Venous-to-arterial carbon dioxide differences and the microcirculation in sepsis

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Assessment of the microcirculation has been of particular interest in the management of septic shock for over a decade (1,2). It has garnered more attention in light of conflicting data recently on oxygen-derived parameters in patients with sepsis (3). Microcirculatory dysfunction has been linked to organ failure despite adequate macro-hemodynamic stability (4). The microcirculatory perfusion is regulated by the myogenic, metabolic and neurohumoral systems, which in turn affect the arteriolar tone, driving pressure, capillary patency and hemorheology (4). In septic states, perfusion pressure and deformability of cells are reduced, and arteriolar constriction ensues; the end-result is shunting of blood, bypassing essential areas of capillary exchange (5). These changes debilitate the microcirculation and impede tissue oxygenation, resulting in impaired organ functions. Moreover, with stasis in the capillary bed and inflammatory factors released from injured cells that cannot be cleared due to deficient flow, the microcirculation becomes a nidus for continued bacterial growth and persistent insult, sustaining the toxemia and acidemia.

It has been shown that timely aggressive interventions and treatment with early improvements in organ functions increases the probability of survival (6,7). However, improvement in global hemodynamics, such as mean arterial pressures and central venous oxygen saturations (ScvO2) do not always translate to improved perfusion in the microcirculation (8). Assessment of the microcirculation, through indices such as the microvascular flow index, heterogeneity index and proportion of perfused vessels have been found to be lower in septic patients compared to healthy volunteers, with more marked abnormalities among patients with severe sepsis (9). Sophisticated and novel imaging techniques including the sidestream dark-field imaging and nailfold videocapillaroscopy can allow for direct visualization of the microcirculation at the bedside (1). In spite of that, the use of such imaging techniques requires the availability of expertise and special equipment, which may not be readily accessible in the clinical setting and in acute resuscitation. Furthermore, more trials are required to determine the applicability of these modalities in clinical evaluation and in how it can guide resuscitation goals.

More commonly, biochemical tests such as serum lactate concentration and blood gas levels are performed in routine practice as attempts to evaluate the microcirculation. Actual correlation of these parameters with the microcirculation is fraught with numerous confounders (10). The early goal directed therapy by Rivers and colleagues incorporated measurements of ScvO2 as part of the resuscitation goals (7). However, normal ScvO2 may not be a good indicator of adequate tissue oxygenation as low ScvO2 is neither a common nor consistent finding among critically ill patients (11). In addition, ScvO2 levels may not correlate well with the true value of mixed venous oxygen saturation (SvO2) (12). The potential of measuring CO2 as a marker of adequacy of resuscitation has been of growing interest in view of its greater solubility in blood compared to O2 and hence allowing it to diffuse out to the venous effluent despite the low perfusion state from capillary bed shunting (13). An increase in arteriovenous difference in pCO2 (normal difference less than 6 mmHg) has been found to reliably reflect tissue hypoxia (14). Conversely, a lower difference has been associated with a higher cardiac index and better lactate clearance (15-17).

Ospina-Tascón and colleagues performed a study that
included 75 patients from a mixed intensive care unit with septic shock to evaluate the adequacy of mixed venous-arterial carbon dioxide difference (Pv-aCO2) in assessing the microcirculatory perfusion during the early stages of resuscitation (18). Data obtained from a sidestream dark-field imaging device to evaluate the sublingual microcirculatory images was correlated with Pv-aCO2. The authors found good agreement between changes in Pv-aCO2 and changes in proportion of perfused vessels ($R^2=0.42$, $P<0.001$) at 0 and 6 h (determined by time of pulmonary artery catheter insertion), reflecting the potential of measuring Pv-aCO2 during resuscitation as a surrogate for adequacy of perfusion in the microcirculation. Apart from the changes in proportion of perfused vessels, changes in Pv-aCO2 were also significantly associated with changes in functional capillary density and heterogeneity index. Hence, changes in Pv-aCO2 could potentially provide a good reflection of the state of the tissue perfusion without direct imaging of the microcirculation. Patients with a Pv-aCO2 of more than 6 mmHg despite a normal ScvO2 remain inadequately resuscitated and further interventions such as continued fluid resuscitation or inotropes should be considered to improve tissue perfusion (15).

In the study by Ospina-Tascón and colleagues, Pv-aCO2 did not correlate with cardiac output ($R^2=0.01$, $P=0.45$). This finding contrasted with previous experimental models, which showed that Pv-aCO2 is inversely related to cardiac index (17,19,20). The results of this study support the evidence that Pv-aCO2 is related to blood flow variations rather than cardiac output alone (21). Nonetheless, knowledge of the cardiac index in septic patients provides clinicians with an idea of the stroke volume index and guides decision making to optimize cardiac function. It is likely that data from Pv-aCO2 will be complementary to macro-hemodynamic parameters in the global management of patients with septic shock.

The use of mixed venous blood in the study by Ospina-Tascón and colleagues requires blood specimens to be obtained from the mixed venous circulation through a pulmonary artery catheter. The insertion of a pulmonary artery catheter requires expertise, is time-consuming and associated with cardiac complications such as dysrhythmias, valve damage and pulmonary infarction (22,23). It is almost exclusively used in the intensive care units. A study by van Beest and colleagues demonstrated strong agreement between central venous-arterial pCO2 difference and mixed venous-arterial pCO2 difference [intraclass coefficient (ICC) =0.70, $P<0.001$]; likewise an inverse relationship between central venous-arterial pCO2 and cardiac index (21). However, we are unable to draw any conclusions between the results and the microcirculation due to the post-hoc nature and lack of prospective direct microcirculatory assessment in the study. Nevertheless, the appeal of potentially fewer cardiac complications using a central venous catheter compared with a pulmonary artery catheter coupled with wider generalizability to other areas such as emergency departments should prompt further research in this area (24).

In conclusion, the field of research in microcirculation in septic shock is gaining momentum. The vast majority of research in the management of sepsis has been targeting the macrohemodynamics (7,25-28). Although important, it merely completes one piece of the complicated management jigsaw in sepsis and septic shock. Ospina-Tascón and colleagues have demonstrated very interesting and useful correlations between Pv-aCO2 and direct assessments of the microcirculation. Though not yet ready for prime time, future research should focus on the microcirculation earlier in the sepsis continuum, even before septic shock develops, and its applicability beyond the walls of the intensive care units.

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Footnote

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References

3. Angus DC, Barnato AE, Bell D, et al. A systematic review and meta-analysis of early goal-directed therapy for septic