



# Contribution of Capillary Refilling Time and Skin Mottling Score to Predict ICU Admission of Patients with Septic or haemorrhagic Shock Admitted to the Emergency Department: A TRCMARBSAU Study

Romain Jouffroy<sup>1</sup> , Emmanuel Bloch-laine<sup>2</sup> , Maxime Maignan<sup>3</sup> , Pierrick Le Borgne<sup>4</sup> , Nicolas Marjanovic<sup>5</sup> , Thomas Lafon<sup>6</sup> , Scarlett Dehdar<sup>7</sup> , Lea Thomas<sup>8</sup> , Pierre Michelet<sup>9</sup> , Benoit Vivien<sup>1</sup> 

<sup>1</sup>Intensive Care Unit, Anaesthesiology, SAMU, Necker Enfants Malades Hospital, Assistance Publique - Hôpitaux de Paris, Paris, France

<sup>2</sup>Department of Emergency, Cochin Hospital, Assistance Publique - Hôpitaux de Paris, Paris, France

<sup>3</sup>Department of Emergency and SAMU, Grenoble Alps University Hospital, Grenoble; Department of Emergency, Haute-pierre Hospital, University Hospital of Strasbourg, Strasbourg, France

<sup>4</sup>INSERM (French National Institute of Health and Medical Research), UMR 1260, Regenerative NanoMedicine (RNM), Fédération de Médecine Translationnelle (FMTS), University of Strasbourg, Strasbourg, France

<sup>5</sup>Department of Emergency and SAMU, Poitiers University Hospital, Poitiers, France

<sup>6</sup>Department of Emergency, SAMU, Inserm CIC 1435, Limoges University Hospital Center, Limoges, France

<sup>7</sup>Department of Emergency, Argenteuil Hospital, Argenteuil, France

<sup>8</sup>Department of Emergency, Begin Military Hospital, Clamart, France

<sup>9</sup>Department of Emergency, Timone Hospital, Aix-Marseille University – CV2N, INSERM, INRA, Assistance Publique Hôpitaux de Marseille, Marseille, France

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## Abstract

**Objective:** In the emergency department (ED), the severity assessment of shock is a fundamental step prior to the admission in the intensive care unit (ICU). As biomarkers are time consuming to evaluate the severity of micro- and macro-circulation alteration, capillary refill time and skin mottling score are two simple, available clinical criteria validated to predict mortality in the ICU. The aim of the present study is to provide clinical evidence that capillary refill time and skin mottling score assessed in the ED also predict ICU admission of patients with septic or haemorrhagic shock.

**Methods:** This trial is an observational, non-randomised controlled study. A total of 1500 patients admitted to the ED for septic or haemorrhagic shock will be enrolled into the study. The primary outcome is the admission to the ICU.

**Results:** The study will not impact the treatments provided to each patient. Capillary refill time and skin mottling score will not be taken into account to decide patient's treatments and/or ICU admission. Patients will be followed up during their hospital stay to determine their precise destination after the ED (home, ICU or ward) and the 28- and 90-day mortality after hospital admission.

**Conclusion:** The results from the present study will provide clinical evidence on the correlation between the ICU admission and the capillary refill time and the skin mottling score in septic or haemorrhagic shock admitted to the ED. The aim of the present study is to provide two simple, reliable and non-invasive tools for the triage and early orientation of these patients.

**Keywords:** Capillary refill time, emergency, intensive care unit, prediction, skin mottling score

## Introduction

Severity assessment is a fundamental step in the initial hospital orientation of patients admitted to the emergency department (ED). Currently, the initial assessment (triage) is based on clinical examination including vital param-

eters and anamnestic history aiming to look for severity elements. This assessment directly impacts subsequent orientation after the ED to intensive care unit (ICU), ward or home. A mild sick patient may be referred to a ward, whereas a more severe patient, or at risk of worsening, is usually admitted to the ICU unless palliative.

As applied to sepsis, the decision-making is based on clinical signs of severe sepsis and/or septic shock according to the 2005 SFAR-SRLF conference (1). The usual severity scores, such as Sequential Organ Failure Assessment (2), Index Gravity Score II (3) and Simplified Acute Physiology Score II (4), are only validated in the ICU and needs time to be evaluated. Thus, these scores are not transposable to the ED and not useful at admission in the ED.

Shock, especially septic or haemorrhagic, induces a decrease of the tissue perfusion reflected by the mottling and/or the lengthening of the capillary refill time (5, 6). An association has been established between the mortality and the mottling (score >2/5) and the lengthening of the capillary refill time in patients suffering from septic shock in the ICU (7-14) and in the pre-hospital setting (15). This highlights the importance of these two simple clinical signs to screen patients with poor outcome. This potential ability to detect patients at risk is even more important in the ED facing a growing number of patients each year in France. Thus, there is a need for simple, reliable and fast screening, triage tools, accessible and repeatable over time.

The aim of the present study is to provide clinical evidence that capillary refill time and skin mottling score predict ICU admission of patients admitted to the ED for septic or haemorrhagic shock.

## Methods

This is a prospective, observational, non-randomised controlled study. The study will be conducted according to the common guidelines for clinical trials (Declaration of Helsinki, International Conference on Harmonisation and WHO Good Clinical Practice standards, including certification by an external audit). The trial protocol has been approved by the French committee on public safety Sud Méditerranée IV (reference no.: 18 10 09) and by the National Heart Agency (ID RCB no.: 2018-A02588-47) on 09/14/2018. The trial is registered on Clinical trials (NCT03831022).

## Population

Patients will be recruited in the ED of the following hospitals: Cochin and Hotel Dieu Hospitals, Assistance Publique Hôpitaux de Paris, Paris, France; University Grenoble Hospital, Grenoble, France; University Strasbourg Hospital, Strasbourg, France; University Poitiers Hospital, Poitiers,

France; University Limoges Hospital, Limoges, France; Victor Dupuy General Hospital, Argenteuil, France and University Marseille Hospital, Assistance Publique Hôpitaux de Marseille, Marseille, France with a target sample size of 1500 subjects.

Physicians will provide information to the patients or their relatives to obtain their oral consent. An information form explaining the purpose of the study will also be given to the patients or their relatives. Participants will be able to withdraw from the study at any time without consequence.

The trial will be executed from December 17, 2018 to December 17, 2020.

All recruitment procedures will be recorded in a computer file.

## Inclusion criteria

Participants admitted to the ED and meeting the following criteria will be included in the study:

1. Aged >18 years either sex.
2. Skin mottling score >2 and/or capillary refill time >3 s associated with at least one of the following measured at the ED admission by the nurse in charge of the patient:
  - a. Systolic blood pressure <90 mm Hg or blood pressure decrease of 30% at least for patients with high blood pressure history
  - b. Heart rate >120 beats per minute
  - c. Respiratory rate >22 movements per minute
  - d. Glasgow coma scale <13.

## Exclusion criteria

Participants meeting one or more of the following criteria will be excluded from the study:

1. Aged <18 years.
2. Pregnancy.
3. Serious comorbid conditions with a not to be reanimated status known at the ED admission.
4. Patients with guardianship or custodian.

## Interventions

Patients who meet the inclusion criteria and none of the exclusion criteria will be followed up during their hospital stay to determine the precise destination after the ED (home, ICU or ward) and the 30- and 90-day mortality after hospital admission.

Capillary refill time and skin mottling score will not be taken into account to decide patient's treatments or orientation even if the physician can know their respective values.

### Outcome measure

The primary endpoint is the rate of ICU admission after the ED. The secondary endpoints are the 30- and 90-day mortality after hospital admission.

### Safety

In the present study, no intervention or treatment will be decided on the capillary refill time and the skin mottling score values.

In the present study, the treatments provided will not depend on the capillary refill time and the skin mottling score values.

### Sample size

The expected ICU admission rate is 30%. The lack of preliminary data did not allow us to perform sample size calculation. Thus, considering the prospective design of this observational study, a total of 1500 patients will be enrolled considering 5% of missing data regarding the primary endpoint.

### Statistical analysis

Descriptive statistics will be used to describe demographic and baseline characteristics of study participants. The predictive ability for ICU admission of the capillary refill time and skin mottling score will be assessed by the receiver operating characteristic curve analysis method. A comparison between both area under the curve will be performed as described by De Long et al. (16). Thereafter, the predictive ability of the capillary refill time and skin mottling score will be assessed by multiple logistic regression. The results will be expressed as odds ratio with 95% confidence interval.

The accepted level of significance for all analyses will be  $p < 0.05$ . Data analysis will be conducted by independent statisticians from the research team. Analysis will be performed using R 3.4.2 (<http://www.R-project.org>; the R Foundation for Statistical Computing, Vienna, Austria).

### Results

Not applicable to date, the study is ongoing.

### Discussion

Currently, to the best of our knowledge, this is the first prospective observational clinical trial on capillary refill time and skin mottling score for the prediction of ICU admission of patients with septic or haemorrhagic shock.

The demonstration of the relationship between capillary refill time and skin mottling score and ICU admission of patients with haemorrhagic or septic shock will suggest its usefulness in clinical routine. These tools will be helpful to anticipate

the needs of care by allowing an adapted orientation since the ED. It will earn valuable minutes during the first “golden hours” directly impacting the prognosis.

Reclassification resulting from the integration of these tools into decision-making will also help to improve in-hospital patient flow. Over-triage leads to the congestion of the ICU, decreasing access for patients requiring it. Conversely, under-triage exposes the patient to aggravation and complications occurrence. Incorporating the measurement of capillary refill time and skin mottling score into the decision-making algorithm could lead to decrease over- and under-triage, allowing a better patients' orientation after the ED.

However, our study presents several limitations. First, this is a non-randomised controlled trial. Second, a bias due to unblinding cannot be ruled out. Third, some patients may not achieve inclusion criteria despite a real underlying shock, that is, young healthy adults and/or patients with beta-blocker therapy. Fourth, only patients with septic and haemorrhagic shock will be recruited; thus, conclusions will not be transposable to other shock aetiology (cardiogenic and anaphylactic).

### Conclusion

The results of the present study will provide a new evidence for capillary refill time and skin mottling score in patients with septic or haemorrhagic shock to anticipate the need of care and to enhance the decision-making of subsequent orientation after the ED. The aim of the present study is to provide two simple, reliable and non-invasive tools for the triage and the early orientation of these patient.

**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of Sud Méditerranée IV (reference no.: 18 10 09) and by the National Heart Agency (ID RCB no.: 2018-A02588-47) on 09/14/2018.

**Informed Consent:** Written informed consent was obtained from patients or relatives who participated in this study.

**Peer-review:** Externally peer-reviewed.

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**Conflict of Interest:** The authors have no conflicts of interest to declare.

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## References

1. Pottecher T, Calvat S, Dupont H, Durand-Gasselín J, Gerbeaux P. Haemodynamic management of severe sepsis: recommendations of the French Intensive Care Societies (SFAR/SRLF) Consensus Conference, 13 October 2005, Paris, France. *Crit Care* 2006; 10: 311. [\[CrossRef\]](#)
2. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonca A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med* 1996; 22: 707-10. [\[CrossRef\]](#)
3. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993; 270: 2957-63. [\[CrossRef\]](#)
4. Le Gall JR, Neumann A, Hemery F, Bleriot JP, Fulgencio JP, Garrigues B, et al. Mortality prediction using SAPS II: an update for French intensive care units. *Crit Care* 2005; 9: R645-52. [\[CrossRef\]](#)
5. Pickard A, Karlen W, Ansermino JM. Capillary refill time: is it still a useful clinical sign? *Anesth Analg* 2011; 113: 120-3. [\[CrossRef\]](#)
6. Bridges E. Assessing patients during septic shock resuscitation. *Am J Nurs* 2017; 117: 34-40. [\[CrossRef\]](#)
7. Ait-Oufella H, Bige N, Boelle PY, Pichereau C, Alves M, Bertinchamp R, et al. Capillary refill time exploration during septic shock. *Intensive Care Med* 2014; 40: 958-64. [\[CrossRef\]](#)
8. Ait-Oufella H, Lemoine S, Boelle PY, Galbois A, Baudel JL, Lemant J, et al. Mottling score predicts survival in septic shock. *Intensive Care Med* 2011; 37: 801-7. [\[CrossRef\]](#)
9. Bourcier S, Joffre J, Dubee V, Preda G, Baudel JL, Bige N, et al. Marked regional endothelial dysfunction in mottled skin area in patients with severe infections. *Crit Care* 2017; 21: 155. [\[CrossRef\]](#)
10. Hernandez G, Pedreros C, Veas E, Bruhn A, Romero C, Rovigno M, et al. Evolution of peripheral vs metabolic perfusion parameters during septic shock resuscitation. A clinical-physiologic study. *J Crit Care* 2012; 27: 283-8. [\[CrossRef\]](#)
11. Lima A, Jansen TC, Van Bommel J, Ince C, Bakker J. The prognostic value of the subjective assessment of peripheral perfusion in critically ill patients. *Crit Care Med* 2009; 37: 934-8. [\[CrossRef\]](#)
12. Lara B, Enberg L, Ortega M, Leon P, Kripper C, Aguilera P, et al. Capillary refill time during fluid resuscitation in patients with sepsis-related hyperlactatemia at the emergency department is related to mortality. *PLoS One* 2017; 12: e0188548. [\[CrossRef\]](#)
13. Mrgan M, Rytter D, Brabrand M. Capillary refill time is a predictor of short-term mortality for adult patients admitted to a medical department: an observational cohort study. *Emerg Med J* 2014; 31: 954-8. [\[CrossRef\]](#)
14. De Backer D, Creteur J, Dubois MJ, Sakr Y, Vincent JL. Microvascular alterations in patients with acute severe heart failure and cardiogenic shock. *Am Heart J* 2004; 147: 91-9. [\[CrossRef\]](#)
15. Jouffroy R, Saade A, Tourtier JP, Gueye P, Bloch-Laine E, Ecolan P, et al. Skin mottling score and capillary refill time to assess mortality of septic shock since pre-hospital setting. *Am J Emerg Med* 2019; 37: 664-71. [\[CrossRef\]](#)
16. DeLong ER, DeLong DM, Clarke-Pearson DL. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988; 44: 837-45. [\[CrossRef\]](#)