HAL
archives-ouvertes.fr

Strategy focused on clinical parameters of microcirculation to resuscitate patients in septic shock: Do not forget any tools

Saber Davide Barbar, Laurent Muller, Vincent Bruckert, Marc Léone, Mervyn Singer

▶ **To cite this version:**

Saber Davide Barbar, Laurent Muller, Vincent Bruckert, Marc Léone, Mervyn Singer. Strategy focused on clinical parameters of microcirculation to resuscitate patients in septic shock: Do not forget any tools. Anaesthesia Critical Care & Pain Medicine, Elsevier Masson, 2019, 38 (3), pp.209-210. 10.1016/j.accpm.2019.04.011 . hal-02159362

HAL Id: hal-02159362
https://hal-amu.archives-ouvertes.fr/hal-02159362

Submitted on 18 Jun 2019

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Strategy focused on clinical parameters of microcirculation to resuscitate patients in septic shock: Do not forget any tools

ARTICLEINFO

Keywords:
ICU
Septic shock
Microcirculation

The current objective of initial resuscitation of patients with septic shock is the optimisation of general haemodynamic variables including heart rate, mean arterial blood pressure, cardiac output and cardiac preload using normalisation of arterial lactate as a marker of presumed success [1–3]. However, microcirculatory blood flow can remain impaired despite restora- tion of macro-haemodynamic parameters. Ait-Oufella et al. clearly showed that persistence of skin mottling [4], an increased capillary refill time (CRT) [5] and an increased toe-to-room temperature gradient [6] were associated with worse patient outcomes. Similarly, Leone et al. reported that low oxygen tissue saturation (StO_2) was associated with poor outcomes in patients with septic shock [7]. Few studies have assessed a strategy targeting the microcirculation. In a recent paper published in JAMA, Hernandez et al. performed a multicentre randomised controlled trial (ANDROMEDA-SHOCK), conducted in 28 intensive care units (ICU) in 5 South American countries comparing peripheral perfusion–targeted (peripheral perfusion group) and lactate– targeted (lactate group) resuscitation in the early phase of septic shock [8]. Between March 2017 and March 2018, 424 patients with septic shock were randomised to a step-by-step resuscitation protocol aimed at normalising CRT (n = 212) or normalising/ decreasing plasma lactate at a rate exceeding 20% every 2 hours (n = 212), over an 8-hour intervention period. The primary outcome was 28-day all-cause mortality. Secondary outcomes were organ dysfunction at 72 hours (using the Sequential Organ Failure Assessment (SOFA) score [9]), Day 90 mortality, organ support-free days (mechanical ventilation, renal replacement therapy, and vasopressor) within 28 days, and intensive care unit (ICU) and hospital lengths of stay. In the final analysis, 416 patients (98% of those enrolled) were assessed. Day 28 mortality was 34.9% versus 43.4% in the peripheral perfusion and lactate groups, respectively (hazard ratio, 0.75 [95% CI, 0.55 to 1.02]; P = .06; risk difference, —8.5% [95% CI, —18.2% to 1.2%]). For secondary outcomes, the 72-hour SOFA score was significantly lower in the peripheral perfusion group (mean SOFA score, 5.6 T 4.3 vs. 6.6 T 4.7, P = .045). No significant differences were found for other secondary outcomes. The authors concluded that a resuscitation strategy targeting CRT normalisation compared to a strategy targeting serum lactate levels did not reduce 28-day all-cause mortality in patients with septic shock.

The investigators produced a strict protocol to reduce variability in patient management, achieving less than 15% non- adherence in both groups. The control group mortality rate of 43.4% is close to that predicted by the Sepsis-3 criteria for septic shock [10]. Although the difference in 28-day mortality did not reach statistical significance, these findings should encourage further assessment of the microcirculation in septic shock patients for the following reasons:

- the primary goal of this study – a 33% relative reduction in mortality rate based on a change in initial management strategy – is considerable and perhaps unrealistic. This highlights the need for appropriate targets in septic shock studies [11], and suggests this study was underpowered [12]. To show a relative mortality reduction <10%, approximately 1500 patients should have been included;
- interestingly, the greater fall in SOFA score at 72 hours suggests that clinical improvement was faster in the peripheral perfusion group. The choice of a composite goal including day-28 survival and delta SOFA score may have resulted in a statistically significant result;
- in less severely ill patients (APACHE II score < 25 or SOFA score < 10), the mortality rate was lower in the peripheral perfusion group, suggesting that such stratification may be therapeutically relevant;
- a possible explanation for the differences seen between the two strategies may relate to the timing of assessment (30 vs. 120 minutes in the peripheral perfusion and lactate groups, respectively). Furthermore, the peripheral perfusion strategy was associated with a lower volume of fluid resuscitation administered in the first 8 hours (2359 T 1344 mL vs. 2767 T 1749 mL, P = 0.01). After the first 6 hours of treatment, a target of 10% lactate clearance should be used with caution [13]. In the present study, some patients could have been included after the first 6 hours, leading to a less efficient application of this strategy;
- this study confirms that a management approach during the early phase of septic shock based on a reproducible, systematic clinical examination is as effective as a biomarker-based

approach. This could explain the lack of added benefit of Early Goal Directed Therapy applied in the first 6 hours of septic shock [14].

In conclusion, this study failed to show outcome superiority of a management strategy based on CRT, as compared with repeated measurements of serum lactate levels. However, its results should at least encourage physicians to evaluate the microcirculation in patients with septic shock using a simple, easy and safe clinical approach aiming at assessing peripheral perfusion such as CRT or mottling. Whether such a clinical strategy should replace or be combined with monitoring of serum lactate requires further evaluation.

Disclosure of interest

Pr M. Singer declares relevant conflicts of interest with Deltex Medical and Oxford Optronix.
Pr M. Leone declares relevant conflicts of interest with MSD, Pfizer, Aspen, Orion, Octapharma, Aguettant, Amomed.
The other authors declare that they have no competing interest.

References

[1] Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med 2017;43(3):304–77. http://dx.doi.org/10.1007/s00134-017-4683-6.

[2] Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, et al. Early Lactate-Guided Therapy in Intensive Care Unit Patients: A Multicenter, Open-Label, Randomized Controlled Trial. Am J Respir Crit Care Med 2010;182(6):752–61. http://dx.doi.org/10.1164/ rccm.200912-1918OC.

[3] Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA, et al. Lactate Clearance vs Central Venous Oxygen Saturation as Goals of Early Sepsis Therapy: A randomized Clinical Trial. JAMA 2010;303(8):739–46. http://dx.doi.org/10.1001/jama.2010.158.

[4] Ait-Oufella H, Lemoinne S, Boelle PY, Galbois A, Baudel JL, Lemant J, et al. Mottling score predicts survival in septic shock. Intensive Care Med 2011;37(5):801–7. http://dx.doi.org/10.1007/s00134-011-2163-y.

[5] 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(7):958–64. http://dx.doi.org/10.1007/s00134-014-3326-4.

[6] Bourcier S, Pichereau C, Boelle PY, Nemlaghi S, Dubé e V, Lejour G, et al. Toe-to- room temperature gradient correlates with tissue perfusion and predicts outcome in selected critically ill patients with severe infections. Ann Intensive Care 2016;6(1):63. http://dx.doi.org/10.1186/s13613-016-0164-2.

[7] Leone M, Blidi S, Antonini F, Meyssignac B, Bordon S, Garcin F, et al. Oxygen Tissue Saturation Is Lower in Nonsurvivors than in Survivors after Early Resuscitation of Septic Shock. Anesthesiology 2009;111(2):366–71. http://dx.doi.org/10.1097/ALN.0b013e3181aae72d.

[8] Herná ndez G, Ospina-Tascó n GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J, et al. Effect of a Resuscitation Strategy Targeting Peripheral Perfusion Status vs Serum Lactate Levels on 28 Day Mortality Among Patients With Septic Shock. ANDROMEDA-SHOCK Randomized Clinical Trial. JAMA 2019;321(7):654–64. http://dx.doi.org/10.1001/jama.2019.0071.

[9] Vincent JL, Moreno R, Takala J, Willatts S, De Mendonç a 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 Pro- blems of the European Society of Intensive Care Medicine. Intensive Care Med 1996;22(7):707–10.

[10] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016;315(8):801–10. http://dx.doi.org/10.1001/jama.2016.0287.

[11] Amrhein V, Greenland S, McShane B. Scientists rise up against statistical significance. Nature 2019;567(7748):305–7. http://dx.doi.org/10.1038/ d41586-019-00857-9.

[12] Angus DC. How Best to Resuscitate Patients With Septic Shock? JAMA 2019;321(7):647–8. http://dx.doi.org/10.1001/jama.2019.0070.

[13] Bakker J, De Backer D. Lactate-guided resuscitation saves lifes: we are not sure. Intensive Care Med 2016;42(3):472–4.

[14] PRISM Investigator, Rowan KM, Angus DC, Bailey M, Barnato AE, Bellomo R, et al. Early, Goal-Directed Therapy for Septic Shock - A Patient-Level Meta- Analysis. N Engl J Med 2017;376(23):2223–34. http://dx.doi.org/10.1056/NEJMoa1701380.

Saber Davide Barbar[a,*], Laurent Muller[a], Vincent Bruckert[b], Marc Leone[c], Mervyn Singer[d]

[a]*EA 2992, service réanimation, université de Montpellier, CHU Nîmes, Nîmes, France*

[b]*Département anesthésie réanimation, institut de cardiologie, hôpital Pitié Salpêtrière, Paris, France*

[c]*Pôle Musca, service d'anesthésie et de réanimation, centre d'investigation Clinique Nord, hôpital Nord, Aix-Marseille université, Assistance publique–Hôpitaux de Marseille, Marseille, France*

[d]*Bloomsbury Institute of Intensive Care Medicine, University College London, London, UK*

*Corresponding author
E-mail address: saber.barbar@chu-nimes.fr (S.D.Barbar).