Original Article

Estimation of blood lactate and bicarbonate levels after stored blood transfusion to predict ICU admission in patients undergoing major head and neck surgeries: A prospective observational study

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Abstract

Background and Aims: Major head neck surgeries are often associated with major blood loss requiring blood transfusion. However, in spite of transfusion, patients usually suffer adverse postoperative outcomes. Biomarkers can help in identifying such events early. This observational study was conducted to compare blood lactate and bicarbonate levels as predictors of adverse postoperative outcomes.

Materials and Methods: Forty-eight adult American Society of Anesthesiologists Physical Status I–III patients met the inclusion criteria. Intraoperative blood loss was managed with stored blood transfusion as per transfusion trigger. Blood lactate and bicarbonate levels were measured preoperatively (Tbas), at the immediate postoperative period (T0), and at 8 h (T8), 16 h (T16), and 24 h (T24) postoperatively. Outcomes such as need for intensive care unit (ICU) admission, length of ICU stay, intraoperative blood transfusion, re-exploration rate, and mortality were recorded.

Results: Blood transfusions and ICU admissions were required in 19 (39.6%) and 24 (50%) patients, respectively. Lactate levels of patients requiring blood transfusion and admission to ICU rose significantly from their baseline (1.30 \pm 0.41 mmol/l) to 2.80 \pm 1.14 mmol/l at the immediate postoperative period, which fell to 2.06 \pm 0.78 mmol/l at 24 h postoperatively, compared to other patients who did not require transfusion and ICU admission (P < 0.001). The bicarbonate value did not show any significant change from its baseline (22.68 \pm 1.83 mEq/l) at all time points (P = 0.8). In addition, no significant difference was noted regarding ICU admissions (P = 0.659) or blood transfusions (P = 0.788).

Conclusions: Following major head and neck surgeries, blood lactate level is a good predictor, but bicarbonate is a poor predictor of the need for blood transfusions and ICU admission. Intraoperative blood transfusion failed to prevent rise in blood lactate level, which is taken as a surrogate marker of tissue hypoxia.

Keywords: Blood lactate, blood transfusion, head and neck surgery, ICU admission, tissue hypoxia

Introduction

The highly vascular anatomy of the head and neck region poses a high risk for significant blood loss during major head and neck surgeries, and it is especially true for oncological

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surgeries. [1] Excessive blood loss encountered during head and neck surgeries could lead to adverse postoperative outcomes such as prolonged intensive care unit (ICU) stay, need for blood transfusions, and even mortality. [2,3] The incidence of allogenic blood transfusions during the perioperative period

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has been reported to be as high as 84%.[2] Although the purpose of blood transfusion is to achieve better oxygen delivery and to improve tissue oxygenation, the ability of stored blood to effectively deliver oxygen to target tissues is a matter of debate.^[4] During the initial hours of blood transfusion, the transfused blood (red blood cells [RBCs]) does not serve as an effective oxygen delivery system. Hence, the tissue may remain in an oxygen-deprived state. Therefore, transfused blood may, in fact, be serving only as volume replacement during the initial hours of transfusion. It is, therefore, important to know the presence and severity of tissue hypoxia, so that appropriate measures can be taken in time. In light of the scientific background, several biomarkers such as lactate, base deficit, blood pH, albumin-corrected anion gap, and bicarbonate have been used as surrogate markers of tissue hypoxia. [5-10] All these surrogate markers of tissue hypoxia have their own sensitivity and specificity either alone or in combination. Some studies have shown that blood lactate and base deficit not only predict tissue hypoxia more accurately than any other marker, [9,11-13] but also predict adverse postoperative outcomes following major surgeries.[12,14-17] However, the best biomarker to predict tissue hypoxia remains a matter of debate.

Bicarbonate, a component of the acid buffer system, is a part of the routine blood chemistry panel and can be assessed using a venous sample. It could serve as a useful surrogate for arterial blood gas analysis, especially in settings where technical and human expertise are lacking. [10,18,19] With the above hypothesis and the questionable ability of stored blood to effectively deliver oxygen to the target tissues, we conducted this study to know whether surrogate markers such as blood lactate and bicarbonate levels are able to predict adverse postoperative outcomes following major head and neck surgeries. We also aimed to know whether intraoperative stored blood transfusions do have any effect on the levels of blood lactate and bicarbonate, which are taken as surrogate markers of tissue hypoxia.

Material and Methods

After obtaining ethical clearance from the Institutional Ethics Committee (AIIMS/IEC/21/299), this study was enrolled in the Clinical Trial Registry of India (CTRI/2021/07/035103). This tertiary care hospital-based prospective, observational, nonrandomized study was conducted from June 2021 to August 2022. Written informed consent was obtained from all patients. The date of the first patient enrollment was August 3, 2021. All adult patients of American Society of Anesthesiologists Physical Status I–III who were posted for elective major head and neck surgery from the Department

of Head and Neck Oncology and ENT during the study period were included. These surgeries included^[14] total laryngopharyngectomy, total laryngectomy, Commando operation, total thyroidectomy, maxillectomy, etc. Patients who were critically ill, patients on ionotropic support, patients with hepatic dysfunction, chronic airway diseases, or chronic kidney disease, and patients on hepatotoxic or nephrotoxic drugs were excluded. The primary outcome variable of this study was determination of blood lactate and bicarbonate levels for predicting ICU admission. The secondary outcome was to determine whether intraoperative allogenic blood transfusion requirement had any effect on blood lactate and bicarbonate levels, need for re-exploration, and mortality after major head and neck surgeries. The criteria for ICU admission were taken from the study of Stretch and Shepherd^[20] and National Early Warning Score (NEWS) with its recent modification, the NEWS-2 criteria. [21] NEWS-2 uses physiological parameters such as respiration rate, oxygen saturation (SpO₂), systolic blood pressure, pulse rate, level of consciousness or new confusion, temperature, and requirement of supplemental oxygen (yes/no). As per NEWS thresholds and triggers, clinical risk stratification was classified as low (score 0-4), lowmedium (red score, a score of 3 in any individual parameter), medium (score 5-6), and high (a score of 7 and above). A score of 3 in any individual parameter or a cumulative score of 5–6 in more than one parameter was taken as the criterion for ICU admission. Taking the primary outcome variable into account, [14] the sample size was calculated to be 48 with 24 ICU and 24 non-ICU admissions, assuming area under the curve (AUC) to be 0.7 at 80% power with the level of significance at 0.05. However, assuming a dropout rate of 5%, we recruited 50 patients, of whom one patient was excluded due to intraoperative change in surgical plan and another patient suffered cardiac arrest during surgery, hence surgery was abandoned tand the patient was transferred to coronary care unit for further management. Anesthesia induction and maintenance were as per the institutional standard protocol for all patients. Intraoperatively, in all patients, continuous monitoring was done for heart rate, invasive blood pressure, central venous pressure (CVP), SpO2, temperature, end-tidal carbon dioxide, and urine output. However, these values were noted at the time of induction and post-induction every 5 min till 30 min, every 15 min till 2 h, and every 30 min till the end of surgery. Arterial blood samples were measured for baseline hemoglobin, blood lactate, and bicarbonate levels before the surgery (Tbas), at the immediate postoperative period (T0), and at 8 h (T8), 16 h (T16), and 24 h (T24) postoperatively.

The inferior vena cava collapsibility index was taken as a guide for the preoperative volume status of patients. Administration of intravenous fluid was started using crystalloids with an intraoperative target CVP between 8 and 10 cmH₂O, with the exclusion of positive end-expiratory pressure. Maximum allowable blood loss (MABL) was calculated using the patient's estimated blood volume and hematocrit. A fall in hematocrit value of more than 25% from baseline was taken as a transfusion trigger, and blood loss was replaced with stored packed red blood cells (PRBCs). Intraoperative total blood loss, number of units of blood transfused, total crystalloid fluids, and total operative time were noted. Postoperative outcomes such as the need for ICU admission as per the criteria, length of ICU stay, blood transfusion requirements, re-exploration surgeries, and mortality were also recorded.

Statistical analysis

The statistical analysis was carried out using the IBM Statistical Package for the Social Sciences (SPSS®) version 24 software. Shapiro-Wilk normality test was applied to identify normally distributed variables. Normally distributed continuous variables (such as age, height, weight, body mass index, hemoglobin, blood lactate, and bicarbonate levels) were expressed as mean and standard deviation. Non-normally distributed variables and categorical variables (operation time, amount of blood loss, blood transfusion) were expressed as median and interquartile range. Binary variables (gender, ICU admission/nonadmission) were expressed as absolute numbers and proportions. Results were analyzed using Chi-square tests for categorical variables and independent t-test for numerical variables. The correlation was analyzed using Pearson correlation. The specificity of blood lactate and bicarbonate levels as a cutoff for ICU admission was evaluated using the receiver operating characteristic (ROC) curve analysis, which was judged by AUC and prediction using bivariate logistic regression analysis. P value < 0.05 was considered statistically significant.

Results

The characteristics of the study population are presented in Table 1. Forty-eight adult patients who underwent major head and neck surgeries fulfilled the inclusion criteria. Majority of the patients (72.9%) were males. The mean age of the study population was 43.44 ± 10.73 years. The mean duration of anesthesia and surgery was 6.49 ± 2.79 and 6.09 ± 2.73 h, respectively. The mean blood loss during surgery was 613.33 ± 370.74 ml. Twenty-eight (58.3%) of the 48 patients underwent surgeries associated with higher blood loss, such as total laryngectomy, maxillectomy, and commando operation. These surgeries encountered an average blood loss of 701.14 ± 335.85 ml, and the rest of the surgeries had an average blood loss of 482 ± 368.13 ml. Of all the patients, 19 (39.6%) patients required allogeneic blood

transfusions. PRBCs were used for transfusions. Surgeries with higher blood loss utilized a median of 1 unit of PRBC (range 1–3), whereas those with lesser blood loss utilized a median of 0 units of PRBC (range 0–3). Many of the patients encountered blood loss within the range of MABL, and hence, no blood was transfused. ICU admission was needed in 24 (50%) patients, and the mean duration of ICU stay was 2.29 ± 1.23 days. The mean duration of hospital stay for all the patients was 10.21 ± 6.81 days. There was a significant association between those who received intraoperative blood transfusions and those who were eventually admitted to the ICU (P < 0.001) [Table 2]. None of the patients underwent surgical re-exploration. No mortality was encountered in the study.

The baseline blood lactate value of the participants was 1.30 ± 0.41 mmol/l, with a peak of 2.80 ± 1.14 mmol/l at the immediate postoperative period, which reduced to 2.06 ± 0.78 mmol/l at 24 h postoperatively [Table 3]. This change in lactate value over time was statistically significant (P < 0.001). There was a significant increase in blood lactate levels with a peak value of 3.92 ± 0.66 mmol/l

Table 1: Baseline characteristics of the study groups (n=48)

Basic details	Values		
Age in years (mean±SD)	43.44±10.73		
Gender, n (%)			
Male	35 (72.9%)		
Female	13 (27.1%)		
Weight in kg, mean±SD	60.02 ± 7.50		
Hemoglobin, mean±SD	13.45 ± 0.8		
ASA status, n (%)			
I	11 (22.9%)		
II	32 (66.7%)		
III	5 (10.4%)		
Anesthesia duration in hours, mean±SD	6.49 ± 2.79		
Surgical duration in hours, mean±SD	6.09 ± 2.73		
Blood loss in ml, mean±SD	613.33±370.74		
Patients requiring blood transfusions, n (%)	19 (39.6%)		
Duration of ICU stay in days, mean±SD	2.29 ± 1.23		
Duration of hospital stay in days, mean±SD	10.21 ± 6.81		
Mortality, n (%)	0 (0)		

ASA=American Society of Anesthesiologists, ICU=intensive care unit, SD=standard deviation

Table 2: Association between intraoperative blood transfusion and ICU admission (*n*=48)

	ICU adı	Total		
	Yes	No		
Blood transfusion				
Yes	18	1	19	
No	6	23	29	
Total	24	24	48	

Chi-square value- 25.176, P<0.001. ICU=intensive care unit

and 3.78 ± 0.75 mmol/l in patients for whom blood was transfused and in patients who required ICU admission, respectively, compared to those who did not. This increase in blood lactate value was significant at all time points, that is, at the immediate postoperative period and at 8, 16, and 24 h postoperatively (P < 0.001) [Table 4, Figure 1]. ROC curve analysis also revealed that lactate levels at each of the time points were predictive of the need for blood transfusions and ICU admissions (P < 0.001).

The baseline blood bicarbonate level of all the participants was 22.68 ± 1.83 mEq/l. There was no significant change in bicarbonate levels at each of the time points [Table 3]. Bicarbonate levels were not significantly different in those requiring blood transfusions or ICU admission compared to those who did not, at each of the time points [Table 5, Figure 2]. The change in bicarbonate levels over time in those requiring blood transfusions or ICU admission was also not found to be significant (P = 0.788 and 0.659, respectively). ROC curve analysis revealed that bicarbonate levels at each of the time points were not predictive of the need for blood transfusions or ICU admission.

Discussion

Major head and neck surgery carries a substantial risk to patients, which is largely attributed to significant blood loss, particularly in cases involving cancer-related procedures. In such surgeries, substantial blood loss often necessitates the use of allogeneic blood transfusions. The main objective behind blood transfusions in these cases is to ensure sufficient oxygenation of tissues, thereby averting tissue hypoxia. Nonetheless, despite receiving allogeneic blood, patients may still face unfavorable postoperative consequences, including prolonged stays in the ICU, continued requirement for blood transfusions, and, in severe cases, mortality.

In this observational study, all patients who underwent elective major head and neck surgery for various reasons were comparatively younger, with an average age of 43.44 ± 10.73 years. Following surgery, half of the participants required postoperative ICU admission, with an average duration of 2.29 \pm 1.23 days in the ICU and 10.21 \pm 6.81 days in the hospital. This study bears some similarities to the research conducted by Ibrahim and Ahmed, [14] although their study encompassed a larger sample size and an older mean age $(64.4 \pm 9.2 \text{ years})$, resulting in a more prolonged ICU stay compared to ours. They also noted extended durations of ICU and hospital stays, averaging 3.2 ± 1.2 and 19.3 ± 5.5 days, respectively. The variance in ICU and hospital stay between our study and theirs could be attributed to the fact that our participants were notably younger, potentially possessing greater physiologic resilience to adverse conditions, thus leading to shorter stays in the ICU and hospital.

Table 3: Change in blood lactate (mmol/l) and bicarbonate (mEq/l) levels over time (n=48)

Timepoint Serum lactate		Repeated me	easures ANOVA	Serum bicarbonate (mEq/l) Mean (SD)	Repeated measures ANOVA	
(mmol/l) Mean (SD)	F	P	F		P	
Baseline	1.30 (0.41)	5.5	< 0.001	22.68 (1.83)	0.8	0.531
Immediate postoperative	2.80 (1.14)			22.36 (2.85)		
8 h postoperative	2.64 (1.02)			22.62 (2.31)		
16 h postoperative	2.34 (0.84)			22.28 (1.72)		
24 h postoperative	2.06 (0.78)			21.82 (1.73)		

ANOVA=analysis of variance, SD=standard deviation

Table 4: Comparison of patients requiring ICU stay and blood transfusions versus those who did not require transfusion in terms of change in lactate over time (n=48)

Lactate levels Timepoint	Blood transfusion Mean (SD) mmol/l		P for comparison of the two groups	ICU admission Mean (SD) mmol/l		P for comparison of the two groups
	Yes	No	at each of the timepoints ^a	Yes	No	at each of the timepoints ^a
Baseline	1.36 (0.60)	1.26 (0.22)	0.915	1.34 (0.54)	1.26 (0.24)	0.992
Immediate postoperative	3.92 (0.66)	2.07 (0.71)	< 0.001	3.78 (0.75)	1.82 (0.33)	< 0.001
8 h postoperative	3.60 (0.62)	2.01 (0.68)	< 0.001	3.48 (0.67)	1.80 (0.47)	< 0.001
16 h postoperative	3.08 (0.63)	1.86 (0.55)	< 0.001	3.01 (0.63)	1.68 (0.35)	< 0.001
24 h postoperative	2.77 (0.61)	1.59 (0.46)	< 0.001	2.64 (0.61)	1.48 (0.41)	< 0.001
<i>P</i> for change in serum lactate over time within each group ^b	< 0.001	<0.001		<0.001	<0.001	
Overall P for comparison of change in serum lactate over time between the two groups ^c	<0.	.001		<0	.001	

ICU=intensive care unit, SD=standard deviation. aWilcoxon-Mann-Whitney test. Friedman test. Generalized estimating equations

Table 5: Comparison of patients requiring ICU stay and blood transfusions versus those who did not require transfusion in terms of change in serum bicarbonate over time (n=48)

Bicarbonate levels Timepoint	Blood transfusion Mean (SD) mEq/l		P for comparison of	ICU admission Mean (SD) mEq/l		P for comparison of
	Yes	No	the two groups at each of the timepoints ^a	Yes	No	the two groups at each of the timepoints ^a
Baseline	22.57 (2.01)	22.74 (1.73)	0.719	22.46 (1.87)	22.89 (1.80)	0.326
Immediate postoperative	22.38 (3.90)	22.34 (1.97)	0.486	21.94 (3.46)	22.77 (2.08)	0.091
8 h postoperative	22.86 (3.00)	22.47 (1.77)	0.891	22.50 (2.76)	22.75 (1.82)	0.297
16 h postoperative	22.61 (1.94)	22.07 (1.57)	0.229	22.30 (1.85)	22.26 (1.63)	0.901
24 h postoperative	22.06 (2.00)	21.66 (1.56)	0.768	21.60 (1.87)	22.04 (1.60)	0.200
<i>P</i> for change in serum bicarbonate over time within each group ^b	0.561	0.091		0.237	0.119	
Overall <i>P</i> for comparison of change in serum bicarbonate over time between the two groups ^c	0.788			0.6	559	

ICU=intensive care unit, SD=standard deviation. aWilcoxon-Mann-Whitney test. Friedman test. Generalized estimating equations

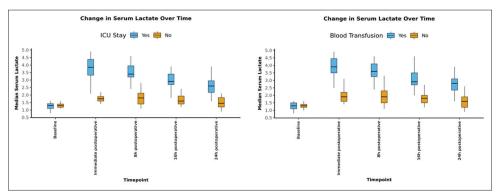


Figure 1: Box and Whisker plot depicting the distribution of serum lactate over different timepoints with respect to ICU stay and blood transfusion. ICU = intensive care unit

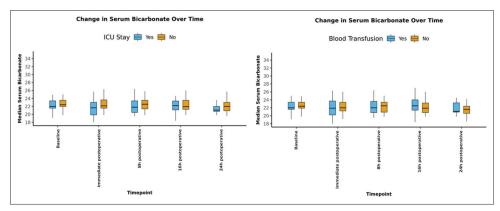


Figure 2: Box and Whisker plot depicting the distribution of serum bicarbonate over different timepoints with respect to ICU stay and blood transfusion. ICU = intensive care unit

Blood loss in head and neck surgery varies with the type and complexity of the operation. In our study, the mean intraoperative blood loss was 613.33 ± 370.74 ml. Among 48 patients, 19 needed allogeneic blood transfusions perioperatively. This contrasts the results of Weber, ^[2] who found a median blood loss of 144.5 ml (range: 0-1600 ml), with 11.7% of 438 patients needing transfusions. Higher blood loss in our study is likely due to a larger proportion (58.3%) of surgeries with high blood loss, such as maxillectomies, total laryngectomies, and

commando operations, averaging 701.14 ± 335.85 ml, compared to other procedures averaging 482 ± 368.13 ml.

In our study, serum lactate and bicarbonate levels were monitored to predict adverse postoperative outcomes, such as ICU admission, and as an indirect measure of tissue hypoxia. The mean serum lactate increased significantly from baseline (1.30 \pm 0.41 mmol/l) to a peak of 2.80 \pm 1.14 mmol/l immediately after surgery and then decreased to 2.06 \pm 0.78 mmol/l at 24 h postoperatively.

This decline suggests maximal tissue hypoxic stress during the immediate postoperative period, which is gradually alleviated by resuscitative measures within the following 24 h. Contrarily, Ibrahim and Ahmed^[14] noted peak serum lactate levels at 16 h postsurgery, which was particularly elevated in nonsurvivors, with no decrease found by 24 h. In our study, the absence of mortality, a younger population, and fewer patients needing blood transfusions may have contributed to the earlier decline in lactate levels. Conversely, serum bicarbonate, with a baseline mean of 22.68 \pm 1.83 mEq/l, decreased nonsignificantly to 21.82 mEq/l at 24 h postoperatively (P = 0.531). This indicates that serum bicarbonate is an unreliable marker for detecting tissue hypoxia in major head and neck surgery patients.

Among the 48 participants, 19 (39.6%) received intraoperative allogeneic blood transfusions. Their mean blood lactate levels peaked at 3.92 ± 0.66 mmol/l immediately after surgery and then declined to 2.77 mmol/l at 24 h postsurgery. Notably, transfused patients exhibited significantly higher lactate elevations compared to nontransfused counterparts (P < 0.001). This suggests that intraoperative transfusions failed to normalize lactate levels. Conversely, there was no significant difference in serum bicarbonate changes between transfused and nontransfused patients (P = 0.788). No patients required surgical re-exploration.

There was a significant association between those patients who received intraoperative allogeneic blood transfusions and those who were eventually admitted to the ICU (P < 0.001). The mean lactate levels in patients who required ICU admission (24, 50%) rose to a peak of 3.78 ± 0.75 mmol/l immediately after surgery and declined to 2.64 ± 0.61 mmol/l after 24 h. These levels were markedly higher compared to those not requiring ICU admission (P < 0.001). Shrestha et al. [22] found that elevated venous lactate levels (>2 mmol/;) at admission were predictive of ICU admissions, need for blood transfusions, and endoscopies. Likewise, in our current study, all patients meeting the previously discussed ICU admission criteria exhibited serum lactate levels of 3.78 ± 0.75 mmol/l immediately after surgery, which decreased to 2.64 ± 0.61 mmol/l after 24 h. Therefore, elevated serum lactate levels can be considered a reliable predictor of ICU admission. Apart from head and neck surgery, the utility of lactate levels in predicting adverse postoperative outcomes across many other kinds of surgeries has been well studied. [16,17,22] Murtuza et al. [16] found that the failure of blood lactate levels to decrease below 6.76 mmol/l within 24 h after surgery was the most specific indicator for predicting mortality. However, none of our patients exhibited such elevated lactate levels, and consequently, there were no instances of mortality. In contrast to blood lactate, we did not observe any statistically significant difference in serum bicarbonate levels between patients requiring ICU admission and those who did not (P = 0.659). Consequently, serum bicarbonate level was not a reliable predictor of ICU admission. However, the optimal predictor for accurately anticipating the necessity for ICU admission, morbidity, and mortality in postsurgical patients remains a subject of debate.

Studies indicate that the current blood banking procedure may not fully maintain the functions of RBCs during storage, potentially reducing their oxygenation capacity over time. After an *in vivo* transfusion of stored blood, its function usually starts to recover within several hours and may take even up to 72 h to reach the normal level. [4,23] We observed in our study that allogenic transfusion of stored blood during the intraoperative period failed to prevent the rise in serum lactate, which is considered to be an indirect evidence of tissue hypoxia. Therefore, we can say that allogenic transfusion of stored blood usually acts only as volume replacement and its effectiveness in oxygen delivery at the tissue level during the initial hours of transfusion is doubtful.

Limitations

The current study has some limitations. Firstly, our research did not intend to establish a correlation between the storage duration of transfused blood and the levels of surrogate biomarkers. In addition, we did not request blood from the blood bank with matching storage durations due to practical difficulties in obtaining blood with identical storage times. Secondly, we did not conduct a comparison between fresh and stored blood transfusions. Furthermore, we did not investigate the immune modulation effects of blood transfusion in cancer patients, which have been associated with cancer progression. Thirdly, the sample size of our study was small. Therefore, further research is necessary to determine whether the allogeneic transfusion of stored blood effectively supports oxygenation during the initial hours post-transfusion.

Conclusion

To sum up, it can be concluded that when mortality is not a factor, fluctuations in lactate levels serve as a sensitive indicator for ICU admission and the need for blood transfusions, whereas bicarbonate levels do not exhibit the same sensitivity. Furthermore, the most reliable predictor for ICU admission, morbidity, and mortality in postsurgical patients remains a topic of debate, reflecting medicine's ever-changing nature and ongoing quest for better predictors in these scenarios. We can also say that patients who undergo substantial blood loss and receive allogeneic blood transfusions do not experience improved tissue oxygenation, as evidenced by failure to prevent the rise in blood lactate, which serves as an indirect

evidence of tissue hypoxia. However, it is important to note that determination of tissue hypoxia relies on elevated lactate levels, which serve as an indirect rather than a direct evidence.

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Conflicts of interest

There are no conflicts of interest.

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