EDITORIAL

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Mind the Gap in Translating Microcirculation Knowledge and Clinical Impact

The paradox of haemodynamic coherence remains one of the most perplexing diagnostic challenges in modern critical care practice. Clinicians may achieve conventional targets of circulatory stability, such as a mean arterial pressure (MAP) above 70 mmHg, a normalised heart rate and adequate cardiac output indices. Nevertheless, a subset of critically ill patients continues to exhibit tissue hypoperfusion and progressive organ dysfunction. Cold extremities, mottled skin, prolonged capillary refill time (CRT) and oliguria exemplify this dissociation between reassuring macrocirculatory parameters and impaired microcirculatory flow. This phenomenon reveals a critical limitation of our current monitoring paradigm, which is the assumption that optimising systemic haemodynamic translate into adequate tissue perfusion. While macrocirculatory interventions can restore global variables, the true determinants of cellular oxygen delivery (DO_2) and tissue viability reside within the intricate microcirculatory network. This network cannot be directly captured by conventional monitoring; nevertheless, it plays a decisive role in determining patient outcomes.[1]

The microcirculation, defined as the vascular network of vessels smaller than 100 μm, represents the functional interface between systemic circulation and cellular metabolism. This intricate system of arterioles, capillaries and venules relies on finely balanced interactions among haemodynamic forces, endothelial function and the protective glycocalyx. Dysfunction within this compartment explains the persistence of organ failure despite apparent macrocirculatory stability. Loss of haemodynamic coherence between macro- and microcirculation can be described by four mechanisms, each impairing tissue DO_2 through distinct pathways. Type 1 is heterogeneous perfusion, where obstructed and patent capillaries coexist, producing patchy hypoxia despite seemingly adequate flow and typifying sepsis. Type 2 arises from haemodilution, lowering capillary haematocrit and extending diffusion distance, reducing oxygen-carrying capacity even with preserved plasma flow. Type 3 involves microcirculatory stasis from elevated arterial resistance or venous congestion, impeding red blood cell transit despite normal driving pressures. Type 4 results from tissue oedema caused by capillary leak, which increases the distance for oxygen diffusion despite adequate perfusion.[2]

Recognition of the four pathophysiological patterns of microcirculatory failure has driven the development of advanced monitoring techniques aimed at translating experimental insights into bedside practice. Among these, handheld videomicroscopy using sidestream dark-field and incident dark-field imaging has emerged as the current gold standard for real-time microvascular assessment. These devices allow quantitative analysis of sublingual microvascular parameters, including functional capillary density, microvascular flow index and perfused boundary region, all of which have demonstrated significant prognostic value in critically ill patients.[3] Multicentre studies have confirmed that reduced capillary density correlates with higher mortality and organ dysfunction scores, independent of conventional haemodynamic variables.[4] Despite this promise, routine clinical adoption remains limited. Image acquisition requires skilled operators, strict standardisation and advanced automated analysis, creating barriers to widespread use. Inter-observer variability, difficulty maintaining optimal probe positioning and challenges with image quality further reduce reproducibility across settings. Current analysis software also demands substantial computational resources and expert oversight, confining these tools largely to research environments. Consequently, only specialised centres can fully characterise sublingual microvascular function and glycocalyx integrity,[5] while most ICUs continue to depend on indirect surrogates of microcirculatory status, reflecting the gap between technological capability and practical bedside accessibility.

Modern intensive care increasingly relies on simple, cost-effective tools to assess microcirculatory function at the bedside. CRT has regained prominence following the landmark ANDROMEDA-SHOCK trial, which demonstrated improved outcomes with CRT-guided rather than lactate-guided resuscitation in septic shock. CRT-targeted therapy accelerated organ recovery, limited fluid overload, and showed a favourable mortality trend. Its main advantages are speed, reproducibility, and sensitivity to changes in perfusion. Other complementary measures include the peripheral mottling score, which quantifies skin discolouration around the knee and reliably predicts mortality in septic and cardiogenic shock.[4] The peripheral perfusion index, derived from routine pulse oximetry, offers real-time insight into peripheral microcirculatory status. Laboratory markers add value but have limitations. Serum lactate remains widely used; however, its delayed clearance and nonspecificity reduce its utility for real-time monitoring. More refined indices, such as the venous-to-arterial carbon dioxide gap and the Pv-aCO_2 to arteriovenous oxygen difference ratio, can reveal persistent flow-oxygen mismatch even when global haemodynamics appear normal.[5] These modalities together create a pragmatic framework for perfusion assessment in diverse settings. No single surrogate fully reflects the complexity of microcirculatory failure. Repeated use of combined tools during early shock resuscitation improves diagnostic precision beyond macrocirculatory endpoints. Current protocols should integrate CRT, mottling scores, and perfusion indices alongside traditional haemodynamic targets.[4,5]

Microcirculatory monitoring is evolving rapidly, with significant implications for critical care practice. Prospective studies in elderly intensive care populations have shown that admission sublingual microvascular dysfunction independently predicts 30-day mortality, confirming prognostic value beyond conventional haemodynamic variable.[4] The integration of automated handheld videomicroscopy with artificial intelligence now allows standardised, operator-independent quantification of capillary density and flow, addressing long-standing concerns about reproducibility and interpretative consistency. Emerging biomarkers reflecting endothelial glycocalyx integrity are also expanding diagnostic possibilities. Perfused boundary region analysis from sublingual imaging, combined with circulating glycocalyx degradation markers, shows early promise as an objective measure of microvascular barrier function.[5] Near-infrared spectroscopy (NIRS) with vascular occlusion testing offers complementary insight into tissue oxygen use and microvascular reactivity, demonstrating prognostic value in cardiac surgery, trauma and septic shock.[6] Despite these advances, robust validation in large-scale randomised controlled trials remains essential before such modalities can be adopted as resuscitation endpoints. An important development is phenotype-based resuscitation, which prioritises tissue perfusion over traditional macrocirculatory targets. The ongoing ANDROMEDA-SHOCK-2 trial illustrates this by testing whether perfusion-guided protocols improve outcomes compared with standard haemodynamic-based care.[7] Positive findings could redefine intensive care, positioning microcirculatory assessment at the centre of evidence-based resuscitation.

The relevance of microcirculatory monitoring extends beyond systemic circulation, particularly in neurointensive care, where cerebral perfusion is far more complex than traditional pressure-based calculations suggest. Cerebral tissue oxygenation depends not only on the relationship between MAP and intracranial pressure (ICP) but also on microvascular flow patterns, autoregulatory capacity and endothelial barrier integrity. Secondary brain injury may persist despite apparently normal systemic haemodynamics because cerebral microcirculation often exhibits heterogeneous perfusion, impaired autoregulation and increased permeability following glycocalyx disruption. Current tools provide limited insight. Transcranial Doppler assesses large-vessel flow but cannot fully capture microvascular disturbances, while NIRS offers practical regional cerebral oxygenation monitoring and has shown utility after cardiac arrest and during cardiac surgery.[6,8] Principles from systemic microcirculatory research, including dynamic assessment and phenotype-guided therapy, should guide cerebral perfusion management and shape the next generation of neuroprotective strategies beyond purely pressure-driven paradigms.

Malaysian intensive care encounters both challenges and opportunities in adopting microcirculatory assessment strategies. While sophisticated videomicroscopy remains largely inaccessible, pragmatic bedside tools can be introduced immediately. Systematic training of medical and nursing staff in CRT assessment, mottling score documentation, peripheral perfusion index measurement, and lactate clearance monitoring could elevate care standards without major infrastructure costs. These parameters should be reassessed dynamically during resuscitation, guiding fluid therapy, vasopressor selection, and inotropic support based on microcirculatory response rather than macrocirculatory targets alone. Simultaneously, academic centres should establish dedicated microcirculation laboratories, standardise imaging techniques, and build patient registries. Such initiatives will enable international collaboration, prepare for emerging technologies, and drive a truly tissue-focused, outcome-driven approach to resuscitation in Malaysian ICUs.

Therefore, clinicians, researchers, and trainees must sustain a strong commitment to advancing the science of microcirculation. We should integrate simple bedside markers into daily practice, invest in the expertise needed to adopt emerging imaging technologies and contribute to multicentre studies.[1,7] Our patients deserve more than reassuring numbers on a monitor; they deserve organs that recover and lives that can be saved. Microcirculation now plays a decisive role in critical illness rather than being just a niche research area. By making microcirculation visible, measurable, and actionable, we can move beyond pressure-driven targets toward a new era of tissue-focused, outcome-driven intensive care.

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