortality and complications were reported, of which the incidence of limb ischemia was 7.4 ~ 9.2 [14]. In our study sample, which included 117 patients undergoing VA-ECMO treatment, 18.8% of the patients experienced lower limb ischemia, and our findings further elucidate the factors that may contribute to this complication.

We observed that patients in the ischemia group had a significantly lower body surface area (BSA) compared to those in the non-ischemia group and the patients in the ischemia group had a larger ratio of arterial catheter diameter to BSA and a lower proportion of patients undergoing bypass surgery. Bypass surgery, which establishes an alternative pathway to ensure normal blood flow [15], may help reduce the risk of lower limb ischemia. Our results are consistent with previous studies that have confirmed catheter size as a critical factor in ischemic complications during VA-ECMO, particularly when the ratio of arterial catheter diameter to BSA exceeds a certain threshold [16–18].

Upon analyzing the laboratory indicators before the occurrence of ischemia in the two groups, it was found that the plasma Fg, WBCC, MONO, and StO_2 were lower in the Ischemic group compared to the Non-Ischemic

Table 5 Multivariable regression analysis of lower limb ischemia

Independent variable	B	Standard error	Wald	*P*	Exp(B)	95% confidence interval	
						Lower bound	Upper bound
StO_2	-0.486	0.176	7.591	0.006	0.615	0.436	0.869
CRT	3.317	1.39	5.691	0.017	27.571	1.807	420.655

Note: CRT (capillary refill time), StO_2 (tissue oxygen saturation)

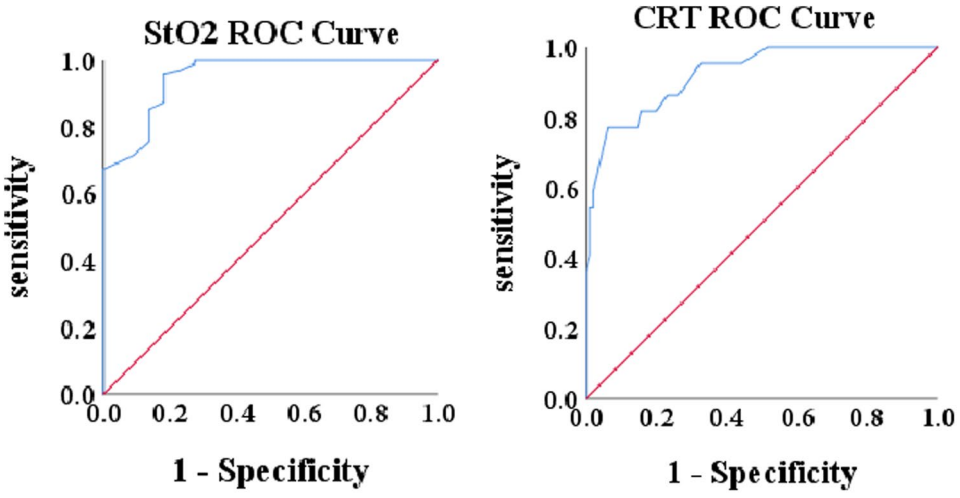

Fig. 2 Receiver operating characteristic curve curve of capillary refill time and tissue oxygen saturation. Note: ROC (receiver operating characteristic curve), CRT (capillary refill time), StO_2 (tissue oxygen saturation)

group, while the levels of D-dimer, HBP, Mb, CK, and CRT were higher in the Ischemic group compared to the Non-ischemic group. These findings suggest that inflammatory and coagulation processes may play a role in the development of ischemia. Biscetti's study also showed that CRP is an inflammatory cytokine associated with failure of lower extremity revascularization (LER) [19]. In Currie's study [20], plasma CK also indicated severe amputation or limb salvage in acute lower limb ischemia. Additionally, studies have shown [21] that remote ischemic postconditioning of the lower limbs during initial percutaneous coronary intervention can safely reduce the enzymatic infarction size in anterior wall myocardial infarction. These findings emphasize the importance of closely monitoring these parameters in patients undergoing VA-ECMO and considering interventions to mitigate their impact on tissue perfusion.

Additionally, we found that after VA-ECMO, the capillary refill time (CRT) was higher in the ischemia group than in the non-ischemia group, while the tissue oxygen saturation (StO_2) was lower. These findings are consistent with previous studies that have shown CRT and StO_2 to be useful indicators of peripheral microcirculation perfusion and tissue oxygenation [22, 23]. CRT involves pressing on the skin to evacuate local capillary blood and observing the time required for blood to refill the skin, making it a simple and non-invasive test for assessing microcirculation status. Cruz's study showed that CRT is a predictor of mortality and postoperative extracorporeal membrane oxygenation requirements in congenital heart disease surgery [24]. Based on physiological and clinical epidemiological data, CRT has been proposed as a marker of inadequate tissue perfusion and is increasingly used as a monitoring agent in shock states and other conditions [25–28].

StO_2 directly reflects tissue oxygenation status. Comerota et al. suggested that StO_2 may help assess patients with peripheral arterial disease [23]. Impaired tissue oxygenation is one of the fundamental causes of various organ dysfunctions and postoperative complications [29]. Lower oxygen saturation is observed in fractures of multiple trauma patients [30]. StO_2 and vascular occlusion testing can identify tissue hypoperfusion in trauma and sepsis [31]. Harrison's study successfully used skin oxygen saturation measurements to predict healing vitality in lower limb amputations due to severe limb ischemia [32]. Kagaya's study showed [33] that StO_2 foot mapping can successfully and non-invasively detect ischemic areas in peripheral tissues of the feet and provides a more suitable assessment than the vascular glomerulus model. Clinically, we found that StO_2 and CRT are convenient and accurate in detecting lower limb ischemia. These two non-invasive tests are highly acceptable to patients and can be repeated [34], facilitating dynamic observation [35]. Kyle's study showed [36] that tissue oxygen saturation monitoring may be a useful adjunct in detecting occult ischemia. As objective quantitative indicators, they accurately reflect the status of lower limb tissues, avoiding subjective errors. In particular, StO_2 has high specificity and sensitivity to ischemia, facilitating early intervention. These findings suggest that CRT and StO_2 can be used not only during VA-ECMO but also for prediction and assessment, providing comprehensive information for patient treatment to ensure safety and efficacy.

The main limitation of this study is the small sample size, with a total of 117 patients enrolled and a single center design. Future studies with larger sample sizes and more comprehensive risk factor assessments are needed to confirm our findings and further elucidate the mechanisms of lower limb ischemia in VA-ECMO patients.

Conclusion

This study adds to or validates the existing knowledge regarding the risk factors for lower limb ischemia in patients undergoing VA-ECMO treatment. The findings emphasize the importance of closely monitoring these patients' CRT, StO_2 levels, CK levels, and the ratio of arterial catheter diameter to BSA, particularly CRT and StO_2, which are independent predictors of lower limb ischemia in VA-ECMO patients. Improving these factors is likely to help reduce the incidence of lower limb ischemia and improve patient outcomes.

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Author contributions

Zhenjia Liu (cohort designing/ sampling/ writing), Lin Han (data collection/ analysis), Li Mo (data collection/analysis), Guangbao Pang (writing/reviewing), Zhongzhi Xie (writing/reviewing), Zhai Huang (study design, data acquisition/ analysis, supervision, writing, revision and final approval).All authors reviewed the manuscript.

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Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Guangxi Zhuang Autonomous Region People's Hospital (No. KY-ZC-2021-072). Clinical trial number: not applicable.

Consent for publication

Not applicable.

Competing interests
The authors declare no competing interests.

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