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FOCUS EDITORIAL

Focus on acute circulatory failure

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A task force of the European Society of Intensive Care Medicine published the results of a consensus conference on the definition, diagnosis, monitoring, and treatment of circulatory failure [1]. Circulatory failure was defined as a life-threatening, generalized form of acute circulatory failure with inadequate oxygen utilization by the cells resulting in cellular dysfunction as a result of dysoxia, i.e., the loss of the physiological independence of oxygen delivery and oxygen consumption associated with increased lactate levels.

However, the interpretation of increased lactate levels may not be as straightforward as suggested. In many cases lactate levels remain elevated after initial resuscitation. Ospina-Tascón et al. [2] showed that under these circumstances, the use of the venous-arterial CO_2 to arterial-venous O_2 content difference ratio as a surrogate of the respiratory quotient could reveal an increased lactate level as a result of persisting anaerobic metabolism. Increased lactate with an abnormal ratio (suggesting anaerobic metabolism) was associated with an excess mortality of almost 30 % compared to APACHE II expected mortality. Therefore, early resolution of tissue hypoperfusion and oxygen delivery-dependent oxygen consumption might prevent excess mortality. As shown by Gu et al. [3] in their meta-analysis of four studies, the use of early therapy aimed at decreasing lactate levels in patients with sepsis is associated with a significant improvement in mortality [risk ratio 0.65 (95 % CI 0.26–1.95)].

Frequently abnormalities in skin perfusion are present in circulatory failure. Coudroy et al. [4] showed that skin mottling was present in 49 % of septic shock patients. Prolonged mottling (more than 6 h) was associated with a 40 % mortality. Similarly, Ait-Oufella et al. [5] showed that persistent abnormal capillary refill time (CRT) after initial resuscitation was related to mortality in septic shock patients. Although these data confirm similar studies in circulatory failure, the effect of using skin perfusion as a goal of therapy on outcome is not yet clear [6].

Fluid resuscitation is an important intervention to improve tissue perfusion. In this regard the results of the FENICE study [7] on the use of fluid challenges in intensive care are remarkable. From this study in 2213 patients admitted to 311 ICUs in 46 countries, it was clear that the use of a fluid bolus was mainly aimed at restoring blood pressure. In the majority of cases, central venous pressure (CVP) was used to predict fluid responsiveness and monitor effectiveness. This is most likely based on the misconception of the original Starling experiments where CVP was the dependent variable on venous return and cardiac function instead of an independent variable of preload [8]. The goal of fluid resuscitation should not be an increase in CVP but rather an increase in stressed volume resulting in an increase in mean systemic filling pressure (MSFP) and a rise in the pressure for venous return (Pvr = MSFP − CVP) thus increasing cardiac output. This concept was studied in post-cardiac surgery patients [9] and in patients with shock [10]. In both cases (using different methods to estimate MSFP) responders were characterized by showing a rise in Pvr whereas in the non-responders the Pvr did not change. Several studies have shown that the effectiveness of a fluid bolus in changing cardiac output (the main variable of interest) is extremely limited in patients following initial fluid resuscitation. In septic shock patients and postsurgical patients it was shown that the increase in cardiac output was met by an increase in arterial elastance to accommodate the increased output thereby limiting the increase in MAP [11] and that 10 min after the completion of the fluid challenge cardiac output had already returned to baseline [12].

Use of other parameters like intrathoracic blood volume (ITBV) and extravascular lung water (EVLW) to

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optimize fluid status in patients with septic shock offers no real advantage over the traditional used parameters. In a large randomized study comparing the use of ITBV and EVLW versus CVP guided fluid resuscitation, the study was discontinued after enrolling 50 % of the projected patients because of futility [13]. These result emphasizes that tissue perfusion instead of hemodynamic parameters should be the goal of initial resuscitation. In a randomized pilot in 30 septic shock patients, Van Genderen et al. [14] studied the safety of restricting fluid resuscitation when normal peripheral perfusion was present despite the persistence of a clinical problem (increased lactate, oliguria, persistent hypotension, etc.). This concept seemed to be safe as the fluid balance was less positive in the protocol patients when compared to the control patients, associated with an improvement in morbidity. The rationale for an endpoint like this was further illustrated by a study on the relationship between CRT and organ perfusion in patients with septic shock. In this pilot study Brunauer et al. [15] showed that the duration of CRT was linearly related to liver, gut, spleen, and kidney perfusion.

Although the current concepts of early goal-directed therapy are still focused on macrohemodynamics the implementation of these endpoints has been associated with improved septic shock survival over the past few years [16], and compliance with the initial resuscitation elements has been recently associated with a 40 % reduction in the odds of in-hospital mortality [17]. Nevertheless, a meta-analysis of early goal-directed therapy for patients with septic shock including the ARISE, the ProCESS, and the ProMISe trials with a total of 4200 patients could not find benefit of therapeutic schedules based on the Surviving Sepsis Guidelines bundles when compared to what was valued as usual care [18].

However, we have to take several aspects into account when evaluating these findings. First, mortality of sepsis and septic shock has decreased dramatically and initial care has many elements of the landmark trial [19] that led to the implementation of these early goal-directed bundles thereby changing the baseline characteristics of patients included. Second, trials randomizing patients to treatment strategies not related to individual needs but to the epidemiology of groups might result in misalignment that may obscure the true positive effect of the intervention [20]. Third, the absence of evidence is not evidence of the absence of a true effect. The use of structured resuscitation, even when using suboptimal macrohemodynamic endpoints, is still associated with an improvement in outcome that could be even more improved with more accurate endpoints. We should therefore develop studies that help to understand the real pathophysiological mechanisms at hand and the effect of available interventions on these mechanisms instead of studying the effect of one-size-fits-all protocols on outcome.

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Compliance with ethical standards

Conflicts of interest
The author has no conflict of interest to declare.

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