Lactate as a Marker of Hypoperfusion During Cardiac Surgery

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ABSTRACT

Background: Tissue hypoperfusion is a major complication during and after cardiac surgery, often associated with increased morbidity, longer ICU stays, and higher mortality. Conventional hemodynamic parameters may not always reflect the adequacy of cellular oxygen delivery, particularly in the context of cardiopulmonary bypass (CPB) where physiological conditions are significantly altered. Among the biochemical indicators of tissue oxygenation, lactate has emerged as a sensitive and dynamic marker of hypoperfusion. Elevated lactate levels often result from anaerobic metabolism due to inadequate oxygen delivery, but they may also reflect stress-induced hypermetabolism, impaired clearance, or microcirculatory dysfunction. Understanding the mechanisms of lactate generation and interpretation in the perioperative setting is essential for timely detection of hypoperfusion and appropriate clinical intervention. This review aims to provide a comprehensive overview of lactate physiology, explore its role as a marker of hypoperfusion in cardiac surgery, and evaluate its diagnostic, prognostic, and therapeutic significance during the perioperative period.

Conclusion: Lactate monitoring offers real-time insight into the adequacy of tissue perfusion and systemic oxygen delivery during cardiac surgery. Unlike static parameters such as blood pressure or central venous pressure, lactate levels reflect metabolic responses at the cellular level. Serial lactate measurements, as well as lactate clearance, are now incorporated into many goal-directed therapy protocols for guiding resuscitation and optimizing outcomes. However, interpretation must be contextual, taking into account factors such as liver dysfunction, drug therapy, and temperature regulation that can influence lactate kinetics. When combined with additional markers like $ScvO_2$ or $Pv\text{-}aCO_2$ gradients, lactate provides a more complete picture of perfusion adequacy. Ultimately, integrating lactate assessment into multimodal monitoring strategies can enhance clinical decision-making and support individualized hemodynamic management in high-risk cardiac surgical patients.

Keywords*: Lactate, Hypoperfusion, Cardiac Surgery*

Lactate Metabolism and Physiology

Lactate is a byproduct of anaerobic metabolism, traditionally viewed as a marker of tissue hypoxia. However, this perspective has evolved. Lactate is constantly produced in small amounts under aerobic conditions and plays a key role in energy transfer between tissues. It is generated primarily in muscle cells and red blood cells through glycolysis, where glucose is broken down into pyruvate. When oxygen supply is limited or cellular metabolism is stressed, pyruvate is converted into lactate by the enzyme lactate dehydrogenase (LDH), regenerating NAD^+ and allowing glycolysis to continue [1].

The balance between lactate production and clearance determines its plasma concentration. Under normal circumstances, lactate is cleared by the liver through gluconeogenesis and oxidation. The kidneys and heart also contribute to lactate metabolism [2]. During cardiac surgery, particularly under cardiopulmonary bypass (CPB), this balance is frequently disrupted. Factors such as hypothermia, hemodilution, reduced hepatic perfusion, and increased catecholamine levels may lead to elevated lactate levels even in the absence of severe hypoxia [3].

Importantly, not all hyperlactatemia reflects true tissue hypoperfusion. Conditions such as beta-agonist administration, hyperglycemia, and stress-related adrenergic surges can increase glycolytic flux and lactate production independently of oxygen delivery [3,4]. Furthermore, impaired clearance — especially in patients with preexisting liver dysfunction — can result in elevated levels without increased production [2].

Therefore, interpreting lactate concentrations requires an understanding of its physiological context. A single elevated lactate value may not confirm tissue hypoxia, but serial measurements and trends are more informative. Rising lactate levels or poor clearance postoperatively often indicate ongoing hypoperfusion or inadequate resuscitation, both of which correlate with poor outcomes [5].

Lactate is thus a key integrative biomarker reflecting the intersection of metabolic demand, oxygen delivery, and organ function — making it invaluable during cardiac surgery for identifying hidden hypoperfusion and guiding clinical decisions [1–5].

Causes and Interpretation of Hyperlactatemia in Cardiac Surgery

Hyperlactatemia during and after cardiac surgery is a common yet complex finding. It is frequently associated with increased morbidity, longer ICU stays, and adverse outcomes. However, interpreting lactate levels in this setting requires an understanding of both its sources and kinetics, as not all elevations are due to hypoperfusion or anaerobic metabolism [6,7].

During cardiac surgery, particularly when using cardiopulmonary bypass (CPB), multiple factors converge to affect lactate production and clearance. First, the use of CPB induces systemic inflammatory response syndrome (SIRS), which triggers metabolic stress and catecholamine release. This, in turn, stimulates glycolysis and accelerates lactate production even in the presence of adequate oxygen delivery, referred to as “stress hyperlactatemia” [8,9]. Adrenergic stimulation through inotropes and vasopressors such as epinephrine further amplifies this response by promoting pyruvate-to-lactate conversion in skeletal muscles and the splanchnic bed [10].

Second, the hemodilution caused by the priming of the CPB circuit results in decreased oxygen-carrying capacity, compromising oxygen delivery (DO_2) despite adequate pump flows. When DO_2 falls below a critical threshold, cells shift toward anaerobic metabolism, leading to increased lactate

generation [6]. This is particularly relevant during phases of hypotension, low cardiac output, or inadequate tissue perfusion, especially in patients with compromised myocardial function or high oxygen demands.

Third, lactate clearance may be impaired due to reduced liver perfusion during surgery. Hepatic blood flow can decrease significantly during CPB or in the context of low cardiac output syndrome, limiting lactate metabolism and contributing to its accumulation [11]. In some cases, a mismatch between oxygen delivery and consumption at the microcirculatory level may also occur, resulting in localized hypoperfusion that standard hemodynamic parameters fail to detect [12].

Importantly, intraoperative hyperglycemia and insulin resistance common during cardiac surgery can also drive anaerobic glycolysis, enhancing lactate production independent of perfusion abnormalities [13]. Other factors such as hypothermia, acidosis, and use of beta-agonists contribute to the multifactorial nature of hyperlactatemia in this context [9].

Thus, elevated lactate should not automatically be equated with tissue hypoxia. A single high value may reflect transient metabolic shifts, whereas persistently rising lactate or failure to clear over time is more suggestive of ongoing hypoperfusion. Integrating lactate trends with clinical data and other perfusion markers such as $ScvO_2$ and $Pv\text{-}aCO_2$ gradients can improve diagnostic accuracy and guide therapy more effectively [14].

Understanding the origin of lactate elevation — whether due to increased production, reduced clearance, or both — is critical to tailoring interventions, avoiding over-resuscitation, and improving outcomes in cardiac surgical patients [6,14].

Lactate as a Marker in Cardiac Surgery

Lactate levels have emerged as powerful prognostic indicators in the context of cardiac surgery. Numerous studies have consistently shown a strong association between intraoperative and postoperative hyperlactatemia and adverse outcomes such as increased morbidity, prolonged mechanical ventilation, longer ICU stays, renal dysfunction, and higher mortality rates [15,16].

What makes lactate particularly valuable is its dynamic nature — not only the absolute values but also the **kinetics of lactate clearance** are critically important. An elevated lactate level immediately after cardiopulmonary bypass (CPB) might reflect temporary perfusion deficits or metabolic stress, but if the level remains high or continues to rise in the postoperative hours, this indicates sustained tissue hypoperfusion or impaired clearance, both of which are linked to poor outcomes [17,18].

In a clinical study involving patients undergoing cardiac surgery, those who failed to reduce lactate levels by more than 10% within 2 hours after surgery had a significantly higher risk of organ dysfunction and death compared to those with effective clearance. This has led to the inclusion of

lactate clearance targets in many goal-directed therapy (GDT) protocols, especially during the early postoperative period [19].

Several thresholds have been proposed to identify high-risk patients. Lactate levels >4 mmol/L are often associated with increased mortality, while levels >2 mmol/L persisting beyond the first 6 hours postoperatively are considered critical warning signs [20]. However, there's no universal cutoff, and interpretation must be tailored to patient-specific factors, surgical complexity, and the presence of comorbidities.

Incorporating lactate trends alongside hemodynamic markers such as central venous oxygen saturation ($ScvO_2$), veno-arterial CO_2 difference ($Pv\text{-}aCO_2$), and clinical indicators of perfusion offers a more accurate risk stratification. For instance, a patient with stable hemodynamics but rising lactate may be experiencing occult hypoperfusion — a phenomenon often missed if lactate monitoring is not emphasized [21].

Moreover, hyperlactatemia in patients with preserved cardiac output might point toward distributive or microcirculatory shock, highlighting the role of lactate beyond global perfusion alone. This makes lactate an indispensable part of the monitoring toolkit, not just for diagnosis but also for guiding therapy and assessing response to interventions during cardiac surgery [22].

Clinical Applications of Lactate Monitoring in Cardiac Surgery

Lactate monitoring during cardiac surgery plays a crucial role in real-time assessment of tissue perfusion and guides perioperative decision-making. It helps identify patients at risk of developing postoperative complications and enables clinicians to tailor interventions based on dynamic perfusion status, especially during cardiopulmonary bypass (CPB) and the immediate recovery phase [23].

One of the key clinical uses of lactate is in guiding fluid resuscitation and inotropic support. In the operating room or ICU, a rising lactate level despite adequate mean arterial pressure (MAP) may indicate hidden hypoperfusion. This can prompt clinicians to evaluate cardiac output, oxygen delivery, and microcirculatory flow, rather than solely relying on static measurements like CVP or MAP [23]. In this way, lactate serves as an early warning marker, often preceding overt signs of organ dysfunction.

Another essential application is in goal-directed therapy (GDT). Monitoring lactate clearance is now incorporated into many GDT protocols for high-risk surgical patients. Achieving a reduction of lactate levels by at least 10–20% every 2 hours in the early postoperative phase is associated with improved outcomes and reduced mortality [24]. This approach helps avoid over-resuscitation by preventing excessive use of fluids and vasoactive drugs once perfusion has normalized, thus minimizing the risk of complications such as pulmonary edema or acute kidney injury [24].

In addition, lactate can act as a triage tool, identifying patients who need closer monitoring or advanced circulatory support. For example, persistently high lactate levels (>4 mmol/L) after CPB may prompt early initiation of mechanical assist devices like intra-aortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) to restore perfusion and oxygen delivery [25].

Furthermore, lactate trends are particularly valuable when interpreted alongside other perfusion markers. For instance, in patients with high $ScvO_2$ but elevated lactate, impaired oxygen utilization at the cellular level should be considered — a phenomenon often seen in sepsis or reperfusion injury after CPB [26]. Similarly, if both $ScvO_2$ and lactate are low, this strongly suggests inadequate global oxygen delivery, often due to reduced cardiac output or severe anemia [27].

In practice, integrating lactate into the multimodal monitoring strategy enables anesthesiologists and intensivists to individualize patient management and optimize outcomes. It offers an inexpensive, rapid, and reproducible tool that reflects the delicate balance between oxygen supply and demand throughout the perioperative course of cardiac surgery [28].

Limitations of Lactate as a Perfusion Marker

While lactate is a widely accepted indicator of tissue hypoperfusion, its interpretation is not always straightforward. One major limitation is that elevated lactate does not always indicate hypoxia or inadequate oxygen delivery. In fact, hyperlactatemia may result from various non-hypoxic mechanisms such as stress-induced catecholamine release, hepatic dysfunction, or use of certain drugs like beta-agonists, which can stimulate glycolysis and lactate production despite adequate tissue perfusion [29].

In the setting of cardiac surgery, especially during and after cardiopulmonary bypass, multiple factors may contribute to lactate elevation. Hemodilution, inflammatory responses, and reperfusion injury can all lead to increased lactate levels independently of perfusion status [30]. Therefore, using lactate in isolation without correlating it with hemodynamic or clinical parameters may lead to misinterpretation and inappropriate management decisions.

Another significant challenge is timing and kinetics. Lactate clearance is a lagging indicator, which means it does not respond immediately to changes in tissue perfusion. After CPB, for instance, lactate levels might remain elevated for hours due to delayed metabolic recovery, even if perfusion is already restored. Relying solely on lactate might result in over-resuscitation, exposing the patient to unnecessary fluid overload or excessive inotropic support [31].

Moreover, hepatic clearance plays a central role in lactate metabolism. Any degree of liver dysfunction—whether pre-existing or acquired intraoperatively—can impair lactate clearance and contribute to persistent hyperlactatemia, irrespective of oxygen delivery. This highlights the importance of integrating lactate interpretation with assessments of liver function and overall metabolic context [32].

Renal dysfunction, although less central to lactate metabolism, may also contribute by altering acid-base balance, further complicating interpretation in critically ill patients [33].

Lastly, it is essential to consider patient-specific variables, such as baseline comorbidities, medications, or intraoperative events (e.g., massive transfusion, prolonged cross-clamp time), which can all influence lactate dynamics. Hence, while lactate remains a valuable biomarker, its utility is maximized only when used in conjunction with other clinical indicators and perfusion markers [34].

Alternative or Complementary Perfusion Markers to Lactate

Despite the importance of lactate as a marker of hypoperfusion, relying solely on it may not provide a complete picture, especially in the dynamic context of cardiac surgery. Several alternative or complementary parameters have been proposed to assess tissue perfusion more accurately and in real time. These markers often serve as adjuncts to lactate, helping clinicians avoid misinterpretation and make more informed decisions.

One of the most widely used adjunctive markers is central venous oxygen saturation ($ScvO_2$), which reflects the balance between oxygen delivery and consumption. A low $ScvO_2$ (<70%) often suggests inadequate oxygen delivery, while a high $ScvO_2$ may indicate impaired oxygen extraction due to microcirculatory or mitochondrial dysfunction. In the setting of elevated lactate and high $ScvO_2$, clinicians should suspect a problem at the cellular level, such as in septic or inflammatory states post-CPB [35].

Another useful parameter is the veno-arterial carbon dioxide difference ($P(v\text{-}a)CO_2$). This marker correlates inversely with cardiac output and venous return, providing insight into the adequacy of perfusion. A $P(v\text{-}a)CO_2$ greater than 6 mmHg often signals reduced flow states even when other parameters appear normal. When used alongside lactate, it may help differentiate between hypoperfusion-related and non-hypoperfusion-related hyperlactatemia [36].

The ratio of $P(v\text{-}a)CO_2$ to the arterial-venous O_2 content difference ($Ca\text{-}vO_2$) has also gained attention. A value >1.4 is considered a marker of anaerobic metabolism and poor perfusion. This index is thought to reflect the respiratory quotient at the bedside, offering early detection of tissue oxygen debt. Unlike lactate, this ratio reacts quickly to resuscitative efforts and can provide earlier clues to tissue hypoxia [37].

Near-infrared spectroscopy (NIRS), a non-invasive method to measure regional tissue oxygenation, especially cerebral or skeletal muscle saturation, has been increasingly used during cardiac surgery. A drop in NIRS values may precede lactate elevation or hypotension, giving an early warning sign of regional hypoperfusion [38].

Lastly, serum base deficit and capillary refill time are simple but effective bedside tools. Although not specific, they offer quick and complementary assessments of global circulatory status, especially in emergency settings or during rapid deterioration [39].

In clinical practice, integrating these parameters with lactate measurement forms a comprehensive strategy. It allows tailored, physiologically sound decisions that reduce both under- and over-resuscitation risks, especially in vulnerable post-cardiac surgery patients [40].

Conclusion

Lactate is a practical and widely used marker of hypoperfusion during cardiac surgery. Elevated levels often reflect poor oxygen delivery and are associated with worse outcomes. However, lactate should be interpreted alongside clinical data and other perfusion indicators like $ScvO_2$ and $P(v\text{-}a)CO_2$ to avoid misinterpretation. Its role in guiding resuscitation is well supported, but it's not without limitations. Future strategies should focus on integrating lactate trends with multimodal monitoring tools for more individualized, timely interventions

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