Microvascular Research 165 (2026) 104924

Contents lists available at ScienceDirect

Microvascular Research

journal homepage: www.elsevier.com/locate/ymvre

Sepsis-induced coagulopathy is associated with impaired tissue oxygen extraction and microvascular reactivity: a prospective observational study

Roberta Domizi [a,b], Andrea Carsetti [a,b], Riccardo Antolini [a,b], Erika Casarotta [a,b], Claudia Scorcella [b], Samuele Zuccari [b], Eva Vitali [a,b], Erica Adrario [a,b], Abele Donati [a,b,*], Elisa Damiani [a,b]

[a] Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, via Tronto 10/a, 60126, Ancona, Italy
[b] Clinic of Anesthesia and Intensive Care Unit, Azienda Ospedaliera Universitaria delle Marche, via Conca 71, 60126, Ancona, Italy

ARTICLE INFO

Keywords:
Sepsis
Coagulopathy
Microcirculation
Tissue oxygenation
Near infrared spectroscopy

ABSTRACT

Background: Coagulopathy is a key driver of organ dysfunction during sepsis/septic shock, yet its relationship with microcirculatory autoregulation is not fully characterized. This study aimed to evaluate the association between sepsis-induced coagulopathy (SIC) and alterations in tissue oxygenation, oxygen extraction capacity and microvascular reactivity.

Methods: Prospective observational study on 23 adult septic patients. Coagulation status was evaluated with standard laboratory parameters and thromboelastography (TEG). A SIC score ≥ 4 was used to identify the presence of coagulopathy. The peripheral (skeletal muscle) tissue oxygen saturation (StO2) was assessed using thenar near infrared spectroscopy (NIRS). By combining a vascular occlusion test, the desaturation rate during ischemia was assessed as an index of oxygen extraction capacity: this was measured separately for the first (StO2 downslope-1) and last part (StO2 downslope-2) of the desaturation curve, and the difference between the two was calculated (delta-downslope). The reoxygenation rate (StO2 upslope) and the area of the hyperemic phase were calculated to evaluate microvascular reactivity.

Results: In patients with SIC, the delta-downslope was higher (1.7 ± 2.5 versus -0.8 ± 3.2, $p = 0.049$) and the StO2 upslope was reduced (96 ± 74 versus 185 ± 91, $p = 0.017$), suggesting altered tissue oxygen extraction capacity and microvascular reactivity. Both parameters were able to discriminate the presence of SIC in the receiver operating characteristics curve analysis. Negative correlations were found between StO2 downslope-1 and TEG maximum amplitude ($r = -0.470$, $p = 0.023$), and Delta-Downslope and platelet count ($r = -0.527$, $p = 0.01$).

Conclusions: SIC is associated with alterations in peripheral tissue oxygen extraction capacity and microvascular reactivity.

1. Introduction

Sepsis is a major cause of mortality and morbidity in the Intensive Care Unit (ICU), characterized by a dysregulated host response to an infection leading to life-threatening organ dysfunction (Singer et al., 2016).

A pivotal driver of organ failure in sepsis is the impairment in microcirculatory perfusion, which represents the critical link between systemic inflammation and cellular metabolic failure (Damiani et al., 2023). This process is fueled by an intricate cross-talk between inflammation and coagulation, often referred to as immunothrombosis (Aklilu et al., 2025). Within this framework, the endothelium acts as a central orchestrator: its activation and subsequent dysfunction trigger a bidirectional relationship where inflammatory mediators and the coagulation cascade create a vicious cycle (Aklilu et al., 2025).

Sepsis-induced coagulopathy (SIC) is characterized by a systemic activation of coagulation and fibrinolysis shutdown, leading to possible microthrombosis (Iba et al., 2020). These pathological processes can lead to an obstruction in microvascular blood flow and disrupt the balance between tissue oxygen delivery and consumption (Marshall,

* Corresponding author at: Clinic of Anesthesia and Intensive Care Unit, Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, via Tronto 10/a, 60126, Ancona, Italy.
E-mail address: a.donati@univpm.it (A. Donati).

https://doi.org/10.1016/j.mvr.2026.104924
Received 30 December 2025; Received in revised form 17 February 2026; Accepted 17 February 2026
Available online 18 February 2026

2001). Despite the known biological link between coagulation and perfusion, the bedside clinical correlation between the coagulopathy and specific indices of microcirculatory function remains to be fully elucidated.

Near-infrared spectroscopy (NIRS) is a non-invasive tool for monitoring peripheral (skeletal muscle) tissue oxygen saturation (StO2) at the bedside. When combined with a vascular occlusion test (VOT), it allows for the assessment of dynamic microvascular reserve. Specifically, it provides insights into tissue oxygen extraction and microcirculatory reactivity, which serves as a proxy for endothelial function and capillary recruitment (Donati et al., 2016).

The goal of this study is to test the hypothesis that sepsis-induced coagulopathy is associated with more severe alterations in tissue oxygenation, oxygen extraction capacity and microvascular reactivity, as assessed by thenar NIRS with a VOT.

2. Methods

This prospective observational study was conducted between June 2023 and June 2025 in a 14-bed Intensive Care Unit (ICU) of a university hospital (Azienda Ospedaliero Universitaria delle Marche) in Ancona, Italy. The study was approved by the Regional Ethical Committee of Marche. Written informed consent was obtained by all patients or their next of kin.

Inclusion criteria were: diagnosis of sepsis within 24 h. Exclusion criteria were: age < 18 years; previous coagulopathy from other causes (including chronic liver failure, previous anticoagulant therapy, hematologic malignancies, congenital coagulation abnormalities); lack of informed consent.

2.1. NIRS monitoring

An InSpectra StO2 Tissue Oxygenation Monitor (model 650; Hutchinson Technology, Hutchinson, MN, USA) with a 15-mm-spaced probe was applied on the thenar eminence and used to measure StO2 at baseline and during a vascular occlusion test (VOT) (Gómez et al., 2008, 2009). In brief, after a 3-minute period of StO2 signal stabilization, a sphygmomanometer cuff on the arm was inflated to 50 mmHg above the systolic arterial pressure in order to arrest the arterial inflow. The cuff was then released after the StO2 was decreased to 40% (Gómez et al., 2008, 2009). StO2 was continuously recorded during the ischemic and the reperfusion phase until stabilization, with a sampling rate of 0.5 Hz. The choice to terminate occlusion based on a threshold value of StO2 (40%) rather than a fixed duration was adopted to ensure that the amount of tissue ischemia was similar between patients, regardless of their basal oxygen extraction rate (Gómez et al., 2009).

The NIRS-derived graph was analysed by means of a software package (version 3.03 InSpectra Analysis Program; Hutchinson Technology Inc.). StO2 and tissue hemoglobin index (THI) (Myers et al., 2009) were measured at baseline. The StO2 downslope (%/minute) was calculated from the regression line of the first (Downslope 1) and the last (Downslope 2) part of StO2 decay after occlusion, providing an index of tissue O2 extraction rate (Donati et al., 2016). The delta-downslope was calculated as the difference between the last and the first part of the desaturation slope (downslope 2 – downslope 1), so that a positive value indicates a flattening in the second part of the slope (slower StO2 decay) (Donati et al., 2016). The StO2 upslope (%/minute) and the area under the curve of the hyperaemic response (area of hyperemia) were calculated as indices of microvascular reactivity (Gómez et al., 2009). The StO2 upslope was calculated by using the entire recovery interval from the StO2 nadir of 40% to baseline StO2 values (Gómez et al., 2008). The linearity of the slopes was confirmed by using the coefficient of determination (R^2). This analysis showed a high degree of linear fit, with average R^2 of 0.991 (range 0.962–0.997) and 0.983 (range 0.956–0.996) for the downslopes and the upslopes, respectively.

2.2. Clinical and coagulation parameters

For all patients we recorded age, gender, admission diagnosis, source of sepsis, comorbidities, the Sequential Organ Failure Assessment (SOFA) (Vincent et al., 1996), the Acute Physiology and Chronic Evaluation II (APACHE II) (Knaus et al., 1985) and the Simplified Acute Physiology Score II (SAPS II) (Le Gall et al., 1993). Moreover, clinical and laboratory data were collected, including mean arterial pressure (MAP), heart rate (HR), arterial lactate levels, use of sedatives and vasoactive agents with dosages, coagulation parameters. The vasoactive-inotropic score (VIS) was calculated (Belletti et al., 2021). The SIC score and the disseminated intravascular coagulation (DIC) score were calculated as described elsewhere (Iba et al., 2019). A SIC score of ≥4 was used to identify patients with sepsis-induced coagulopathy (Iba et al., 2019).

A thromboelastography (TEG) was performed in all patients. A 2-ml whole blood sample was collected in a 3.2% sodium citrate Vacutainer tube and processed at the earliest and within 1 h by an automated device with a multichannel assay cartridge (TEG 6 s System, Haemonetics). The following clot formation parameters were obtained from the citrated kaolin assay: (a) reaction time (R-CK), time between the start of the test and the initial fibrin formation; (B) kinetic time (K-CK), time from initial fibrin formation to reach an amplitude of 20 mm, (c) alpha angle, the speed at which fibrin builds up and cross-linking takes place, (d) maximum amplitude (MA-CK), as a measure of the ultimate strength of the fibrin clot, and (e) clot lysis at 30 min (CLI30-CK), as the percentage decline in amplitude at 30 min. In addition, the MA-CFF was obtained from the citrated functional fibrinogen assay, which activates coagulation using tissue factor and excludes the platelet contribution to clot strength using abciximab, allowing for an assessment of fibrinogen contribution to clot strength (Luo et al., 2020).

2.3. Statistical analysis

This was performed with IBM SPS Statistics for Data Analysis (v. 30) and GraphPad Prism v. 11 (GraphPad software, La Jolla, CA, USA). Normality of distribution was checked using the Kolmogorov-Smirnov test. Continuous variables were expressed as mean ± standard deviation or median (25th–75th percentile), as appropriate. Student's *t*-test, or the Mann–Whitney *U* test, was used to compare continuous variables between two groups. Nominal variables were compared across groups using the chi-square test. The area under the receiver operating characteristic (ROC) curve was calculated to evaluate the discriminant value of the variables for SIC. The Spearman rho was calculated to evaluate correlations between non-normally distributed variables. A $p < 0.05$ was used to indicate statistical significance.

3. Results

A total of 23 septic patients was included in the study. Of these, 12 showed a SIC score of ≥4 (SIC+), with 3 patients out of 12 showing a DIC score ≥ 5 (Iba et al., 2019). General data for SIC+ and SIC- patients are reported in Table 1. Patients in the two groups were similar for age, gender, comorbidities and severity scores. All patients were sedated and required invasive mechanical ventilation. No major differences were found for the sedative agents used in the two groups, although the dose of remifentanyl was higher in the SIC(−) group. All patients received a norepinephrine infusion and the dose was similar between the two groups. However, 5 patients in the SIC(+) group had lactate levels higher than 2 mmol/l, meeting the criteria for septic shock, whereas lactate was <2 mmol/l in all patients in the SIC(−) group.

3.1. Coagulation parameters

These are reported in Table 2. SIC(+) patients had lower platelet counts and higher INR. Fibrinogen levels were increased above normal

Table 1
General clinical data.

	SIC+ ($n = 12$)	SIC− ($n = 11$)	p
Age (years)	53 ± 13	58 ± 17	0.460
Gender (nr of males, %)	6 (50%)	7 (63%)	0.680
Comorbidities (nr, %)			0.776
Arterial hypertension	2 (17%)	5 (45%)	
Cardiovascular disease	2 (17%)	1 (9%)	
Chronic respiratory disease	0 (0%)	1 (9%)	
Diabetes mellitus	2 (17%)	1 (9%)	
Immunosuppression	1 (8%)	1 (9%)	
Obesity	1 (8%)	3 (27%)	
Admission diagnosis (nr, %)			0.737
Sepsis	9 (75%)	6 (54%)	
Polytrauma	2 (17%)	2 (18%)	
Acute respiratory failure	3 (25%)	5 (45%)	
Post-surgery	2 (17%)	1 (9%)	
Sepsis source (nr, %)			0.541
Respiratory	5 (42%)	7 (64%)	
Blood	1 (8%)	0 (0%)	
Abdominal	4 (33%)	1 (9%)	
Genito-urinary	1 (8%)	2 (18%)	
Soft tissue	1 (8%)	2 (18%)	
SOFA score	8 ± 3	9 ± 2	0.410
APACHE II score	11 ± 8	15 ± 8	0.385
SAPS II score	33 [26–63]	44 [33–53]	0.535
Sedation			
Propofol (nr, %)	8 (67%)	9 (82%)	0.640
Propofol (mg/kg/h)	2 [1.5–2]	2 [1.5–3]	0.738
Dexmedetomidine (nr, %)	1 (8%)	0 (0%)	0.999
Dexmedetomidine (mcg/kg/h)	0.8	–	–
Midazolam (nr, %)	3 (25%)	2 (18%)	0.999
Midazolam (mg/kg/h)	0.1 [0.1–0.35]	0.35 [0.3–0.4]	0.400
Remifentanyl (mcg/kg/min)	10 (83%)	11 (100%)	0.478
Remifentanyl (nr, %)	0.05 [0.04–0.07]	0.1 [0.07–0.1]	0.009
Septic shock (nr, %)	5 (42%)	0 (0%)	0.037
Vasoactive drugs			
Norepinephrine tartrate (nr, %)	12 (100%)	11 (100%)	0.999
Norepinephrine tartrate (mcg/kg/min)	0.3 [0.13–0.53]	0.4 [0.15–0.5]	0.575
Terlipressin (nr, %)	1 (8%)	0 (0%)	0.999
Dobutamine (nr, %)	1 (8%)	1 (9%)	0.999
Levosimendan (nr, %)	3 (25%)	1 (9%)	0.590
Vasoactive-inotropic score	15 [7–27]	20 [8–25]	0.683
Heart rate (bpm)	94 ± 27	78 ± 21	0.123
Mean arterial pressure (mmHg)	84 ± 13	83 ± 13	0.801
Lactate (mmol/L)	2.1 ± 1.0	1.4 ± 0.3	0.051
White blood cell count (nr/mmc)	7680 [4443–19,050]	15,370 [9240–21,580]	0.287
Lymphocyte count (nr/mmc)	600 [290–850]	880 [330–1070]	0.277
Procalcitonin (ng/ml)	19 [8–45]	5 [3–73]	0.118

Data are expressed as number (%), mean ± standard deviation or median [1st–3rd quartile], as appropriate.

range in both groups, but were significantly higher in the SIC(−) group as compared to the SIC(+) group. TEG showed no significant differences between the groups for R-CK, K-CK and alpha angle-CK. Both MA-CK and MA-CFF were significantly lower in the SIC(+) group, despite remaining on average within the normal range. These parameters, especially the MA-CFF, were increased above the upper limit of normality in the SIC (−) group. Despite being in the normal range for both groups, the CLI30-CK was significantly lower among SIC(−) patients.

3.2. NIRS-derived parameters

StO2 was similar between the two groups, while THI tended to be higher among SIC(+) patients (Fig. 1). No significant differences were found for the StO2 downslope, both for the first (downslope 1) and the last part (downslope 2) of the desaturation curve, although the latter tended to be lower in the SIC(−) group, suggesting a faster O2 extraction. The delta-downslope was higher among SIC(+) patients (Fig. 2).

Table 2
Coagulation parameters.

	SIC+ (n = 12)	SIC− (n = 11)	p
Platelets (nr * 10^3/mmc)	121 [79–235]	225 [191–341]	0.022
INR	1.3 [1.2–1.8]	1.2 [1.1–1.3]	0.036
aPTT (s)	43 [35–59]	38 [35–40]	0.308
Fibrinogen (mg/dl)	524 ± 161	822 ± 281	0.005
Antithrombin III (%)	70 ± 19	78 ± 22	0.364
D-Dimer (ng/ml)	3596 [2448–5177]	3698 [2784–7552]	0.695
Thromboelastography			
R-CK (min)	8.5 [5.7–11.7]	8.4 [6.6–12]	0.960
K-CK (min)	1.5 ± 0.6	1.4 ± 0.6	0.763
Alpha angle -CK (°)	71 ± 6	74 ± 6	0.230
MA-CK (mm)	63 ± 4	68 ± 5	0.012
MA-CFF (mm)	33 ± 6	49 ± 13	0.001
CLI30-CK (%)	0.3 [0–1.5]	0 [0–0.02]	0.011
Anti-coagulants			
Low-molecular-weight heparin (nr, %)	3 (25%)	8 (73%)	0.039
Low-molecular-weight heparin (UI/day)	6000 [6000–12,000]	5000 [4000–6000]	0.115
Calcium heparin (nr, %)	0 (0%)	2 (18%)	0.217
Calcium heparin (UI/day)	–	5000 [5000–5000]	–
None (nr, %)	9 (75%)	1 (9%)	0.003

Data are expressed as number (%), mean ± standard deviation or median [1st–3rd quartile], as appropriate. *INR* International Normalized Ratio, *aPTT* activated partial thromboplastin clotting time, *R-CK* reaction time – citrated kaolin, *K-CK* kinetics – citrated kaolin, *MA-CK* maximum amplitude – citrated kaolin, *MA-CFF* maximum amplitude – citrated functional fibrinogen, *CLI30-CK* clot lysis index at 30 min – citrated kaolin.

The StO2 upslope was significantly lower in the SIC(+) group, while no difference was observed for the area of hyperemia (Fig. 3). NIRS graphs from two representative patients with and without SIC are shown in Fig. 4. In the ROC curve analysis, a higher delta-downslope and a lower StO2 upslope were able to discriminate the presence of SIC similarly to lactate levels (Fig. 5). Negative correlations were found between StO2 downslope (1) and MA-CK ($r = -0.470$, $p = 0.023$) and Delta-Downslope and platelet count ($r = -0.527$, $p = 0.01$). No other significant correlations were found between NIRS parameters and other variables.

4. Discussion

By using thenar NIRS with a VOT to evaluate peripheral tissue oxygenation in septic patients, we found that sepsis-induced coagulopathy is associated with more severe derangements in tissue oxygen extraction capacity and microvascular reactivity.

In several previous studies, baseline StO2 seemed to predict mortality and identify patients with more severe circulatory shock (Varis et al., 2020). Nonetheless, we previously failed to show any robust association between lower StO2 and worse outcome in a heterogenous population of critically ill patients (Donati et al., 2016). In the present study, StO2 did not differ between patients with and without SIC. Of note, StO2 in this cohort of septic patients was similar to the average StO2 that we previously reported in healthy volunteers (Donati et al., 2016). Similarly as to central venous SO2, StO2 reflects the balance between oxygen delivery and consumption at the tissue level: a reduction in tissue oxygen extraction may thus result in normal/higher StO2 irrespectively of tissue O2 availability.

The integration of NIRS with a VOT enables to assess the dynamic response of the microvascular bed to a transient period of ischemia. Under physiological conditions, the microcirculation can autoregulate blood flow distribution in the tissue through a complex interplay of local mechanisms, including the release of metabolic vasodilators (such as nitric oxide, adenosine, prostaglandins) and the myogenic response of the precapillary sphincters (Bateman et al., 2015). This autoregulation ensures that blood flow is matched to the metabolic demand. All these

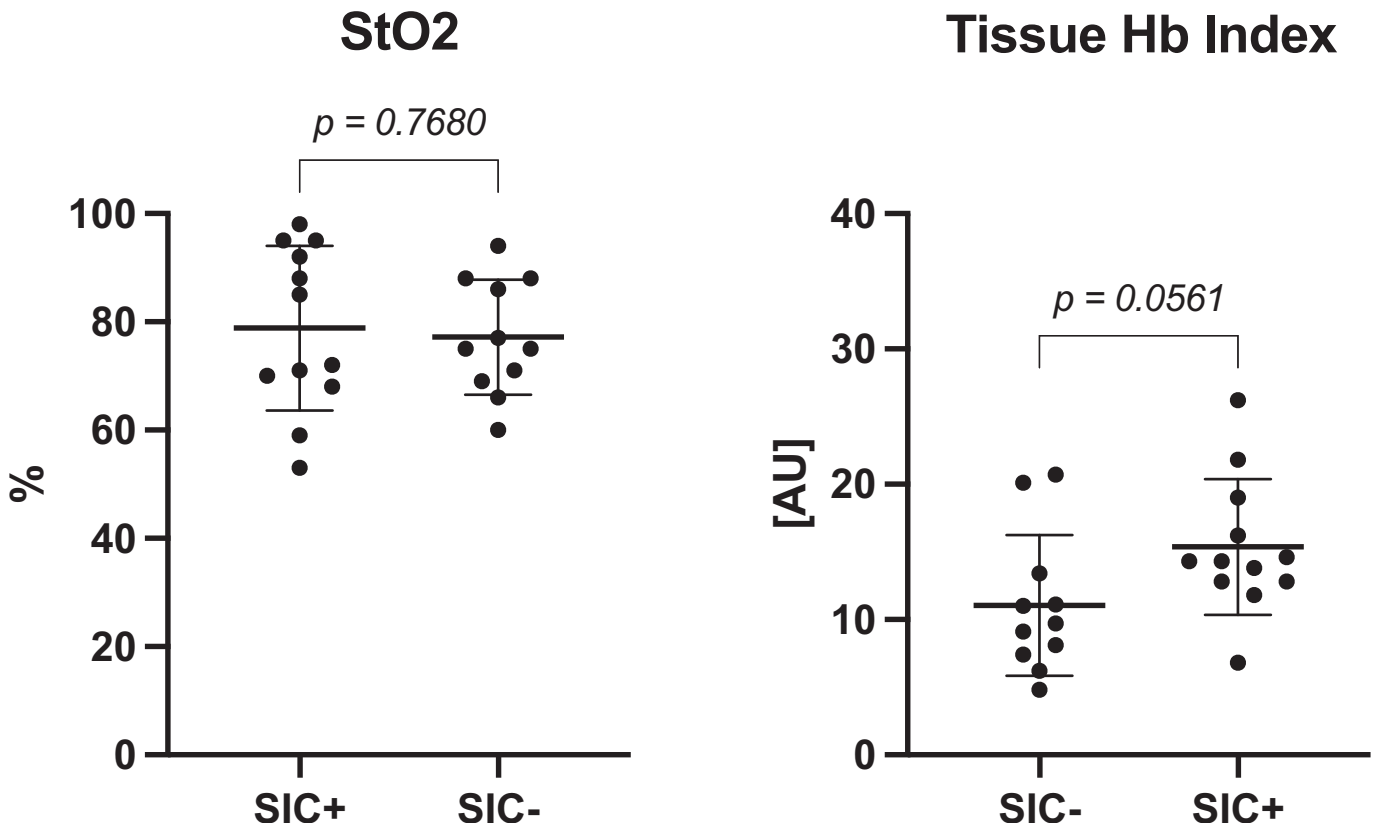

Fig. 1. StO2 and tissue hemoglobin index.

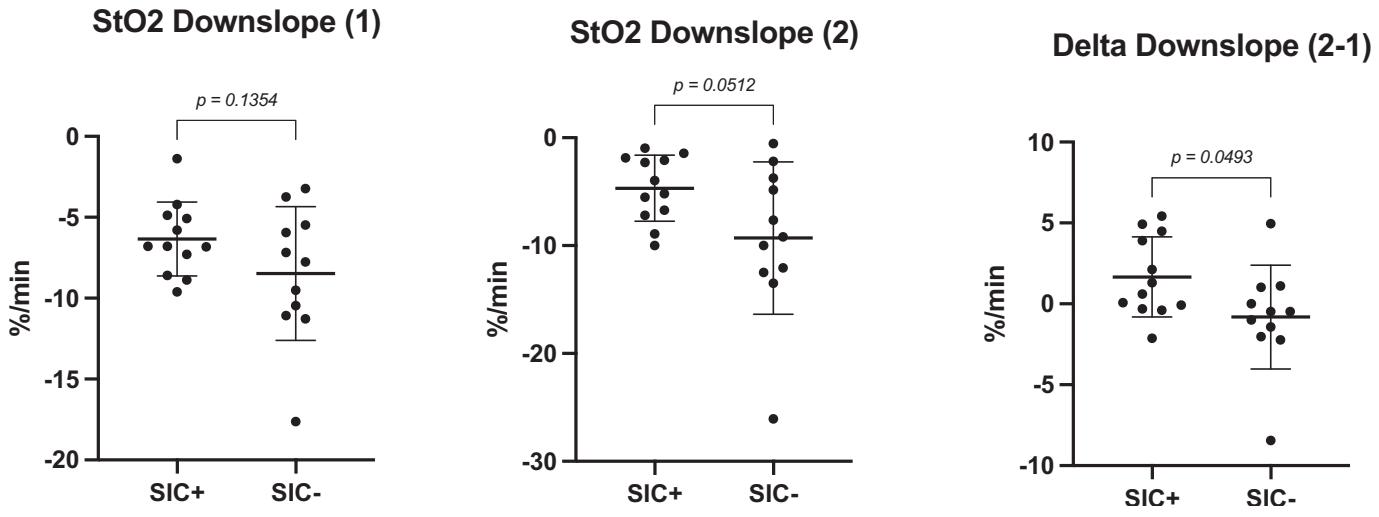

Fig. 2. Parameters of tissue oxygen extraction capacity.

mechanisms can be compromised during sepsis when endothelial dysfunction occurs (Bateman et al., 2015; Ince, 2015). SIC may be either an epiphenomenon of more severe endothelial derangement, or a primary contributor to microcirculatory perfusion failure, where the formation of microthrombi and fibrin deposition physically obstruct the capillary bed, thereby compromising the intrinsic autoregulatory mechanisms and oxygen extraction capacity (Marshall, 2001).

In our study, the desaturation slope under ischemia was similar between SIC(+) and SIC(−) patients in its first part, but tended to be steeper among those without coagulopathy. The delta-downslope, i.e. the difference between the final and the first part of the desaturation slope, was significantly higher among patients with SIC. We were the first to explore the potential meaning of this "flattening" in the desaturation slope during the ischemic phase of the VOT: in critically ill patients, a higher delta-downslope was independently associated with higher 90-day mortality, whereas a constant (or increasing) desaturation rate could reflect a more effective redistribution of blood flow to more hypoxic regions (Donati et al., 2016).

Our findings highlight a significant reduction in the reoxygenation rate (StO2 upslope) during the reperfusion phase among patients with SIC. The NIRS-derived StO2 upslope is a well-established functional index of microvascular reactivity, reflecting the efficiency of capillary recruitment and the hyperemic response following the ischemic challenge (Mesquida et al., 2013). Several studies showed an association

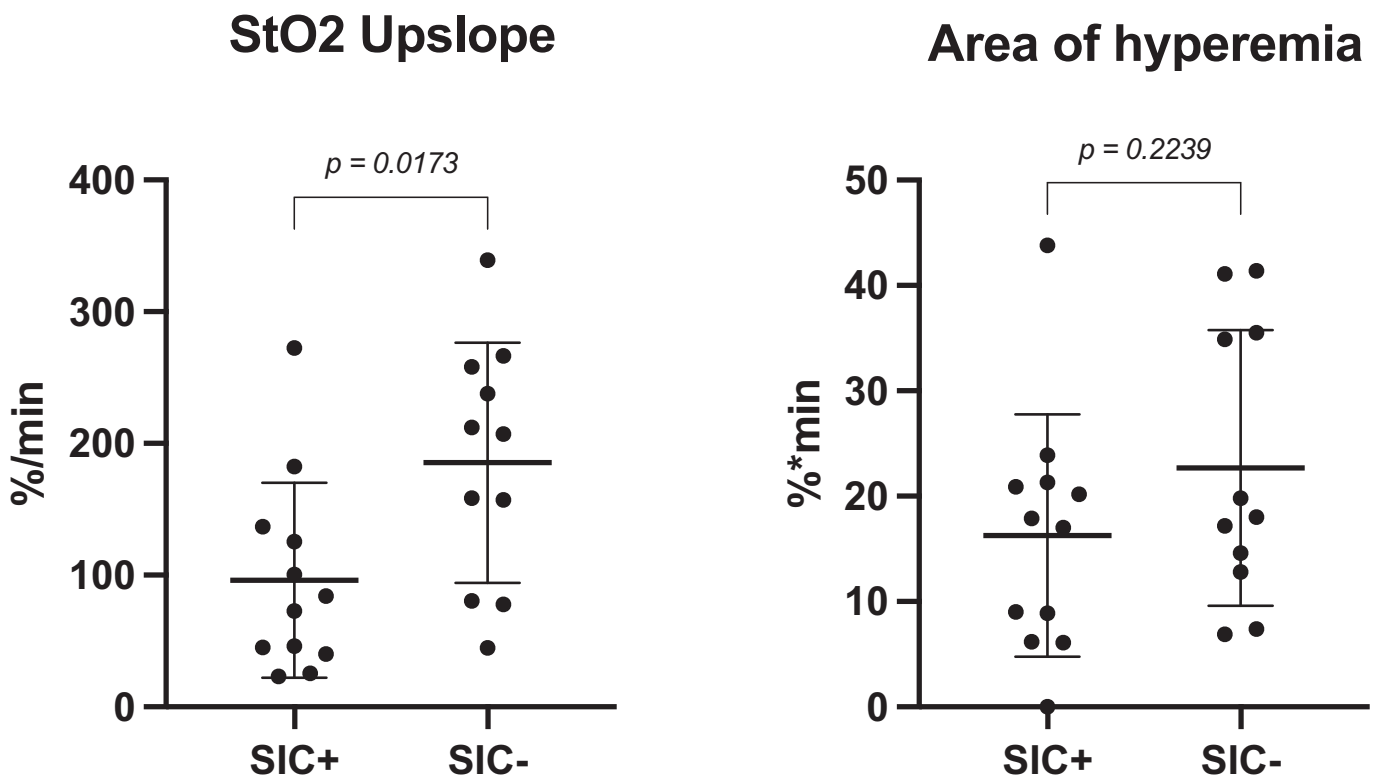

Fig. 3. Parameters of microvascular reactivity.

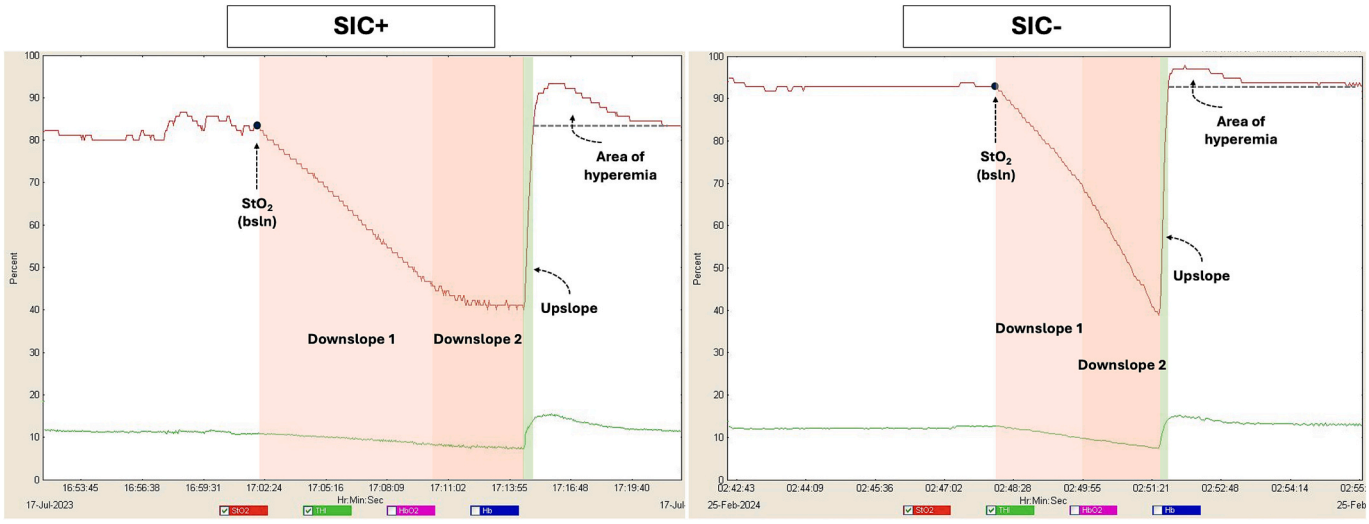

Fig. 4. Representative NIRS tracings during the Vascular Occlusion Test (VOT) for a patient with sepsis-induced coagulopathy (SIC+) and a patient without coagulopathy (SIC−).
The time windows used for parameter calculation are highlighted in different colors: light red indicates the ischemic phase used to calculate the desaturation slopes (Downslope 1 and Downslope 2), light green indicates the reperfusion phase used to calculate the reoxygenation slope (Upslope). These representative graph illustrates the difference in microvascular response between the two groups, showing a flatter desaturation slope in the second phase (Downslope 2) and a slower reoxygenation (Upslope) in the SIC+ patient. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

between a slower re-oxygenation rate and worse outcome in septic patients (Pareznik et al., 2006; Creteur et al., 2007; Skarda et al., 2007). A blunted usplope suggests an impairment in the vasodilatory capacity. While a reduced bioavailability of NO and other endothelium-derived relaxing factors was hypothesized as a mechanism for blunted reactive hyperemia (Mesquida et al., 2013; Kolb et al., 2017), other studies suggests inwardly rectifying potassium channels and Na+/K+-ATPase activation playing a more substantial role in mediating the hyperemic response (Crecelius et al., 2013). In SIC, the physical presence of microthrombi and fibrin strands within the capillary bed may further obstruct microvascular reperfusion.

Sepsis almost invariably triggers a hypercoagulable state (Aklilu et al., 2025). While the SIC score is specifically designed to early identify patients transitioning toward consumption coagulopathy (Iba et al.,

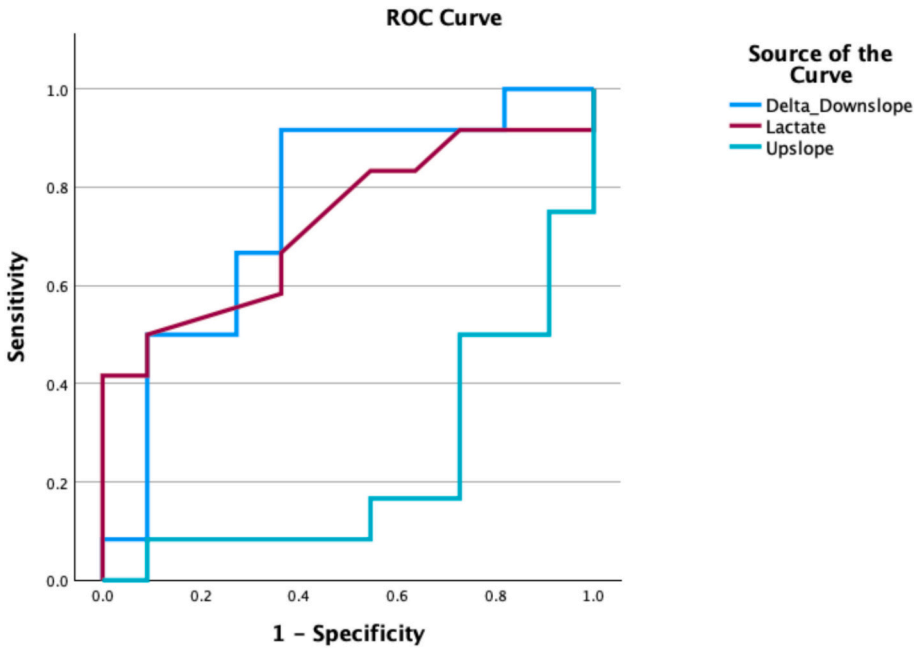

Fig. 5. Receiver operating characteristics curve for the presence of sepsis-induced coagulopathy.
Areas under the ROC curve were: 0.76 [95% CI 0.55–0.96] for delta-downlospe ($p = 0.015$), 0.23 [95% CI 0.03–0.43] for StO2 upslope ($p = 0.007$), 0.73 [95% CI 0.52–0.94] for lactate ($p = 0.035$).

2019), our findings highlight a significant discrepancy between functional clot assessment with TEG and conventional laboratory markers. TEG analysis in SIC(+) patients demonstrated that clot formation and strength remained normal or even enhanced, suggesting that conventional assays fail to capture the true functional hemostatic balance. Of note, 75% of patients in the SIC(+) group were not receiving any pharmacological thromboprophylaxis: this undertreatment was likely driven by the alterations observed in standard laboratory parameters (platelet count, INR, aPTT), which were likely interpreted as high bleeding risk.

Our study has several limitations. First, the small sample size and the single-center nature of the study may limit the generalizability of our findings. Second, as an observational study, we can describe associations but cannot establish a causal link between microthrombosis and tissue oxygenation abnormalities. Third, NIRS measures the skeletal muscle oxygenation in a peripheral localized area (the thenar eminence), which may not always reflect the microcirculatory status of other vital organs. Finally, we used a predefined StO_2 threshold to terminate the ischemic phase rather than a fixed occlusion duration, which may have influenced the assessment of the hyperemic response (Murias et al., 2026). However, our approach was chosen to ensure a comparable level of tissue ischemia across patients with varying basal oxygen extraction rates, thereby reducing inter-individual variability in the metabolic demand during the test (Gómez et al., 2009).

5. Conclusions

Our study shows a significant association between SIC and microcirculatory dysfunction. By employing NIRS combined with a VOT, we observed that patients with SIC exhibit a reduced tissue oxygen extraction capacity and blunted microvascular reactivity. NIRS monitoring may provide clinicians with valuable insights into the functional state of the microcirculation, thus potentially identifying patients at higher risk for adverse outcome.

CRediT authorship contribution statement

Roberta Domizi: Writing – review & editing, Methodology, Investigation, Formal analysis, Conceptualization. **Andrea Carsetti:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Riccardo Antolini:** Writing – original draft, Methodology, Investigation. **Erika Casarotta:** Writing – original draft, Investigation, Formal analysis, Data curation. **Claudia Scorcella:** Writing – original draft, Methodology, Formal analysis, Data curation. **Samuele Zuccari:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Eva Vitali:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Erica Adrario:** Writing – review & editing, Validation, Supervision, Conceptualization. **Abele Donati:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Elisa Damiani:** Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Funding

No external funding was received for the realization of this work.

Declaration of competing interest

The authors declare that they have no competing interests in relation to the submitted manuscript entitled “Sepsis-induced coagulopathy is associated with impaired tissue oxygen extraction and microvascular reactivity: a prospective observational study”.

Acknowledgements

We thank the medical and nurse staff of the Clinic of Anesthesia and Intensive Care of Azienda Ospedaliera Universitaria delle Marche (Ancona, Italy) for their support in the realization of this work.

Data availability

Data will be made available on request.

References

Aklilu, A., Lai, M.S., Jiang, Z., Yip, S.P., Huang, C.L., 2025. Immunothrombosis in sepsis: cellular crosstalk, molecular triggers, and therapeutic opportunities-a review. Int. J. Mol. Sci. 26, 6114.

Bateman, R.M., Sharpe, M.D., Jagger, J.E., Ellis, C.G., 2015. Sepsis impairs microvascular autoregulation and delays capillary response within hypoxic capillaries. Crit. Care 19, 389.

Belletti, A., Lerose, C.C., Zangrillo, A., Landoni, G., 2021. Vasoactive-inotropic score: evolution, clinical utility, and pitfalls. J. Cardiothorac. Vasc. Anesth. 35, 3067–3077.

Crecelius, A.R., Richards, J.C., Luckasen, G.J., Larson, D.G., Dinenno, F.A., 2013. Reactive hyperemia occurs via activation of inwardly rectifying potassium channels and Na+/K+-ATPase in humans. Circ. Res. 113, 1023–1032.

Creteur, J., Carollo, T., Soldati, G., Buchele, G., De Backer, D., Vincent, J.L., 2007. The prognostic value of muscle StO2 in septic patients. Intensive Care Med. 33, 1549–1556.

Damiani, E., Carsetti, A., Casarotta, E., Domizi, R., Scorcella, C., Donati, A., Adrario, E., 2023. Microcirculation-guided resuscitation in sepsis: the next frontier? Front. Med. 10, 1212321.

Donati, A., Damiani, E., Domizi, R., Scorcella, C., Carsetti, A., Tondi, S., Monaldi, V., Adrario, E., Romano, R., Pelaia, P., Singer, M., 2016. Near-infrared spectroscopy for assessing tissue oxygenation and microvascular reactivity in critically ill patients: a prospective observational study. Crit. Care 20, 311.

Gómez, H., Torres, A., Polanco, P., Kim, H.K., Zenker, S., Puyana, J.C., et al., 2008. Use of non-invasive NIRS during a vascular occlusion test to assess dynamic tissue O2 saturation response. Intensive Care Med. 34, 1600–1607.

Gómez, H., Mesquida, J., Simon, P., Kim, H.K., Puyana, J.C., Ince, C., et al., 2009. Characterization of tissue oxygen saturation and the vascular occlusion test: influence of measurement sites, probe sizes and deflation thresholds. Crit. Care 13, S3.

Iba, T., Levy, J.H., Yamakawa, K., Thachil, J., Warkentin, T.E., Levi, M., The Scientific and Standardization Committee on DIC of the International Society on Thrombosis and Hemostasis, 2019. Proposal of a two-step process for the diagnosis of sepsis-induced disseminated intravascular coagulation. J. Thromb. Haemost. 17, 1265–1268.

Iba, T., Levi, M., Levy, J.H., 2020. Sepsis-induced coagulopathy and disseminated intravascular coagulation. Semin. Thromb. Hemost. 46, 89–95.

Ince, C., 2015. Hemodynamic coherence and the rationale for monitoring the microcirculation. Crit. Care 19, S8.

Knaus, W.A., Draper, E.A., Wagner, D.P., Zimmerman, J.E., 1985. APACHE II: a severity of disease classification system. Crit. Care Med. 13, 818–829.

Kolb, L., Orbegozo, D., Creteur, J., Preiser, J.C., Vincent, J.L., De Backer, D., 2017. Oral nitrate increases microvascular reactivity and the number of visible perfused microvessels in healthy volunteers. J. Vasc. Res. 54, 209–216.

Le Gall, J.R., Lemeshow, S., Saulnier, F., 1993. A new Simplified Acute Physiology Score (SAPS II) based on European/North Americal multicenter study. JAMA 270, 2957–2963.

Luo, C., Hu, H., Gong, J., Zhou, Y., Chen, Z., Cai, S., 2020. The value of thromboelastography in the diagnosis of sepsis-induced coagulopathy. Clin. Appl. Thromb. Hemost. 26, 1076029620951847.

Marshall, J.C., 2001. Inflammation, coagulopathy and the pathogenesis of multiple organ dysfunction syndrome. Crit. Care Med. 29, S99–106.

Mesquida, J., Gruartmoner, G., Espinal, C., 2013. Skeletal muscle oxygen saturation (StO2) measured by near-infrared spectroscopy in the critically ill patients. Biomed. Res. Int. 2013, 502194.

Murias, J.M., Inglis, E.C., Alvares, T.S., Rasica, L., Soares, R.N., 2026. New insigths into the influence of tissue desaturation on skeletal muscle reactive hyperemia: implications for sex-related differences. Med. Sci. Sports Exerc. 58, 174–181.

Myers, D., McGraw, M., George, M., Mulier, K., Beilman, G., 2009. Tissue hemoglobin index: a non-invasive optical measure of total tissue hemoglobin. Crit. Care 13 (S2), 15.

Pareznik, R., Knezevic, R., Voga, G., Podbregar, M., 2006. Changes in muscle tissue oxygenation during stagnant ischemia in septic patients. Intensive Care Med. 32, 87–92.

Singer, M., Deutschman, C.S., Seymour, C.W., Shankar-Hari, M., Annane, D., Bauer, M., Bellomo, R., Bernard, G.R., Chiche, J.D., Coopersmith, C.M., Hotchkiss, R.S., Levy, M.M., Marshall, J.C., Martin, G.S., Opal, S.M., Rubenfeld, G.D., van der Poll, T., Vincent, J.L., Angus, D.C., 2016. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 315, 801–810.

Skarda, D.E., Mulier, K.E., Myers, D.E., Taylor, J.H., Beilman, G.J., 2007. Dynamic near-infrared spectroscopy measurements in patients with severe sepsis. Shock 27, 348–353.

Varis, E., Pettila, V., Wilkman, E., 2020. Near-infrared spectroscopy in adult circulatory shock: a systematic review. J. Intensive Care Med. 35, 943–962.

Vincent, J.L., Moreno, R., Takala, J., et al., 1996. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure: on behalf of the working group on sepsis-related problems of the European Society of Intensive Care Medicine. Intensive Care Med. 22, 707–710.