



**INTERNATIONAL JOURNAL OF
PHARMACEUTICAL SCIENCES**
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: <https://www.ijpsjournal.com>



Research Article

Intraoperative Lactate as a Predictor of Complications in Major Surgery

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ARTICLE INFO

Published: 21 Oct 2026

Keywords:

lactate, intraoperative lactate, major surgery, postoperative complications, perioperative medicine, hyperlactatemia, surgical outcomes, mortality

DOI:

10.5281/zenodo.23525260

ABSTRACT

Background: Major surgery is associated with substantial physiological stress, alterations in tissue perfusion, changes in oxygen delivery, and metabolic disturbances that may contribute to postoperative complications. Serum lactate is a widely available biomarker that reflects the balance between lactate production and clearance and has been increasingly investigated as a prognostic marker in the perioperative setting. **Objective:** To review the available evidence regarding the role of intraoperative lactate as a predictor of postoperative complications in patients undergoing major surgery, with emphasis on its prognostic value, timing of measurement, and potential clinical implications. **Methods:** A narrative review of the literature was conducted to evaluate studies assessing intraoperative lactate concentrations in adult patients undergoing major surgical procedures. Evidence regarding the association between intraoperative lactate levels and postoperative complications, organ dysfunction, intensive care requirements, and mortality was considered. **Results:** Elevated intraoperative lactate concentrations have been associated with an increased risk of adverse postoperative outcomes in several major surgical populations. In particular, higher lactate concentrations measured during or at the end of surgery have been associated with postoperative morbidity, prolonged intensive care and hospital stay, organ dysfunction, and mortality. However, the prognostic value of lactate varies according to the type of surgery, timing of measurement, magnitude and persistence of elevation, and the clinical context. Importantly, intraoperative hyperlactatemia may result from multiple mechanisms, including tissue hypoperfusion and impaired oxygen utilization, but also from catecholamine-mediated glycolysis, hepatic dysfunction, pharmacological effects, and other metabolic processes.

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



Conclusions: : Intraoperative lactate is a promising perioperative biomarker for identifying patients at increased risk of complications following major surgery. Its interpretation, however, should be integrated with hemodynamic parameters, surgical characteristics, comorbidities, and other markers of organ dysfunction rather than considered an isolated predictor. Further prospective studies are needed to establish standardized sampling strategies, clinically meaningful thresholds, and its role within multimodal perioperative risk assessment.

INTRODUCTION

Major surgery induces a complex physiological response characterized by profound changes in hemodynamics, oxygen delivery, tissue perfusion, metabolic activity, and inflammatory signaling. During this period, alterations in circulating lactate may reflect an imbalance between lactate production and clearance and can therefore provide information regarding the adequacy of systemic and regional oxygen delivery. Although lactate has traditionally been interpreted as a marker of tissue hypoperfusion and oxygen debt, its elevation may also result from increased glycolytic activity, catecholamine stimulation, impaired hepatic clearance, pharmacological effects, and other mechanisms unrelated to global tissue hypoxia.¹

In the perioperative setting, the identification of patients at increased risk of postoperative complications remains a major clinical challenge. Conventional risk assessment relies predominantly on preoperative characteristics and intraoperative variables such as age, comorbidities, surgical complexity, blood loss, duration of surgery, hemodynamic instability, and transfusion requirements. However, these parameters do not always adequately capture the cumulative physiological burden experienced during a major surgical procedure. Biomarkers capable of integrating the metabolic consequences of intraoperative events may therefore provide complementary prognostic information.

Lactate is particularly attractive in this context because it is inexpensive, rapidly available, and routinely measured through arterial or venous blood gas analysis in patients undergoing major surgery. Evidence from major abdominal surgery has demonstrated an association between elevated lactate concentrations and postoperative morbidity. In one observational study, an

initial serum lactate concentration above 2.7 mmol/L was independently associated with postoperative complications after major abdominal surgery, even after adjustment for disease severity.² These findings support the concept that perioperative hyperlactatemia may identify patients who have experienced clinically relevant physiological stress during surgery.

Importantly, the timing of lactate measurement appears to influence its prognostic value. Studies evaluating lactate at the end of surgery have demonstrated particularly relevant associations with postoperative outcomes. In a large prospective study involving patients undergoing elective hepatectomy, an end of surgery arterial lactate concentration greater than 3 mmol/L independently predicted severe morbidity and 90 day mortality, while incorporation of this measurement into clinical prediction models substantially improved their accuracy.³ Similarly, studies of liver resection have demonstrated that elevated end of surgery lactate is associated with severe postoperative complications and appears to reflect reductions in oxygen delivery related to blood loss, anemia, prolonged surgery, and intraoperative ischemic events.⁴

The prognostic relevance of intraoperative lactate is not restricted to hepatic surgery. In cardiac surgery, an increase in lactate during the procedure, independent of the baseline concentration at induction, has been associated with mortality, prolonged intensive care unit stay, and postoperative renal failure requiring renal replacement therapy.⁵ These findings suggest that the dynamic change in lactate during surgery may provide additional prognostic information beyond a single absolute value. More recently, evidence from emergency noncardiac surgery has demonstrated a dose dependent, nonlinear association between peak intraoperative lactate and in-hospital mortality across different types of major emergency procedures, further supporting its potential role as an early risk marker.⁶

Nevertheless, the interpretation of intraoperative lactate remains challenging. Surgical trauma itself, adrenergic activation, administration of vasopressors, transient vascular occlusion, blood loss, transfusion, hypoxemia, impaired hepatic perfusion, and changes in oxygen delivery can all influence lactate concentrations. In addition, the relationship between



intraoperative lactate and postoperative outcomes may differ according to the type of surgery and the underlying organ function. A systematic review of perioperative lactate measurements in liver resection found consistent associations between elevated perioperative lactate and adverse outcomes, but substantial heterogeneity in sampling times, thresholds, and clinical endpoints prevented quantitative meta analysis and highlighted the need for standardized approaches.⁷

Therefore, although increasing evidence supports intraoperative lactate as a prognostic biomarker, important questions remain regarding the most informative measurement time, clinically meaningful thresholds, the importance of lactate trajectories compared with isolated measurements, and whether lactate provides independent prognostic information beyond established clinical and hemodynamic variables. The objective of this review is to examine the current evidence regarding intraoperative lactate as a predictor of complications in major surgery, focusing on its physiological basis, prognostic performance, interpretation according to surgical context, potential thresholds, limitations, and implications for perioperative risk stratification.

METHODS

Study Design

A narrative literature review was conducted to examine the current evidence regarding the role of intraoperative lactate as a predictor of postoperative complications in patients undergoing major surgery. The review focused on the physiological basis of intraoperative hyperlactatemia, its prognostic significance, the influence of measurement timing and lactate trajectories, and its association with postoperative morbidity, organ dysfunction, intensive care utilization, and mortality.

Evidence Selection

The literature search focused on studies evaluating serum or plasma lactate concentrations obtained during major surgical procedures or at the end of surgery and their association with postoperative outcomes. Priority was given to prospective and retrospective observational cohorts, systematic reviews, meta analyses, and clinical studies conducted in adult surgical populations.

Studies involving major abdominal, hepatic, cardiac, vascular, and emergency surgery were considered because these procedures frequently involve substantial physiological stress, alterations in oxygen delivery, blood loss, hemodynamic instability, or temporary impairment of organ perfusion. Studies evaluating exclusively postoperative lactate were considered when they provided relevant information for understanding the prognostic continuum between intraoperative and early postoperative hyperlactatemia.

The principal outcomes of interest were postoperative complications, severe morbidity, acute kidney injury, prolonged intensive care or hospital stay, need for organ support, and short and long term mortality. Particular attention was given to studies assessing absolute lactate concentrations, peak intraoperative values, changes in lactate during surgery, and measurements obtained at the end of the surgical procedure.

Because considerable heterogeneity exists among surgical populations, lactate sampling protocols, analytical thresholds, and definitions of postoperative complications, the available evidence was synthesized narratively rather than through a quantitative pooled analysis. The interpretation of lactate was considered within the clinical context of each surgical population, recognizing that hyperlactatemia may result from tissue hypoperfusion as well as non hypoxic mechanisms such as catecholamine mediated glycolysis, impaired hepatic clearance, pharmacological effects, and metabolic stress.

DEVELOPMENT

Physiological Basis of Lactate During Major Surgery

Lactate is a normal intermediate of cellular metabolism rather than merely a toxic by product of anaerobic glycolysis. Under physiological conditions, pyruvate generated through glycolysis is converted predominantly to acetyl-CoA and enters the tricarboxylic acid cycle; however, a proportion of pyruvate is continuously converted to lactate through lactate dehydrogenase. Lactate can subsequently be transported between tissues and used as an oxidative substrate, particularly by the heart, skeletal muscle, and other metabolically active organs. Consequently, an increase in circulating



lactate does not necessarily indicate tissue hypoxia, and its interpretation during major surgery requires consideration of both production and clearance.^{1,2}

The traditional interpretation of hyperlactatemia has centered on inadequate oxygen delivery and a shift toward anaerobic metabolism. During major surgery, this mechanism may become clinically important when hypotension, hemorrhage, anemia, low cardiac output, hypoxemia, regional ischemia, or impaired microcirculatory flow reduce oxygen delivery below tissue requirements. Under these circumstances, pyruvate accumulates and is increasingly converted to lactate, while reduced hepatic and renal perfusion may simultaneously impair lactate clearance. The resulting increase in circulating lactate may therefore represent an integrated marker of the physiological consequences of intraoperative hypoperfusion.³

However, perioperative hyperlactatemia is considerably more complex. Surgical stress activates the sympathetic nervous system and increases circulating catecholamines, particularly epinephrine. β_2 -adrenergic stimulation can accelerate glycolysis and increase pyruvate production beyond the oxidative capacity of mitochondria, leading to increased lactate generation even when oxygen delivery remains adequate.⁴ This phenomenon is particularly relevant during cardiac surgery and other procedures associated with marked neuroendocrine activation. Consequently, a high intraoperative lactate concentration should not automatically be interpreted as evidence of global tissue hypoxia.

This distinction has important implications for prognostic interpretation. Lactate may function less as a direct measurement of tissue oxygenation and more as an integrated biomarker reflecting the interaction between oxygen delivery, metabolic stress, catecholamine activity, regional perfusion, and organ specific clearance. The clinical value of the measurement therefore depends not only on its absolute concentration but also on its temporal behavior, the circumstances under which it was obtained, and the concurrent hemodynamic and metabolic variables.^{2,5}

Intraoperative Determinants of Hyperlactatemia

Several mechanisms operating simultaneously during major surgery can increase circulating lactate. The first is inadequate systemic oxygen delivery. Oxygen delivery depends principally on cardiac output and arterial oxygen content, which in turn are determined by hemoglobin concentration and arterial oxygen saturation. Significant blood loss, acute anemia, hypotension, reduced cardiac output, hypoxemia, or combinations of these factors may therefore generate an oxygen supply demand mismatch and promote lactate accumulation. This mechanism has been particularly well characterized in hepatic surgery, in which elevated end of surgery lactate has been associated with reductions in oxygen delivery during the procedure.⁶

The second major mechanism is increased metabolic production without necessarily occurring tissue hypoxia. Surgical trauma activates the adrenergic response and increases glycolytic flux. Catecholamine administration, particularly epinephrine, may further stimulate β_2 -adrenergic receptors and accelerate glycolysis, resulting in increased pyruvate and lactate generation.^{4,5} This mechanism is clinically relevant because vasopressor therapy may improve arterial pressure and systemic perfusion while simultaneously contributing to an increase in lactate. A rising lactate concentration should therefore be interpreted together with the dose and type of vasoactive agents being administered.

The third determinant is impaired lactate clearance. The liver is the principal organ responsible for lactate removal, with additional contributions from the kidneys and other tissues. Major hepatic surgery, reduced hepatic blood flow, temporary vascular occlusion, preexisting liver dysfunction, or extensive hepatic resection can therefore alter lactate kinetics.^{6,7} This is one reason why the same lactate concentration may have different prognostic implications in a patient undergoing hepatectomy compared with a patient undergoing another type of major abdominal operation.

Cardiac surgery introduces additional mechanisms. Cardiopulmonary bypass can modify systemic and regional perfusion, temperature, oxygen delivery, acid-base status, and substrate metabolism. Lactate production may increase in the myocardium, skeletal muscle,



lungs, and splanchnic circulation during cardiopulmonary bypass, while alterations in hepatic perfusion may simultaneously influence clearance.⁸ The resulting hyperlactatemia may therefore represent a combination of inadequate oxygen delivery and increased glycolytic activity rather than a single pathological process.

These mechanisms explain why the prognostic interpretation of intraoperative lactate should be contextual rather than binary. A lactate concentration of 4 mmol/L in a patient with severe hemorrhage, declining hemoglobin, reduced oxygen delivery, and escalating vasopressor requirements has a different clinical meaning from the same concentration in a hemodynamically stable patient receiving high dose epinephrine during cardiopulmonary bypass. The biomarker becomes more informative when integrated with the physiological events occurring during the operation.

Timing of Lactate Measurement and Prognostic Significance

The timing of lactate measurement is one of the most important methodological considerations when evaluating its predictive capacity. A single preoperative value primarily reflects the patient's baseline metabolic and physiological condition, whereas an intraoperative value incorporates the effects of anesthesia, surgical manipulation, blood loss, fluid administration, vasoactive therapy, ischemia, and changes in oxygen delivery. An end of surgery measurement therefore represents a cumulative signal of the physiological burden experienced during the procedure.

Evidence from hepatic surgery provides some of the clearest support for this concept. In a prospective study including 985 patients undergoing elective liver resection, arterial lactate measured at the end of surgery was independently associated with severe postoperative morbidity, a high Comprehensive Complication Index, and 90 day mortality. An end of surgery lactate concentration above approximately 3 mmol/L provided clinically meaningful discrimination, and incorporation of the measurement into predictive models improved their accuracy.³

Subsequent work has reinforced the association between end of surgery lactate and postoperative morbidity after hepatic resection. In a study evaluating

oxygen delivery during elective liver surgery, an end of surgery arterial lactate concentration above 5 mmol/L was associated with severe postoperative complications. Patients with higher lactate had longer procedures, greater blood loss, greater transfusion requirements, and more pronounced reductions in hemoglobin concentration and oxygen delivery. Multi-variable analysis identified the lowest intraoperative oxygen delivery and duration of surgery as major determinants of the end of surgery lactate concentration.⁶ These findings are important because they provide a physiological explanation for the prognostic association rather than simply demonstrating statistical correlation.

Nevertheless, evidence from liver surgery also demonstrates that postoperative measurements may outperform isolated intraoperative measurements. A systematic review of seven studies involving 2,573 patients undergoing liver resection found that perioperative lactate concentrations were consistently associated with adverse outcomes, but substantial heterogeneity in sampling strategies and endpoints prevented quantitative meta-analysis. The authors concluded that lactate appears to be a useful prognostic marker, while emphasizing that the strongest evidence was concentrated in the early postoperative period and that standardized thresholds remained uncertain.⁷

This distinction is relevant when defining the concept of intraoperative lactate as a predictor. The prognostic signal may not depend exclusively on the absolute value obtained during surgery. Rather, the trajectory from induction through the end of the procedure and into the early postoperative period may provide a more complete representation of the patient's physiological response. A patient whose lactate remains low or decreases despite major surgery may have a substantially different risk profile from one whose concentration progressively rises throughout the operation.

Dynamic Lactate Changes as a Prognostic Marker

Dynamic lactate assessment has emerged as a potentially more informative strategy than reliance on a single measurement. An increasing intraoperative concentration may indicate ongoing metabolic stress, persistent oxygen supply demand mismatch, inadequate



correction of blood loss, or progressive organ dysfunction. Conversely, stabilization or reduction may suggest restoration of adequate perfusion and metabolic recovery.

This concept has been particularly investigated in cardiac surgery. In a retrospective analysis of adults undergoing cardiac surgery, patients were categorized according to the magnitude of the increase in lactate between induction and the intraoperative period. Greater increases were associated with progressively worse outcomes. The group with the greatest lactate increase had substantially higher mortality, longer intensive care unit stays, and a higher incidence of postoperative renal failure requiring renal replacement therapy. Importantly, the increase in lactate remained a significant predictor after accounting for the baseline concentration, supporting the concept that lactate kinetics may contain prognostic information independent of the initial value.⁹

The importance of lactate trajectories is also supported by studies of major abdominal surgery. Although much of the available evidence focuses on the early postoperative period, serial measurements demonstrate that persistence of hyperlactatemia is more strongly associated with complications than an isolated value. In a prospective cohort of patients undergoing major elective abdominal surgery, lactate concentrations remained significantly higher among patients who developed postoperative complications, and both the time-weighted lactate concentration and lactate clearance during the first 24 hours were independently associated with postoperative morbidity.¹⁰

These findings suggest a clinically relevant distinction between transient hyperlactatemia and persistent hyperlactatemia. A transient increase may occur as a physiological consequence of surgical stress or catecholamine stimulation and subsequently resolve without major clinical consequences. In contrast, persistent elevation or progressive accumulation may indicate unresolved physiological abnormalities and therefore carry greater prognostic significance. This distinction should be incorporated into future perioperative risk models rather than relying exclusively on a single absolute threshold.

Lactate in Hepatic Surgery

Hepatic surgery represents one of the surgical settings in which the prognostic value of intraoperative lactate has been most extensively investigated. The liver is central to lactate clearance, and hepatectomy directly modifies both hepatic mass and hepatic blood flow. At the same time, liver surgery may involve prolonged procedures, vascular occlusion, blood loss, transfusion, and changes in systemic oxygen delivery, creating several mechanisms through which lactate may increase.^{6, 7}

The landmark prospective study by Vibert and colleagues demonstrated that end of surgery lactate was a powerful early predictor of postoperative outcome after elective hepatectomy. In the training cohort, lactate thresholds of approximately 3 mmol/L provided the best discrimination for high complication burden and 90 day mortality, while a threshold around 2.8 mmol/L was most informative for severe morbidity. Importantly, the predictive performance of clinical models improved when end of surgery lactate was incorporated, supporting its potential role as a complementary biomarker rather than merely a surrogate of baseline disease severity.³

The association appears to have a mechanistic basis. Patients with higher end of surgery lactate have been shown to experience greater reductions in oxygen delivery, greater blood loss, longer operative times, and higher transfusion requirements.⁶ Thus, intraoperative lactate may capture the cumulative physiological consequences of surgical events that are not fully represented by conventional postoperative variables.

At the same time, the interpretation of lactate following liver resection requires caution. A high concentration may reflect impaired clearance caused by reduced functional liver mass rather than persistent systemic hypoperfusion. Preexisting cirrhosis and diabetes may also influence postoperative lactate kinetics.⁷ Consequently, although lactate is prognostically useful in hepatic surgery, the same threshold cannot necessarily be extrapolated to other surgical populations.

Lactate in Cardiac Surgery

Cardiac surgery provides another important model for studying intraoperative lactate because



cardiopulmonary bypass produces profound alterations in perfusion, oxygen delivery, temperature, metabolism, and vascular tone. Hyperlactatemia during and after cardiac surgery has traditionally been interpreted as evidence of inadequate tissue perfusion; however, contemporary evidence demonstrates that its pathophysiology is multifactorial.^{5,8}

During cardiopulmonary bypass, lactate may increase because of inadequate oxygen delivery, low pump flow, anemia, tissue hypoperfusion, or regional ischemia. At the same time, catecholamine driven glycolysis, hypothermia and rewarming, changes in substrate metabolism, and pharmacological interventions may contribute to lactate production.^{5,8} The resulting concentration should therefore be interpreted alongside perfusion parameters rather than used as a standalone measure of oxygen debt.

Despite these limitations, the prognostic association is consistent. In adults undergoing cardiac surgery, an increase in intraoperative lactate has been associated with mortality, prolonged intensive care unit stay, and postoperative renal failure requiring renal replacement therapy.⁹ This observation is particularly relevant because the change in lactate, rather than simply the absolute concentration, was predictive of adverse outcomes.

Recent physiological perspectives further emphasize that lactate should be viewed as a metabolically active substrate and signaling molecule rather than solely as the end product of anaerobic metabolism.¹¹ This conceptual shift does not eliminate its prognostic value; rather, it reinforces the need to understand why lactate is elevated in each individual patient.

Lactate in Major Abdominal and Noncardiac Surgery

The prognostic value of lactate has also been examined in major abdominal surgery outside the hepatic setting. Initial postoperative lactate concentrations have been associated with postoperative morbidity, and serial measurements appear to improve prognostic discrimination. In patients undergoing major abdominal procedures, lactate concentrations were significantly higher among patients who subsequently developed complications, and an early postoperative concentration above

approximately 2.7 mmol/L was independently associated with morbidity after adjustment for physiological severity.¹²

Other prospective evidence demonstrates that the temporal behavior of lactate may be more informative than a single postoperative measurement. In a cohort of patients undergoing elective major abdominal surgery, the time weighted average lactate concentration during the first 24 hours was independently associated with overall and major complications, while greater lactate clearance was associated with a lower risk of major complications.¹⁰ Although these studies primarily evaluate the postoperative period, they provide important support for the concept that lactate kinetics should be considered when interpreting intraoperative values.

More recent studies have also extended the concept to emergency noncardiac surgery. In patients undergoing emergency operations, a higher peak intraoperative lactate has been associated with increased in-hospital mortality in a dose dependent and nonlinear manner.⁶ These findings are clinically relevant because emergency surgery differs substantially from elective surgery: patients frequently arrive with established physiological derangements, sepsis, trauma, hemorrhage, intestinal ischemia, or organ dysfunction. In this context, intraoperative lactate may represent both the preoperative disease burden and the additional physiological stress imposed by surgery.

Relationship Between Intraoperative Lactate and Postoperative Complications

The association between intraoperative lactate and postoperative complications is biologically plausible because the biomarker integrates several processes capable of producing organ injury. Persistent oxygen delivery deficits can promote cellular dysfunction, mitochondrial stress, endothelial injury, and inflammatory activation. When these processes are sufficiently severe or prolonged, they may contribute to acute kidney injury, respiratory failure, cardiovascular instability, hepatic dysfunction, prolonged intensive care requirements, and death.

However, lactate should not be interpreted as a direct mediator of these complications. Rather, it is primarily a marker of physiological disturbance. The elevation

may identify patients exposed to the same intraoperative processes that subsequently cause organ dysfunction. This distinction is essential because treating the lactate concentration itself is not necessarily equivalent to correcting the underlying pathological process.

The predictive value of lactate therefore appears strongest when it is incorporated into a broader physiological assessment. Hemoglobin concentration, arterial oxygen saturation, cardiac output, mean arterial pressure, vasopressor requirement, blood loss, temperature, acid base status, urine output, and other indicators of organ perfusion can help determine whether an elevated lactate reflects clinically significant oxygen delivery impairment or an alternative mechanism. In hepatic surgery, for example, the association between elevated lactate and postoperative morbidity is strengthened by concurrent evidence of reduced oxygen delivery and blood loss.⁶

Potential Lactate Thresholds and Their Clinical Interpretation

One of the major limitations of the literature is the absence of a universally applicable intraoperative lactate threshold. Different studies have reported different cutoffs depending on surgical population, sampling time, outcome definition, and analytical method. In elective liver surgery, end of surgery concentrations around 3 mmol/L have shown prognostic relevance in large cohorts, while other studies have identified thresholds above 5 mmol/L for severe morbidity.^{3,6}

These differences should not be interpreted as contradictions. A threshold of 3 mmol/L measured at the end of an uncomplicated elective hepatectomy is not necessarily equivalent to 3 mmol/L measured during cardiopulmonary bypass or emergency laparotomy. The baseline metabolic state, hepatic clearance, surgical duration, blood loss, vasoactive therapy, and expected physiological response differ substantially between procedures.

For this reason, the most clinically appropriate approach may be to interpret lactate according to trajectory and context rather than a universal cutoff. An increasing concentration, failure to normalize after correction of hemodynamic abnormalities, or persistent elevation at the end of a major operation may be more

concerning than a single moderately elevated measurement. Future studies should therefore prioritize validated dynamic models rather than attempting to identify a single threshold applicable to all surgical patients.

Integration With Perioperative Risk Stratification

The potential clinical value of intraoperative lactate lies in its ability to complement established risk assessment rather than replace it. Traditional models based on age, comorbidity, ASA classification, surgical complexity, physiological variables, and intraoperative events provide important information but may not fully capture the metabolic consequences of those events. Lactate can potentially serve as a biological readout of the cumulative physiological stress imposed by surgery.

This is particularly relevant at the end of major procedures. A patient with substantial blood loss, prolonged surgery, vasopressor requirements, and an elevated end of surgery lactate may warrant closer postoperative monitoring than a patient with similar demographic characteristics but stable lactate kinetics and preserved physiological parameters. In this context, lactate could contribute to decisions regarding postoperative intensive care admission, frequency of laboratory monitoring, hemodynamic surveillance, and early assessment for organ dysfunction. Evidence from hepatic surgery specifically suggests that end of surgery lactate may help identify patients requiring critical care.³

Nevertheless, the use of lactate as a trigger for intervention must be approached cautiously. An elevated concentration should prompt investigation of its cause rather than automatic administration of fluids or vasoactive agents. Excessive fluid administration in a patient whose lactate elevation results primarily from catecholamine mediated glycolysis or impaired hepatic clearance may produce harm without addressing the underlying mechanism. Conversely, failure to recognize a rising lactate in a patient with ongoing hemorrhage or inadequate oxygen delivery may delay correction of a potentially reversible cause.

The most rational clinical model is therefore lactate-guided physiological assessment rather than lactate directed treatment. Serial measurements can identify trends, while concurrent evaluation of perfusion,



oxygen delivery, hemoglobin, blood loss, cardiac function, vasoactive requirements, and organ function can establish whether the lactate elevation represents a clinically actionable abnormality.

Limitations of Lactate as an Intraoperative Biomarker

Despite its potential, several limitations prevent intraoperative lactate from being considered a definitive predictor of postoperative complications. First, there is substantial heterogeneity in the timing and frequency of measurements across studies. Some investigations use a single value at the end of surgery, whereas others evaluate serial intraoperative concentrations or combine intraoperative and postoperative measurements. This heterogeneity makes direct comparison difficult and limits the ability to establish standardized thresholds.⁷

Second, surgical populations are highly heterogeneous. The determinants of lactate during liver resection are not identical to those during cardiac surgery, vascular surgery, trauma, or emergency abdominal procedures. A universal cutoff may therefore have limited clinical applicability.

Third, lactate is affected by several non hypoxic mechanisms. Catecholamine exposure, hepatic dysfunction, pharmacological agents, metabolic disorders, and changes in regional perfusion can all increase circulating lactate.^{4,5} Consequently, hyperlactatemia should not be equated automatically with global tissue hypoxia.

Fourth, the relationship between lactate and outcomes may be confounded by disease severity. Patients who develop severe intraoperative instability are more likely to have high lactate concentrations and are also more likely to develop postoperative complications. Although multivariable analyses have demonstrated independent associations in several studies, residual confounding remains possible.

Finally, most available evidence is observational. Although the prognostic association between intraoperative lactate and adverse outcomes is increasingly consistent, there is insufficient evidence to establish that using lactate prospectively to guide intraoperative interventions improves outcomes. Future

interventional studies are therefore required to determine whether lactate-guided hemodynamic optimization can translate prognostic information into improved clinical outcomes.

Future Directions

Future research should move beyond the simple question of whether intraoperative lactate predicts complications and focus on how lactate should be measured and integrated into clinical decision making. Prospective multicenter studies should establish standardized sampling points, ideally including baseline, key intraoperative milestones, end of surgery, and early postoperative measurements. Such designs would allow investigators to determine whether absolute lactate concentrations, rate of increase, peak concentration, or lactate clearance provides the strongest prognostic information.

Another important direction is the development of multimodal prediction models incorporating lactate with oxygen delivery, hemodynamic variables, blood loss, hemoglobin concentration, vasopressor exposure, surgical duration, and markers of organ function. This approach is likely to be more clinically meaningful than using lactate as an isolated biomarker because its interpretation is intrinsically dependent on physiological context.

Emerging technologies may further expand the role of lactate monitoring. Continuous or near continuous lactate monitoring could theoretically allow detection of rapid metabolic changes during high risk procedures, although this remains an evolving field and requires validation before routine clinical application. Recent reviews in cardiac surgery have highlighted growing interest in continuous lactate monitoring and a more sophisticated interpretation of lactate as a metabolic substrate, shuttle, and signaling molecule.¹¹

Ultimately, the most important question is not whether lactate rises during major surgery, but whether its trajectory identifies a modifiable physiological disturbance. If future studies demonstrate that early recognition of clinically significant hyperlactatemia followed by targeted correction of the underlying cause reduces postoperative morbidity, intraoperative lactate could become an important component of precision



perioperative medicine. Until such evidence is available, its principal role should remain that of a readily accessible prognostic biomarker that complements, rather than replaces, comprehensive clinical assessment.

DISCUSSION

The available evidence supports the concept that intraoperative lactate is a clinically relevant prognostic biomarker in patients undergoing major surgery, but its interpretation requires considerably greater nuance than the traditional association between hyperlactatemia and tissue hypoxia. Across different surgical populations, elevated lactate concentrations during surgery or at the end of the procedure have been consistently associated with postoperative morbidity, organ dysfunction, prolonged intensive care utilization, and mortality.^{3,5,6,9} However, the strength and meaning of this association vary according to the type of procedure, timing of measurement, baseline physiological condition, and mechanisms responsible for lactate accumulation.

One of the most important findings emerging from the literature is that lactate kinetics may be more informative than an isolated concentration. An increasing intraoperative lactate concentration can reflect ongoing physiological stress, whereas stabilization or subsequent clearance may indicate recovery from a transient metabolic insult. This distinction is particularly relevant in cardiac surgery, where the magnitude of lactate increase during the operation has been associated with mortality, prolonged intensive care stay, and renal replacement therapy.⁹ Similarly, studies of major abdominal surgery suggest that persistent hyperlactatemia and impaired lactate clearance are more strongly associated with adverse outcomes than a single elevated value.¹⁰ Thus, serial assessment may provide a more comprehensive representation of perioperative physiological burden.

The evidence from hepatic surgery is particularly compelling because it provides a strong association between an end of surgery lactate concentration and clinically relevant postoperative outcomes.^{3,6} The prognostic signal in this population is biologically plausible because hepatectomy simultaneously exposes

patients to blood loss, alterations in oxygen delivery, prolonged operative time, changes in hepatic perfusion, and a reduction in functional hepatic mass. Lactate therefore reflects not only systemic oxygen imbalance but also the capacity of the liver to clear the metabolite. This makes liver surgery an important model for understanding the prognostic potential of intraoperative lactate, but it also demonstrates why thresholds derived from one surgical population should not automatically be extrapolated to another.

A central issue is that lactate is not synonymous with anaerobic metabolism. Catecholamine mediated stimulation of glycolysis can produce substantial lactate elevations despite preserved systemic oxygen delivery.^{4,5} This phenomenon is especially important in patients receiving epinephrine or undergoing procedures characterized by intense adrenergic activation. Therefore, an elevated intraoperative lactate should trigger a search for its mechanism rather than an automatic assumption of global tissue hypoperfusion. Hemorrhage, anemia, hypotension, low cardiac output, hypoxemia, and impaired regional perfusion remain important causes, but medication effects and metabolic activation must also be considered.

This distinction has direct implications for clinical practice. If lactate is interpreted as an isolated surrogate of hypoperfusion, there is a risk of inappropriate interventions, particularly excessive fluid administration or escalation of vasoactive therapy without identifying the underlying cause. Conversely, dismissing an elevated lactate as merely a consequence of surgical stress may delay recognition of ongoing hemorrhage, inadequate oxygen delivery, or organ dysfunction. The most appropriate approach is therefore to interpret lactate within a multidimensional physiological framework, integrating hemodynamic parameters, hemoglobin concentration, blood loss, oxygenation, vasopressor requirements, urine output, acid-base status, and evidence of organ dysfunction.

Another important consideration is the heterogeneity of reported lactate thresholds. Values around 3 mmol/L have demonstrated prognostic relevance at the end of elective liver surgery, whereas higher thresholds have been reported for severe morbidity in other cohorts.^{3,6} This variability indicates that a universal intraoperative



cutoff is unlikely to adequately characterize risk across all major surgical procedures. Rather than defining a single value as pathological, future risk models should probably incorporate the patient's baseline concentration, the magnitude and rate of lactate increase, the peak value, and the degree of subsequent clearance.

The distinction between prognostic association and clinical utility is also critical. Current evidence demonstrates that intraoperative lactate identifies patients at higher risk, but this does not establish that lactate-guided interventions improve outcomes. Most available studies are observational, and patients with elevated lactate are inherently more likely to have experienced severe surgical stress, hemorrhage, hemodynamic instability, or organ dysfunction. Lactate may therefore function primarily as a marker of the severity of an underlying process rather than an independent causal determinant of complications. Before lactate can be incorporated into standardized treatment algorithms, prospective interventional studies are needed to determine whether acting on its trajectory changes postoperative outcomes.

Nevertheless, its practical characteristics make lactate particularly attractive for perioperative risk stratification. It is rapidly available, relatively inexpensive, routinely obtained in many high-risk operations, and capable of providing information before postoperative complications become clinically evident. In this regard, its greatest potential may be at the transition between the operating room and postoperative care. An elevated or progressively increasing end of surgery lactate could identify patients who require more intensive hemodynamic surveillance, closer assessment of organ function, or admission to a higher level of postoperative monitoring.³

Overall, the current evidence supports a contextual and dynamic interpretation of intraoperative lactate. Its prognostic value is strongest when it is considered as an integrated marker of metabolic and physiological stress rather than as a direct measurement of tissue hypoxia. The future role of lactate will likely depend on combining its trajectory with established clinical variables and other biomarkers in multimodal perioperative prediction models. Such an approach could transform lactate from a descriptive laboratory

abnormality into a clinically useful component of individualized perioperative risk assessment.

CONCLUSION

Intraoperative lactate is a promising prognostic biomarker in patients undergoing major surgery and is consistently associated with an increased risk of postoperative complications, organ dysfunction, prolonged critical care requirements, and mortality. Its predictive value appears particularly relevant when lactate is measured at the end of surgery or evaluated dynamically throughout the procedure. However, lactate should not be interpreted as an isolated marker of tissue hypoperfusion because its concentration is influenced by multiple factors, including oxygen delivery, blood loss, catecholamine activation, vasoactive medications, hepatic clearance, and the type and duration of surgery. The available evidence therefore supports a contextual, serial interpretation of lactate rather than reliance on a universal cutoff. Integration of intraoperative lactate kinetics with hemodynamic variables, surgical characteristics, and markers of organ function may improve perioperative risk stratification and facilitate earlier identification of patients requiring intensified postoperative monitoring. Nevertheless, further prospective and interventional studies are required to establish standardized measurement strategies and determine whether lactate guided management can translate its prognostic value into improved clinical outcomes.

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HOW TO CITE: Esteban Diaz Rivadeneira, Javier Tuiran Alvarez, Ana Carranza Montiel, Julian Amaya Perez, Jhon Alvarez Molina, Alder Gomez Angulo, Intraoperative Lactate as a Predictor of Complications in Major Surgery, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 10, 3109-3120. <https://doi.org/10.5281/zenodo.23525260>

