

Mottling Incidence and Mottling Score According to Arterial Lactate Level in Septic Shock Patients

Arnaud Ferraris¹, Camille Bouisse², Fabrice Thiollière³, Vincent Piriou⁴, Bernard Allaouchiche⁵

ABSTRACT

Objectives: Mottling score is estimated from 0–5 according to mottling over the knee and described as clinical evaluation of tissue perfusion. This score was developed with ancient definitions of sepsis without lactate level, a major prognostic parameter when superior to 2 mmol/L. This study describes mottling incidence and mottling score in septic shock patients according to lactate level.

Materials and methods: We reanalyzed our prospective study in a French tertiary hospital in the intensive care unit (ICU) which studied mottling score and thermography correlation. Patients admitted to septic shock diagnosis and requiring vasoactive drugs were included. We recorded hemodynamic variables, mottling score, and lactate. Data collection was realized at ICU admission (H0) and after six hours (H6).

Results: Forty-three patients were included. Mean age was 67 (± 4), mean sequential organ failure assessment (SOFA) score was 11 (8–12), and SAPS II 58 ± 20 . Mortality rate at day 28 was 30%. Among patients with lactate ≥ 2 mmol/L, mottling was more prevalent in 82.6% vs 47.4% (p value = 0.016), and at H6 mottling score was higher (p value = 0.009). Although, mottling incidence was not different between dead (85%) and survivors (81%; p value = 0.795).

Conclusion: A new sepsis definition implies a new epidemiology in mottling according to lactate threshold. Patients with lactate ≥ 2 mmol/L presented a higher incidence and score of mottling. However, mortality was not influenced by mottling in this study.

Clinical significance:

- Arterial lactate is a major prognostic parameter when superior to 2 mmol/L.
- A new definition of sepsis was published in 2016 with a new paradigm and epidemiology of septic shock
- Patients with lactate ≥ 2 mmol/L presented a higher incidence and score of mottling.
- Mottling score is a clinical sign of microcirculatory alteration, related to lactate level in septic shock.

Keywords: Lactate, Microcirculation, Mottling score, Septic shock.

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INTRODUCTION

Microcirculation is a vascular network responsible for the distribution of oxygen from arteries to capillaries and tissues of the body.¹ In septic shock, peripheral perfusion is altered, generating hypoxia and organ failure.² Many studies explored microcirculatory alterations, a crucial point in physiopathology of septic shock.^{3,4} Microcirculation evaluation is feasible at bedside with capillary refill time, mottling score, diuresis, or skin temperature gradients. Nevertheless, technical devices are in development to direct evaluation of microvascular perfusion, such as sublingual videomicroscopy with sidestream dark field (SDF)⁵ or near-infrared spectroscopy technology (NIRS) that indirectly evaluates tissue perfusion and global oxygenation alteration.⁶ None of these devices has showed superiority on the other. No gold standard is available to compare these methods, which makes microcirculation monitoring uneasy. We decided to focus on skin perfusion of the knee by mottling score, basing our choice on previous studies.⁷

Skin mottling is defined as a violaceous coloration due to blood flow reduction in small vessels secondary to heterogeneous microcirculation alterations. An example is depicted in Figure 1 with schematized 5 mottling areas. In a previous observational study, skin mottling ratio reached 29% in an intensive care unit (ICU) population of 791 patients and increased to 49% in patients admitted for septic shock. Specific scores such as SAPS II were higher in patients with mottling in comparison to those free of mottling [mean SAPS II 46 (34–59) vs 32 (21–45), respectively].⁸ Mottling is

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a clinical sign of septic shock,² easy to recognize over the knee in ICU or in emergency settings and identified as a negative outcome in critically ill patients.⁹

A new definition of sepsis was published in 2016 with a septic shock defined by a sepsis associated with lactate ≥ 2 mmol/L and vasopressor requirement to maintain mean arterial pressure (MAP) ≥ 65 mm Hg.¹⁰ A new definition implies a new paradigm and repartition in septic shock epidemiology. As a major prognostic parameter, we presumed that patients with arterial lactate ≥ 2 mmol/L present more microcirculatory disorders such as mottling.

We analyzed our data issued from our prospective observational study, including all patients admitted in the ICU for septic shock

which compared mottling score with skin temperature around the knee involving infrared thermography.¹¹ The objective of the current study is to analyze mottling incidence and mottling score in septic shock patients according to lactate threshold of 2 mmol/L.

MATERIALS AND METHODS

We resumed data of our prospective cohort of 46 patients published in 2018¹¹ which focused on correlation between skin temperature measured by thermography with mottling score during septic shock. Briefly, we achieved over 8-month period a prospective observational study in an ICU in a French tertiary hospital of Lyon from January to August 2016. We enrolled adult consecutive patients with a diagnosis of septic shock. Patients were enrolled with a suspected sepsis associated with systolic arterial pressure <90 mm Hg or MAP <65 mm Hg, despite initial crystalloid resuscitation and requiring norepinephrine at admission

in ICU. Those excluded include black skin, pregnancy, peripheral arterial disease, cutaneous infection of the lower limbs, and patient or relatives refusal. This study was purely observational, and verbal information was authorized (local ethics committee). Oral information was given to all patients. Institutional approval was issued from the local ethics committee (Comité de Protection des Personnes sud est IV Lyon, France; Ref L15-2013, approved on December 15 of 2015).

Management of Patients

Patient care with septic shock was guided according to local protocol and adapted from reference guidelines.^{10,12} Briefly, patient resuscitation at admission was intravenous volume expansion with crystalloids and initiation of vasoactive drugs (norepinephrine) to reach specified end points: MAP >65 mm Hg (or 70 mm Hg in patients with chronic arterial hypertension) and urine output >0.5 mL/kg/hour. Continuous and invasive arterial pressure, central venous catheter, and mechanical ventilation were provided when needed. We used transthoracic echocardiography (Vivid S6, General Electric Healthcare®) or transpulmonary thermodilution (PiCCO, Pulsion medical system®) as hemodynamic monitoring. According to local protocol, sedation and analgesia were performed with midazolam and sufentanil, respectively.

Study Protocol

Demographic and clinical characteristics of the patients were recorded: age, sex, severity scores with sequential organ failure assessment (SOFA) and Simplified Acute Physiologic Score II (SAPS II) determined at admission.^{13,14} Measurements were performed at study inclusion (H0) and 6 hours after initial resuscitation (H6): global macrocirculatory variables (MAP, heart rate, and cardiac output), arterial lactate, mechanical ventilation, norepinephrine requirements, and mottling score (from 0 to 5). Thermography was realized with a thermic camera FLIR-E® at H0 and H6 at bedside for the previous analysis (Fig. 2). We recorded ICU mortality rate at day 28, length of stay, mechanical ventilation-free days, and SOFA score on discharge.

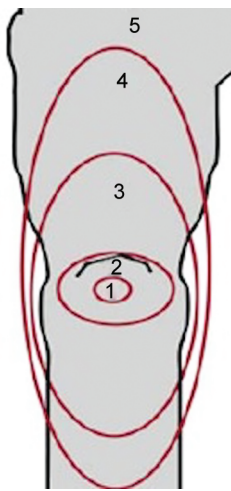


Fig. 1: Mottling score defined by five zones around the knee. Schema from Ref. 9

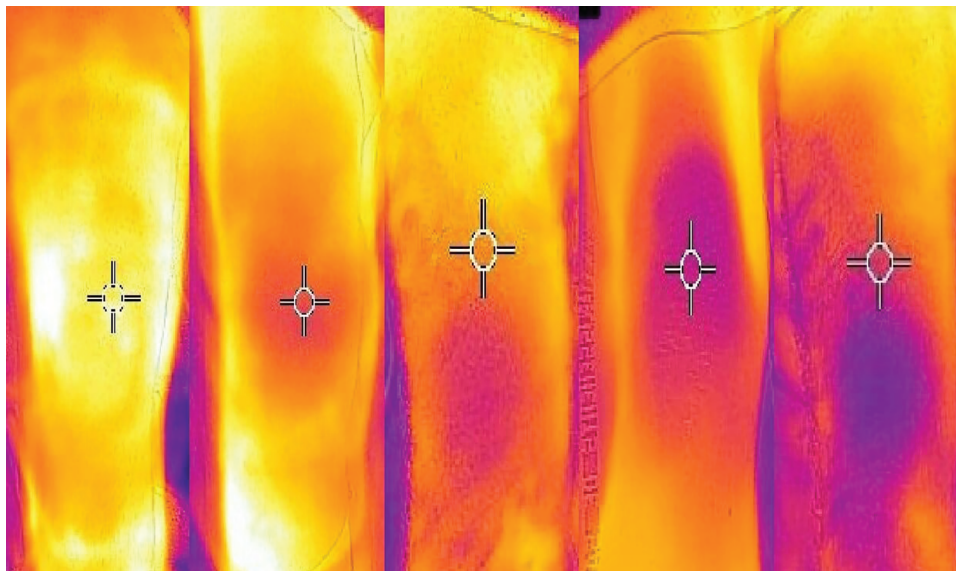


Fig. 2: Examples of thermography, from mottling score 0–4 (from left to right)

Endpoints

Primary endpoint is a difference in mottling incidence and mottling score according to arterial lactate level during a septic shock. We supposed that patients with lactate ≥ 2 mmol/L presented higher mottling frequency and higher mottling score than patients with lactate < 2 mmol/L.

Secondary endpoints are first to compare hemodynamic parameters and vasopressor requirements according to lactate level and second the relationship between mottling and ICU mortality, 28-day survival, severity scores at admission and discharge, and norepinephrine level.

Statistical Analysis

Data are presented as number (%), mean \pm SD (standard deviation) or median (25th–75th) for non-normally distributed variables (Shapiro–Wilk test) as appropriate. A Chi-square test and a student test were performed to compare patients with a lactate ≥ 2 mmol/L or inferior. A p value < 0.05 was considered statistically significant. Statistical analysis was performed using JMP 13.1 software (SAS institute).

RESULTS

Forty-six patients were prospectively included for septic shock during an 8-month period in the ICU. Clinical characteristics of the patients are summarized in Table 1. Save 3 patients weaned from vasopressors at H6 time point after initial resuscitation, and all patients received norepinephrine. ICU mortality was 30% ($n = 14$).

We compared hemodynamic parameters, mottling, and prognostic factors between patients with an arterial lactate ≥ 2

mmol/L and those with a lactate < 2 mmol/L. Results are presented in Table 2 for H0 (ICU admission) and in Table 3 for H6.

Among patients with arterial lactate ≥ 2 mmol/L at H0, 77% of nonsurvivors presented mottling vs 72% in survivors (p value = 0.795). Similarly, at H6 85% of nonsurvivors presented mottling vs 81% in survivors (p value = 0.795).

DISCUSSION

We resumed analysis from our cohort of a prospective observational study to describe mottling incidence and mottling score in septic shock patients according to lactate threshold of 2 mmol/L. In this analysis, mottling repartition was different at H6 according to arterial lactate level. Patients with a lactate ≥ 2 mmol/L required higher norepinephrine doses, mottling incidence, and mottling score at H6. Furthermore, no difference was demonstrated in this study with severity score such as SOFA and day-28 mortality.

Skin temperature is a paramount parameter in microcirculation monitoring, including other exploration such as capillary refill time, where normal threshold is debated.¹⁵ Most of the studies focused on septic shock,^{16,17} and they confirmed microvascular alterations. Nevertheless, microcirculatory alterations are described in various critical situations: cardiogenic shock¹⁸ and severe trauma.¹⁹ In the present study, we focused on septic shock to generate a homogeneous cohort with the physiopathology of sepsis.

Many microcirculation analyzes are published, some are clinical assessments easy to perform at bedside but often subjective measures: capillary refill time,²⁰ toe-to-room temperature gradients,²¹ and mottling score.⁹ Some devices are developed as videomicroscopy, spectral orthogonal polarization, or side stream dark field imaging to directly visualization of microcirculation.⁵ However, these techniques are not daily practice and remain in development. Moreover, in absence of gold standard, we focus on mottling score that is an easy and simple exploration. Initially developed by Ait-Oufella, this exploration is correlated with mortality and ICU outcomes in septic shock in a single-center study.⁹ Among 60 patients in septic shock, the authors established a strong

Table 1: General characteristics. Values are expressed as absolute values (n), %, mean (\pm SD) or median (25th–75th)

Patients (n)	46	
Age, years	67 (± 4)	
Male gender	21 (45%)	
Body mass index (kg/m^2)	25 (± 2)	
SOFA at admission	11 (8–12)	
SAPS II at admission	57 (± 20)	
Hemodynamic parameters	H0	H6
Mean arterial pressure (mm Hg)	67 (± 5)	73 (± 12)
Heart rate (/minute)	101 (± 9)	97 (± 7)
Cardiac output (mL/minute)	4.9 (4.5–5.4)	5.1 (4.2–5.7)
Mottling at examination, n /total	25/37 (68%)	29/43 (67%)
Volume expansion (mL)	1,000 (750–2,250)	1,000 (100–2,000)
Norepinephrine doses ($\mu\text{g}/\text{kg}/\text{minute}$)	0.37 (0.13–0.8)	0.42 (0.15–0.9)
Lactate level (mmol/L)	2.4 (1.2–4.7)	2.2 (1.4–4)
Mechanical ventilation	31 (67%)	
Outcomes		
28-day mortality	14 (30%)	
ICU length-of-stay, days	12 (5–24)	
SOFA at ICU discharge	2 (0–6)	
Vasopressor-free days	4.5 (1–11)	
Ventilator-free days	3 (1–6)	

Table 2: Hemodynamic parameters, mottling score at ICU admission (H0) according to lactate level. Values are expressed as absolute values (n), %, mean (\pm SD) or median (25th–75th)

	Lactate ≥ 2 mmol/L	Lactate < 2 mmol/L	p value
H0 (admission)			
SOFA score	10.5 (8–12)	10 (6–12)	0.578
Hemodynamic SOFA	4 (4–4)	4 (4–4)	0.578
MAP (mm Hg)	61 \pm 6	76 \pm 7	0.001
Heart rate (/minute)	107 \pm 13	91 \pm 12	0.084
Norepinephrine doses ($\mu\text{g}/\text{kg}/\text{minute}$)	0.69 (0.14–1)	0.26 (0.12–0.4)	0.033
Mottling patients (n)	75%	69%	0.716
Mottling score			
0	25%	31%	
1	20%	23%	
2	25%	31%	
3	20%	15%	
4	10%	0%	
5	0%	0%	0.805
28-day mortality (n)	45%	23%	0.21

Table 3: Hemodynamic parameters, mottling score after initial resuscitation (H6) according to lactate level. Values are expressed as absolute values (n), %, mean (\pm SD) or median (25th–75th)

H6	Lactate \geq 2 mmol/L	Lactate < 2 mmol/L	p value
MAP (mm Hg)	74 \pm 5	73 \pm 5	0.634
Heart rate (/minute)	100 \pm 10	95 \pm 13	0.551
Norepinephrine doses(μ g/kg/minute)	0.75 (0.36–1.1)	0.18 (0.06–0.45)	0.006
Mottling patients (n)	86.2%	47.4%	0.016
Mottling score			
0	17.4%	52.6%	
1	43.5%	0%	
2	17.4%	21.1%	
3	13%	21.1%	
4	8.7%	0%	
5	0%	5.3%	0.009
28-day mortality (n)	30.4%	25%	0.692

relation between 14-day mortality and mottling score (p value < 0.0001) as well as its variation between admission H0 and H6.

In this study, H0 and H6 time points were empirically determined similar to previous studies^{9,22} when measures were related to mortality. At H0, we expect the worst microcirculation situation and at H6 a stabilization after initial resuscitation.

This current work is the first study to analyze mottling score according to new sepsis definition. As a meta parameter of severity of septic shock, arterial lactate is related to circulatory and metabolic disorders. This study confirms relationship between arterial lactate and peripheral circulatory disorders, such as mottling. Nevertheless, no correlation was found between ICU outcomes or mortality and arterial lactate groups. This point corroborates the lack of power hypothesis in our study. Negative results could be explained with a limited cohort. Moreover, the study was not designed to establish relationship between mottling and mortality but to compare mottling score distribution according to lactate threshold, and this work is a second analysis of a previous study designed to another objective. We note some limitations to illustrate the lack of results: We conducted a monocentric study, and number of patients is limited without previous calculation of the number of subjects required. This study was neither randomized nor blinded. Moreover, mottling score is not a gold standard in microcirculatory monitoring. Other studies are required to confirm these data with a larger cohort. Measurement and comparison of others microcirculatory parameters, such as capillary refill time, temperature gradients between central to peripheral, and vascular occlusion test with a NIRS device according to lactate threshold, are further studies to be conducted.

CONCLUSION

A new sepsis definition implies a new epidemiology in mottling according to lactate threshold. Patients with lactate \geq 2 mmol/L presented a higher incidence and score of mottling. However, mortality was not influenced by mottling in this study.

AVAILABILITY OF DATA AND MATERIAL

Data are available in Data Archiving and Networked Services: <https://doi.org/10.17026/dans-za5-xs39>

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