

Normal Oxygen, Starving Tissue

Paper 02 · Editorial concept paper · Created 15 October 2026

Abstract. A patient may have acceptable arterial oxygen saturation and global hemodynamics while individual tissue regions receive insufficient effective oxygen. Microvascular flow heterogeneity, diffusion distance and impaired extraction provide a mechanistic explanation, established most clearly in critical-illness research.

Oxygen availability has several gates

A pulse oximeter estimates peripheral arterial hemoglobin saturation. It does not tell us how many capillaries are exchanging oxygen in a particular organ, how far oxygen must diffuse to a cell, or whether mitochondria can use it. Oxygen delivery depends on cardiac output and arterial oxygen content, but delivery at organ scale still differs from exchange at tissue scale. A fully saturated red blood cell flowing rapidly through a shunting capillary pathway need not supply cells distant from that pathway.

Functional capillary density

The microcirculation is a network of exchanging units, not a uniform downstream extension of large vessels. In a healthy tissue, recruitment and flow regulation keep diffusion distances compatible with metabolism. In severe inflammation and shock, some microvessels become poorly perfused while others retain or accelerate flow. This heterogeneity can undermine extraction even when systemic delivery seems adequate. Research in sepsis offers striking examples of this macro–micro dissociation; extrapolation to every form of chronic fatigue or cognitive complaint is not justified.

Tissue supply and tissue utilization must be separated

Reduced oxygen use can arise from impaired delivery, altered mitochondrial function or both. These can produce similar clinical consequences but require different explanations. A high venous oxygen saturation, for example, does not always imply generous cellular oxygenation; it may coexist with impaired extraction and heterogeneous tissue hypoxia. Likewise, lactate elevation has several mechanisms and cannot be treated as a direct map of oxygen lack. Properly describing the problem matters more than choosing a single preferred biomarker.

How this could alter clinical reasoning

In critical care the distinction suggests that normalization of blood pressure or oxygen saturation cannot always be the final endpoint; perfusion and organ function remain essential. In chronic conditions it is a hypothesis-generating lens: vascular rarefaction, anemia, microthrombi, endothelial dysfunction and metabolic impairment may each change tissue performance.

But a patient with normal saturation and fatigue has not thereby been diagnosed with occult tissue hypoxia. Differential diagnosis and validated measurements are required.

Counterargument and bounds

Some tissues tightly match perfusion to demand, and systemic measurements remain enormously useful. Demonstrating regional oxygen heterogeneity in a specific disease does not show that correcting that heterogeneity improves patient outcomes. Indeed, attempts to optimize physiological surrogates can cause harm. The defensible proposition is narrower: **oxygen transport is a multiscale process**, and the adequacy of its earliest measurements must be judged against organ function and the evidence for the clinical setting.

A quantitative intuition

The distinction between supply and extraction can be expressed using oxygen content and flow. At a macroscopic level, oxygen delivery is cardiac output multiplied by arterial oxygen content. Yet a high measured delivery does not imply uniform diffusion and utilization. Imagine two tissues receiving the same net flow: in one, blood travels through many evenly perfused capillaries; in the other, flow is concentrated in a smaller number of channels while neighboring units are poorly perfused. The second geometry can leave patches of tissue disadvantaged despite unchanged total flow. This is an explanatory illustration, not a validated patient-specific calculation.

Why this must not become a catch-all fatigue diagnosis

The problem is most clearly demonstrated in critical illness and specified microvascular disorders. Its intuitive appeal makes it easy to transfer indiscriminately to common complaints. That would be a mistake. Anemia may lower arterial oxygen content; sleep apnea may cause intermittent hypoxemia; primary muscle disease may impair function despite normal supply; depression can change fatigue perception; medication effects can cause exertional intolerance. Each may produce symptoms without any need to postulate an inaccessible capillary lesion. The task is to determine whether the proposed mechanism has discriminating clinical evidence.

Measuring the right endpoint

If an intervention raises a tissue oxygen proxy but worsens patient outcomes, the proxy was not an adequate target. The literature on hemodynamic optimization teaches the same lesson: physiology requires outcome confirmation. Research designs should compare perfusion measures, organ-function endpoints and adverse effects rather than assuming 'more oxygen' is always better. Oxygen can itself become toxic under certain conditions; flow redistribution may carry costs elsewhere. The useful question is whether tissue delivery is appropriate for demand, not whether every measurable supply number can be maximized.

Selected scientific reading

1. Ince C. The microcirculation is the motor of sepsis. Crit Care. 2005;9(Suppl 4):S13–S19.

2. [Ellis CG, Jagger J, Sharpe M. The microcirculation as a functional system. Crit Care. 2005;9\(Suppl 4\):S3–S8.](#)
3. [Østergaard L et al. Microcirculatory dysfunction and tissue oxygenation in critical illness. Acta Anaesthesiol Scand. 2015;59:1246–1259.](#)

Editorial status: Conceptual scientific essay, not peer reviewed. Not original clinical data, a treatment protocol or medical advice. Selected readings are not a systematic review. Evidence and interpretation should be assessed independently.