Alterations in Skin Blood Flow at the Fingertip Are Related to Mortality in Patients With Circulatory Shock

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Objectives: Skin blood flow is rapidly altered during circulatory shock and may remain altered despite apparent systemic hemodynamic stabilization. We evaluated whether changes in skin blood flow during circulatory shock were related to survival.

Design: Prospective study.

Setting: Thirty-five-bed medical-surgical university hospital department of intensive care.

Subjects: Twenty healthy volunteers and 70 patients with circulatory shock (< 12 hr duration), defined as the need for vasopressors to maintain mean arterial pressure greater than or equal to 65 mm Hg and signs of altered tissue perfusion.

Interventions: We assessed skin blood flow using skin laser Doppler on the fingertip for 3 minutes at basal temperature (SBF_{BT}) and at 37°C (SBF_{37}) (thermal challenge test) once in volunteers and at the time of inclusion and after 6, 24, 48, 72, and 96 hours in patients with shock. Capillary refill time and peripheral perfusion index were measured at the same time points on the contralateral hand.

Measurements and Main Results: The thermal challenge response (ΔSBF/ΔT) was calculated using the following formula: (SBF_{37}–SBF_{BT})/(37–basal temperature). Area under the receiver operating characteristic curves were calculated to evaluate variables predictive of ICU mortality. At inclusion, skin blood flow and ΔSBF/ΔT were lower in patients than in volunteers. Baseline skin blood flow (31 [17–113] vs 16 [9–32] arbitrary perfusion units; $p = 0.01$) and ΔSBF/ΔT (4.3 [1.7–10.9] vs 0.9 [0.4–2.9] arbitrary perfusion unit/s) were greater in survivors than in nonsurvivors. Capillary refill time was shorter in survivors than in nonsurvivors; peripheral perfusion index was similar in the two groups. ΔSBF/ΔT (area under the receiver operating characteristic curve 0.94 [0.88–0.99]) and SBF_{BT} (area under the receiver operating characteristic curve 0.83 [0.73–0.93]) had the best predictive value for ICU mortality with cutoff values less than or equal to 1.25 arbitrary perfusion unit/°C (sensitivity 88%, specificity 89%) and less than or equal to 21 arbitrary perfusion unit (sensitivity 84%, specificity 81%), respectively.

Conclusions: Alterations in fingertip skin blood flow can be evaluated using a laser Doppler thermal challenge technique in patients with circulatory shock and are directly related to outcome. These novel monitoring techniques could potentially be used to guide resuscitation. (*Crit Care Med* 2019; XX:00–00)

Key Words: laser Doppler flowmetry; microcirculation; peripheral tissue perfusion; skin reactivity; thermal challenge

Circulatory shock, recognized as arterial hypotension with signs of tissue hypoperfusion (1), leads to abnormal cellular oxygen availability and organ dysfunction (1). Alterations in skin perfusion can occur early in patients with shock, even before global hemodynamic variables are altered (2–6), and remain altered despite hemodynamic stabilization after resuscitation (6–10). Therefore, any alteration in skin perfusion could be a valuable alarm signal (4, 5). However, evaluation of peripheral perfusion at the bedside remains challenging. Clinical assessment, for example, using the capillary refill time (CRT) or the mottling score, has been used, but remains subjective.

The CRT measures the time required for a distal capillary bed to regain its color after pressure has been applied to cause blanching. Alterations in capillary perfusion prolong the time needed for distal capillaries to refill with blood, leading to longer CRTs. Although the criteria for prolonged CRT are debatable (11), it has been associated with high blood lactate concentrations (12), more severe organ dysfunction (7) and increased ICU mortality (7–9, 12). CRT assessment can be influenced by many factors, including the degree of pressure applied and ambient light and temperature, and there is poor interobserver agreement in those with limited training or without a chronometer (13–15). Nevertheless, precise CRT examination using chronometry was shown to be at least as good as serial blood lactate levels as a resuscitation target (16).

The presence of mottling, patchy skin discoloration that usually starts around the knees and is believed to reflect abnormal skin perfusion, has been related to worse outcomes (17).

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Ait-Oufella et al (10) developed a mottling score, in which the extent of mottling on the legs was scaled from 0 to 5, and reported that higher scores were associated with increased 14-day mortality in patients with septic shock and that patients whose mottling score decreased during resuscitation had better outcomes. However, mottling can persist up to 3 hours after initial treatment of circulatory shock (17), limiting its use to guide resuscitation.

Because of the difficulties in reliably assessing skin perfusion by clinical evaluation, several techniques have been developed to more precisely quantify peripheral perfusion, including transcutaneous monitoring of carbon dioxide and oxygen tensions using cutaneous electrodes (2), monitoring of muscle oxygen saturation using near-infrared spectroscopy (NIRS) (4, 18–20), and assessment of skin blood flow (SBF) using skin laser Doppler (SLD) (21–23).

SBF monitoring using SLD is an attractive technology because of its noninvasive character and simplicity (21–23). An interesting approach is to measure SBF while local skin temperature is increased (thermal challenge test), thus evaluating endothelial vasodilatory function (24–29). We previously showed that a decrease in the microcirculatory recruitment capabilities of forearm SBF after a thermal challenge test was related to worse outcomes in patients with circulatory shock (22). To investigate the value of this technique further using the same area as is used in CRT monitoring, we decided to measure SBF at the fingertip using SLD and to explore whether the variables measured were associated with outcome in patients with circulatory shock. Although there is some evidence (26, 27) to suggest that impairment of SBF at the fingertip measured using SLD is correlated with severity of disease, these studies were conducted in patients with systemic sclerosis and no studies have been performed in circulatory shock. We hypothesized that a blunted fingertip SBF response to a thermal challenge would be associated with increased mortality in patients with circulatory shock.

MATERIALS AND METHODS

This prospective study was conducted between October 2015 and July 2017 in our 35-bed Department of Intensive Care. Local ethical committee approval was obtained (protocol number P2015/365/B406201525438) and informed consent was signed by the volunteers and patients or their next of kin.

All adult ICU admissions during the study period were screened. Patients were eligible if they fulfilled the following criteria for circulatory shock: need for norepinephrine to maintain a mean arterial pressure (MAP) greater than or equal to 65 mm Hg with at least one sign of poor tissue perfusion (mottled skin, altered level of consciousness, oliguria) and an arterial lactate concentration greater than or equal to 2 mmol/L. We only included patients within the first 12 hours after the onset of shock. We excluded patients with any of the following criteria: presence of any skin lesion that rendered study measurements difficult, a previous history of Raynaud's phenomenon (26), a previous diagnosis of systemic sclerosis (27) or peripheral vascular disease, or previous inclusion in this study. Volunteers were recruited from the hospital personnel for convenience, using the same exclusion criteria.

SBF Measurements

SBF was evaluated using a SLD device (PeriFlux System 5000; Perimed, Jarfalla, Sweden) with a small thermostatic SLD probe (Reference number 457, Perimed; **Fig. S1**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265). This probe allows SBF measurement and for the temperature at the place where it is positioned to be changed. The probe is attached to the skin with the aid of double-sided tape. The emitted laser beam has a wavelength of 780 nm, which allows evaluation of a depth between 0.5 and 1.0 mm under the skin. The backscattered light is collected by the probe and the shift in light wavelength is proportional to the RBC velocity in the studied skin area, thus providing a noninvasive measurement of SBF expressed as arbitrary perfusion units (APUs).

Volunteers were studied once in the supine position. They were asked to rest calmly for 30 minutes before the measurements and to refrain from any movement during the measurements. In patients, SBF was measured as soon as possible (baseline) after the identification of circulatory shock and 6, 24, 48, 72, and 96 hours thereafter. Patients were asked not to move their fingers during measurements. If a patient became agitated during the procedure, the measurements were repeated as soon as possible after the patient had settled.

At each time point, the thermostatic probe was positioned on the tip of the index finger, and the basal SBF (SBF_{BT}) and basal temperature (T) were recorded after 3 minutes. The skin probe temperature was then immediately increased to 37°C, and the SBF (SBF_{37}) was again recorded after 3 minutes. Data were registered continuously for future off-line analyses using PeriSoft software 2.5.5 (Perimed). To standardize the change in SBF by the change in temperature, we calculated the $\Delta SBF/\Delta T$ as (SBF_{37}–SBF_{BT})/(37–basal temperature).

TABLE 1. Baseline Skin Blood Flow at Basal Temperature (SBF_{BT}) and at 37°C (SBF_{37}) and Response to Thermal Challenge Test ($\Delta SBF/\Delta T$) in Healthy Volunteers and Patients in Circulatory Shock

Characteristic	Healthy Volunteers ($n = 20$)	Patients ($n = 70$)	p
Male	13 (65%)	37 (53%)	0.6
Age, yr	29 (30–31)	63 (53–73)	0.01
Finger temperature (°C)	30.1 (29.8–30.2)	26.9 (25.3–29.3)	0.03
SBF_{BT} (APU)	201 (158–245)	18 (12–73)	< 0.01
SBF_{37} (APU)	558 (554–602)	61 (26–107)	< 0.01
$\Delta SBF/\Delta T$	59.5 (40.4–62.5)	1.9 (0.9–6.3)	< 0.01

APU = arbitrary perfusion units, SBF = skin blood flow, SBF_{BT} = SBF at basal temperature, SBF_{37} = SBF at 37°C.
Values shown as counts (%) or median (25–75th percentiles).

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TABLE 2. Baseline Clinical Characteristics of Survivors and Nonsurvivors in Patients With Circulatory Shock[a]

Characteristic	Total ($n = 70$)	Survivors ($n = 41$)	Nonsurvivors ($n = 29$)	p
Age, yr	63 (53–73)	62 (51–67)	63 (54–74)	0.5
Acute Physiology and Chronic Health Evaluation II score	26 (21–31)	22 (18–27)	28 (24–32)	0.01
Sequential Organ Failure Assessment score	13 (9–15)	10 (7–14)	15 (12–16)	0.01
Mean arterial pressure (mm Hg)	75 (68–83)	77 (69–84)	75 (66–83)	0.2
Heart rate (beats/min)	96 (76–109)	97 (76–113)	96 (75–107)	0.6
Cardiac index (L/min/m^2) ($n = 55$)	2.3 (2.0–2.8)	2.4 (2.0–2.8)	2.2 (2.0–2.6)	0.4
Central venous pressure (mm Hg)	9 (6–14)	8 (5–14)	11 (8–14)	0.1
Norepinephrine dose (µg/kg/min)	0.2 (0.1–0.5)	0.1 (0.1–0.9)	0.3 (0.1–0.7)	0.02
Lactate (mmol/L)	2.9 (2.3–4.1)	2.5 (2.1–3.5)	3.3 (2.5–5.7)	0.01
Central venous oxygen saturation (%)	73 (59–77)	73 (65–78)	71 (57–77)	0.8
Type of shock (%)				
Septic	47	28	19	0.8
Cardiogenic	22	13	9	
Hemorrhagic	1	0	1	
Capillary refill time at finger (s)	2 (1–3)	2 (1–2)	3 (2–4)	< 0.05
Finger temperature (°C)	27 (26–30)	28 (26–30)	26 (24–28)	0.02
Perfusion index	1.3 (0.5–2.1)	1.4 (0.5–1.3)	1.2 (0.6–1.8)	0.6
SBF (APU)	18 (12–73)	31 (17–113)	16 (9–32)	0.01
ΔSBF/ΔT (APU/°C)	1.9 (0.9–6.3)	4.3 (1.7–10.9)	0.9 (0.4–2.9)	< 0.01
Hemoglobin (g/dL)	11 (8–13)	12 (9–14)	10 (9–13)	0.7
Mechanical ventilation, *n* (%)	56 (83)	31 (77)	25 (89)	0.4
Renal replacement therapy, *n* (%)	24 (34)	11 (27)	12 (41)	0.3
Time on ICU before study inclusion (hr)	6 (4–8)	6 (4–9)	6 (3–8)	0.4

APU = arbitrary perfusion units, SBF = skin blood flow.
[a]Time of first SBF measurement.
Values shown as median (25–75th percentiles) unless stated otherwise.

Protocol and Data Collection

Patients with circulatory shock were managed according to current guidelines (30) by a team of intensivists different from those who performed the SLD measurements. Demographic data were collected at admission. We recorded the presence of mechanical ventilation at study inclusion and the need for renal replacement therapies during the first 24 hours after inclusion. The type of shock was classified as septic or nonseptic (cardiogenic or hypovolemic). At each SBF time-point, hemodynamic variables and blood gas analyses were obtained, the peripheral perfusion index (PPI) was recorded from the bedside monitor (IntelliVue MP70 monitor; Philips Medical Systems, Boblingen, Germany) and the CRT assessed on the opposite hand to that used for SBF measurements. CRT was determined by applying pressure to the tip of the finger for at least 15 seconds until the skin showed whitening; the time until return of baseline coloration after release of the pressure was measured with a chronometer.

The Acute Physiology and Chronic Health Evaluation (APACHE) II score (31) was calculated using the worst data during the first 24 hours in the ICU and the Sequential Organ Failure Assessment (SOFA) score (32) was calculated at admission and at each SBF measurement point. Survival status was recorded at ICU discharge.

Statistical Analysis

Variables were assessed for normality of distribution using a Kolmogorov-Smirnov test and data are presented as median (25–75th percentiles) or mean with SD as appropriate. The differences between groups were assessed using a chi-square test, Fisher exact test, Mann-Whitney *U* test, analysis of variance (ANOVA) with Bonferroni post hoc analysis, or Kruskal-Wallis test as appropriate. We also grouped patients according to interquartile ranges of initial SOFA score and lactate concentration to assess the association between SBF and these variables. ANOVA

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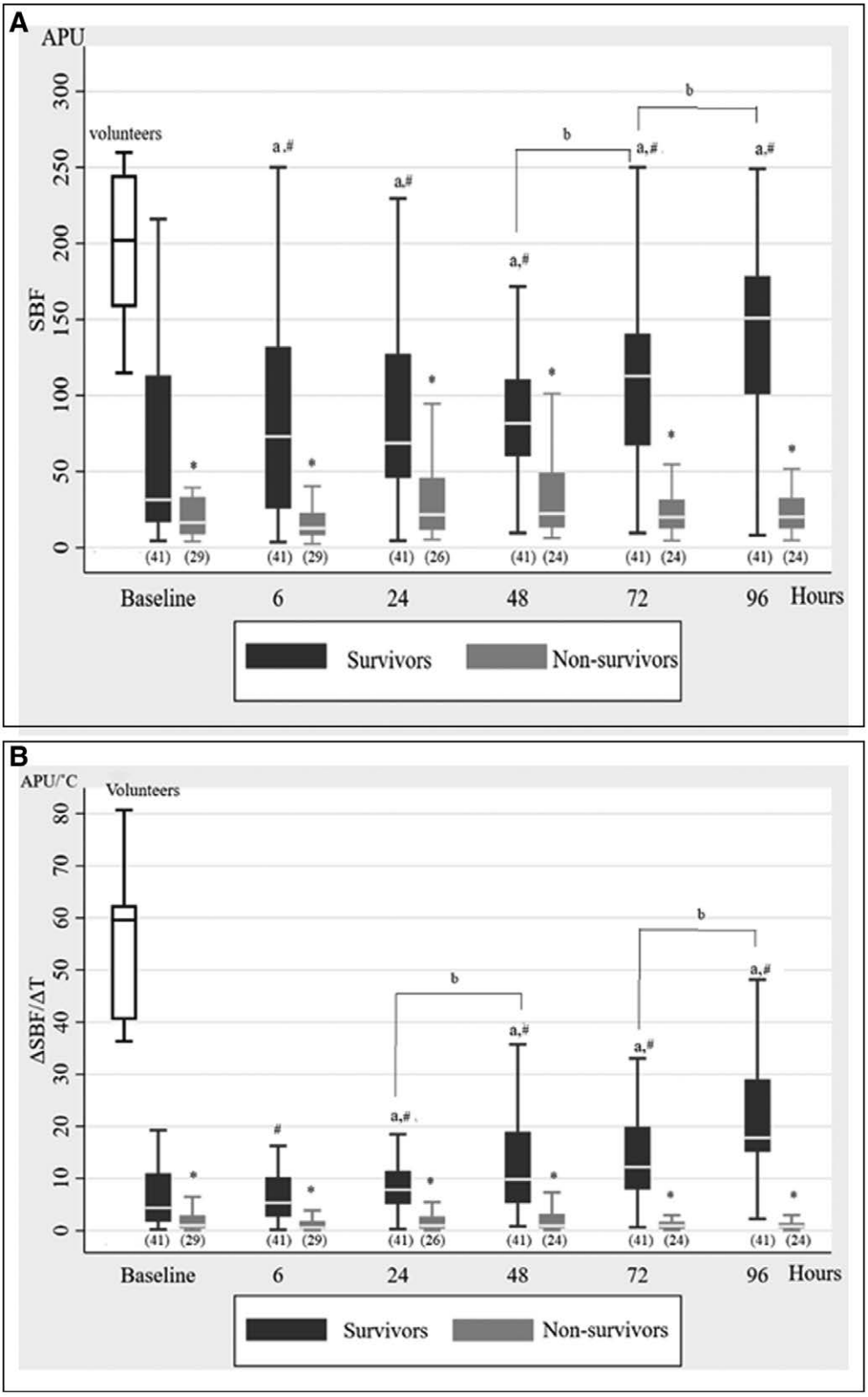

Figure 1. Skin blood flow (SBF) and thermal challenge response (ΔSBF/ΔT) during the study period in survivors and nonsurvivors. **A**, SBF. **B**, ΔSBF/ΔT. Data are expressed as medians with 95% CIs. $^{*}p < 0.05$ versus survivors; $^{a}p < 0.05$ versus baseline in the same group; $^{b}p < 0.05$ versus the indicated time point within the same group; $\#p < 0.05$ versus volunteers. APU = arbitrary perfusion units.

was used to evaluate the time course of SBF between groups (survivors vs nonsurvivors, sepsis vs nonsepsis). We plotted sensitivity and specificity using a receiving operating characteristics (ROCs) graph, and the area under the ROC curve (AUROC) was calculated for the different variables as a measure of their ability to predict ICU mortality. AUROCs are presented as means with 95% CI and compared using the Hanley and McNeil method. To assess correlations of possible variables with the different SBF-derived variables, we plotted individual data on graphs and calculated the Pearson or Spearman correlation coefficient (r) as appropriate. A two-sided p value of less than 0.05 was considered statistically significant. All analyses were performed using STATA 15.0 (StataCorp LLC, College Station, TX).

RESULTS

Of the 74 patients who met the inclusion criteria during the study period, four refused to participate, so 70 were studied. Patients were older than the healthy volunteers (**Table 1**). All patients had reached an MAP greater than or equal to 65 mm Hg by the time of the baseline measurements. Twenty-nine patients died (41%) in the ICU, five within the 96-hour study period. The cause of death was multiple organ failure for all patients. Two patients became severely agitated during the test and their SBF measurements were delayed by 20 minutes at T6 and T24, respectively. Initial blood lactate concentration, APACHE II score and SOFA score were higher in the nonsurvivors than in the survivors (**Table 2**). MAP, cardiac index (CI), and central venous oxygen

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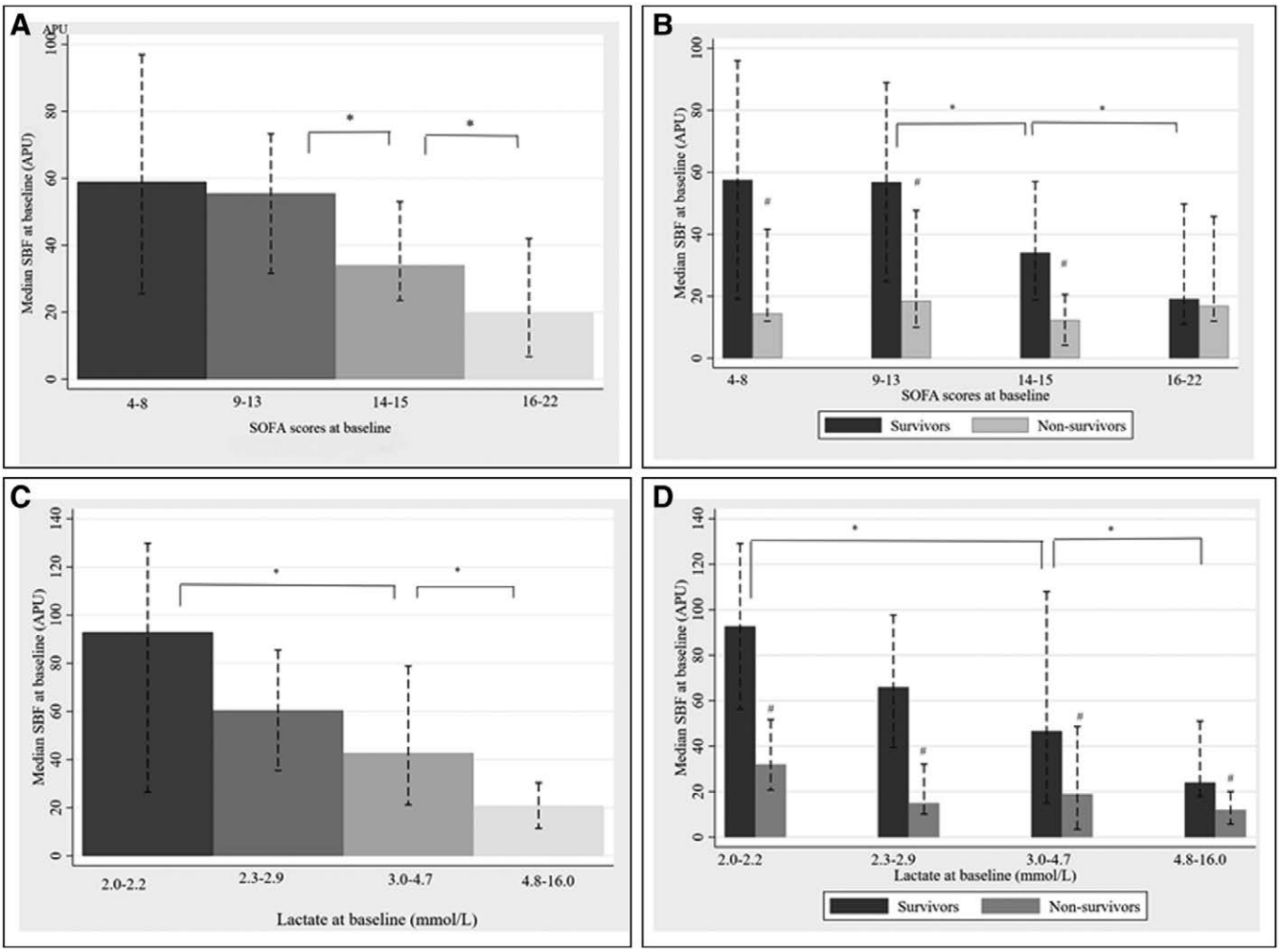

Figure 2. Median baseline skin blood flow (SBF) for different quartiles of Sequential Organ Failure Assessment (SOFA) score and blood lactate level. Median baseline SBF for different quartiles of SOFA score in all patients (**A**) and in survivors and nonsurvivors (**B**). Median baseline SBF for different quartiles of lactate level in all patients (**C**) and in survivors and nonsurvivors (**D**). Data are expressed as medians with 95% CIs. *$p < 0.05$ between quartiles, #$p < 0.05$ versus survivors. APU = arbitrary perfusion units.

saturation ($ScvO_2$) were not significantly different in survivors and nonsurvivors (Table 2). Lactate levels decreased in the first 6 hours in survivors and nonsurvivors and remained relatively stable thereafter (**Fig. S2**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265).

SBF and SBF-Derived Variables

SBF_{BT}, SBF_{37}, ΔSBF/ΔT ratio, and finger temperature were lower in the patients at baseline than in the healthy volunteers (Table 1).

In the patients, SBF_{BT} (**Fig. 1*A***), SBF_{37} (**Fig. S3**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265), and ΔSBF/ΔT ratio (**Fig. 1*B***) were lower in the nonsurvivors than in the survivors at baseline (Table 2) and throughout the study period. Finger temperature was also lower in the nonsurvivors than in the survivors throughout the study (**Fig. S4**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265).

In survivors, SBF_{BT} (Fig. 1*A*) was significantly higher than the value at baseline from 6 hours. SBF_{37} (Fig. S3, Supplemental Digital Content 1, http://links.lww.com/CCM/F265) and the ΔSBF/ΔT ratio (Fig. 1*B*) increased significantly in survivors from 24 hours compared with baseline. SBF_{BT}, SBF_{37}, and ΔSBF/ΔT in survivors and nonsurvivors remained below values in healthy volunteers at all time points ($p < 0.01$). These patterns were similar in septic and nonseptic shock subgroups (**Figs. S5** and **S6**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265)

Baseline median CRT was higher in the nonsurvivors than in the survivors (Table 2) but decreased to less than 2 seconds in survivors and nonsurvivors during the first 6 hours after inclusion (data not shown). Three of the nonsurvivors had a CRT greater than or equal to 4 seconds for more than 6 hours after inclusion. There was no significant difference in baseline PPI between the survivors and the nonsurvivors but PPI was higher in the survivors than in the nonsurvivors at T6 and T24 (**Fig. S7**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265).

Correlations Between SBF, Other Variables, and Mortality

At study inclusion, there was a weak but significant correlation between SBF and blood lactate level ($r = 0.26$; $p = 0.01$) and SOFA score ($r = 0.29$; $p < 0.01$), but not with the

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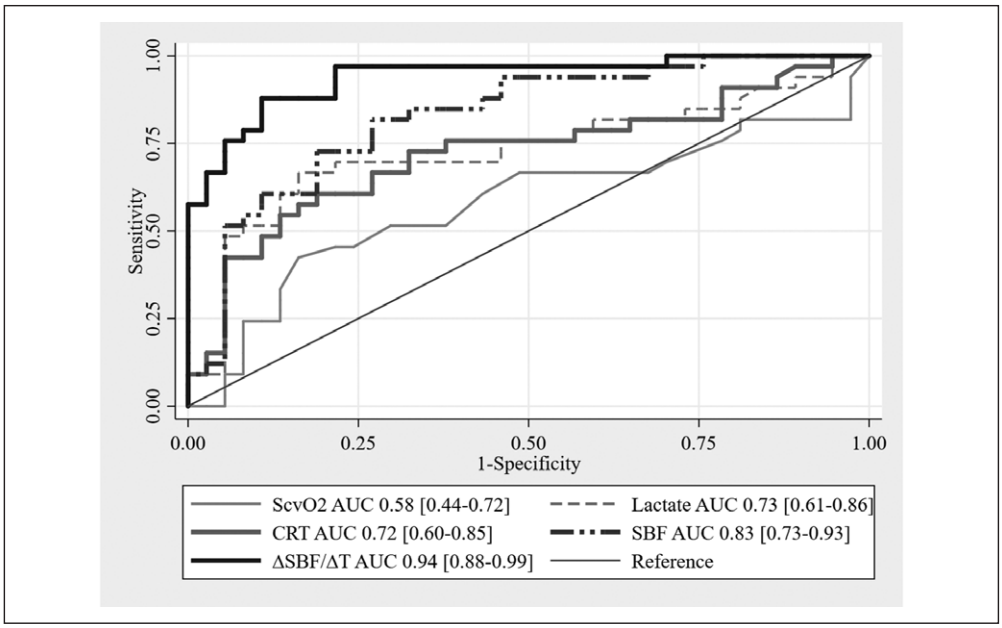

Figure 3. Prediction of ICU mortality by baseline variables. AUC = area under the curve, CRT = capillary refill time, SBF = skin blood flow, $Scvo_2$ = central venous oxygen saturation, ΔSBF/ΔT = skin blood flow/ thermal challenge response.

APACHE II score ($r = 0.28$; $p = 0.1$), MAP ($r = 0.1$; $p = 0.2$), CI ($r = 0.2$; $p = 0.1$; **Fig. S8**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265), or norepinephrine dose ($r = 0.2$; $p = 0.3$; **Fig. S9**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265).

When the patients were grouped by interquartile range of initial SOFA score and lactate concentrations, patients with the highest SOFA scores and lactate concentrations had the lowest SBF values. Within each interquartile range of SOFA score and lactate concentrations, SBFs were lower in the nonsurvivors than in the survivors (**Fig. 2**).

The AUROC for baseline ΔSBF/ΔT ratio and SBF were higher than those for blood lactate ($p < 0.01$), $Scvo_2$ ($p < 0.01$), CRT ($p < 0.01$), and PPI (area under the curve 0.51; $p < 0.01$) for predicting ICU mortality (**Fig. 3**). Baseline ΔSBF/ΔT ratio had a greater AUROC than baseline SBF ($p = 0.02$) with cutoff values less than or equal to 1.25 APU/°C (sensitivity 88%, specificity 89%) and less than or equal to 21 APU (sensitivity 84%, specificity 81%), respectively.

Similar results were obtained in patients with and without septic shock (**Figs. S10** and **S11**, Supplemental Digital Content 1, http://links.lww.com/CCM/F265).

DISCUSSION

In this prospective study, SBF was altered in patients with circulatory shock compared with healthy volunteers, even though the patients were hemodynamically stabilized, with MAP greater than or equal to 65 mm Hg. SBF at baseline was related to the SOFA score and initial lactate concentration, but not to MAP or CI. SBF was lower in nonsurvivors than in survivors at baseline and throughout the study period. Furthermore, the nonsurvivors had a persistently blunted SBF response to the thermal challenge test, reported as the ΔSBF/ΔT ratio. Baseline SBF and ΔSBF/ΔT were both predictive of ICU mortality.

During the initial phase of circulatory shock, skin perfusion is reduced in order to preserve blood flow to vital organs (2–6). This alteration is usually present before the deterioration of hemodynamic variables and is reversed quite late during resuscitation; it may persist even when systemic variables seem to have returned to acceptable values (2–6, 33, 34), as shown in the current study, and has been related to an unfavorable course and increased mortality (7–11). Monitoring of peripheral perfusion could therefore help to detect occult perfusion deficits.

The evolution of peripheral perfusion variables during resuscitation may be even more important than baseline values. Our results are consistent with results from studies by Ait-Oufella et al (8) and Hernandez et al (9) who reported that prolonged CRT was related to mortality, although our patients were less severely ill than in those studies. The patients in the studies by Ait-Oufella et al (8) and Hernandez et al (9) had lactate levels of 4.5 mmol/L and 3.3 mmol/L (1.6–4.5 mmol/L), respectively, versus 2.9 mmol/L (2.3–4.1 mmol/L) in the present study and CRT values of 3.5 seconds and 5 seconds (2–6 s), versus 2 seconds (1–3 s). Hernandez et al (9) demonstrated that the recovery of CRT to normal values within 6 hours was associated with successful resuscitation, which they defined as a blood lactate concentration less than 2 mmol/L in the 24 hours after resuscitation. A recent multicenter study showed that there was less organ dysfunction in the 72 hours after resuscitation in patients in whom CRT normalized during the treatment of circulatory shock (16). In our study, there was a significant increase in SBF in the first 6 hours after resuscitation only in survivors, suggesting that the recovery of SBF during the treatment of circulatory shock may be associated with the severity of disease. Furthermore, this change in SBF could not be detected by systemic variables and was similar regardless of the etiology of shock (septic vs nonseptic). This disparity between microcirculatory and global systemic variables has been reported previously using other techniques, such as NIRS (18, 19, 35) and PPI (36, 37).

One may argue that the higher dose of norepinephrine in nonsurvivors than in survivors could have reduced fingertip SBF because of the activation of alpha-receptors resulting in

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peripheral vasoconstriction. However, norepinephrine dose and SBF were not correlated. Similar findings have been reported in the thenar muscle with NIRS (38) and the sublingual area using side stream dark-field imaging (39, 40).

SBF measurement coupled with a thermal challenge test can be applied to evaluate the capillary vasodilation induced by a temporary increase in skin temperature (27–29). The response to a thermal challenge test requires good capillary endothelial function so that the SBF can increase during the rise in skin temperature (27–29, 41, 42). This test is usually performed at temperatures of 43°C on the forearm to obtain a maximal vasodilatory effect (27–29, 41, 42), but we used 37°C instead of 43°C for several reasons. First, in patients with endothelial dysfunction, such as those in circulatory shock, a thermal challenge test at temperatures greater than 40°C may cause skin burn (25, 26) and, in our experience (unpublished), patients complain of a burning sensation in the finger with a temperature of 43°C. Second, in patients with septic shock, Vallée et al (43) reported altered cutaneous blood flow, evaluated by P_{CO_2} monitoring on the ear lobe at 37°C, with changes more severe in nonsurvivors than in survivors.

We demonstrated that the response to the thermal challenge test (ΔSBF/ΔT) at 37°C was greater in survivors than in nonsurvivors both at baseline and subsequently and was not related to systemic variables. Furthermore, we observed an improvement in the ΔSBF/ΔT in the first 24 hours in the survivors, suggesting that the evolution of ΔSBF/ΔT is linked to disease severity. Additionally, there was no difference in ΔSBF/ΔT between patients with septic and nonseptic shock, suggesting that the capillary vasodilatory effect was similar in different types of circulatory shock.

ΔSBF/ΔT was more accurate at predicting ICU mortality than SBF at basal temperature (about 28°C). Nevertheless, the change in ΔSBF/ΔT occurred later than the change in SBF. SBF measurement at basal temperatures may therefore be the better variable for monitoring peripheral tissue perfusion during resuscitation so that treatments can be adjusted rapidly.

Our study has several limitations. First, it was a single-center study, limiting its external validity. However, this reduced any effect of variability in the treatment of shock that may have occurred if several centers had been involved. Second, the volunteers were younger than the patients, which may have affected the results. Tsuchida (44) demonstrated that SBF on the dorsum of the hand was 30% lower in elderly (age 70 yr) than in younger (age 20 yr) healthy volunteers. By contrast, Vionnet et al (45) observed no age-related differences on the forearm. These different results suggest that age-related change in SBF may depend on the area studied, but this needs further investigation. Third, although we excluded patients and volunteers with a history of peripheral vascular disease as this may interfere with the vasodilatory response to local hyperthermia (thermal challenge test) (46), we have no information on the smoking history of patients or volunteers, which may also potentially impact on the results (47, 48).

To our knowledge, these are the first observations describing the evolution of fingertip SBF measurements using SLD during circulatory shock and reporting a persistently blunted response to a thermal challenge test in nonsurvivors. Further study is needed to determine whether the SLD technique could be used to detect an improvement in peripheral perfusion during initial fluid administration and thus guide fluid resuscitation.

CONCLUSIONS

SBF measured by SLD was altered in patients with circulatory shock and the magnitude of this alteration was proportional to the SOFA score and to lactate levels and predictive of ICU mortality. SBF evaluation by SLD may be a valuable tool for monitoring tissue perfusion in circulatory shock.

Drs. Mongkolpun, Orbegozo, Vincent, and Creteur designed the study. Drs. Mongkolpun, Orbegozo, Cordeiro, and Franco performed the skin blood flow and capillary refill time measurements. Drs. Mongkolpun, Vincent, and Creteur analyzed the data. Dr. Mongkolpun wrote the first draft of the article. Drs. Orbegozo, Cordeiro, Franco, Vincent, and Creteur revised the article for critical content. All authors read and approved the final version.

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Alterations in skin blood flow at the fingertip of patients with circulatory shock are related to disease severity and mortality

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Digital Supplementary Content

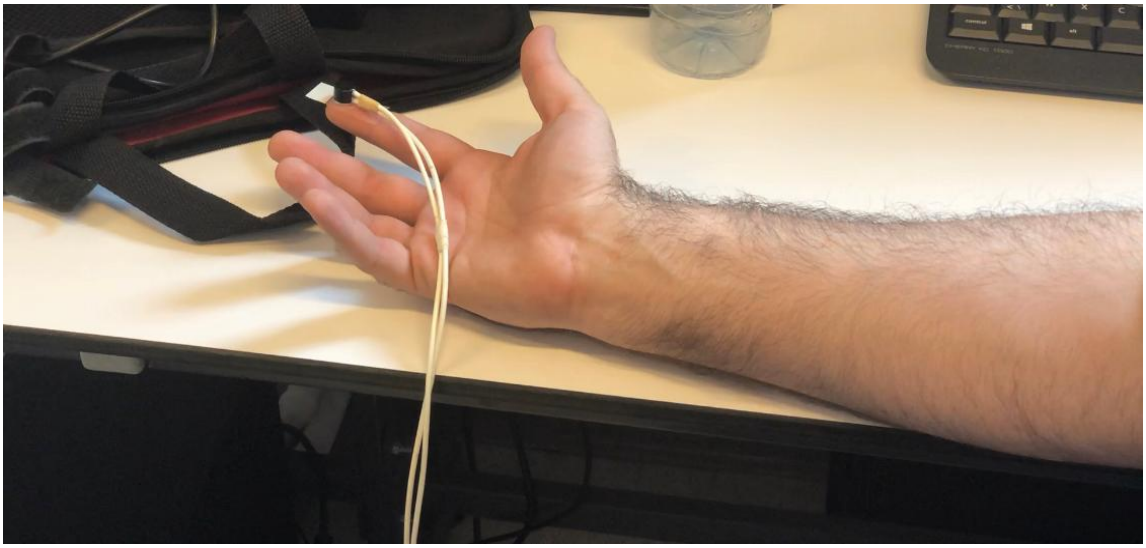

Figure S1. Thermostatic skin laser Doppler (SLD) probe (Reference number 457, Perimed, Jarfalla, Sweden)

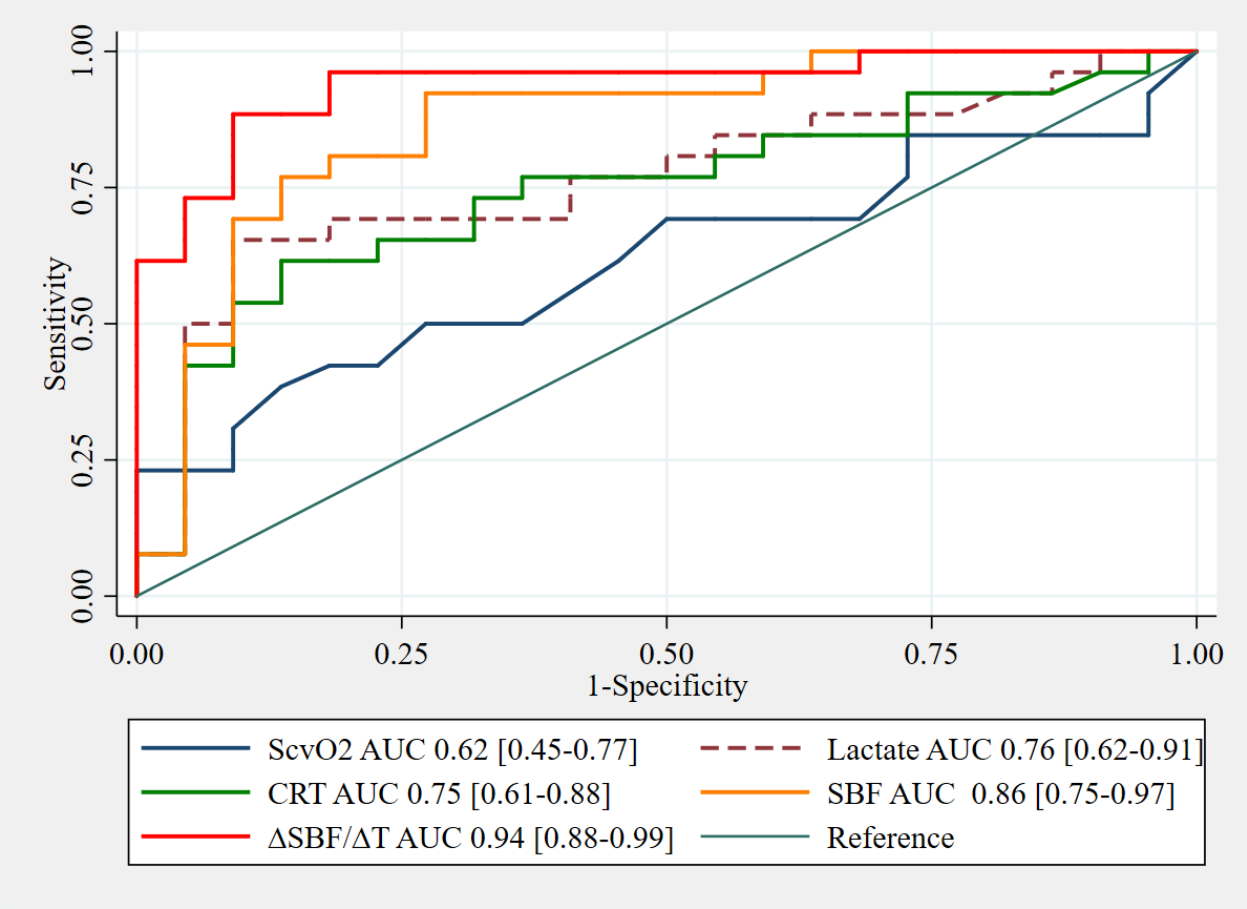

Figure S10. Receiver operating characteristic (ROC) curves of baseline parameters for prediction of mortality in patients with septic shock. $ScvO_2$: central venous oxygen saturation; CRT: capillary refill time; SBF: skin blood flow; AUC: area under the curve

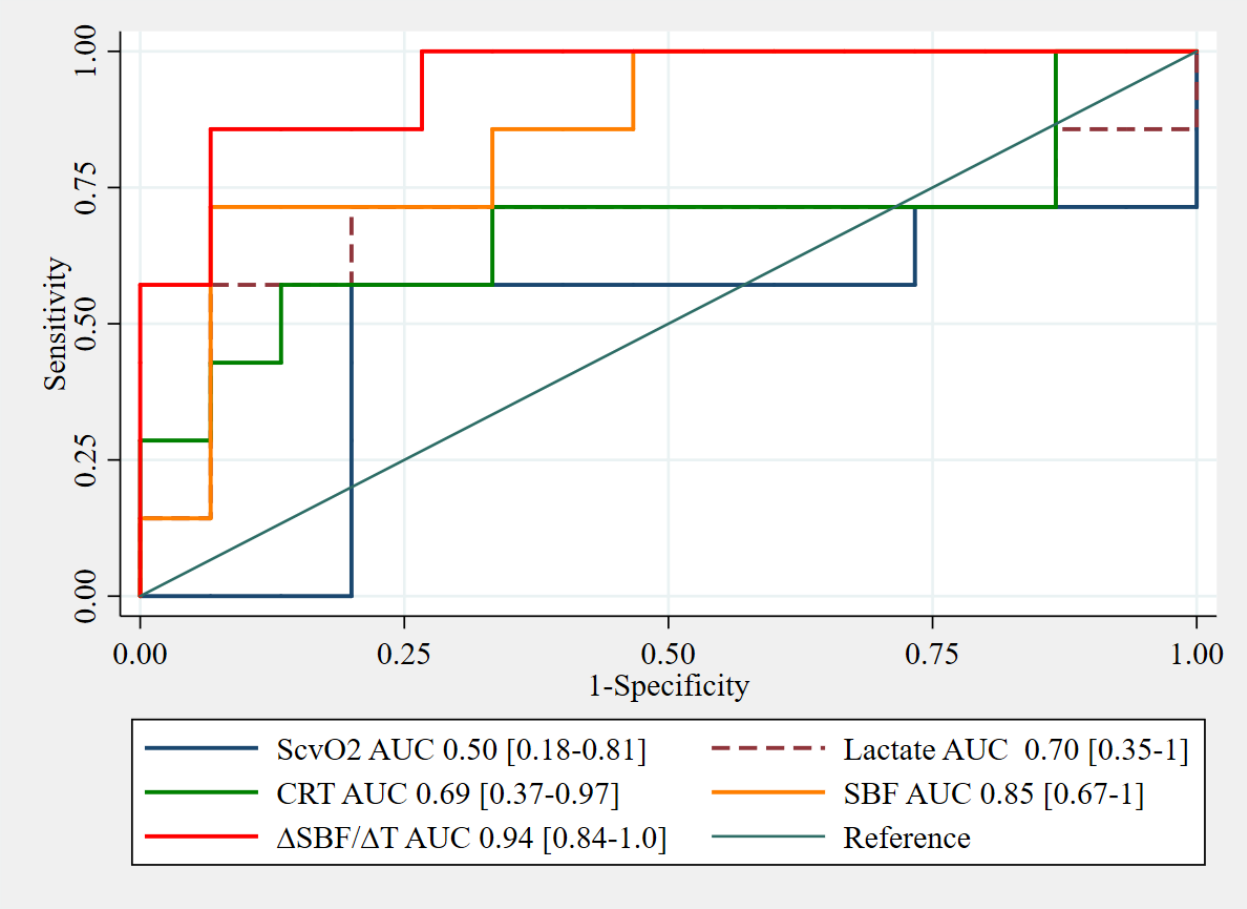

Figure S11. Receiver operating characteristic (ROC) curves of baseline parameters for prediction of mortality in patients with non-septic shock. $ScvO_2$: central venous oxygen saturation; CRT: capillary refill time; SBF: skin blood flow; AUC: area under the curve