The prognostic value of the subjective assessment of peripheral perfusion in critically ill patients

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Objective: **The physical examination of peripheral perfusion based on touching the skin or measuring capillary refill time has been related to the prognosis of patients with circulatory shock. It is unclear, however, whether monitoring peripheral perfusion after initial resuscitation still provides information on morbidity in critically ill patients. Therefore, we investigated whether subjective assessment of peripheral perfusion could help identify critically ill patients with a more severe organ or metabolic dysfunction using the Sequential Organ Failure Assessment (SOFA) score and lactate levels.**

Design: **Prospective observational study.**

Setting: **Multidisciplinary intensive care unit in a university hospital.**

Patients: **Fifty consecutive adult patients admitted to the intensive care unit.**

Interventions: **None.**

Measurements and Main Results: **Patients were considered to have abnormal peripheral perfusion if the examined extremity had an increase in capillary refill time (>4.5 seconds) or it was cool to the examiner hands. To address reliability of subjective inspection and palpation of peripheral perfusion, we also measured forearm-to-fingertip skin-temperature gradient ($T_{skin-diff}$), central-to-toe temperature difference (T_{c-toe}), and peripheral flow index. The measurements were taken within 24 hours of admission to the intensive care after hemodynamic stability was obtained (mean arterial pressure >65 mm Hg). Changes in SOFA score during the first 48 hours were analyzed (δ-SOFA). Individual SOFA score was significantly higher in patients with abnormal peripheral perfusion than in those with normal peripheral perfusion (9 ± 3 vs. 7 ± 2, $p < 0.05$). $T_{skin-diff}$, T_{c-toe}, and peripheral flow index were congruent with the subjective assessment of peripheral perfusion. The proportion of patients with δ-SOFA score >0 was significantly higher in patients with abnormal peripheral perfusion (77% vs. 23%, $p < 0.05$). The logistic regression analysis showed that the odds of unfavorable evolution are 7.4 (95% confidence interval 2–19; $p < 0.05$) times higher for a patient with abnormal peripheral perfusion. The proportion of hyperlactatemia was significantly different between patients with abnormal and normal peripheral perfusion (67% vs. 33%, $p < 0.05$). The odds of hyperlactatemia by logistic regression analysis are 4.6 (95% confidence interval 1.4–15; $p < 0.05$) times higher for a patient with abnormal peripheral perfusion.**

Conclusions: **Subjective assessment of peripheral perfusion with physical examination following initial hemodynamic resuscitation in the first 24 hours of admission could identify hemodynamically stable patients with a more severe organ dysfunction and higher lactate levels. Patients with abnormal peripheral perfusion had significantly higher odds of worsening organ failure than did patients with normal peripheral perfusion following initial resuscitation. (Crit Care Med 2009; 37:934–938)**

KEY WORDS: physical examination; capillary refill; skin temperature; body temperature; critically ill; multiple organ failure

Clinical signs of poor peripheral perfusion have been shown to be an early marker of inadequate tissue perfusion in acute circulatory shock (1–3). The rationale of monitoring peripheral perfusion is based on the concept that during hypotension the sympathetic neurohumoral response predominates on peripheral tissues resulting in a decreased skin perfusion and temperature (4, 5). Thus, monitoring of peripheral perfusion can assess the effect of the neurohumoral compensatory mechanism induced by low flow shock states in an acute stage of the disease.

Studies have showed that the subjective assessment of peripheral perfusion, in particular, the physical examination by touching the skin or measuring capillary refill time, can identify patients at high risk of complications from acute circulatory shock (6–9). Hasdai et al (7) showed the importance of the physical examination of peripheral perfusion in determining the prognosis of patients with cardiogenic shock. In their study, the presence of a cold and clammy skin was an independent predictor of 30-day mortality. Although septic shock is associated with peripheral vasodilation, cool extremities may be present in the early stage of sepsis. In another recent study, Thompson et al (8) studied the time course of the clinical features of meningococcal disease in children and adolescents before the admission to the hospital, and they identified cold hands and feet together with abnormal skin color as the main important clinical signs within the first 12 hours of the onset of illness. From these studies, it is clear that subjective assessment of peripheral perfusion is a valuable adjunct in hemodynamic monitoring during circulatory shock, and should be the first approach to assess critically ill patients.

However, most studies on clinical assessment of peripheral perfusion have fo-

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cused on specific populations of patients or have been performed during resuscitation in an acute stage of the disease (3, 8–10). It is unclear whether monitoring peripheral perfusion with physical examination in a general population of the intensive care unit (ICU) after initial resuscitation still provides information about organ derangements and whether it predicts outcome in terms of organ dysfunction.

In view of these observations, we carried out a prospective study to evaluate whether subjective assessment of peripheral perfusion in the postresuscitation phase of patients admitted to a general ICU could predict organ dysfunction. In particular, we wished to investigate if clinical monitoring of peripheral perfusion could help identify patients with a more severe organ dysfunction or metabolic dysfunction, as expressed by high Sequential Organ Failure Assessment (SOFA) score and lactate levels.

MATERIALS AND METHODS

Study Design and Patients. This prospective observational study was conducted in the intensive care of a university hospital, admitting all patients except those following cardiac surgery. We enrolled consecutive critically ill patients who had undergone initial resuscitation and stabilization within 24 hours of ICU admission. Patients were excluded if they had severe peripheral vascular disease (with a history of vascular surgery). The Institutional Review Board approved the study. Each patient or relative provided written informed consent.

Measurements. The assessment of peripheral perfusion was based on the subjective evaluation of the examiner, and patients were considered to have abnormal peripheral perfusion if the examined extremity had an increase in capillary refill time or it was cool to the examiner's hands. Capillary refill time was measured by applying firm pressure to the distal phalanx of the index finger for 15 seconds. A chronometer recorded the time for return of the normal color and 4.5 seconds was defined as the upper limit of normality (11). To address the reliability of the subjective assessment of peripheral perfusion by the examiner, we also measured forearm-to-fingertip skin-temperature gradient ($T_{skin\text{-}diff}$), central-to-toe temperature difference ($T_{c\text{-}toe}$), and peripheral flow index (PFI) simultaneously with clinical observation. The $T_{skin\text{-}diff}$ was obtained from two skin probes (Hewlett Packard 21078A, Palo Alto, CA) attached to the index finger and on the radial side of the forearm, mid-way between the elbow and the wrist. The $T_{c\text{-}toe}$ was calculated from central temperature, with an infrared tympanic thermometer (First Temp Genius Thermometer—3000A; Kendall Healthcare, Mansfield, MA), and great toe temperature measured on the ventral face with a skin probe (Hewlett Packard 21078A). The temperature gradients $T_{skin\text{-}diff}$ and $T_{c\text{-}toe}$ can better reflect cutaneous blood flow than the skin temperature itself. Considering a constant environment condition, $T_{skin\text{-}diff}$ and $T_{c\text{-}toe}$ increases during vasoconstriction (12, 13). PFI provides a noninvasive method to evaluate and to reflect changes in peripheral perfusion (14, 15). PFI is derived from the pulse oximetry signal and it was measured using the Nellcor-OxiMax pulse oximetry (Boulder, CO) and the Hewlett Packard monitor (Viridia/56S). To confirm the subjective assessment of abnormal peripheral perfusion condition, this study used the following definition of vasoconstriction: $T_{skin\text{-}diff} > 0$°C (12), $T_{c\text{-}toe} > 7$°C (13), and PFI < 1.4 (14). Although the ambient temperature at each patient's bedside was not directly measured, the ICU has one-person closed rooms and the ambient temperature in each patient room was individually and actively controlled at 22°C. Thereafter, routine global hemodynamic variables such as heart rate, mean arterial pressure, central venous pressure, and urine output were obtained.

Basic demographic characteristics and all the variables of SOFA score were collected for each patient. The investigator registered the measurements within 24 hours of admission to the intensive care after hemodynamic stability was obtained (mean arterial pressure >65 mm Hg and no change in vasopressor infusion rate for 2 hours). Changes in SOFA score during the first 48 hours (δ-SOFA) were also analyzed and was calculated as the difference between the 48-hour SOFA score and the admission score (16). Arterial blood samples were withdrawn for the determination of blood gases and lactate levels. Hyperlactatemia was defined as a blood lactate level >2 mmol/L. We were interested in evaluating whether subjective assessment of peripheral perfusion could help identify patients with unfavorable evolution defined as δ-SOFA score >0 and hyperlactatemia.

Statistics. The results are presented as mean ± SD, unless otherwise specified. Differences between group means were tested by Student's *t* tests, and for variables that were not normally distributed, by Mann-Whitney *U* test. The chi-square test was used to compare frequencies. To estimate the association between abnormal peripheral perfusion and both δ-SOFA score and hyperlactatemia, logistic regression analysis was performed. *p* values ≤0.05 were considered statistically significant.

RESULTS

Of 50 patients included in the study, 39 had circulatory shock at admission to ICU, of whom 21 had septic shock and 18 had no septic shock. Table 1 summarizes the clinical data of the patients. During the first 24 hours of ICU admission, 23 patients (46%) had abnormal peripheral perfusion following resuscitation and stabilization. Individual SOFA score was significantly higher in patients with abnormal peripheral perfusion than in those with normal peripheral perfusion (9 ± 3 vs. 7 ± 2, $p < 0.05$). $T_{skin\text{-}diff}$, $T_{c\text{-}toe}$, and PFI measurements were congruent with the subjective assessment of peripheral perfusion (Table 2). Hemodynamic variables were similar in patients with abnormal and normal peripheral perfusion (Table 3). In patients who received vasopressor therapy (n = 33), the dose of vasopressor did not differ between normal (n = 17) and abnormal (n = 16) peripheral perfusion condition (0.19 ± 0.11 vs. 0.17 ± 0.10; $p = 0.80$).

The proportion of patients with unfavorable evolution was significantly higher in patients with abnormal peripheral perfusion (Table 4). Logistic regression analysis showed that the odds of unfavorable evolution are 7.4 (95% confidence interval 2–19; $p < 0.05$) times higher for a patient with abnormal peripheral perfusion than for a patient with normal peripheral perfusion. Differences in global hemodynamic variables, such as heart rate, mean arterial pressure, central venous pressure, and urine output were not

Table 1. Demographic data of the patients

Number of patients	50
Age (yrs)	51 (17–80)
Male/female	39/11
Sequential Organ Failure Assessment score admission	8 (2–15)
Acute Physiology and Chronic Health Evaluation II	23 (13–35)
Admission category	
Pneumonia	9
Trauma	8
Abdominal sepsis	7
Postoperative	5
Chronic obstructive pulmonary disease	3
Cardiogenic shock	2
Hepatic encephalopathy	2
Hypovolemic/hemorrhagic shock	2
Mediastinitis	2
Meningitis	2
Pancreatitis	2
Postcardiac arrest	2
Cerebrovascular accident	1
Lung cancer	1
Systemic lupus erythematosus	1
Urosepsis	1
Survivor/nonsurvivor	35/15

Values are given as mean (range) whereappropriate.

Table 2. Objective parameters of peripheral circulation according to the subjective evaluation of peripheral perfusion

Objective Parameters	Subjective Evaluation		
	Normal (n = 27)	Abnormal (n = 23)	*p*
$T_{skin-diff}$ (°C)	−0.2 ± 2.8	4.6 ± 2.8	<0.01
T_{c-toe} (°C)	6.5 ± 3.4	10 ± 4.1	<0.01
PFI	2.3 ± 1.6	0.7 ± 0.8	<0.01

$T_{skin-diff}$, forearm-to-fingertip skin-temperature gradient; T_{c-toe}, central-to-toe temperature difference; PFI, peripheral flow index.

Table 3. Global hemodynamics variables in abnormal and normal peripheral perfusion

	Peripheral Perfusion		
	Normal (n = 27)	Abnormal (n = 23)	*p*
HR (bpm)	90 ± 22	94 ± 20	0.53
MAP (mm Hg)	80 ± 14	81 ± 18	0.87
CVP (mm Hg)	14 ± 6	13 ± 7	0.84
Urine output (mL/hr)	111 ± 83	72 ± 30	0.14

HR, heart rate; MAP, mean arterial blood pressure; CVP, central venous pressure.

Table 4. Proportion of patients with unfavorable evolution (δ-SOFA >0) and favorable evolution (δ-SOFA score ≤0) stratified by normal and abnormal peripheral perfusion[a]

	Peripheral Perfusion	
	Normal (n = 27)	Abnormal (n = 23)
δ-SOFA ≤0 (N = 33), percent of patients	70	30
δ-SOFA >0 (N = 17), percent of patients	23	77

SOFA, Sequential Organ Failure Assessment score.

[a] $p < 0.05$, by chi-square test.

Table 5. Proportion of hyperlactatemia and normal blood lactate levels between patients with abnormal and normal peripheral perfusion[a]

	Peripheral Perfusion	
	Normal (n = 27)	Abnormal (n = 23)
Normal lactate levels (N = 29), percent of patients	69	31
Hyperlactatemia (N = 21), percent of patients	33	67

[a] $p < 0.05$, by chi-square test.

statistically significant between patients with and without unfavorable evolution (data not shown). The proportion of patients with hyperlactatemia was significantly higher in patients with abnormal peripheral perfusion (Table 5). Logistic regression analysis showed that the odds of hyperlactatemia in a patient with abnormal peripheral perfusion are 4.6 (95% confidence interval 1.4–15; $p < 0.05$) times higher than in a patient with normal peripheral perfusion.

DISCUSSION

This prospective observational study shows that the subjective assessment of peripheral perfusion could discriminate patients with a more severe organ dysfunction, as expressed by high SOFA score and lactate levels in patients with abnormal peripheral perfusion. One may argue that high SOFA score in the abnormal peripheral perfusion group may be related to the level of mean arterial pressure or to the use of vasopressor support. However, our patients were all resuscitated and stabilized at the moment that data were collected, and global hemodynamic variables or dose of vasopressor was similar between patients with normal and abnormal peripheral perfusion. This finding suggests that abnormal peripheral perfusion is not related to hypotension or vasoconstriction from a pharmacologic intervention. This lack of association between abnormal peripheral perfusion and global hemodynamic variables is not unexpected, because some studies have reported a poor correlation between clinical examination of peripheral perfusion and heart rate, blood pressure, or cardiac output (3, 10, 17). In addition, recent observations suggest that microcirculatory alterations in circulatory shock are independent of systemic variables (18, 19) and that systemic variables may not be sensitive enough to reflect changes in peripheral blood flow in critically ill patients (20).

Delta-SOFA score has been suggested to monitor the evolution of organ failure (16). In our study, we investigated whether the condition of peripheral perfusion in resuscitated patients could predict an increase in severity of organ dysfunction. Our results show that patients who persist with abnormal peripheral perfusion after initial resuscitation have a significantly higher probability of unfavorable evolution, as indicated by an increase in the δ-SOFA score. Thus, monitoring peripheral perfusion could identify these patients who do not improve despite initial resuscitation and stabilization. Similarly, the logistic regression analysis showed that patients who have an abnormal peripheral perfusion following resuscitation are more likely to remain hyperlactatemic. The interpretation of hyperlactatemia in critically ill patients is complex, and factors other than hypoperfusion may be involved (21). Nevertheless, our findings are in agreement with those of Kaplan et al (6) showing that patients with cold extremities are associated with higher blood lactate levels. The correlation between abnormal peripheral perfusion and high blood lactate levels in our patients is not surprising as hyperlactatemia in most cases takes place in the presence of organ dysfunction (22–24). This prospective study does not show a causal relation between poor peripheral perfusion and organ dysfunction or tissue hypoperfusion, but some reports indicate this relation (1, 25–27). Studies on measurements of blood flow and oxygenation in peripheral tissues suggest that compensatory vasoconstriction results in maldistribution of microcirculatory flow, which has been associated with organ dysfunction and multiple organ failure (1, 25–27).

In a recent consensus conference on hemodynamic monitoring in shock, it was recognized that the definition of shock requires evidence of circulatory and cellular dysfunction, manifested by markers of hypoperfusion such as elevated blood lactate levels, regardless of the presence of hypotension (20). Because data were collected in the post-

resuscitation period, our patients exhibited no other clinical signs of circulatory shock apart from hyperlactatemia and abnormal peripheral perfusion. Normotension with persisting hyperlactatemia following initial resuscitation has been associated with a high incidence of organ failure (28, 29). Our study is in agreement with these findings, demonstrating that abnormal peripheral perfusion in patients with no other clinical signs of shock is predictive of progressing organ dysfunction. Thus, if the clinician stops the resuscitation after the traditional endpoints have been normalized, a majority of patients will remain in a state of compensated shock. The absence of abnormal peripheral perfusion after initial resuscitation identifies patients with a more favorable outcome. Therefore, clinical assessment of peripheral perfusion during resuscitation has the potential to optimize resuscitation procedures. However, this was not the topic of this study. The subjective inspection and palpation of peripheral perfusion is safe, noninvasive, and easy to perform at the bedside and enables physicians to identify those patients with tissue hypoperfusion before continuing to invasive procedures. The subsequent potential of subjective assessment of peripheral perfusion in a general ICU population applied by multiple clinicians must be investigated further to address whether aiming at normalization of peripheral perfusion will have an impact on outcome.

As the focus on our study was to address the relationship between abnormal peripheral perfusion and organ failure, we minimized the variability of the subjective assessment of peripheral perfusion by having only one investigator collecting the data. In addition, we compared this subjective assessment of peripheral perfusion with three objective measurements: $T_{skin\text{-}diff}$, $T_{c\text{-}toe}$, and PFI. These parameters are independent indicators of peripheral blood flow (30). We found that the subjective clinical assessment of peripheral perfusion was in agreement with the objective measurements of $T_{skin\text{-}diff}$, $T_{c\text{-}toe}$, and PFI (Table 2).

This study has several limitations that should be acknowledged. First, measurements of global blood flow (cardiac output) were not made in this study. The main focus was to assess the relationship between the presence of abnormal peripheral perfusion following our standard hemodynamic optimization protocol and organ dysfunction. Second, we did not include other methods of peripheral perfusion monitoring, such as cutaneous laser Doppler flowmetry, transcutaneous oximetry, or sublingual capnometry as we emphasized the subjective assessment of peripheral perfusion. In addition, we speculate that these noninvasive methods could have shown the same association with $T_{skin\text{-}diff}$, $T_{c\text{-}toe}$, and PFI. Third, although $T_{c\text{-}toe}$ is a well-validated method to estimate peripheral blood flow, central temperature in our study was obtained using a tympanic thermometer, which may not be a reliable representation of core temperature. However, the impact of central temperature in $T_{c\text{-}toe}$ calculation is small compared with the skin temperature of the great toe, as abnormalities in $T_{c\text{-}toe}$ are a result mainly of changes in peripheral vasoconstriction (30). Fourth, changes in ambient temperature may have influenced the subjective assessment of the skin temperature. Differences in ambient temperature at each patient's bedside were not directly measured. However, the ICU consists of one-person closed rooms and the ambient temperature in each patient room was individually controlled at 22°C. Furthermore, the differences in subjective skin temperature were in agreement with differences in $T_{skin\text{-}diff}$ in our study. As a change in ambient temperature similarly affects forearm and fingertip temperature producing little influence in the gradient between forearm and fingertip (30), we think the effect of ambient temperature was small. Last, peripheral perfusion is not static; it alters over time in a constant dynamic situation, and our measurements were made within 24 hours of ICU admission.

CONCLUSION

In conclusion, we found that a clinical assessment of peripheral perfusion by physical examination following initial hemodynamic optimization during the first 24 hours of admission could discriminate hemodynamically stable patients with more severe organ dysfunction. In addition, patients with abnormal peripheral perfusion following this initial resuscitation had significantly higher odds of worsening organ failure and higher lactate levels compared with patients with normal peripheral perfusion at this time point. The easy application of this clinical assessment of peripheral perfusion at the bedside has a potential as a simple and inexpensive tool for early detection of worsening organ dysfunction and possibly the adequacy of treatment in critically ill patients.

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