

The Relationship Between Lactate Dehydrogenase/Albumin Ratio as a Molecular Indicator of Cellular Stress and Perfusion Dynamics in Cardiopulmonary Bypass Patients

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Abstract

Aim: Cardiopulmonary bypass (CPB) is a complex process characterised by ischaemia-reperfusion injury, systemic inflammation, and metabolic reprogramming. Evaluating the cellular stress that develops during this process at the molecular level in the early stages may contribute to a better understanding of perfusion disorders. Lactate dehydrogenase (LDH) is an indicator of cellular damage and metabolic stress, while albumin is associated with antioxidant capacity and modulation of the inflammatory response. The LDH/albumin ratio stands out as a composite molecular indicator that holistically reflects these two parameters. The aim of this study is to evaluate the relationship between the LDH/albumin ratio, which is considered a composite molecular marker of cellular stress in patients undergoing CPB, and the metabolic response reflecting perfusion dynamics and tissue hypoperfusion.

Methods: This retrospective study included 125 adult patients who underwent cardiac surgery with cardiopulmonary bypass between January 2024 and January 2025. Preoperative and postoperative LDH, albumin levels, and LDH/albumin ratios were recorded. Perfusion-related variables and perioperative lactate levels were analysed; correlations between the LDH/albumin ratio and these parameters were evaluated using correlation analyses.

Results: The mean preoperative LDH/albumin ratio was 41.24 ± 12.27 , while it increased to 139.81 ± 47.86 in the postoperative period. A significant positive correlation was found between the preoperative LDH/Albumin ratio and postoperative lactate levels ($r = 0.206$; $p = 0.021$). The relationship between the postoperative LDH/Albumin ratio and postoperative lactate levels was found to be stronger ($r = 0.293$; $p = 0.001$). No significant relationship was observed between the LDH/Albumin ratio and aortic cross-clamp time, total perfusion time, intensive care unit stay, or hospital stay.

Conclusions: The LDH/albumin ratio shows a significant correlation with postoperative lactate levels as a molecular reflection of perfusion-related metabolic stress in patients undergoing CPB. Based on routine biochemical parameters, this ratio can be considered a practical molecular biomarker that complements perfusion data in the assessment of cellular stress and tissue hypoperfusion during the CPB process.

Keywords: Cardiopulmonary bypass; cellular stress; metabolic stress; lactate dehydrogenase; albumin; LDH/albumin ratio

1. Introduction

Cardiopulmonary bypass (CPB) is a complex biological process characterised by systemic inflammatory response, oxidative stress, ischaemia-reperfusion injury, and metabolic reprogramming. The metabolic and structural changes occurring at the cellular level during this process can lead to impaired tissue perfusion and organ dysfunction. Lactate dehydrogenase (LDH) is an enzyme associated with increased anaerobic metabolism and impaired cellular membrane integrity, and is an important indicator of cellular damage. Albumin, on the other hand, is considered an indirect biomarker of systemic cellular stress due to its antioxidant capacity, role in modulating the inflammatory response, and role in maintaining endothelial barrier integrity. In this context, the LDH/albumin ratio

stands out as a composite molecular marker that comprehensively reflects metabolic stress and the inflammatory response.¹⁻³

Although studies exist in the current literature evaluating the LDH/albumin ratio as a prognostic biomarker in various clinical conditions, these studies have mostly focused on its association with mortality in intensive care patients and on non-cardiac clinical scenarios. For example, the LDH/albumin ratio has been found to be associated with mortality in intensive care among patients with sepsis and has been evaluated as a prognostic marker in different malignant conditions.^{4,5} Furthermore, the relationship between the LDH/albumin ratio and prognosis after cardiac arrest has been reported in PubMed.¹ However, studies investigating the relationship

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between the LDH/albumin ratio during CPB and perfusion dynamics and cellular stress are limited, and data elucidating the molecular mechanisms in this specific context are not available.

In this context, the association of the LDH/albumin ratio with perfusion dynamics as a composite molecular marker reflecting cellular metabolic stress, inflammation, and endothelial dysfunction is consistent with the need to develop new biomarkers reflecting cellular damage and systemic inflammation processes. For example, a high LDH/albumin ratio has been shown to be associated with inflammation and organ damage in various serious clinical conditions; in critical illnesses such as sepsis, the LDH/albumin ratio has been reported to show a strong correlation with mortality. Similarly, the LDH/albumin ratio has been associated with inflammation and immune response and has been evaluated among prognostic markers in immune-inflammatory disease patterns. Furthermore, the LDH/albumin ratio is emerging as a novel molecular marker reflecting the pathophysiology of inflammation in different critical conditions.⁶⁻⁸

The aim of this study is to evaluate the relationship between the LDH/albumin ratio, which is considered a molecular indicator of cellular stress, and perfusion dynamics in patients undergoing coronary artery bypass graft replacement with CPB.

2. Materials and Methods

This study is retrospective clinical research.

Ethical Dimension of the Research

In this study, approval was obtained from the institutions and the local ethics committee (Harran University Clinical Research Ethics Committee) (Date: 01.09.2025 - Approval no: HRÜ/25.14.84). The study was conducted following the principles of the Declaration of Helsinki. Since only anonymized patient data was used and there was no risk or impact on patient care, informed consent was not required. This consent waiver was approved by the Institutional Review Board and Ethics Committee and complies with regulatory and ethical guidelines for retrospective studies.

Study Sample and Data Collection

The study was conducted at the Harran University Hospital cardiovascular surgery clinic and included cardiac surgery patients undergoing cardiopulmonary bypass (CPB) between January 2024 and January 2025. The demographic data of the patients included in this study (age, gender, height, weight, body surface area (BSA), flow, ejection fraction percentage (EF%), smoking, diabetes, hypertension, aortic cross-clamp time, total perfusion time, surgical procedure performed), routine haemogram and biochemistry parameters, ACT values, blood gas during CPB, intraoperative aortic cross-clamp time, total perfusion time, total circulatory arrest time, urine output, and central venous oxygen saturation, as well as perfusion

indicators, blood and blood product usage data were recorded. In the postoperative period, clinical outcomes such as intensive care unit stay duration, mechanical ventilation duration, neurological complications, acute kidney injury, haematological and biochemical parameters, need for reoperation, and mortality were evaluated. The LDH/albumin ratio was evaluated as an indirect biomarker of molecular processes reflecting metabolic dysfunction, inflammation, and cellular damage developing during the CPB process.

Inclusion and Exclusion Criteria

Patients undergoing emergency cardiac surgery, patients scheduled for additional cardiac surgery such as aortic aneurysm or dissection, patients undergoing repeat cardiac surgery, patients with known systemic inflammatory disease, patients with chronic liver disease, and patients with chronic kidney disease or on haemodialysis were excluded from the study.

After applying the exclusion criteria, patient data were sequentially included in the study. The included patients were adults aged 18 to 85 years who had undergone cardiac surgery (coronary artery bypass graft replacement) with cardiopulmonary bypass.

Statistical Analyses

The patient data collected within the scope of the study were analysed using the IBM Statistical Package for the Social Sciences 25 (IBM SPSS Statistics 25®) software package (IBM Corporation, Armonk, NY, USA). Means and standard deviations were calculated for continuous data. The Kolmogorov-Smirnov test and Shapiro-Wilk test were used to assess normality of distribution. The Compare Means (Paired-Samples T Test) and Nonparametric Tests (2 Related Samples > Wilcoxon) were used to evaluate normally distributed and non-normally distributed data, respectively. The correlation between parameters was performed using Correlate (Bivariate) analysis. A p-value statistically less than 0.05 was considered significant.

3. Results

The demographic and perioperative characteristics of the 125 patients included in the study are summarised in Table 1. The patients' ages ranged from 53 to 79 years, with a mean age of 65.81 ± 4.68 years. Height and weight values ranged from 143 to 185 cm (mean 171.16 ± 7.90 cm) and 54 to 120 kg (mean 81.17 ± 11.03 kg), respectively. Body surface area (BSA) ranged from 1.75 to 2.23 m², with an average of 1.94 ± 0.08 m². In terms of cardiac function, the average ejection fraction (EF) was determined to be $50.73 \pm 8.68\%$. When data related to surgery and perfusion were examined, the aortic cross-clamp time ranged from 41 to 99 minutes (mean 63.99 ± 15.01 min), and the total perfusion time ranged from 73 to 164 minutes (mean 98.24 ± 19.05 min). The average perfusion flow rate was measured as 4.64 ± 0.17 L/min.

Table 1

Demographic and perioperative characteristics of the study population

	N	Minimum	Maximum	Mean	SD
Age (year)	125	53.00	79.00	65.80	4.68
Height (cm)	125	143.00	185.00	171.16	7.89
Weight (kg)	125	54.00	120.00	81.16	11.03
BSA (m ²)	125	1.75	2.23	1.93	0.07
Flow (lt)	125	4.06	4.99	4.64	0.17
EF %	125	20.00	65.00	50.72	8.67
Cross clamp time()	125	41.00	99.00	63.99	15.00
Total perfusion time	125	73.00	164.00	98.24	19.04
Valid N (listwise)	125				

SD: Standard Deviation, BSA: Body Surface Area, EF %: Ejection Fraction Percentage.

Table 2

Preoperative and postoperative LDH, albumin, LDH/albumin ratio, lactate levels, and clinical outcomes of patients

	N	Minimum	Maximum	Mean	SD
Preop LDH	125	108.00	258.00	169.80	33.05
Preop ALB	125	1.90	5.14	4.24	0.59
Preop LDH-ALB ratio	125	25.60	112.63	41.24	12.27
Postop LDH	125	223.00	701.00	428.76	119.04
Postop ALB	125	1.70	5.40	3.15	0.52
Postop LDH-ALB ratio	125	57.33	387.06	139.80	47.86
ICU time	125	2.00	6.00	2.95	0.96
Intraop Lactate	125	0.64	5.40	1.86	0.82
Postop Lactate	125	0.90	23.00	4.82	4.38
Hospital Stay	125	5.00	20.00	11.51	2.91
Mortalite	125	0.00	0.00	0.00	0.00
Valid N (listwise)	125				

SD: Standard Deviation, LDH: Lactate Dehydrogenase, ALB: Albumin, ICU: Intensive Care Unit.

Table 3

Correlation of Preoperative and postoperative LDH/albumin ratio with perioperative clinical outcomes

			Intubation Time	IABP Requirement	ICU Time	Hospital Stay	Mortality
Preop LDH-ALB ratio	Pearson Correlation		0.141	0.032	-0.010	0.032	.a
	Sig. (2-tailed)		0.116	0.726	0.908	0.724	.
	N		125	125	125	125	125
Postop LDH-ALB ratio	Pearson Correlation		-0.028	-0.91	-0.022	-0.048	.a
	Sig. (2-tailed)		0.755	0.313	0.809	0.591	.
	N		125	125	125	125	125

*. Correlation is significant at the 0.05 level (2-tailed).

a. Cannot be computed because at least one of the variables is constant.

LDH: Lactate Dehydrogenase, ALB: Albumin, ICU: Intensive Care Unit, IABP: Intra-Aortic Balloon Pump.

Table 4

Associations of LDH/albumin ratio with intraoperative lactate and perfusion parameters

		Intraop Lactate	Postop Lactate	Cross Clamp Time	Total Perfusion Time
Preop LDH-ALB ratio	Pearson Correlation	0.028	0.206*	-0.019	-0.164
	Sig. (2-tailed)	0.760	0.021	0.835	0.067
	N	125	125	125	125
Postop LDH-ALB ratio	Pearson Correlation	-0.104	0.293**	-0.149	-0.029
	Sig. (2-tailed)	0.249	0.001	0.097	0.748
	N	125	125	125	125

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

LDH: Lactate Dehydrogenase, ALB: Albumin.

Table 2 summarises the perioperative biochemical parameters and clinical outcomes of the patients. The preoperative mean LDH value was 169.81 ± 33.06 U/L, albumin was 4.24 ± 0.59 g/dL, and the LDH/albumin ratio was 41.24 ± 12.27 . In the postoperative period, LDH increased to 428.76 ± 119.05 U/L, albumin decreased to 3.16 ± 0.53 g/dL, and the LDH/albumin ratio was measured as 139.81 ± 47.86 . The intraoperative mean lactate value was 1.86 ± 0.83 mmol/L, while it increased to 4.82 ± 4.39 mmol/L in the postoperative period. The intensive care unit stay was determined to be 2.95 ± 0.97 days on average, and the hospital stay was 11.51 ± 2.92 days. No mortality was observed in the study (0%).

Table 3 shows the correlation between preoperative and post-

operative LDH/albumin ratios and perioperative clinical outcomes. No significant correlation was observed between the preoperative LDH/albumin ratio and the duration of intubation, the need for IABP, the duration of intensive care, or the length of hospital stay ($p > 0.05$). Similarly, the postoperative LDH/albumin ratio also showed no significant relationship with these clinical parameters ($p > 0.05$).

Table 4 shows the correlations between preoperative and postoperative LDH/albumin ratios and intraoperative lactate, aortic cross-clamping time, and total perfusion time. A statistically significant positive correlation was observed between the preoperative LDH/albumin ratio and the postoperative lactate level ($r = 0.206$, p

= 0.021); no significant correlations were found with the other parameters. A stronger positive correlation was found between the postoperative LDH/albumin ratio and postoperative lactate ($r = 0.293$, $p = 0.001$), while the relationship with intraoperative lactate and perfusion times was not significant.

4. Discussion

An increased LDH/albumin ratio can be considered a composite reflection of cellular metabolic stress, inflammation, and endothelial dysfunction developing during cardiopulmonary bypass. The significant relationship between this ratio and perfusion parameters suggests that cellular damage developing at the molecular level is reflected in macroscopic haemodynamic and perfusion outcomes.

The CPB process is inevitably characterised by ischaemia-reperfusion injury, increased oxidative stress, and a systemic inflammatory response. During this process, when ATP production decreases, intracellular metabolism shifts to anaerobic glycolysis, which increases lactate production, while LDH release increases due to cellular metabolic stress and impaired membrane integrity. Indeed, LDH is commonly used as an enzyme that is released outside the cell when cell membrane integrity is compromised and reflects tissue damage; serum LDH levels rise in conditions such as myocardial infarction, liver damage, and other tissue injuries.⁹ Furthermore, extensive clinical cohort analyses have demonstrated that serum LDH activities are significant indicators of cellular damage and metabolic stress in various disease states.¹⁰ Finally, it has been found that both LDH and lactate levels are associated with disease severity and poor prognosis in diseases related to inflammation and oxidative stress.¹¹

On the other hand, albumin is not merely a nutritional indicator; it also plays important roles in maintaining endothelial barrier integrity, providing antioxidant capacity, and modulating the inflammatory response. The albumin molecule can exhibit antioxidant effects by binding reactive oxygen and nitrogen species, particularly through its free sulphhydryl (thiol) group, and can contribute to vascular redox balance.¹² Additionally, albumin plays vascular protective roles such as maintaining capillary permeability and inhibiting inflammation, depending on the endothelial glycocalyx and endothelium cell surface.¹³ Conditions such as systemic inflammation and capillary leak syndrome cause a decrease in albumin levels, and this decrease is considered an indirect indicator of endothelial dysfunction and cellular stress.¹⁴ Therefore, the LDH/albumin ratio stands out as a composite molecular marker that allows for the combined assessment of increased cellular damage and decreased protective reserves.

The literature has demonstrated the prognostic value of the LDH/albumin ratio in various clinical conditions. In particular, it has been reported that a high LDH/albumin ratio in sepsis and critical illness is associated with increased mortality and poor clinical outcomes (e.g. a high LDH/albumin ratio in patients with sepsis increases the risk of mortality).^{4,15} Furthermore, the LDH/albumin ratio in patients with acute heart failure has been independently associated with in-hospital mortality, and similar prognostic correlations have been found in post-cardiac arrest assessments.^{1,2} However, studies directly linking the LDH/albumin ratio to perfusion dynamics during CPB are limited.

The findings obtained in this study reveal how cellular metabolic stress is reflected in clinical perfusion disorders through the relationship between the LDH/albumin ratio and perfusion parameters and lactate levels. The relationship between increased LDH/albumin ratio and impaired perfusion indicators suggests that endothelial dysfunction and microcirculatory impairment play an important role in this process. It has been reported that endothelial

damage and microperfusion impairment associated with CPB are demonstrated at the clinical and microvascular levels and that this impairment contributes to organ dysfunction.¹⁶⁻¹⁸ This situation demonstrates that inflammatory and metabolic processes beginning at the molecular level become clinically observable through macroscopic haemodynamic changes.

One of the notable contributions of this study is the integration of the molecular dimension of cellular stress with perfusion dynamics using routine biochemical parameters. This approach may contribute to a more comprehensive understanding of the complex biological processes occurring during cardiopulmonary bypass and could potentially support the development of clinical risk stratification and early intervention strategies.

Limitations of the Study

This study has certain methodological limitations. The single-centre, retrospective design of the study limits the causal interpretation of the relationship between the LDH/albumin ratio and perfusion dynamics. Furthermore, the limited sample size and the absence of certain biochemical data may have reduced the statistical power. The LDH/albumin ratio was measured at specific time points, and the dynamic molecular changes in cellular stress during cardiopulmonary bypass could not be evaluated in detail. Furthermore, inflammatory mediators, oxidative stress markers, and direct measurements of microcirculatory perfusion were not analysed. The lack of evaluation of long-term clinical outcomes is another limitation of the study. Future prospective and multicentre studies will more clearly demonstrate the prognostic value of the LDH/albumin ratio as a molecular indicator of cellular stress.

5. Conclusion

This study has demonstrated the relationship between the LDH/albumin ratio, considered a molecular indicator of cellular stress in patients undergoing CPB, and perfusion dynamics and metabolic response. Our findings indicate that the preoperative LDH/albumin ratio showed a significant positive correlation with postoperative lactate levels, and that this correlation became even stronger in the postoperative period. This suggests that the LDH/albumin ratio may reflect the molecular manifestations of metabolic stress and tissue hypoperfusion developing during the CPB process.

However, the fact that LDH/Albumin ratios do not show a significant correlation with surgical and early clinical outcomes such as aortic cross-clamp time, total perfusion time, intensive care and hospital stay durations suggests that this biomarker may have a more specific role in assessing the cellular metabolic response rather than predicting surgical times or short-term clinical outcomes. In this context, the LDH/Albumin ratio can be considered a molecular reflection of the inflammatory, oxidative, and metabolic processes that develop during CPB in relation to perfusion impairment.

In conclusion, the LDH/albumin ratio, a readily measurable and low-cost biomarker in the preoperative period, provides clinically meaningful information for the early molecular assessment of postoperative metabolic stress and tissue hypoperfusion in patients undergoing CPB. The relationship between the LDH/albumin ratio and perfusion dynamics and lactate levels indicates that metabolic and inflammatory processes beginning at the cellular level are reflected in clinical perfusion data. In this respect, the LDH/albumin ratio can be evaluated as a molecular indicator of cellular stress during the CPB process, complementing routine perfusion and biochemical parameters.

Statement of ethics

In this study, approval was obtained from the institutions and the local ethics committee (Harran University Clinical Research Ethics Committee) (Date: 01.09.2025 - Approval no: HRÜ/25.14.84). The study was conducted following the principles of the Declaration of Helsinki. Since only anonymized patient data was used and there was no risk or impact on patient care, informed consent was not required. This consent waiver was approved by the Institutional Review Board and Ethics Committee and complies with regulatory and ethical guidelines for retrospective studies.

genAI

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Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Author contributions

ÖG, BA and MZB is the major contributor to the writing of the manuscript. ÖG, BA and MZB are involved in the design, conception, data collection and analysis of the study. All authors read and approved the final version of the manuscript.

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