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REVIEW

Indexed Oxygen Delivery and Cerebral Near-Infrared Spectroscopy During 28 °C Hypothermic Cardiopulmonary Bypass in Aortic Valve Surgery: A Physiological and Clinical Perspective

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ABSTRACT

Maintaining adequate tissue oxygenation during cardiopulmonary bypass requires matching oxygen transport to metabolic demand rather than relying on fixed flow or pressure targets. During aortic valve (AV) surgery, moderate hypothermia may reduce oxygen consumption; however, hemodilution, low pump flow, altered autoregulation, and increasing metabolism during rewarming can still result in systemic or cerebral oxygen debt. To evaluate indexed oxygen delivery (DO_2i) and cerebral near-infrared spectroscopy (NIRS) as complementary monitoring tools and propose a phase-specific physiologic framework for their combined interpretation. PubMed/MEDLINE and major scientific society guidelines were searched through June 30, 2026, prioritizing adult cardiac surgery guidelines, randomized trials, observational cohorts, systematic reviews, and mechanistic studies. DO_2i quantifies global oxygen transport, whereas NIRS reflects regional supply-demand balance in frontal cerebral tissue. Concurrent decreases in DO_2i and bilateral NIRS values may suggest inadequate global oxygen delivery, whereas discordance should prompt assessment of regional, technical, or regulatory causes. Low DO_2i exposure is most consistently associated with acute kidney injury; NIRS-guided protocols may reduce desaturation burden, although their effects on major neurologic outcomes remain uncertain. Cumulative exposure incorporating both depth and duration may be more informative than a single nadir. In patients undergoing AV surgery, age, ventricular hypertrophy, renal vulnerability, and cerebrovascular atherosclerosis may heighten the clinical relevance of individualized interpretation, particularly during rewarming, when metabolic demand rises. The proposed DO_2i-NIRS framework is not a prospectively validated treatment algorithm but a physiology-based conceptual model supporting individualized multimodal perfusion management across cardiopulmonary bypass initiation, cooling, hypothermic maintenance, rewarming, and separation from bypass.

Keywords: Aortic valve surgery, cardiopulmonary bypass, moderate hypothermia, oxygen delivery, near-infrared spectroscopy, cerebral oximetry, goal-directed perfusion

INTRODUCTION

Cardiopulmonary bypass (CPB) temporarily replaces native circulation and gas exchange while introducing several non-physiologic conditions, including hemodilution, non-pulsatile flow, blood contact with artificial surfaces, temperature shifts, and microcirculatory heterogeneity. Consequently, apparently adequate pump flow and mean arterial pressure do not necessarily ensure sufficient cellular oxygenation. Contemporary perfusion practice increasingly emphasizes the relationship among systemic oxygen transport, metabolic demand, and regional organ perfusion rather than relying on isolated hemodynamic targets.[1]

AV surgery provides a clinically relevant setting in which this approach is particularly important. Patients undergoing AV surgery are often older and may have concentric left ventricular hypertrophy, limited diastolic and coronary reserve, chronic kidney disease, and cerebrovascular or aortic atherosclerosis. These comorbidities may cause similar macrohemodynamic targets to result in substantially different levels of organ oxygenation and tolerance to impaired oxygen delivery.

Moderate hypothermia can reduce metabolic oxygen demand; however, no single CPB temperature target has been universally accepted for adult AV surgery.[1] In this review, 28 °C is not proposed as a mandatory institutional protocol or universal target but rather as a physiologic reference point within the spectrum of moderately hypothermic CPB. Complex aortic procedures involving arch reconstruction, hypothermic circulatory arrest, or selective cerebral perfusion are beyond the scope of this study. The principal conceptual contribution of this review is the proposal that indexed oxygen delivery (DO_2i) and cerebral near-infrared spectroscopy (NIRS) be interpreted jointly in relation to changing metabolic demand across the distinct phases of CPB, including initiation, cooling, hypothermic maintenance, rewarming, and separation from bypass.

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Literature Search and Review Approach

PubMed/MEDLINE and the guideline websites of major scientific societies were searched through June 30, 2026, using a focused narrative search strategy. Search terms included "cardiopulmonary bypass," "oxygen delivery," "DO_2i," "goal-directed perfusion," "hypothermia," "rewarming," "near-infrared spectroscopy," "cerebral oximetry," and "AV surgery," both individually and in relevant combinations. Adult cardiac surgery guidelines, randomized studies, large observational cohorts, systematic reviews, and mechanistic studies were prioritized. Older studies establishing physiologic thresholds or fundamental principles of temperature management were also retained when clinically relevant.

Studies were selected based on their direct contribution to physiologic or clinical questions related to DO_2i, cerebral NIRS, hypothermic CPB, rewarming, and AV surgery. Because few studies have simultaneously evaluated continuous DO_2i and bilateral NIRS specifically during AV surgery at exactly 28 °C, the indirectness of evidence derived from mixed adult cardiac surgical populations is explicitly acknowledged. This article was not designed as a systematic review or meta-analysis; therefore, no formal risk-of-bias assessment, PRISMA-based study selection, or quantitative evidence synthesis was performed.

Physiological Basis of DO_2i

Systemic oxygen delivery is determined by blood flow and arterial oxygen content. During CPB, DO_2i is calculated as the pump flow index multiplied by arterial oxygen content and by 10; CaO_2 is determined primarily by hemoglobin concentration and arterial oxygen saturation, with a much smaller contribution from dissolved oxygen. Accordingly, a high PaO_2 cannot compensate for marked hemodilution, and pump flow and hematocrit should not be considered independent targets.

When oxygen delivery decreases, tissues initially preserve oxygen consumption (VO_2) by increasing oxygen extraction. Once extraction reserve is exhausted, oxygen consumption becomes delivery-dependent, and anaerobic metabolism increases. No single DO_2i value represents a universal biologic threshold because temperature, anesthesia, inflammation, microcirculatory function, and organ reserve can shift the critical point. Nevertheless, low DO_2i nadirs and cumulative exposure below approximately 260-300 mL/min/m^2 have been consistently associated with acute kidney injury.[2-4] Randomized studies targeting DO_2i levels of approximately 280-300 mL/min/m^2 have primarily demonstrated reductions in mild AKI, without reproducible benefits for severe acute kidney injury (AKI), mortality, or major neurologic events.[5-7] DO_2i should therefore be regarded as a modifiable risk marker rather than an absolute safety threshold.

Mixed venous oxygen saturation (SvO_2), oxygen extraction, carbon dioxide-derived indices, and lactate provide complementary information to DO_2i. Hypothermia may suppress metabolism and maintain a deceptively high SvO_2, whereas lactate is a delayed and non-specific marker. Normal global values do not exclude microcirculatory dysfunction.[8] Non-pulsatile perfusion, endothelial activation, altered erythrocyte deformability, and inflammatory shunting can uncouple macrohemodynamic variables from capillary flow. This hemodynamic incoherence helps explain why normal DO_2i or blood pressure does not guarantee adequate microcirculation in every organ.

Oxygen Balance and Rewarming During Moderate Hypothermia

Cooling reduces enzymatic activity and cerebral and systemic oxygen consumption. NIRS and SvO_2 may therefore remain stable or increase; however, pump flow should not be reduced solely on the basis of temperature. When hemodilution is substantial, even a modest reduction in flow may lower DO_2i below the reserve capacity of the kidneys or splanchnic organs. Hypothermia shifts the oxyhemoglobin dissociation curve to the left, increases blood viscosity, and alters tissue oxygen unloading. Safe management requires a dynamic balance among flow, hemoglobin concentration, pressure, temperature, and measured metabolic response.

In adults undergoing mild-to-moderate hypothermia, alpha-stat management is generally preferred to preserve cerebral autoregulation.[1,9] pH-stat management can increase $PaCO_2$ and cerebral blood flow, thereby increasing NIRS values; however, this numerical increase does not necessarily indicate superior neuroprotection.

Rewarming is the most vulnerable phase. Oxygen consumption increases rapidly, and a previously adequate DO_2i may become relatively insufficient. Controlled rewarming, avoidance of cerebral hyperthermia, and monitoring of the arterial outlet-to-venous return temperature gradient are recommended.[1,10,11] A decrease in NIRS and SvO_2, increased oxygen extraction, and a subsequent rise in lactate should be interpreted as complementary indicators of evolving oxygen debt. The rewarming rate should be assessed together with arterial outlet temperature and the risk of cerebral temperature overshoot because rapid warming can amplify the supply-demand mismatch despite apparently acceptable macrohemodynamic values.

Cerebral NIRS: Measurement and Limitations

Cerebral NIRS estimates frontal regional oxygen saturation from the differential absorption of near-infrared light by oxyhemoglobin and deoxyhemoglobin. The signal is predominantly venous-weighted and is influenced by arterial flow, hemoglobin concentration, SaO_2, venous drainage, $PaCO_2$, temperature, anesthesia, head position, cannula direction, and autoregulation.[12-14] NIRS may reveal an oxygen supply-demand imbalance early, but it cannot identify the underlying cause by itself.

When feasible, a baseline value should be obtained before induction and administration of supplemental oxygen, with the head in a neutral position; however, emergency conditions, preoperative oxygen therapy, or late monitor placement may preclude this. In such cases, the earliest reliable measurement should be used as the reference, and the conditions under which it was obtained should be documented. Studies have used a decrease of approximately 20% from baseline or an absolute rSO_2 value of approximately 50% as intervention criteria; however, absolute and relative thresholds are not equivalent, and no single universal boundary has been validated.[15]

Because devices differ in wavelength selection, source-detector spacing, algorithms, and calibration, absolute rSO_2 values are not directly interchangeable across systems.[13,16] Extracranial tissues can influence the signal, and the effect of skin pigmentation may vary according to the technology and algorithm used.[16-26] Forehead sensors sample only a limited region of the frontal cortex; therefore, normal bilateral

values do not exclude posterior or focal ischemia outside the field of view.[27] A unilateral decrease may reflect sensor artifact, head rotation, jugular compression, carotid disease, cannula direction, embolic events, or regional malperfusion. NIRS is not a direct diagnostic test for embolism, cannula malposition, or focal cerebral ischemia. The depth, duration, recurrence, and laterality of desaturation are more informative than a single measurement.

Phase-Specific DO_2i-Nirs Integration During CPB

The value of combined monitoring lies in recognizing patterns rather than normalizing isolated values. When DO_2i and bilateral NIRS decrease concurrently and SvO_2 also decreases, inadequate global oxygen delivery becomes more likely. When DO_2i remains acceptable but NIRS decreases, regional or regulatory causes, such as pressure-dependent cerebral flow, hypocapnia, cannula-related asymmetry, impaired autoregulation, venous congestion, or increased cerebral metabolic demand, should be considered. Conversely, low DO_2i with stable or elevated NIRS during cooling may reflect metabolic suppression but does not exclude renal or splanchnic risk.

At CPB initiation, hemodilution and transient changes in flow and pressure may reduce both measures. During cooling, NIRS and SvO_2 may be preserved as metabolic demand decreases. During hypothermic maintenance, trends and cumulative exposure are more informative than a single nadir. During rewarming, an equivalent decrease in NIRS carries greater clinical significance because metabolic demand is increasing. During separation from bypass, a decline in NIRS may accompany low cardiac output, inadequate preload, ventricular dysfunction, arrhythmia, anemia, hypoxemia, or hypotension.

This DO_2i-NIRS approach is not a prospectively validated treatment algorithm and has not been validated against clinical outcomes. It is a conceptual decision-support model derived from physiologic principles, observational associations, and indirect evidence. Because identical monitoring patterns may arise from different underlying mechanisms, combinations of monitoring variables should not be used as automatic diagnostic or intervention rules. Phase-specific relationships among DO_2i, NIRS, SvO_2, and lactate are summarized in Figure 1.

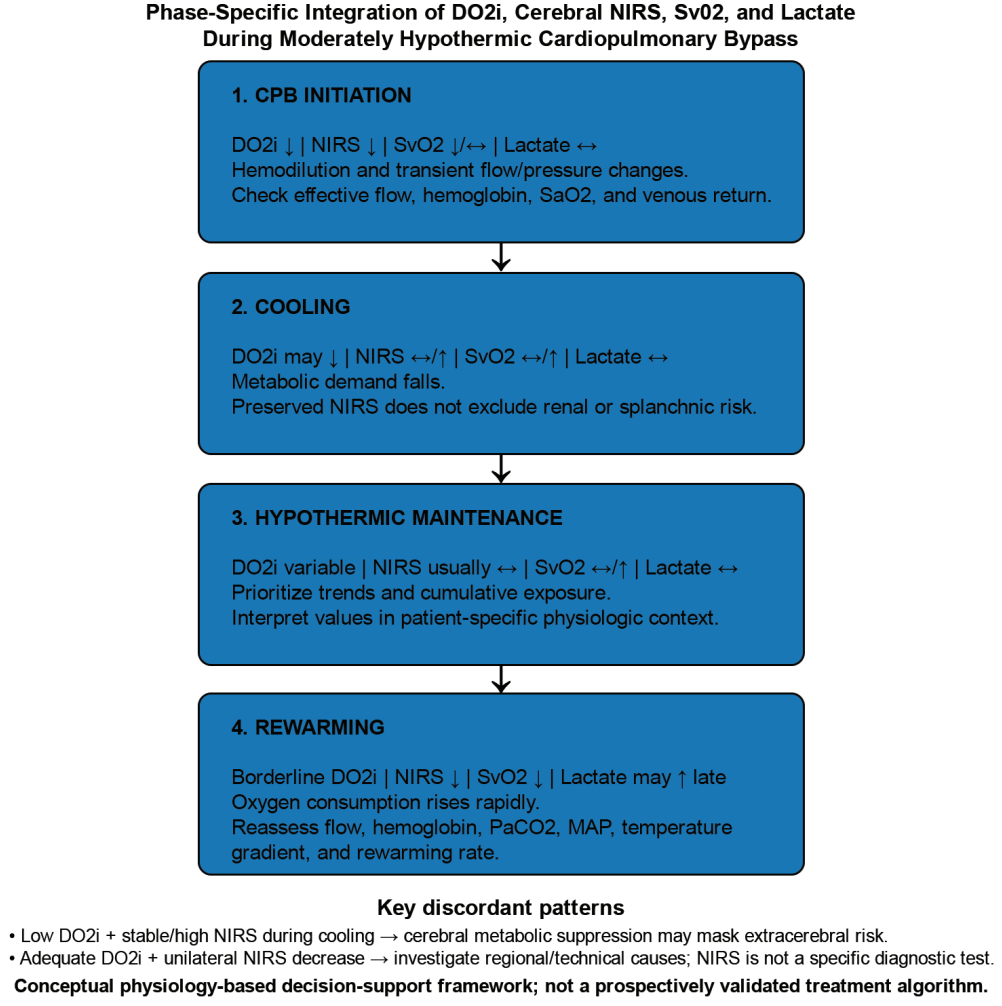

Figure 1. Integrated physiologic interpretation of DO_2i, cerebral NIRS, SvO_2, and lactate across phases of moderately hypothermic cardiopulmonary bypass. The schematic depicts expected patterns during initiation, cooling, hypothermic maintenance, and rewarming. Discordance among parameters does not establish a specific diagnosis. The figure represents a physiology-based conceptual decision-support framework rather than a prospectively validated treatment algorithm

Fixed Thresholds, Cumulative Exposure, and Multiparameter Interpretation

Thresholds can aid standardization but may also create false reassurance when interpreted without considering time and clinical context. The same DO_2i may be adequate during hypothermic maintenance yet become borderline during rewarming, particularly when hemoglobin concentration decreases or venous congestion develops. Likewise, the same rSO_2 value may have different clinical implications in patients with different baseline values.

Cumulative or time-dependent exposure considers not only the magnitude of a physiologic deviation but also its duration. A brief, rapidly corrected decrease is not biologically equivalent to an equally deep but prolonged decrease. "Time-dose burden" describes the combined depth and duration of exposure below a target or patient-specific reference value. Deeper and longer deviations result in a greater cumulative burden; however, validated universal time-dose limits for DO_2i or NIRS based on patient characteristics and CPB phase are not yet available.

Pressure, flow, and hemoglobin targets require the same caution. Vasopressor-mediated increases in arterial pressure may improve NIRS without necessarily increasing capillary flow or overall oxygen transport, whereas higher pump flow may increase DO_2i while worsening venous congestion, line pressure, or hemolysis. Transfusion increases arterial oxygen content but carries inflammatory and volume-related risks. The multiparameter matrix in Table 1 is therefore not a validated algorithm for standardizing practice but a conceptual framework for systematically evaluating plausible mechanisms. Interventions should be individualized according to baseline reserve, CPB phase, surgical conditions, and concordant monitoring data.

Multiparameter Matrix for Clinical Application

Clinical decisions should be based on patterns across multiple parameters rather than on normalization of a single variable. Low DO_2i, low bilateral NIRS, falling SvO_2, and rising lactate should prompt evaluation of global oxygen delivery. Adequate DO_2i with a unilateral reduction in NIRS and stable systemic variables makes a regional flow problem or technical artifact more likely. During cooling, low DO_2i with preserved NIRS may reflect cerebral metabolic suppression; during rewarming, borderline DO_2i with falling NIRS and SvO_2 may indicate an increasing supply-demand mismatch. Table 1 summarizes these patterns and should be interpreted as a conceptual matrix rather than a validated management algorithm.

Practical Approach to Desaturation

The goal of management is to correct the underlying mechanism rather than merely increase a monitor value. Signal quality, sensor contact, head and neck position, and external compression should first be checked, followed by assessment of whether the change is bilateral or unilateral and whether it coincides with a surgical event. Actual pump flow, venous drainage, oxygenator function, SaO_2, hemoglobin concentration, DO_2i, mean arterial pressure, $PaCO_2$, SvO_2, temperature, and anesthetic depth should then be assessed together.

When DO_2i and SvO_2 are low, effective pump flow and venous return should be optimized when technically feasible, unnecessary hemodilution should be minimized, and transfusion decisions should not be based solely on NIRS or hematocrit. When DO_2i is adequate but NIRS remains low, cerebral perfusion pressure, $PaCO_2$, head position, cannula direction, and rewarming rate should be reassessed. Persistent unilateral changes require direct communication among the clinical team and, when appropriate, additional imaging or flow assessment. NIRS-guided protocols may reduce desaturation burden but have not demonstrated consistent benefits for stroke, mortality, or long-term cognitive outcomes.[17-21] A successful intervention should improve the overall physiologic pattern rather than NIRS alone.

Clinical Evidence and Specific Relevance to AV Surgery

Renal evidence is more consistent than neurologic evidence. DO_2i-guided perfusion has primarily reduced mild AKI in several studies and meta-analyses, although the effect size varies according to the threshold used, temperature, transfusion practices, and patient risk.[5-7,22,23] Cerebral desaturation is associated with delirium, cognitive dysfunction, and prolonged hospitalization, but correcting the monitor value has not been proven to alter the underlying clinical outcome. Randomized studies have reduced desaturation duration, while major neurologic outcomes have remained inconsistent.[17-20] Contemporary syntheses suggest a possible reduction in delirium but emphasize the limited certainty of the evidence.[24,25] Low baseline NIRS may also reflect anemia, low cardiac output, lung disease, frailty, or cerebrovascular disease; therefore, a prognostic association does not establish a single treatable mechanism.

Table 1. Pattern-based interpretation of DO_2i and cerebral NIRS during cardiopulmonary bypass

Observed pattern	Likely interpretation	Initial checks and approach
Low DO_2i+low bilateral NIRS+falling SvO_2	Inadequate global oxygen delivery is likely.	Verify effective pump flow, hemoglobin, SaO_2, venous return, oxygenator function, temperature, and metabolic demand.
Adequate DO_2i+low unilateral NIRS	Regional or technical problem is more likely; NIRS is not diagnostic.	Check sensor, head-neck position, jugular compression, cannula direction, carotid/aortic pathology, and surgical events.
Low DO_2i+stable/high NIRS during cooling	Reduced cerebral metabolism may mask systemic or extracerebral risk.	Assess depth/duration of low DO_2i, SvO_2/extraction, renal vulnerability, hemoglobin, and splanchnic risk.
Falling NIRS during rewarming±falling SvO_2	Increasing oxygen consumption may be exceeding delivery.	Increase effective flow when appropriate; reassess hemoglobin, $PaCO_2$, MAP, temperature gradient, and rewarming rate.

Note: This table is not a prospectively validated clinical management algorithm. The same monitoring pattern may arise from more than one physiologic or technical mechanism; NIRS does not directly diagnose embolism, cannula malposition, or focal cerebral malperfusion. NIRS: Near-infrared spectroscopy

In AV disease, ventricular hypertrophy, limited coronary and diastolic reserve, renal vulnerability, and cerebrovascular atherosclerotic burden may reduce tolerance to changes in oxygen delivery. Accordingly, apparently normal flow, pressure, or hematocrit may not provide equivalent organ protection in every patient. Combined interpretation of DO_2i and NIRS may help reveal this heterogeneity; however, direct studies evaluating isolated AV surgery with continuous DO_2i and bilateral NIRS at a defined temperature remain limited. The recommendations should therefore be interpreted as a conceptual approach adapted to the physiologic vulnerabilities of AV surgery rather than as disease-specific fixed thresholds.

Study Limitations and Future Research

This review is limited by heterogeneity in NIRS devices, temperature targets, perfusion protocols, transfusion practices, and outcome definitions. Most studies include both coronary and valve procedures, and few have reported cumulative DO_2i, NIRS, and SvO_2 burden in the same patients. Moderate hypothermia itself encompasses a broad temperature range, and inferences specific to 28 °C are based on limited direct evidence.

Future studies should stratify AV disease phenotype, cerebral and renal reserve, acid-base strategy, and CPB phase and evaluate time-weighted DO_2i-NIRS exposure rather than relying on a single nadir. The clinical benefit of this multiparameter framework should be evaluated prospectively.

CONCLUSION

Safe perfusion during moderately hypothermic CPB for AV surgery cannot be defined by a single flow, pressure, hematocrit, DO_2i, or NIRS value. DO_2i quantifies global oxygen transport, whereas NIRS reflects regional frontal cerebral supply-demand balance. Concordant deterioration supports inadequate global oxygen delivery, whereas discordance warrants investigation of regional, technical, or regulatory causes.

The central message of this review is that DO_2i and cerebral NIRS should not be interpreted as independent thresholds but rather considered together across the changing physiologic phases of CPB. Because metabolic demand differs during cooling, hypothermic maintenance, and especially rewarming, the same numerical value may have different clinical significance. The proposed integration is not a validated treatment algorithm but a conceptual decision-support framework that incorporates trends, cumulative exposure, baseline vulnerability, and corroborating physiologic variables.

The potential contribution of individualized perfusion management is to support selection of the lowest-risk corrective intervention based on the most plausible mechanism rather than applying identical targets to every patient. During rewarming in particular, trends in DO_2i, NIRS, hemoglobin, SvO_2, $PaCO_2$, mean arterial pressure, lactate, and temperature should be interpreted together. These monitoring measures should complement, rather than replace, the clinical judgment of experienced perfusion, anesthesia, and surgical teams.

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