*Editorial*

# Beyond vital signs: oxygen delivery, oxygen utilization, and the limits of physiologic signal after red cell transfusion

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Red blood cell (RBC) transfusion is among the most frequently administered hospital interventions. Its physiologic rationale appears straightforward: increase hemoglobin concentration, augment oxygen delivery ($DO_2$), and thereby improve tissue oxygenation. However, in stable, non-bleeding patients, the physiologic signal of transfusion is often far less evident than its biochemical effect, and structured follow-up beyond the immediate transfusion window remains limited[1-3].

In this issue of Blood Transfusion, Trentino and colleagues report a longitudinal study of continuously monitored ward patients receiving 1- or 2-unit RBC transfusions[1]. Using high-frequency heart rate (HR), respiratory rate (RR), and oxygen saturation ($SpO_2$) measurements analyzed with segmented mixed-effects regression, they demonstrate that despite predictable increases in hemoglobin concentration, there were no clinically meaningful changes in continuously monitored vital signs before or after transfusion[1].

These findings require careful interpretation. They do not suggest that transfusion lacks value. They do, however, challenge two persistent assumptions: that vital signs reliably reflect transfusion need or benefit, and that increasing hemoglobin necessarily increases oxygen utilization. In the Trentino cohort, hemoglobin declined over 48 hours before transfusion and increased appropriately afterward[1]. Yet HR, RR, and $SpO_2$ remained largely unchanged during the 10 hours pre-transfusion and the 24 hours post-transfusion. Even during infusion, observed shifts were small and clinically trivial[1].

If anemia at hemoglobin levels near contemporary restrictive thresholds (ideally 7 g/dL) consistently produced clinically relevant oxygen delivery impairment in stable patients, compensatory tachycardia or tachypnea would be expected. Instead, vital signs changes were notably not present. This does not imply that anemia is benign or that transfusion is unwarranted. It does suggest that hemoglobin concentration alone is an imperfect surrogate in measuring physiologic instability in stable ward patients. Current transfusion guidelines appropriately caution against decisions based solely on hemoglobin concentration and rather emphasize clinical context and symptoms[2,3]. Subjective monitoring of patients in this population through the entire multidisciplinary team thus becomes crucial in developing this context. Nonetheless, hemoglobin thresholds continue to exert substantial influence in daily practice. The absence of measurable physiologic signal in this carefully monitored cohort raises an uncomfortable possibility: in stable patients, transfusion may sometimes be laboratory-driven rather than physiology-driven.

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Though this study was centered around concrete endpoints that were continuously measured, the importance of clinical context remains vital in determining true need for transfusion, especially in stable patients. Current practice around transfusion culturally aims to correct a hemoglobin value without analysis of the clinical context. As such, assessment of the patient is as important as monitoring of these objective values. Presentation of symptoms of physiologically significant anemia –e.g., end-organ dysoxia (impaired renal function, respiratory compensatory mechanisms)– should further guide the rationale of a transfusion before a decision is made. Perhaps the physiologic signal for transfusion rather lies in the decompensated anemic patient as opposed to what is presenting in quantitative values.

The deeper physiological issue concerns the distinction between oxygen delivery and oxygen utilization. Transfusion increases hemoglobin concentration and therefore arterial oxygen content ($CaO_2$). Given stable cardiac output, $DO_2$ increases. This is fundamental physiology. However, oxygen consumption ($VO_2$) depends on tissue demand, microcirculatory flow, mitochondrial integrity, and extraction capacity[4]. When $VO_2$ is supply-independent, increasing $DO_2$ does not increase oxygen utilization. Multiple physiological investigations demonstrate that RBC transfusion often increases $DO_2$ without increasing $VO_2$ in stable, non-bleeding patients[4,5]. In such settings, transfusion augments transport capacity without correcting an oxygen deficit because no deficit is present.

Furthermore, stored RBCs are not physiologically identical to native circulating cells. Reduced 2,3-diphosphoglycerate levels in banked blood shift the oxygen-hemoglobin dissociation curve leftward, potentially impairing early post-transfusion oxygen unloading[6]. Storage-related alterations –including reduced deformability, nitric oxide scavenging, oxidative injury, and accelerated senescence– may further affect microvascular flow and effective tissue oxygen delivery[6]. Thus, while hemoglobin increases, effective tissue oxygenation may not rise proportionally. The absence of meaningful change in HR, RR, or $SpO_2$ after transfusion in the present study[1] is consistent with this physiological framework. If systemic oxygen debt had been present and reversed, measurable physiologic changes might reasonably have been anticipated in the endpoints. Their absence underscores the need for physiological precision rather than reflexive correction.

RBC transfusion increases oxygen delivery. It does not necessarily increase oxygen utilization. Transfusion practice rightly emphasizes vigilance during infusion to detect acute reactions. Yet structured assessment beyond the immediate post-transfusion window is uncommon. Outside critical care settings, few systems track longer-term trajectories of functional recovery, infection, thrombosis, inflammation, or cumulative exposure burden attributable to transfusion.

In the Trentino study, monitoring extended 24 hours after transfusion[1]. Even this degree of observation is unusual. Beyond that period, physiological and clinical follow-up typically ceases. Transfusion is often conceptualized as a discrete intervention rather than a biologic exposure with potential downstream effects. Immunomodulation, endothelial activation, inflammatory signaling, and thrombotic risk may evolve over days to weeks[7]. When assessment is confined to hemoglobin increment and short-term vital signs, a complex biologic intervention is reduced to a numeric transaction. Physiological tolerance of moderate anemia in stable patients is well documented[4,5]. Compensatory increases in oxygen extraction and redistribution of flow may preserve adequate tissue oxygenation at hemoglobin levels below traditional transfusion triggers.

The stability of vital signs prior to transfusion monitored in this cohort[1] aligns with that principle. Many stable ward patients near restrictive thresholds are not in overt oxygen debt. This reframes the clinical imperative. In stable, non-bleeding patients, priority should shift toward identifying and treating the underlying cause of anemia –iron deficiency, inflammation, renal disease, marrow suppression, occult blood loss– rather than defaulting to hemoglobin correction alone. Treating anemia addresses pathophysiology. Transfusion addresses transport capacity. This perspective does not diminish the importance of transfusion in hemorrhage, ischemia, or hemodynamic instability. It does emphasize that in stable patients with preserved compensatory reserve, reflexive transfusion warrants reconsideration.

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## CONCLUSIONS

Continuous monitoring data challenge the assumption that declining hemoglobin inevitably produces measurable physiologic instability, or that transfusion predictably restores physiologic equilibrium[1]. In stable ward patients, neither assumption appears consistently valid. RBC transfusion increases oxygen delivery. It does not guarantee increased oxygen utilization. It may correct hemoglobin concentration without correcting tissue hypoxia.

The relevant question in stable patients is not simply, "*What is the hemoglobin?*" but rather, "*Is oxygen utilization impaired - and will transfusion meaningfully improve outcome?*" (treat the patient, not the number).

Greater precision in distinguishing delivery from utilization, combined with systematic attention to diagnosis and treatment of anemia itself, will strengthen transfusion practice and align intervention with demonstrable physiologic need.

### Implications for practice

- In stable, non-bleeding patients, hemoglobin concentration alone should not be interpreted as proof of impaired oxygen utilization.
- Absence of measurable physiologic instability near restrictive thresholds suggests that transfusion decisions require integration of symptoms, context, and alternative therapies.
- Oxygen delivery and oxygen utilization are distinct physiologic constructs; increasing hemoglobin does not guarantee improved tissue oxygenation.
- Priority should be directed toward diagnosis and treatment of underlying anemia whenever feasible.

*The Authors declare no conflicts of interest.*

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