Editorial Commentary

Association and dissociation of microcirculation and macrocirculation in critically ill patients with shock

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Pitfalls of macrocirculation

Early goal-directed therapy with maintenance of adequate central venous pressure (CVP), mean arterial pressure (MAP), and central venous oxygen saturation ($ScvO_2$) fails to improve survival (1-3) in patients with shock, which emphasizes the fact that normal values of macrocirculation parameters may be inadequate to prevent shock.

Poor macrocirculation is associated with poor microcirculation, but microcirculatory dysfunction may exist despite the normalization of macrocirculation. CVP is affected and limited by several factors (4). The predictability of fluid responsiveness of CVP is low (5). Increased CVP may reduce renal perfusion (6). In addition, maintaining a high MAP with high dose vasopressor may cause excessive vasoconstriction, which may lead to a reduced number of perfused small vessels in the tissue (7). However, maintaining a high MAP by using adequate dose of vasopressor in patients with a past history of hypertension may improve microcirculation (8,9). Furthermore, during disseminated intravascular coagulation, microthrombosis may occlude tissue microvascular blood flow and result in shunting of the microvascular blood flow, which may eventually lead to a falsely high $ScvO_2$. Because of the frequent dissociation between microcirculation and systemic hemodynamics, only direct measurement of the microcirculation in different tissues may indicate microcirculatory dysfunction in patients with shock exhibiting normal macrocirculation parameters.

Techniques for clinical microcirculation research

Several methods can be used to measure or evaluate microvascular perfusion (10). Laser Doppler is used to measure the velocity of red blood cells (RBCs) (11). Near-infrared spectroscopy (NIRS) is used to measure tissue oxygen saturation (12). Microvascular reactivity can be evaluated using laser Doppler or NIRS (13). Laser speckle imaging is used to compare the perfusion intensity of microvascular blood flow and reveal the heterogeneity of microcirculation (14). Videomicroscopy is used to measure the density of perfused small vessels and evaluate the microvascular blood flow classification (15-17). The sublingual area is most frequently used to evaluate and measure the microcirculation in clinical studies. The most frequently used microcirculation parameters include total small vessel (less than 20 μm) density (TSVD), blood flow classification of small vessels, perfused small vessel density (PSVD), proportion of perfused small vessels (PPV), microvascular flow index (MFI) score, and heterogeneity index (HI) (18). The quality of microcirculation videos is crucial for correct evaluation of the microcirculation (19).

Microcirculatory dysfunction in critically ill patients with shock

In patients with sepsis or septic shock, microvascular blood flow is altered; microcirculatory dysfunction is more severe in non-survivors than in survivors (20). Various damages may result in microcirculatory dysfunction in patients with septic shock. Hypovolemia, loss of vascular reactivity and autoregulation, and microthrombosis reduce the density of perfused small vessels and may lead to shunting of oxygen from the hypoperfused area to the hyperperfused area. Systemic inflammations may cause glycocalyx degradation and manifest capillary leakage and subsequent tissue edema. Although excessive use of vasopressors may

reduce the density of perfused small vessels, adequate use of vasopressors may be required to increase microvascular perfusion (8). In patients with sepsis and septic shock, microcirculatory dysfunction was more severe in the 28-day nonsurvivor group than in the 28-day survivor group (21). In patients with surgical or traumatic hemorrhagic shock, our previous study revealed that early TSVD and PSVD are correlated with the lactate level 24 h after surgery (22). Tachon *et al.* found that the sublingual microcirculation was impaired for at least 72 h after restoration of the macrocirculation in patients with traumatic hemorrhagic shock (23). In patients with cardiogenic shock, decreased cardiac output impairs microvascular perfusion, and subsequent systemic inflammation may result in further impairment of microcirculation (24). In patients with out-of-hospital cardiac arrest, persistent microcirculatory dysfunction is associated with poor survival (25). For patients on venoarterial extracorporeal membrane oxygen (VA-ECMO) life support, microcirculatory dysfunction is more severe in non-survivors than in survivors (26,27). Akin *et al.* used sublingual microcirculation as a novel potential marker to identify successful weaning from VA-ECMO (28).

Limitations of microcirculation in clinical practice

There exist several limitations of using microcirculation in clinical practice and shock resuscitation. First, the unavailability of expensive devices and time-consuming analysis of microcirculation videos limit the possibility of frequent microcirculation monitoring for every patient. Second, some microcirculation parameters are semi-quantified and time-consuming. High adherence to the consensus and internal validation in the study group are crucial to maintain a high-quality examination of microcirculation. A new, real-time, and automated analysis software for microcirculatory videos is required. Third, most microcirculation studies can only measure the tissue surface in several specific areas. However, the microcirculation in the deeper layers of the tissue and in different organs may not always correlate with the microcirculation in the investigated area. The kidneys and intestine are vulnerable to hypoperfusion in patients with different types of shock. Novel techniques or specific biomarkers are required to investigate the microcirculation in the kidneys and intestine.

How to resuscitate microcirculation without information of microcirculation parameters?

Increasing cardiac output, early fluid supplementation, adequate use of vasopressors, careful transfusion of RBCs, avoid excessive vasoconstriction, and blood purification are strategies to improve PSVD and microvascular blood flow (29). However, during the unavailability of a device to evaluate the microcirculation, substitute parameters may be helpful. Several measurements are suggested to represent microcirculation, including lactate levels (30), the gap between the venous and arterial carbon dioxide (31), and capillary filling time (32).

Conclusions

Normal values of macrocirculation parameters may be inadequate for shock resuscitation. The first step is to combine several macrocirculation parameters for appropriate decision—to guide the resuscitation of systemic hemodynamics. The second step is to evaluate the microcirculation or use substitute measurement to resuscitate the microcirculation. New techniques and software are required for timely evaluation and resuscitation of the microcirculation to maintain adequate tissue perfusion.

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Footnote

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

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