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Association between mean hemodynamic variables during the first 24 h and outcomes in cardiogenic shock: identification of clinically relevant thresholds

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Abstract

Purpose Cardiogenic shock (CS) remains a critical condition with high mortality rates despite advances in treatment. This study aims to comprehensively evaluate both macrocirculatory and tissue perfusion variables over the initial 24 h post-admission to determine their impact on patient prognosis and identify potential hemodynamic thresholds for optimal outcomes. Secondary aims were to explore the correlation between macrocirculatory and tissue perfusion variables.

Design This is a post hoc analysis of data from two prospective studies, OptimaCC (NCT01367743) and MicroShock (NCT03436641), involving only patients with CS. Both studies applied regular assessment of hemodynamic variables at specific time points (admission, 6, 12, and 24 h) to ensure consistency in data collection, enrolling 118 patients between September 2011 and July 2021, with similar inclusion criteria and care processes.

Results The median age of the cohort was 69 years, 59% being male. The primary outcome, 30-day mortality, occurred in 37% of patients. Average macrocirculation variables over the first 24 h of CS such as mean arterial pressure (MAP), cardiac output (CO), cardiac index (CI), and cardiac power index (CPI) were significantly lower in patients meeting the primary outcome. Accordingly, average tissue perfusion variables (ΔPCO_2 and $\Delta PCO_2/C(a\text{-}v)O_2$) over the first 24 h of CS were also consistently impaired in patients meeting the primary outcome. The optimal clinically relevant thresholds of the first 24 h time course for poor outcomes, closely approximating the optimal values identified in the analysis, were: mean SAP < 95 mmHg, MAP < 70 mmHg, CO < 3.5 L/min, CI ≤ 1.8 L/min/m^2, CPI < 0.27 W/m^2, $ScvO_2$ < 70%, $\Delta PCO_2 \geq 9$ mmHg, and $\Delta PCO_2/C(a\text{-}v)O_2 \geq 1.5$ mmHg/mL.

Conclusions This study is the first to identify critical hemodynamic thresholds, encompassing both macrocirculatory and tissue perfusion variables, within the initial 24 h of CS that are associated with adverse outcomes. The identified thresholds suggest specific hemodynamic targets that may guide resuscitation strategies.

Keywords Cardiogenic shock, Heart failure, Macrocirculation, Tissue perfusion variables

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Take-home message

This study introduces two novel contributions in cardiogenic shock management: a comprehensive longitudinal assessment of macrocirculatory variables during early treatment and the first-ever longitudinal evaluation of tissue perfusion variables in early cardiogenic shock. These findings offer new hemodynamic targets for optimizing early intervention.

A 140-character Tweet

New breakthroughs in cardiogenic shock: first study to assess macrocirculatory & tissue perfusion variables longitudinally in early management. #CriticalCare

Introduction

Cardiogenic shock (CS) presents a significant challenge, requiring a thorough approach to guide resuscitation strategies [1, 2]. Understanding both macrocirculatory and tissue perfusion variables is crucial for gaining insights into hemodynamic intricacies [3]. Despite advancements in pharmaceuticals and acute mechanical circulatory support (aMCS), mortality rates in CS patients remain high at 30–50% at 6 to 12 months [4]. To address this, the Shock Academic Research Consortium (SHARC) has proposed a refined definition of CS as a cardiac disorder characterized by clinical and biochemical evidence of sustained tissue hypoperfusion [5]. Diagnosis includes systolic blood pressure (SBP) < 90 mmHg for ≥ 30 min or the need for vasopressors, inotropes, or mechanical circulatory support to maintain systolic blood pressure ≥ 90 mmHg, with additional hemodynamic criteria such as cardiac index (CI) < 2.2 L/min/m^2 measured by invasive or non-invasive methods. This definition completes the recently updated Society for Cardiovascular Angiography and Interventions (SCAI) Shock classification [6].

While various hemodynamic variables, especially those related to prognosis, have shown utility in isolated analyses typically conducted upon admission, subsequent hemodynamic management remains a matter of debate [7, 8]. To date, no studies have accurately reported a temporal longitudinal assessment of these macrocirculatory and tissue perfusion variables correlated with prognosis during the first hours of patient care. Consequently, this study aims to comprehensively evaluate hemodynamic variables, including tissue perfusion variables, along with their mean values over the initial 24 h post-admission, elucidating their dynamic impact on patient prognosis. Secondary aims were to explore the correlation between macrocirculatory and tissue perfusion variables. We hypothesized that hospital mortality in CS patients would rise with progressively lower hemodynamic variables. Furthermore, we aimed to identify potential thresholds that might delineate optimal hemodynamic ranges.

Materials and methods

Study design and study settings

We performed a post hoc analysis of data collected prospectively in two studies of CS: OptimaCC [9] and MicroShock [10]. These two studies were chosen because they enrolled similar populations of patients with CS, with closely regular assessment of hemodynamic variables at the same time point (admission *i.e.* H0, H6, H12, H24). Also, the process of care and the inclusion window were similar in the two studies. OptimaCC was conducted in nine French intensive care units (ICUs) and MicroShock in two ICUs. The two trials enrolled 118 patients between September 2011 and July 2021, namely 57 patients from the OptimaCC study and 61 patients from the MicroShock study.

Ethics

The protocol of each of the two studies was approved by the appropriate ethics committees. OptimaCC (NCT01367743) received the approval of the Nancy Hospital Institutional Review Board, France. MicroShock (NCT03436641) received approval from the Comité de Protection des Personnes, Sud-Est V, France (Comité de Protection des Personnes, Sud-Est V; reference 18-STRA-01).

Study population

All patients admitted to the participating centers during each trial period were screened for eligibility. Inclusion criteria were age 18 years or older and ICU admission for CS. We did not include data from patients who withdrew consent after initial inclusion.

While OptimaCC included only acute myocardial infarction complicated by CS (AMI-CS), the MicroShock study included all types of CS except CS following cardiac arrest.

Study definitions

Definitions of CS were nearly identical in the two studies. In OptimaCC, CS was defined by simultaneous presence of all the following criteria: (1) CS due to acute myocardial infarction (AMI) successfully revascularized by using percutaneous coronary intervention (PCI); (2) SBP < 90 mmHg or mean arterial pressure (MAP) < 65 mmHg without a vasopressor agent or need for vasopressor therapy to correct hypotension; (3) CI < 2.2 l/min/m2 in the absence of vasopressor or inotrope therapy; (4) pulmonary artery occlusion pressure > 15 mmHg or echocardiographic evidence of high

pressure; (5) echocardiographic left ventricular ejection fraction (LVEF) < 40% without inotrope support (this criterion was not taken into account in instances of treatment with dopamine, norepinephrine, epinephrine, dobutamine, or milrinone); (6) at least one evidence of tissue hypoperfusion (e.g., skin mottling, oliguria, elevated lactate level, altered consciousness) and (7) an inserted pulmonary artery catheter. All these seven criteria had to be met for a patient to be included in the study. In MicroShock, CS was defined according to the definition used in the FRENSHOCK registry which considers all CS shock regardless of the etiology [11], and patients were included if they met at least one criterion of each of the following three main components: (1) Low cardiac output, defined by systolic blood pressure < 90 mmHg and/or the need for amines (dobutamine and/or norepinephrine and/or epinephrine) to maintain systolic blood pressure > 90 mmHg and/or cardiac index < 2.2 L/min/m^2 on echocardiography or right heart catheterization; (2) Elevation of left and/or right heart pressures, defined by clinical signs, radiology (overload signs on chest X-ray or computed tomography scan), biological tests (natriuretic peptide elevation), echocardiography (usual signs of left ventricular filling pressure elevation) or invasive hemodynamic overload signs (elevation of mean pulmonary artery pressure or pulmonary capillary wedge pressure); (3) Signs of malperfusion, which could be clinical (oliguria, mottling, confusion) and/or biological (lactate > 2 mmol/L, hepatic insufficiency, renal failure).

The SCAI shock classification was evaluated at admission for all patients enrolled in the MicroShock study. In contrast, for the patients included in the OptimaCC study, the classification was retrospectively and independently determined in a blinded manner by two expert authors based on admission characteristics. The vasoactive-inotropic score (VIS) was calculated based on its latest version [12].

At each time point (admission i.e. H0, H6, H12, H24), variables reflecting macrocirculation and tissue perfusion were collected. Data used at H0 were obtained from the measurement closest to the time of admission, typically within the first hour, even for variables derived from pulmonary artery catheter or central venous catheters implanted in the superior vena cava territory. Macrocirculation was assessed using invasive blood pressure monitoring (intra-arterial catheter), heart rate, LVEF, and CI by echocardiography for the MicroShock study and pulmonary artery catheters for the OptimaCC study. Echocardiography variables were assessed by physicians with adult echocardiography certification [13, 14] using the Vivid-S5 or S70 system (General Electric). Cardiac index (L/min/m^2) assessment with echocardiography was calculated by using standard formulae, as CI is the quotient of the cardiac output (CO) divided by the body surface area. The CO is the product of the stroke volume by the heart rate. Stroke volume is calculated as the product between aortic velocity–time integral (measured using pulsed-wave Doppler) and aortic cross-sectional area. The latter is calculated in the long-axis parasternal window using the left ventricular outflow tract diameter measurement. Thus, stroke volume = [(3.1416) × (left ventricular outflow tract diameter/2)^2] × aortic velocity–time integral. Cardiac power index (CPI, W/m^2) is the cardiac power output indexed to body surface area and was calculated as MAP × cardiac index/451 [15]. In the OptimaCC cohort, pulmonary artery catheter variables have been collected, such as right atrial pressure (RAP), pulmonary artery systolic pressure (PASP), pulmonary artery occlusion pressure (PAOP), systemic vascular resistance index (SVRI), pulmonary vascular resistance index (PVRI) and pulmonary artery pulsatility index (PAPi) was calculated as followed [PASP–diastolic pulmonary arterial pressure]/right atrial pressure.

Tissue perfusion variables were assessed using pairs of arterial and central venous blood samples to determine the following variables: arterial partial pressure of oxygen (PaO_2), arterial partial pressure of carbon dioxide ($PaCO_2$), central venous partial pressure of oxygen (PvO_2), central venous partial pressure of carbon dioxide ($PvCO_2$), arterial oxygen saturation (SaO_2), and central venous oxygen saturation ($ScvO_2$). In order to use the measurement values from the central venous catheter implanted in the superior vena cava territory as a reference, a correction factor was therefore applied to the OptimaCC data (obtained via a pulmonary artery catheter) by adding 5% from the raw values of SvO_2, based on previous data showing a mean difference of 5% between mixed venous oxygen saturation (SvO_2) and $ScVO_2$ with minimal impact regarding the CO [16, 17]. The hemoglobin (Hb) and lactate concentrations were measured from the arterial blood. The arterial oxygen content (CaO_2), central venous oxygen content (CvO_2), C(a-v)O_2, P(v-a)CO_2, and ratio of venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference *i.e.* P(v-a)CO_2/C(a-v)O_2 ratio were defined as follows:

- $CaO_2 = (1.34 \times SaO_2 \times Hb) + (0.0031 \times PaO_2)$
- $CvO_2 = (1.34 \times ScvO_2 \times Hb) + (0.0031 \times PvO_2)$
- $C(a\text{-}v)O_2 = CaO_2 - CvO_2$
- $P(v\text{-}a)CO_2 = \Delta PCO_2 = PvCO_2 - PaCO_2$
- $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio $= \Delta PCO_2/C(a\text{-}v)O_2 = (PvCO_2 - PaCO_2)/(CaO_2 - CvO_2)$

As mentioned, Pv-aCO_2, also named PCO_2 gap or ΔPCO_2, was calculated by subtracting arterial partial

pressure of carbon dioxide ($PaCO_2$) from partial pressure of CO_2 in superior vena cava blood ($PvCO_2$) measured in arterial and central venous samples taken simultaneously. However, in the OptimaCC cohort, $PvCO_2$ was collected via the pulmonary artery catheter and thus corresponded to mixed venous partial pressure of CO_2 ($PmvCO_2$), whereas, in the MicroShock cohort, it was collected via a central venous catheter implanted in the superior vena cava territory and thus corresponded to $PcvCO_2$, which may be overestimated according to literature data [18]. In order to use the measurements values from the central venous catheter implanted in the superior vena cava territory as a reference, a correction factor was therefore applied to the OptimaCC data (obtained via a pulmonary artery catheter) by adding 2.7 mmHg from the raw values of $PvCO_2$, based on data from the work of Cavaliere et al. [18].

In the supplementary material, data were analyzed using the pulmonary artery catheter as a reference by subtracting 5% from the raw $ScvO_2$ values and subtracting 2.7 mmHg from the raw $PcvCO_2$ values.

In the MicroShock study, skin mottling of the anterior aspect of the knee was assessed visually on both legs, as a variables of tissue hypoperfusion. Patients were placed supine with the legs straight and at the level of the heart. Mottling score which describes the extent of the mottled area on the knee and thigh was determined on a 6-point scale ranging from 0 to 5 in the MicroShock cohort as described previously [19, 20]. If mottling was present, then the leg with more prominent mottling was chosen for scoring.

If patients were put under VA-ECMO support within the first 24 h, the hemodynamic variables were no longer taken into account for the analysis once they were under VA-ECMO support.

Data collection

For each patient in each study, a dedicated study nurse or investigator at each participating center collected the baseline clinical data and comorbidities; characteristics of the CS; clinical and laboratory features at ICU admission; treatments delivered in the ICU; ICU length of stay; invasive mechanical ventilation duration; and vital and functional status at ICU discharge, hospital discharge and at long-term follow-up.

Outcome measures

For the present study, the primary outcome was the 30-day mortality. The 30-day mortality was a secondary outcome in the MicroShock study and OptimaCC study. As objective judgment criteria, these elements were collected in a precise manner in both studies.

Statistical analysis

Continuous variables were expressed as medians with interquartile ranges and categorical variables as frequencies and percentages. Baseline characteristics were compared between the two cohorts using Wilcoxon test for continuous variables and Fisher's exact test for categorical variables. The hemodynamic variables were also compared between patients who experienced the primary outcome (death at 30 days) and those who did not, using the same tests. The mean value of each hemodynamic variable was calculated from the 4 measurements at H0, H6, H12, and H24 when at least one of the four measurements was available. Missing values were not imputed and were not accounted for in the analyses. However, missing data were rare during the study period. For each hemodynamic variable, most patients had all four measurements.

The association between hemodynamic variables and the outcome was assessed using univariable Cox model. Hazard Ratios (HR) are reported with 95% confidence interval (CI 95%). For each hemodynamic variable, an optimal threshold was determined by maximizing the Harrell's C-index in univariable Cox model.

Kaplan–Meier analyses were performed to provide event-free survival curves based on the optimal thresholds for hemodynamic variables. Differences between the curves were analyzed using the log-rank test.

The relationship between macrocirculation indices and tissue perfusion variables was assessed by calculating Spearman's rank correlation coefficients.

The two-tailed significance level was set at $p < 0.05$. All statistical analyses were performed using R software version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

Data from 118 patients were analyzed in two pooled prospective multicenter observational cohorts. The comprehensive characteristics are summarized in Table 1. The median age of our cohort was 69 (60–77 years) years. The study population consisted predominantly of males (59%). The median LVEF was 30% (IQR 20–40). Admission lactate level was 3.4 mmol/l (IQR 1.9–6). At admission, the median SAPS II score was 61 (45–74) points, median SOFA was 9 (7–11) points, and median VIS was 39 (13–83). The distribution of post-hoc calculated SCAI shock classification at admission was as follows: B (2%), C (53%), D (29%), and E (16%). A total of 90% of the patients were under mechanical ventilation. Prior to study enrollment, 28% of patients had experienced a cardiac arrest event necessitating cardiopulmonary resuscitation.

Table 1 Baseline characteristics of the study population

Variable	Overall (*n* = 118)	MicroShock (*n* = 61)	OptimaCC (*n* = 57)
Demographic			
Age (years)	69 (60–77)	70 (65–77)	67 (55–77)
Sex			
Male	70 (59%)	32 (52%)	38 (67%)
Female	48 (41%)	29 (48%)	19 (33%)
BMI (kg/m^2)	26.1 (22.5–28.1) [*n* = 115]	27.0 (23.1–30.4)	25.4 (22.3–27.4) [*n* = 54]
Medical history			
Hypertension	54 (46%)	40 (66%)	14 (25%)
Diabetes	30 (25%)	24 (39%)	6 (11%)
Smoker	19/94 (20%)	9/37 (24%)	10 (18%)
Coronary artery disease	42/116 (36%)	38/59 (64%)	4/57 (7%)
Clinical presentation			
Heart rate (bpm)	90 (72–115) [*n* = 117]	85 (71–117) [*n* = 60]	94 (75–115)
Systolic BP (mmHg)	103 (90–122) [*n* = 117]	100 (84–122) [*n* = 60]	104 (95–123)
Diastolic BP (mmHg)	60 (50–68) [*n* = 117]	61 (50–67) [*n* = 60]	59 (48–69)
Mean BP (mmHg)	73 (64–86) [*n* = 116]	72 (62–79) [*n* = 60]	76 (68–88) [*n* = 56]
CI at H0 (L/min/m^2)	1.9 (1.5–2.3) [*n* = 110]	1.8 (1.3–2.1) [*n* = 56]	1.9 (1.7–2.6) [*n* = 54]
CPI at H0 (W/m^2)	0.3 (0.2–0.4) [*n* = 110]	0.3 (0.2–0.3) [*n* = 56]	0.3 (0.2–0.4) [*n* = 54]
LVEF (%)	30 (20–40) [*n* = 109]	25 (20–38) [*n* = 57]	34 (25–40) [*n* = 52]
Ischemic cause	74 (63%)	19 (31%)	55 (96%)
Arterial lactate (mmol/L)	3.4 (1.9–6.0) [*n* = 110]	3.2 (1.7–6.2) [*n* = 56]	3.9 (2.3–5.7) [*n* = 54]
Cardiac arrest before inclusion	33 (28%)	4 (7%)	29 (51%)
SCAI shock classification			
SCAI classification	[*n* = 117]		[*n* = 56]
B	2 (2%)	2 (3%)	0 (0%)
C	62 (53%)	24 (39%)	38 (68%)
D	34 (29%)	18 (30%)	16 (29%)
E	19 (16%)	17 (28%)	2 (4%)
Severity scores			
SAPS II score	61 (45–74) [*n* = 116]	64 (50–77) [*n* = 60]	56 (44–69) [*n* = 56]
SOFA score	9 (7–11) [*n* = 110]	8 (7–10) [*n* = 53]	9 (8–12)
VIS at H0	39 (13–83)	30 (5–69)	44 (21–99)
Management			
Assisted ventilation	101/112 (90%)	55 (90%)	46/51 (90%)
Extra-renal purification	27 (23%)	18 (30%)	9 (16%)
ECMO	9 (8%)	5 (8%)	4 (7%)
Outcomes			
Death at 30 days	44 (37%)	23 (38%)	21 (37%)
Death and/or ECMO at 30 days	48 (41%)	25 (41%)	23 (40%)

Categorical variables are expressed as absolute counts (%) and continuous variables as median (25th to 75th percentile). BMI = body mass index; CI: cardiac index; CPI: cardiac power index; LVEF = left ventricular ejection fraction; SCAI: Society for Cardiovascular Angiography and Interventions; SAPS = simplified acute physiology score; SOFA = sequential organ failure assessment; ICU = intensive care unit; VA-ECMO = venoarterial extracorporeal membrane oxygenation

Values are median (1st quartile–3rd quartile) for continuous variables and n (%) for categorical variables

* *p* value from Wilcoxon test for continuous variables and Fisher's exact test for categorical variables

Primary outcome

The primary outcome, 30-day mortality, occurred in 44 patients (37%) (Table 1). When analyzing the average values over the first 24 h of CS, the mean of macrocirculatory variables were consistently and significantly lower in the group meeting the primary outcome criteria (except for CI; $p = 0.07$ and $ScVO_2$; $p = 0.09$) (Table 2). Conversely, the average values for tissue

Table 2 Comparison of macrocirculatory hemodynamic and tissue perfusion variables between 30-day survivors and 30-day non-survivors

Variable	Overall ($n=118$)	30-day survivors ($n=74$)	30-day non-survivors ($n=44$)	p value*
Mean SAP (mmHg)	105 (96–114)	106 (97–120)	104 (91–112)	0.024
Mean MAP (mmHg)	72 (68–79)	74 (70–81)	70 (65–76)	0.010
Mean CO (L/min)	4.0 (3.3–4.8) [$n=114$]	4.3 (3.4–5.2) [$n=71$]	3.5 (3.0–4.3) [$n=43$]	0.004
Mean CI (L/min/m^2)	2.2 (1.8–2.5) [$n=117$]	2.2 (1.9–2.7) [$n=73$]	2.2 (1.7–2.4)	0.074
Mean CPI (W/m^2)	0.4 (0.3–0.4) [$n=117$]	0.4 (0.3–0.5) [$n=73$]	0.3 (0.3–0.4)	0.027
Mean $ScvO_2$ (mmHg/mL)	71 (64–77) [$n=115$]	72 (64–77) [$n=72$]	69 (64–76) [$n=43$]	0.095
Mean ΔPCO_2 (mmHg)	7.5 (5.8–9.4) [$n=114$]	7.2 (5.7–8.5) [$n=71$]	8.5 (6.5–11.7) [$n=43$]	0.034
Mean $\Delta PCO_2/C(a\text{-}v)O_2$ (mmHg/mL)	1.7 (1.2–2.3) [$n=113$]	1.7 (1.1–2.1) [$n=71$]	1.9 (1.5–2.6) [$n=42$]	0.052
Mean arterial lactate (mmol/L)	2.8 (1.7–4.6) [$n=116$]	2.2 (1.5–3.3)	4.5 (2.3–9.0) [$n=42$]	< 0.0001

SAP: systolic arterial pressure; MAP: mean arterial pressure; CO: cardiac output; CI: cardiac index; CPI: cardiac power index; $ScvO_2$: central venous oxygen saturation; $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio: ratio of venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference (or $\Delta PCO_2/C(a\text{-}v)O_2$)

Values are median (1st quartile–3rd quartile) for continuous variables and *n* (%) for categorical variables

* *p* value from Wilcoxon test for continuous variables and Fisher's exact test for categorical variables

hypoperfusion variables, ΔPCO_2, $\Delta PCO_2/C(a\text{-}v)O_2$, and arterial lactate, during the first 24 h were significantly higher (i.e. worst) in the group meeting the primary outcome criteria (except for $\Delta PCO_2/C(a\text{-}v)O_2$; $p=0.05$) (Table 2). In Table S1, the primary outcome was analyzed using the pulmonary artery catheter as a reference, showing almost similar results.

Exclusively within the OptimaCC cohort, where pulmonary artery catheter variable were prospectively measured in nearly all patients at each time point (H0, H6, H12, and H24), comparisons of the mean of these variables (during the first 24 h) between 30-day survivors and non-survivors are presented in Table S2. Notably, a lower mean PAOP during the first 24 h was significantly associated with improved 30-day survival.

Exclusively within the MicroShock study cohort, where mottling scores were prospectively assessed (as a clinical sign of tissue hypoperfusion) in nearly all patients at each time point, the mottling score was consistently and significantly associated with 30-day mortality across all time points within the first 24 h (Table S3, Fig. S1).

Critical threshold for longitudinal time course of hemodynamic variables

To identify the best thresholds for predicting the primary outcome, univariate Cox regression analysis was performed on mean macrocirculatory variables measured within the first 24 h. The optimal clinically relevant thresholds, closely approximating the optimal values identified in the analysis, for predicting the primary outcome were as follows: a mean SAP in the first 24 h < 95 mmHg with a Hazard Ration (HR): 2.1 (95% CI 1.1–3.9), a mean MAP in the first 24 h < 70 mmHg with a HR: 1.9 (95% CI 1.04–3.4), a mean $ScvO_2$ in the first 24 h < 70% with an HR: 1.8 (95% CI 0.9–3.3), a mean CO in the first 24 h < 3.5 L/min with a HR: 2.4 (95% CI 1.3–4.3), a mean CI in the first 24 h ≤ 1.8 L/min/m^2 with a HR: 1.8 (95% CI 0.9–3.4), and a mean CPI in the first 24 h < 0.27 W/m^2 with a HR: 2.4 (95% CI 1.2–4.6) (Table 3). Exclusively within the OptimaCC cohort, the optimal clinically relevant thresholds for pulmonary arterial catheter variables—closely aligning with the optimal values identified in the analysis—for predicting the primary outcome are presented in Table S4.

Regarding tissue perfusion variables, the optimal clinically relevant thresholds, closely approximating the optimal values identified in the analysis, for predicting the primary outcome were as follows: a mean ΔPCO_2 in the first 24 h ≥ 9 mmHg with an HR: 2.7 (95% CI 1.5–5.02), a mean $\Delta PCO_2/C(a\text{-}v)O_2$ in the first 24 h ≥ 1.5 mmHg/mL with an HR: 2.1 (95% CI 1.1–4.3) (Table 3).

Longitudinal time courses of hemodynamic variables and 30-day mortality

Figure 1 shows the statistically significant association between the average value of macrocirculatory hemodynamic variables over the first 24 h and 30-day mortality. During the first 24 h, an average SAP < 95 mmHg, MAP < 70 mmHg, $ScvO_2$ < 70%, CO < 3.5 L/min, CI ≤ 1.8 L/min/m^2, as well as CPI < 0.27 W/m^2 were significantly associated with a worse prognosis (C-index = 0.58 (0.51–0.65), C-index = 0.58 (0.51–0.66), C-index = 0.58 (0.51–0.66), C-index = 0.62 (0.54–0.69), C-index = 0.57 (0.5–0.65) and C-index = 0.58 (0.51–0.65) respectively) (Table 3).

Patients with an average ΔPCO_2 over the first 24 h ≥ 9 mmHg were significantly more likely to achieve the primary outcome ($p=0.0005$) (Fig. 2). Similarly, for

Table 3 Association of macrocirculatory hemodynamic and tissue perfusion variables with endpoints in univariable Cox model

	N_{events}/N (%)	Univariable cox model		Prognostic value	
		HR (CI 95%)	*p* value	C-index (CI 95%)	*p* value
Outcome = death at 30 days					
Mean SAP (per 10 mmHg decrease)	44/118 (37%)	1.41 (1.14–1.74)	0.001	0.635 (0.552–0.718)	0.001
Mean SAP < 95 mmHg	44/118 (37%)	2.09 (1.10–3.94)	0.024	0.580 (0.510–0.650)	0.025
Mean MAP (per 10 mmHg decrease)	44/118 (37%)	1.74 (1.25–2.41)	0.0010	0.644 (0.560–0.728)	0.0008
Mean MAP < 70 mmHg	44/118 (37%)	1.89 (1.04–3.43)	0.037	0.584 (0.510–0.657)	0.027
Mean $ScvO_2$ (per 1% decrease)	43/115 (37%)	1.03 (1.00–1.06)	0.023	0.600 (0.506–0.693)	0.036
Mean $ScvO_2$ < 70%	43/115 (37%)	1.80 (0.99–3.28)	0.054	0.586 (0.511–0.661)	0.025
Mean CO (per 1 L/min decrease)	43/114 (38%)	1.62 (1.24–2.13)	0.0004	0.668 (0.581–0.756)	0.0002
Mean CO < 3.5 L/min	43/114 (38%)	2.38 (1.30–4.33)	0.005	0.617 (0.544–0.691)	0.002
Mean CI (per 1 L/min/m^2 decrease)	44/117 (38%)	2.04 (1.24–3.34)	0.005	0.626 (0.538–0.715)	0.005
Mean CI ≤ 1.8 L/min/m^2	44/117 (38%)	1.81 (0.96–3.41)	0.068	0.577 (0.503–0.651)	0.042
Mean CPI (per 0.1 W/m^2 decrease)	44/117 (38%)	1.57 (1.19–2.08)	0.001	0.648 (0.563–0.732)	0.0006
Mean CPI < 0.27 W/m^2	44/117 (38%)	2.37 (1.22–4.61)	0.011	0.584 (0.516–0.653)	0.016
Mean ΔPCO_2 (per 1 mmHg increase)	43/114 (38%)	1.14 (1.07–1.22)	0.0001	0.623 (0.529–0.717)	0.010
Mean $\Delta PCO_2 \geq 9$ mmHg	43/114 (38%)	2.75 (1.51–5.02)	0.0010	0.629 (0.556–0.702)	0.0005
Mean $\Delta PCO_2/C(a\text{-}v)O_2$ (per 1 mmHg/mL increase)	42/113 (37%)	1.10 (1.02–1.18)	0.012	0.610 (0.527–0.694)	0.009
Mean $\Delta PCO_2/C(a\text{-}v)O_2 \geq 1.5$ mmHg/mL	42/113 (37%)	2.15 (1.08–4.29)	0.029	0.598 (0.532–0.665)	0.004
Mean arterial lactate (per 1 mmol/L increase)	42/116 (36%)	1.29 (1.20–1.38)	< 0.0001	0.764 (0.685–0.842)	< 0.0001
Mean arterial lactate ≥ 3 mmol/L	42/116 (36%)	4.18 (2.13–8.19)	< 0.0001	0.687 (0.623–0.751)	< 0.0001

SAP: systolic arterial pressure; MAP: mean arterial pressure; CO: cardiac output; CI: cardiac index; CPI: cardiac power index; $ScvO_2$: central venous oxygen saturation; $P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio: ratio of venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference (or $\Delta PCO_2/C(a\text{-}v)O_2$)

CI: confidence interval, HR: hazard ratio

an average $\Delta PCO_2/C(a\text{-}v)O_2 \geq 1.5$ mmHg/mL ($p = 0.004$) and an arterial lactate ≥ 3 mmol/L (< 0.0001) (Fig. 2).

In Table S5 and Fig. S2, these hemodynamic variables were analyzed using the pulmonary artery catheter as a reference.

Interaction of out-of-hospital cardiac arrest (OHCA) status with hemodynamic variables on 30-day mortality

Interaction terms in Cox models revealed no significant difference in the effect of mean macrocirculatory hemodynamic and tissue perfusion variables during the first 24 h of CS on 30-day mortality between patients with and without OHCA. Indicating no difference in effect between the two groups, with one exception: mean SAP (over the first 24 h) as a continuous variable (interaction $p = 0.017$) which was associated with 30-day mortality in patients without OHCA, but not in those with OHCA (Table S6).

Correlations between macrocirculation and tissue perfusion variables

No relationship was observed between the longitudinal time courses of macrocirculatory variables and tissue perfusion variables, with correlation coefficients close to zero (Fig. 3). The macrocirculatory variables showed a strong correlation with each other (MAP, CO, CI, and CPI), as did those of tissue perfusion (ΔPCO_2 and $\Delta PCO_2/C(a\text{-}v)O_2$), with correlation coefficients between 0.62 and 0.93.

Discussion

Our study is among the first to longitudinally evaluate macrocirculatory and tissue perfusion variables within the first 24 h of CS admission, addressing a critical gap as over 50% of randomized controlled trials in AMICS don't even report cardiac index [21]. We found that specific thresholds of systemic hemodynamics, such as a mean MAP < 70 mmHg, a mean CO < 3.5 L/min and a mean CI ≤ 1.8 L/min/m^2, were significantly associated with increased 30-day mortality. Additionally, tissue hypoperfusion variables such as $\Delta PCO_2 \geq 9$ mmHg and $\Delta PCO_2/C(a\text{-}v)O_2 \geq 1.5$ mmHg/ml emerged as significant predictors of poor outcomes.

Mean arterial pressure threshold in cardiogenic shock

Our results identified a critical MAP threshold of 70 mmHg during the first 24 h, below which outcomes were poorer. These findings highlight the importance of early hemodynamic monitoring and target-setting in managing CS, given the lack of international consensus

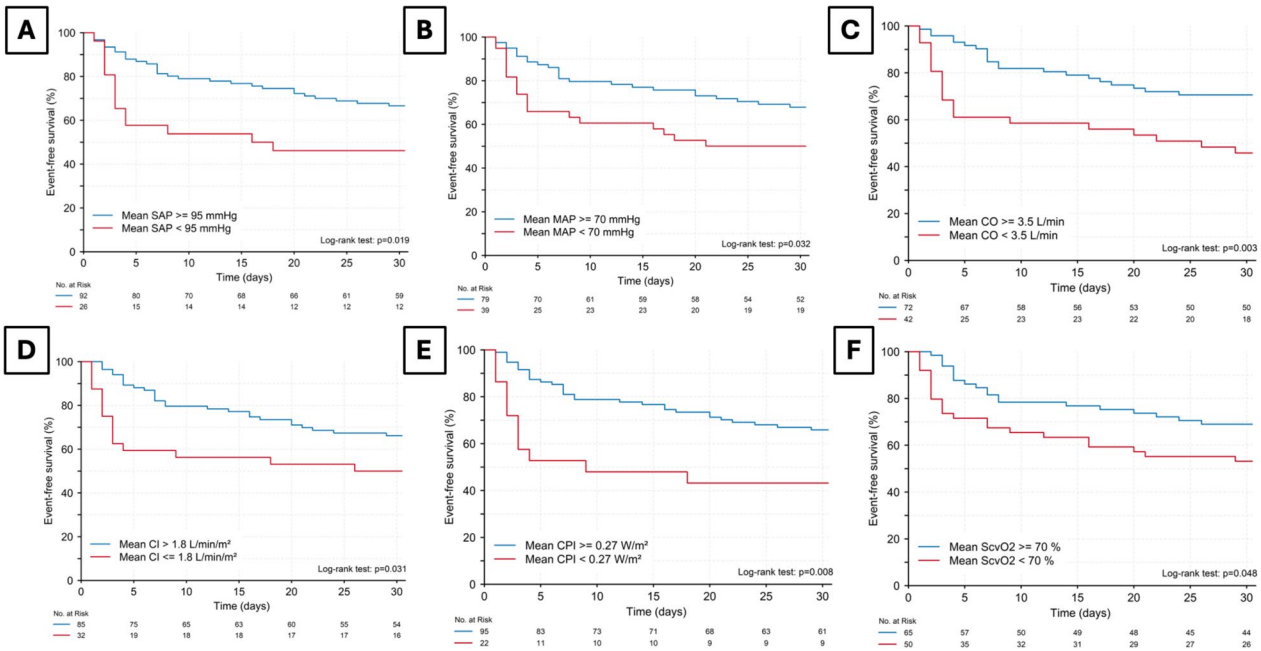

Fig. 1 Kaplan–Meier showing 30-day mortality in cardiogenic shock according to mean macrocirculatory variables during the first 24 h. **A** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean SAP during the first 24 h. **B** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean MAP during the first 24 h. **C** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean CO during the first 24 h. **D** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean CI during the first 24 h. **E** Kaplan–Meier showing 30-day mortality support in cardiogenic shock according to the mean CPI during the first 24 h. **F** Kaplan–Meier showing 30-day mortality support in cardiogenic shock according to the mean $ScVO_2$ during the first 24 h

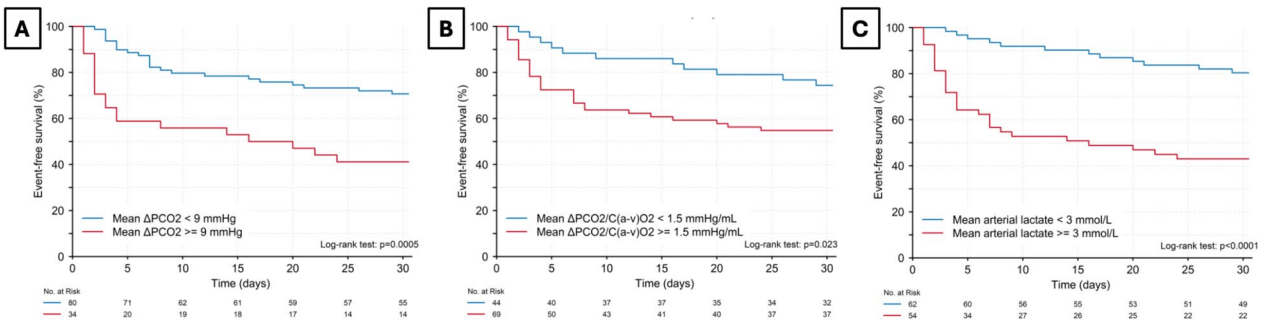

Fig. 2 Kaplan–Meier showing 30-day mortality in cardiogenic shock according to mean perfusion variables during the first 24 h. **A** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean ΔPCO_2 during the first 24 h. **B** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean $\Delta PCO_2/C(a\text{-}v)O_2$ during the first 24 h. **C** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean arterial lactate level during the first 24 h

on hemodynamic targets in CS. Some guidelines advise using inotropes in CS patients with SBP < 90 mmHg [22], while others suggest a MAP target ≥ 65 mmHg in all circulatory shock states [23], but these targets lack validation in randomized clinical trials to date [24]. Recent retrospective studies indirectly provide evidence supporting a MAP target of 65 mmHg during the first 24 h after ICU admission for CS [25], or a MAP target of 70 mmHg during the first 36 h after ICU admission [26], due to poorer outcomes associated with MAP below these thresholds.

Mean $ScvO_2$ threshold in cardiogenic shock

Few studies have precisely addressed the prognostic value of $ScvO_2$ (or SvO_2) in CS. Traditionally, a decrease in $ScvO_2$ has been primarily attributed to inadequate oxygen delivery due to low CO [27, 28]. However, a recent study found a weak correlation between CO and $ScvO_2$

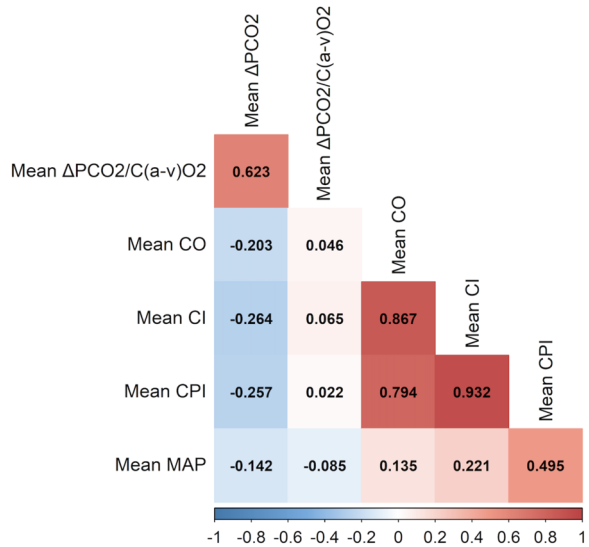

Fig. 3 Correlation between longitudinal trends of macrocirculatory hemodynamic variables and tissue perfusion variables. Spearman rank correlation between longitudinal trends of macrocirculatory hemodynamic variables and tissue perfusion variables. MAP, mean arterial pressure; CO, cardiac output; CI, cardiac index; CPI, cardiac power index; ΔPCO_2, delta PCO_2; $\Delta PCO_2/C(a\text{-}v)O_2$, ratio of venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference

in CS patients [29]. Interestingly, in line with our results, this study also showed a strong association between an early increase in $ScvO_2$ (>60% at 24 h) and improved patient outcomes.

Cardiac output/cardiac index threshold in cardiogenic shock

There is no consensus on target CO or CI during the initial hours of CS, even though improving these variables has long been a primary goal since Gunnar et al. reported a low CO in patients with CS following AMI in their pioneering work of 1966 [30]. One major limitation, however, is that most studies used a single value (CO, CI, CPO, or CPI) assessed at admission, neglecting the dynamic nature of hemodynamic variables in CS [30–35]. Historical studies have used various thresholds for CI, but precise cut-offs have been considered impractical due to cases of end-organ hypoperfusion with higher CI values. A sub-analysis of the SHOCK trial describes cardiac power output (CPO) as one of the best hemodynamic variables for predicting mortality in CS [15]. In our analysis, a CPI threshold of 0.27 W/m^2 within the first 24 h was associated with increased mortality at day 30.

CO_2-derived threshold in cardiogenic shock

In patients experiencing circulatory shock states, an elevation in tissue partial pressure of CO_2 is observed, reflecting impaired tissue perfusion. This might result from higher CO_2 production without a corresponding increase in blood flow to wash it out (due to increased heterogeneity of blood flow and/or a reduction in functional capillary density), or it could also result from anaerobic metabolism and elevated lactate production, which requires bicarbonate buffering, leading to increased CO_2 production. In septic shock, a $\Delta PCO_2 > 6$ mmHg has been associated with higher mortality, reflecting inadequate CO [36]. Studies have shown inconsistent correlations between ΔPCO_2 and macrocirculatory hemodynamics, but significant associations with microcirculatory perfusion have been noted [10, 37], even in a cohort of patients under VA-ECMO support [38]. The $\Delta PCO_2/C(a\text{-}v)O_2$ ratio, also named PCO_2 gap/Da-vO_2, usually studied in septic shock, is another relevant variable reflecting tissue perfusion. By quantifying the relationship between the venous-to-arterial PCO_2 difference and the arterial-to-venous oxygen content difference, this index offers earlier and potentially more dynamic insights into the adequacy of tissue oxygenation and perfusion in critically ill patients [39]. Our study found a mean above 1.5 mmHg/ml during the first 24 h to predict 30-day mortality, indicating increased anaerobic metabolism, as already described [40].

Loss of hemodynamic coherence in cardiogenic shock

A key finding of our study is the notable dissociation between macrocirculatory and tissue perfusion variables in patients with CS. While strong correlations were observed within each variable group—macrocirculatory variables (MAP, CO, CI, CPI) and tissue perfusion variables (ΔPCO_2 and $\Delta PCO_2/C(a\text{-}v)O_2$)—the longitudinal trajectories of these two sets of variables showed no correlation. This dissociation suggests that optimizing macrohemodynamic variables, although essential for overall stabilization, does not necessarily equate to improved tissue perfusion, which is more strongly associated with CS outcomes [3]. This finding underscores the complexity of hemodynamic management in CS and highlights the need for comprehensive monitoring strategies that include direct assessment of tissue perfusion alongside traditional macrohemodynamic targets.

Strengths and study limitations

On the one hand, our results are consistent with recent studies emphasizing the benefits of longitudinal assessment of CS during the initial hours [41]. This approach refines classification and is strongly associated with in-hospital mortality. The identification of significant thresholds for tissue perfusion markers despite an absence of correlation with systemic markers indirectly but strongly argues for a multimodal

monitoring. On the other hand, this study spans 10 years and includes CS patients from various causes, introducing some heterogeneity. The prolonged inclusion period partly resulted from logistical challenges. In the OptimaCC study, for instance, the final center was only initiated in June 2013, limiting early recruitment. Similarly, the MicroShock study faced multiple enrollment disruptions due to COVID-19. The OptimaCC study's criteria, requiring both successful PCI and a Swan-Ganz catheter, may have introduced selection bias by excluding more unstable patients, explaining the lower proportion of SCAI Stage E patients (4%) compared to MicroShock (28%). However, integrating both cohorts improves overall representation. Despite being one of the largest investigations of early hemodynamic variables in CS, the relatively small sample size limits statistical power. Although all C-index values achieved statistical significance, their relatively low magnitude indicates that the model had limited discriminatory power to differentiate between low- and high-risk subjects. Differences in measurement methods (pulmonary artery catheter in OptimaCC vs. echocardiography in MicroShock) and the evolving CS management over time are additional limitations. The use of a fixed correction factor constitutes another limitation of the study. Non-blinded measurements, reflecting clinical practice for CS management, likely introduced minimal bias. Due to the absence of standardized perfusion-based management guidelines, any bias from peripheral assessments was likely negligible. Finally, a more granular analysis incorporating time-based hemodynamic variables and threshold-exceedance durations could potentially refine our results. Lastly, as an observational study, it establishes associations rather than causality, emphasizing the need for prospective trials. Our work advocates for detailed and comprehensive hemodynamic assessment of CS patients, integrating its evolving nature during the crucial first few hours [41].

Conclusions

This study is among the first to identify critical hemodynamic thresholds within the initial 24 h of CS that are associated with adverse outcomes. Lower macrocirculatory variables and higher (i.e. worst) tissue hypoperfusion variables within the first 24 h are associated with increased mortality in CS patients. These findings highlight the importance of early, comprehensive hemodynamic monitoring and suggest specific thresholds that may guide resuscitation strategies. Further research is warranted to refine these thresholds and improve clinical outcomes in CS management.

What is new?

Monitoring the longitudinal average trend of hemodynamic variables during the first hours of cardiogenic shock significantly improved the ability to predict 30-day mortality.

What are the clinical implications?

- Defining hemodynamic targets: These new data might help define hemodynamic targets in the early management of cardiogenic shock.
- Evaluating future therapies: Better-defined hemodynamic targets, including both macrocirculatory and tissue perfusion variables, will aid in the design and evaluation of future therapies for cardiogenic shock, with greater precision.

Abbreviations

AMI-CS	Acute myocardial infarction complicated by cardiogenic shock
CaO_2	Arterial oxygen content
CvO_2	Central venous oxygen content
CI	Cardiac index
CO	Cardiac output
CPI	Cardiac power index
CPO	Cardiac power output
CS	Cardiogenic shock
ΔPCO_2	Delta PCO_2
LVEF	Left ventricular ejection fraction
MAP	Mean arterial pressure
OHCA	Out-of-hospital cardiac arrest
PaO_2	Arterial partial pressure of oxygen
$PaCO_2$	Arterial partial pressure of carbon dioxide
PvO_2	Central venous partial pressure of oxygen
$PvCO_2$	Central venous partial pressure of carbon dioxide
$P(v\text{-}a)CO_2/C(a\text{-}v)O_2$ ratio	Ratio of venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference (or $\Delta PCO_2/C(a\text{-}v)O_2$)
SAPS II	Simplified acute physiology score
SCAI	Society for cardiovascular angiography and interventions
$ScvO_2$	Central venous oxygen saturation
SOFA	Sequential organ failure assessment
SvO_2	Mixed venous oxygen saturation
VA-ECMO	Venoarterial extracorporeal membrane oxygenation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-025-05356-0.

Supplementary Material 1: Figure S1. Comparison of the time course of mottling score from H0 to H24 between survivors and non-survivors at day 30, exclusively within the MicroShock cohort.

Supplementary Material 2: Figure S2. Kaplan–Meier showing 30-day mortality in cardiogenic shock according to mean macrocirculatory and mean tissue perfusion variables during the first 24 h, using pulmonary artery catheter as reference. **A** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean $ScvO_2$ during the first 24 h. **B** Kaplan–Meier showing 30-day mortality in cardiogenic shock according

to the mean ΔPCO_2 during the first 24 h. **C** Kaplan–Meier showing 30-day mortality in cardiogenic shock according to the mean $\Delta PCO_2/C(a\text{-}v)O_2$ during the first 24 h. ΔPCO_2: delta PCO_2, $ScvO_2$: central venous oxygen saturation, $P(v\text{-}a)CO_2/ C(a\text{-}v)O_2$ ratio: ratio of venous-arterial carbon dioxide tension difference to arterial-venous oxygen content difference (or $\Delta PCO_2/C(a\text{-}v)O_2$).

Supplementary Material 3: Table S1. Comparison of macrocirculatory hemodynamic and tissue perfusion variables between 30-day survivors and 30-day non-survivors, calculated using pulmonary artery catheter as reference.

Supplementary Material 4: Table S2. Comparison of pulmonary artery catheter variables between 30-day survivors and 30-day non-survivors, exclusively within OptimaCC cohort.

Supplementary Material 5: Table S3. Comparison of mottling score between 30-day survivors and 30-day non-survivors, exclusively within MicroShock cohort.

Supplementary Material 6: Table S4. Association of pulmonary artery catheter variables with death at 30 days in univariable Cox model, exclusively within OptimaCC cohort.

Supplementary Material 7: Table S5. Association of macrocirculatory hemodynamic and tissue perfusion variables with endpoints in univariable Cox model, calculated using pulmonary artery catheter as reference.

Supplementary Material 8: Table S6. Association of macrocirculatory hemodynamic and tissue perfusion variables with death at 30 days in univariable Cox model and interaction with out-of-hospital cardiac arrest (OHCA).

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Author contributions
BL, FM, and HM conceived the study. BL, AC, JD, JH, FM, AK, and HM have been involved in the care of patients and hemodynamic assessment. BL, AC, and HM collected the data and wrote the manuscript. KD and NG performed statistical analysis. BL, AC, JD, CD, NG, CEG, JH, FM, AK, and HM participated in the revising of a manuscript. All authors approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Availability of data and materials
The study data will be shared with investigators upon reasonable request to the corresponding author.

Declarations

Ethical approval and consent to participate
The protocol of each of the two studies was approved by the appropriate ethics committees. OptimaCC (NCT01367743) received the approval of the Nancy Hospital Institutional Review Board, France. MicroShock (NCT03436641) received approval from the Comité de Protection des Personnes, Sud-Est V, France (Comité de Protection des Personnes, Sud-Est V; reference 18-STRA-01).

Consent for publication
All authors of the manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript in accordance with ICMJE criteria. This is an original article which has not already been published in a journal and is not currently under consideration by another journal. All authors agree to the terms of the BioMed Central Copyright and License Agreement.

Competing interests
The authors declare no competing interests.

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References

1. Arrigo M, Blet A, Morley-Smith A, Aissaoui N, Baran DA, Bayes-Genis A, Chioncel O, Desch S, Karakas M, Moller JE, et al. Current and future trial design in refractory cardiogenic shock. Eur J Heart Fail. 2023;25(5):609–15.
2. Jung C, Bruno RR, Jumean M, Price S, Krychtiuk KA, Ramanathan K, Dankiewicz J, French J, Delmas C, Mendoza AA, et al. Management of cardiogenic shock: state-of-the-art. Intensiv Care Med. 2024;50:1814.
3. Merdji H, Levy B, Jung C, Ince C, Siegemund M, Meziani F. Microcirculatory dysfunction in cardiogenic shock. Ann Intensiv Care. 2023;13(1):38.
4. Aissaoui N, Puymirat E, Delmas C, Ortuno S, Durand E, Bataille V, Drouet E, Bonello L, Bonnefoy-Cudraz E, Lesmeles G, et al. Trends in cardiogenic shock complicating acute myocardial infarction. Eur J Heart Fail. 2020;22(4):664–72.
5. Waksman R, Pahuja M, van Diepen S, Proudfoot AG, Morrow D, Spitzer E, Nichol G, Weisfeldt ML, Moscucci M, Lawler PR, et al. Standardized definitions for cardiogenic shock research and mechanical circulatory support devices: scientific expert panel from the shock academic research consortium (SHARC). Circulation. 2023;148(14):1113–26.
6. Naidu SS, Baran DA, Jentzer JC, Hollenberg SM, van Diepen S, Basir MB, Grines CL, Diercks DB, Hall S, Kapur NK, et al. SCAI SHOCK stage classification expert consensus update: a review and incorporation of validation studies: this statement was endorsed by the American college of cardiology (ACC), American college of emergency physicians (ACEP), American heart association (AHA), European society of cardiology (ESC) association for acute cardiovascular care (ACVC), international society for heart and lung transplantation (ISHLT), society of critical care medicine (SCCM), and society of thoracic surgeons (STS) in december 2021. J Am Coll Cardiol. 2022;79(9):933–46.
7. Berg DD, Kaur G, Bohula EA, Baird-Zars VM, Alviar CL, Barnett CF, Barsness GW, Burke JA, Chaudhry SP, Chonde M, et al. Prognostic significance of haemodynamic parameters in patients with cardiogenic shock. Eur Heart J Acute Cardiovasc Care. 2023;12(10):651–60.
8. Jentzer JC, Burstein B, Ternus B, Bennett CE, Menon V, Oh JK, Anavekar NS. Noninvasive hemodynamic characterization of shock and preshock using echocardiography in cardiac intensive care unit patients. J Am Heart Assoc. 2023;12(22):e031427.
9. Levy B, Clere-Jehl R, Legras A, Morichau-Beauchant T, Leone M, Frederique G, Quenot JP, Kimmoun A, Cariou A, Lassus J, et al. Epinephrine versus norepinephrine for cardiogenic shock after acute myocardial infarction. J Am Coll Cardiol. 2018;72(2):173–82.
10. Merdji H, Curtiaud A, Aheto A, Studer A, Harjola VP, Monnier A, Duarte K, Girerd N, Kibler M, Ait-Oufella H, et al. Performance of early capillary refill time measurement on outcomes in cardiogenic shock: an observational, prospective multicentric study. Am J Respir Crit Care Med. 2022;206:1230.
11. Delmas C, Roubille F, Lamblin N, Bonello L, Leurent G, Levy B, Elbaz M, Danchin N, Champion S, Lim P, et al. Baseline characteristics, management, and predictors of early mortality in cardiogenic shock: insights from the FRENSHOCK registry. ESC Heart Fail. 2022;9(1):408–19.
12. Belletti A, Lerose CC, Zangrillo A, Landoni G. Vasoactive-inotropic score: evolution, clinical utility, and pitfalls. J Cardiothorac Vasc Anesth. 2021;35(10):3067–77.

13. Expert Round Table on Echocardiography in ICU. International consensus statement on training standards for advanced critical care echocardiography. Intensiv Care Med. 2014;40(5):654–66.
14. Wiegers SE, Ryan T, Arrighi JA, Brown SM, Canaday B, Damp JB, Diaz-Gomez JL, Figueredo VM, Garcia MJ, Gillam LD, et al. 2019 ACC/AHA/ASE advanced training statement on echocardiography (revision of the 2003 ACC/AHA clinical competence statement on echocardiography): a report of the ACC competency management committee. Catheter Cardiovasc Interv. 2019;94(3):481–505.
15. Fincke R, Hochman JS, Lowe AM, Menon V, Slater JN, Webb JG, LeJemtel TH, Cotter G, Investigators S. Cardiac power is the strongest hemodynamic correlate of mortality in cardiogenic shock: a report from the SHOCK trial registry. J Am Coll Cardiol. 2004;44(2):340–8.
16. Ladakis C, Myrianthefs P, Karabinis A, Karatzas G, Dosios T, Fildissis G, Gogas J, Baltopoulos G. Central venous and mixed venous oxygen saturation in critically ill patients. Respiration. 2001;68(3):279–85.
17. Berridge JC. Influence of cardiac output on the correlation between mixed venous and central venous oxygen saturation. Br J Anaesth. 1992;69(4):409–10.
18. Cavaliere F, Antoniucci ME, Arlotta G, Bevilacqua F, Calabrese M, Corrado M, Corsi F, De Paulis S, Guarneri S, Scapigliati A. Is the pCO_2 gap obtained from the superior vena cava in agreement with that from the pulmonary artery? Minerva Anestesiol. 2019;85(12):1308–14.
19. Ait-Oufella H, Lemoinne S, Boelle PY, Galbois A, Baudel JL, Lemant J, Joffre J, Margetis D, Guidet B, Maury E, et al. Mottling score predicts survival in septic shock. Intensiv Care Med. 2011;37(5):801–7.
20. Merdji H, Bataille V, Curtiaud A, Bonello L, Roubille F, Levy B, Lim P, Schneider F, Khachab H, Dib JC, et al. Mottling as a prognosis marker in cardiogenic shock. Ann Intensiv Care. 2023;13(1):80.
21. Tyler JM, Brown C, Jentzer JC, Baran DA, van Diepen S, Kapur NK, Garberich RF, Garcia S, Sharkey SW, Henry TD. Variability in reporting of key outcome predictors in acute myocardial infarction cardiogenic shock trials. Catheter Cardiovasc Interv. 2022;99(1):19–26.
22. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Bohm M, Burri H, Butler J, Celutkiene J, Chioncel O, et al. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J. 2021;42(36):3599–726.
23. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, Jaeschke R, Mebazaa A, Pinsky MR, Teboul JL, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European society of intensive care medicine. Intensiv Care Med. 2014;40(12):1795–815.
24. Mathew R, Fernando SM, Hu K, Parlow S, Santo PD, Brodie D, Hibbert B. Optimal perfusion targets in cardiogenic shock. JACC Adv. 2022;1(2):1–14.
25. Burstein B, Tabi M, Barsness GW, Bell MR, Kashani K, Jentzer JC. Association between mean arterial pressure during the first 24 hours and hospital mortality in patients with cardiogenic shock. Crit Care. 2020;24(1):513.
26. Parlow S, Di Santo P, Mathew R, Jung RG, Simard T, Gillmore T, Mao B, Abdel-Razek O, Ramirez FD, Marbach JA, et al. The association between mean arterial pressure and outcomes in patients with cardiogenic shock: insights from the DOREMI trial. Eur Heart J Acute Cardiovasc Care. 2021;10(7):712–20.
27. Sumimoto T, Takayama Y, Iwasaka T, Sugiura T, Takeuchi M, Hasegawa T, Tarumi N, Takashima H, Nakamura S, Taniguchi H, et al. Mixed venous oxygen saturation as a guide to tissue oxygenation and prognosis in patients with acute myocardial infarction. Am Heart J. 1991;122(1 Pt 1):27–33.
28. Muir AL, Kirby BJ, King AJ, Miller HC. Mixed venous oxygen saturation in relation to cardiac output in myocardial infarction. Br Med J. 1970;4(5730):276–8.
29. Gallet R, Lellouche N, Mitchell-Heggs L, Bouhemad B, Bensaid A, Dubois-Rande JL, Gueret P, Lim P. Prognosis value of central venous oxygen saturation in acute decompensated heart failure. Arch Cardiovasc Dis. 2012;105(1):5–12.
30. Gunnar RM, Cruz A, Boswell J, Co BS, Pietras RJ, Tobin JR Jr. Myocardial infarction with shock. Hemodynamic studies and results of therapy. Circulation. 1966;33(5):753–62.
31. Forrester JS, Diamond GA, Swan HJ. Correlative classification of clinical and hemodynamic function after acute myocardial infarction. Am J Cardiol. 1977;39(2):137–45.
32. Reynolds HR, Hochman JS. Cardiogenic shock: current concepts and improving outcomes. Circulation. 2008;117(5):686–97.
33. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, Kern M, Garratt KN, Goldstein JA, Dimas V, et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care: endorsed by the American heart association, the cardiological society of India, and sociedad Latino Americana de cardiologia intervencionista; affirmation of value by the Canadian association of interventional cardiology-association canadienne de cardiologie d'intervention. J Am Coll Cardiol. 2015;65(19):2140–1.
34. Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, Buller CE, Jacobs AK, Slater JN, Col J, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. SHOCK investigators. Should we emergently revascularize occluded coronaries for cardiogenic shock. N Engl J Med. 1999;341(9):625–34.
35. Hsu S, Kambhampati S, Sciortino CM, Russell SD, Schulman SP. Predictors of intra-aortic balloon pump hemodynamic failure in non-acute myocardial infarction cardiogenic shock. Am Heart J. 2018;199:181–91.
36. Ospina-Tascon GA, Bautista-Rincon DF, Umana M, Tafur JD, Gutierrez A, Garcia AF, Bermudez W, Granados M, Arango-Davila C, Hernandez G. Persistently high venous-to-arterial carbon dioxide differences during early resuscitation are associated with poor outcomes in septic shock. Crit Care. 2013;17(6):R294.
37. Ospina-Tascon GA, Umana M, Bermudez WF, Bautista-Rincon DF, Valencia JD, Madrinan HJ, Hernandez G, Bruhn A, Arango-Davila C, De Backer D. Can venous-to-arterial carbon dioxide differences reflect microcirculatory alterations in patients with septic shock? Intensiv Care Med. 2016;42(2):211–21.
38. Ellouze O, Nguyen M, Missaoui A, Berthoud V, Aho S, Bouchot O, Guinot PG, Bouhemad B. Prognosis value of early veno arterial PCO_2 difference in patients under peripheral veno arterial extracorporeal membrane oxygenation. Shock. 2020;54(6):744–50.
39. Mekontso-Dessap A, Castelain V, Anguel N, Bahloul M, Schauvliege F, Richard C, Teboul JL. Combination of venoarterial PCO_2 difference with arteriovenous O_2 content difference to detect anaerobic metabolism in patients. Intensiv Care Med. 2002;28(3):272–7.
40. Lim HS, Howell N. Cardiogenic shock due to end-stage heart failure and acute myocardial infarction: characteristics and outcome of temporary mechanical circulatory support. Shock. 2018;50(2):167–72.
41. Jentzer JC, Van Diepen S, Patel PC, Henry TD, Morrow DA, Baran DA, Kashani KB. Serial assessment of shock severity in cardiac intensive care unit patients. J Am Heart Assoc. 2023;12(23):e032748.

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