REPEn
Revista Paulista de Enfermagem

PESQUISA

Submited: 08.04.2021
Accepted: 06.11.2021

Como citar este artigo

Horak ACP, Ferretti-Rebustini REL, Oliveira LB, Crespo JCL, Wilson AMMM, Oliveira JC, Santana-Santos E. Hyperlactatemia and worse outcomes in patients undergoing cardiac surgery: a retrospective cohort study. Rev Paul Enferm. 2022;33. https://doi.org/10.33159/25959484.repen.2022v33a03

Hyperlactatemia and worse outcomes in patients undergoing cardiac surgery: a retrospective cohort study

Hiperlactatemia e piores desfechos em pacientes submetidos à cirurgia cardíaca: um estudo de coorte retrospective

Hiperlactatemia y peores resultados en pacientes sometidos a cirugía cardíaca: un estudio de cohorte retrospective

Ana Clara Peneluppi Horak[I] ORCID: 0000-0003-4663-8328
Renata Eloah de Lucena Ferretti-Rebustini[I] ORCID: 0000-0002-6159-5787
Larissa Bertachini de Oliveira[I] ORCID: 0000-0001-9509-4422
Jeiel Carlos Lamonica Crespo[I] ORCID: 0000-0002-6910-9819
Ana Maria Miranda Martins Wilson[I] ORCID: 0000-0003-3608-8158
Jussiely Cunha Oliveira[II] ORCID: 0000-0001-6782-8994
Eduesley Santana-Santos[II] ORCID: 0000-0001-8545-5677

[I] Universidade de São Paulo. São Paulo, SP, Brazil
[II] Universidade Federal de Sergipe. Aracaju, SE, Brazil

ABSTRACT

Objective: Identify the factors, complications, and outcomes associated with hyperlactatemia in patients undergoing cardiac surgery. **Methods:** A retrospective cohort study including patients with hyperlactatemia admitted to the surgical intensive care unit (SICU) immediately after cardiac surgery. Patients were divided into 2 groups based on baseline lactate levels: hyperlactatemia group (HL, lactate levels ≥ 3 mmol/L) and normal lactate group (NL, lactate levels < 3 mmol/L). **Results:** Of 1304 patients, 589 (45.2%) had hyperlactatemia in the postoperative period of cardiac surgery. The LH group when compared to the NL group, respectively, presented a higher mean value for the EuroSCORE (3.5 ± 2.4 vs 3.2 ± 2.3, p = 0.018), higher mortality rates (13.6% vs 3.9%, p <0.001), acute kidney injury (52.6% vs. 36.8%; p <0.001), longer ICU stay (4 days [3 - 6]) vs. 5 days [3 - 7]; p <0.001), required mechanical ventilation for longer in the first 24 hours (9.4% vs. 18.1%; p <0.001) and 48 hours (7.7% vs. 15.1%; p <0.001) after admission to the ICU and had higher rates of use of IABP (8.1% vs. 5.5%; p = 0.034). The survival curves show that the overall survival was better in the patients in the NL group. **Conclusions:** In the postoperative period of cardiac surgery, the prevalence of hyperlactatemia was 45.2% with worse outcomes for this group. Patients in the HL group had higher mortality, higher frequency of mechanical ventilation in the first 24 and 48 hours, higher incidence of acute kidney injury, more need for the use of IABP, and longer length of stay SICU.
Descriptors: Perioperative procedures, Hyperlactatemia, Hospital mortality, Critical care outcomes

Corresponding Author

Eduesley Santana-Santos
eduesley.santos@gmail.com

RESUMO

Objetivo: Identificar os fatores, complicações e desfechos associados à hiperlactatemia em pacientes submetidos à cirurgia cardíaca. **Métodos:** Estudo de coorte retrospectivo incluindo pacientes com hiperlactatemia internados na unidade de terapia intensiva cirúrgica (UTI) imediatamente após cirurgia cardíaca. Os pacientes foram divididos em 2 grupos com base nos níveis basais de lactato: grupo hiperlactatemia (HL, níveis de lactato ≥ 3 mmol / L) e grupo de lactato normal (NL, níveis de lactato <3 mmol / L). Resultados: Dos 1.304 pacientes, 589 (45,2%) apresentaram hiperlactatemia no pós-operatório de cirurgia cardíaca. O grupo LH quando comparado ao grupo NL, respectivamente, apresentou maior valor médio do EuroSCORE (3,5 ± 2,4 vs 3,2 ± 2,3, p = 0,018), maiores taxas de mortalidade (13,6% vs 3,9%, p <0,001), lesão renal aguda (52,6% vs. 36,8%; p <0,001), maior permanência na UTI (4 dias [3 - 6]) vs. 5 dias [3 - 7]; p <0,001), necessitou de ventilação mecânica por mais tempo nas primeiras 24 horas (9,4% vs. 18,1%; p <0,001) e 48 horas (7,7% vs. 15,1%; p <0,001) após admissão na UTI e teve maior taxas de uso de Balão Intra-Aórtico (BIA) (8,1% vs. 5,5%; p = 0,034). As curvas de sobrevida mostram que a sobrevida global foi melhor nos pacientes do grupo NL. Conclusões: No pós-operatório de cirurgia cardíaca, a prevalência de hiperlactatemia foi de 45,2% com piores desfechos para este grupo. Os pacientes do grupo LH apresentaram maior mortalidade, maior frequência de ventilação mecânica nas primeiras 24 e 48 horas, maior incidência de lesão renal aguda, maior necessidade de uso de BIA e maior tempo de internação na UTI.
Descritores: Procedimentos perioperatórios, Mortalidade, Procedimentos cirúrgicos cardiovasculares

RESUMEN

Objetivo: Identificar los factores, complicaciones y resultados asociados a la hiperlactatemia en pacientes sometidos a cirugía cardíaca. **Métodos:** estudio de cohorte retrospectivo que incluyó pacientes con hiperlactatemia hospitalizados en la unidad de cuidados intensivos quirúrgicos (UCI) inmediatamente después de la cirugía cardíaca. Los pacientes se dividieron en 2 grupos según los niveles basales de lactato: grupo de hiperlactatemia (HL, niveles de lactato ≥ 3 mmol/L) y grupo de lactato normal (NL, niveles de lactato <3 mmol/L). **Resultados:** De los 1.304 pacientes, 589 (45,2%) presentaron hiperlactatemia en el postoperatorio de cirugía cardíaca. El grupo LH en comparación con el grupo NL, respectivamente, tuvo un valor medio más alto del EuroSCORE (3,5 ± 2,4 vs. 3,2 ± 2,3, p = 0,018), mayores tasas de mortalidad (13,6% vs. 3, 9%, p <0,001) , lesión renal aguda (52,6% frente a 36,8%; p <0,001), estancia más prolongada en la UCI (4 días [3 - 6]) vs. 5 días [3 - 7]; p <0,001), requirieron ventilación mecánica durante más tiempo en las primeras 24 horas (9,4% vs.18,1%; p <0,001) y 48 horas (7,7% vs.15,1%; p <0,001) después de la admisión en UCI y tuvieron mayores tasas de uso del Balón Intraaórtico (BIA) (8,1% vs.5,5%; p=0,034). Las curvas de supervivencia muestran que la supervivencia global fue mejor en los pacientes del grupo NL.
Conclusiones: En el postoperatorio de cirugía cardíaca, la prevalencia de hiperlactatemia fue del 45,2% con los peores resultados para este grupo. Los pacientes del grupo LH presentaron mayor mortalidad, mayor frecuencia de ventilación mecánica en las primeras 24 y 48 horas, mayor incidencia de daño renal agudo, mayor necesidad de uso de BIA y mayor estancia en UCI.
Descriptores: Procedimientos perioperatorios, Hiperlactatemia, Mortalidad hospitalaria, Resultados en cuidados críticos.

INTRODUCTION

Hyperlactatemia (HL) is commonly found in the postoperative period cardiac surgery, an important procedure for many patients with cardiac dysfunctions[1,2]. The increase in lactate occurs as a result of anaerobic glycolysis caused by oxygen deficit and tissue hypoperfusion associated with high metabolic expenditure and its monitoring is used as an important prognostic marker. In cases of cardiac surgery, the metabolic alteration associated with the use of cardiopulmonary pulmonary circulation (CPB) and its relationship with cardiac biochemical processes alters tissue oxygenation and increases the serum blood lactate value above

2 mmol/L, which characterizes the state of hyperlactatemia, can lead to negative outcomes and increased morbidity and mortality [2, 3].

The increase in lactate levels may be type A, resulting from tissue hypoxia with oxygenation imbalance and occurs during or shortly after the onset of CPB due to hypoperfusion, or type B, which manifests itself within 4-14 h after surgery in the intensive care unit (ICU), resulting from different causes besides tissue hypoxia[4,5]. Early hyperlactatemia may be associated with a much higher probability of negative outcomes with increased morbidity and mortality that may be caused by the effects of the use of cardiopulmonary pulmonary bypass (CPB) during the surgical procedure associated with impaired tissue oxygenation and consequent tissue hypoxia and, postoperatively, by the administration of vasoactive drugs increased body temperature, tremors, recovery of spontaneous ventilation, among others[2, 6].

It is attested that the adequate involvement of the multidisciplinary team in knowing the factors and strategies to reduce the morbidity and mortality of patients undergoing cardiac surgery should be tied to the adequate knowledge of the entire team in both the operating room and the ICU on lactate measurement as a prognostic marker necessary to monitor tissue perfusion[1]. It is worth mentioning the role of nursing in monitoring and recording hemodynamic parameters and vital signs, CPB time, provision of sedatives and/or analgesics, besides being aware of the presence of arrhythmias, administration of blood products, vasopressors, peak lactate leveling both intraoperatively and postoperatively[7].

However, although studies on hyperlactatemia report possible complications, especially associated with a higher mortality and morbidity rate of patients after cardiac surgery[8], there are gaps in the international and national literature on which risk factors and other outcomes are associated with increased serum lactate levels to assist professionals who provide care to patients in the postoperative period of cardiac surgery. Therefore, this study aimed to identify the factors, complications, and outcomes associated with hyperlactatemia in patients undergoing cardiac surgery.

MATERIALS AND METHODS

This is a retrospective cohort study conducted at the Heart Institute (InCor), Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), a tertiary-level teaching hospital specialized in cardiology and pulmonology, also considered a quaternary reference center in São Paulo - Brazil. The hospital has 570 beds, with 40 beds equipped for the Adult Intensive Care Unit for care in the postoperative period of cardiac surgery. The study was approved by the number 1.685.984 / CAAE: 58258816.4.0000.0068, by the Institutional Ethics Committee and had the waiver of the informed consent form because it is a study with retrospective data collection in electronic medical records.

All records of patients admitted to the surgical intensive care unit (SICU) between January 2015 and December 2015 after cardiac surgery (coronary artery bypass graft, valve replacement, and/or aortic surgery) were included into study. Patients submitted to surgery to correct congenital heart defects, percutaneous implantation of the aortic valve, or incomplete data in the electronic medical records were excluded. Patients were divided into two groups based on lactate levels of admission to the surgical intensive care unit (basal lactate levels). Patients with lactate levels of admission of 3 mmol/L or more were classified as a hyperlactatemia group (HL), and those with levels below 3 mmol/L, normal lactate group (NL), as shown in Figure 1. In this study, hyperlactatemia was defined as lactate levels >3.0mmol/L, in the literature and this cutoff value was previously associated with major complications after cardiac surgery[1, 2, 4].

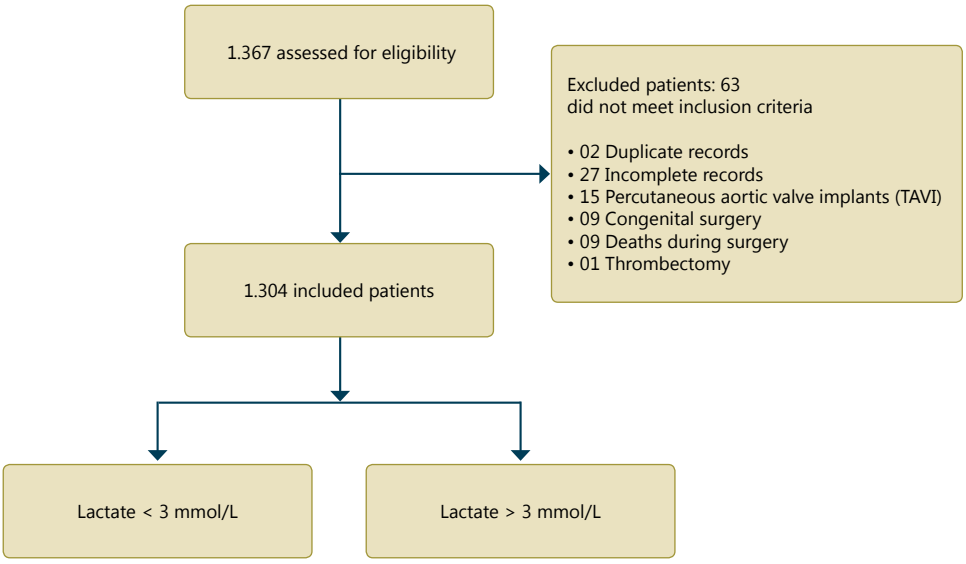

Figure 1 - Flowchart of adult patients included in the study

The electronic medical records were reviewed and required information was recorded on a questionnaire developed for this purpose. Blood lactate levels were assessed routinely iRadiometer ABL 835 blood gas analyzer (Radiometer Medical A/S, Bronshoj, Denmark) immediately on the arrival to the SICU (baseline). Samples were obtained from a radial arterial line and immediately sent to the laboratory in a time not greater than five minutes. A database was created including the variables of interest and statistical analysis was performed. All information was collected in a database whose source was the electronic medical record.

The data collection instrument was composed of variables for clinical and demographic characterization, as well as data from the pre, intra, and postoperative periods of the patients included. The outcomes evaluated in this study included: mortality during hospitalization, acute kidney injury (AKI) defined by the KDIGO[9]criteria, use of mechanical ventilation for more than 24 and 48 hours after admission to SICU, need for intra-aortic balloon (IABP), return to the operating room, length of stay in SICU and length of hospital stay.

The normality was evaluated with the Kolmogorov-Smirnov test. A descriptive analysis of the variables was carried out, using means with standard deviation (SD) and medians with interquartile range (IQR), and was compared using Student t-test or Mann-Whitney U test, as appropriate. Categorical variables were compared using the chi-square test or Fisher exact test, as appropriate. Logistic regression was used to determine hyperlactatemia as a predictor of adverse outcomes. Survival curves with the Kaplan-Meier method were used to estimate the difference in mortality between groups. And all tests were 2-tailed. $P<0.05$ was considered significant for the analysis. The SPSS version 21.0 program was used for data analysis.

RESULTS

Hyperlactatemia in the postoperative period (lactate $\geq$ 3.0mmol/L) was observed in 589 (45.2%) patients. A comparison between normal lactate and hyperlactatemic group was performed and comparative analysis revealed that HL group had a mean EuroSCORE of 3.5 ± 2.4 compared with a score of 3.2 ± 2.3 with statistical significance (P = 0.018) (Table 1).

Table 1 - Clinical, demographics and surgical characteristics between NL group and HL group

Variable	NL Group (n=715)	HL Group (n=589)	p-value
Preoperative characteristics			
Male Gender, n (%)	441 (61.7)	353 (59.9)	0.531
Age in years, mean ± SD	60 ± 13	61 ± 13	0.070
LVEF, mean ± SD	60.0 ± 11.3	58.8 ± 10.6	0.055
EuroSCORE, mean ± SD	3.2±2.3	3.5 ± 2.4	0.018
Heart Failure, n (%)	117 (16.4)	99 (16.8)	0.881
NYHA, n (%)			
I	7 (6.8)	9 (9.8)	0.422
II	43 (41.7)	44(47.8)	
III	49 (47.6)	33(35.9)	
IV	4 (3.9)	5 (5.4)	
Myocardial Infarction (prior), n (%)	167 (23.4)	137 (23.3)	1.000
Hypertension, n (%)	461 (64.5)	400 (67.9)	0.197
Dyslipidemia, n (%)	321 (44.9)	254 (43.1)	0.538
Active smoking, n (%)	99 (13.8)	71 (12.1)	0.364
Diabetes, n (%)	254 (35.5)	209 (35.5)	1.000
Stroke (prior), n (%)	29 (4.1)	19 (3.2)	0.463
Cardiac Sugery (prior), n (%)	90 (12.6)	92 (15.6)	0.127
CKD, n (%)	98 (13.7)	98 (16.6)	0.161
Intraoperatives characteristics			
CABG, n (%)	333 (46.6)	251 (42.6)	0.162
Valve Replacement, n (%)	304 (42.5)	264 (44.8)	0.432
Aortic surgery, n (%)	21 (2.9)	13 (2.2)	0.486
CABG+Valve Replacement, n (%)	11 (1.5)	27 (4.6)	0.001
Cardiopulmonary bypass use, n (%)	674 (94.3)	547 (92.9)	0.308
Cardiopulmonary bypass time, mean ± SD	93.6 ± 34.8	97.9 ± 40.0	0.043
Time of anoxia in minutes, mean ± SD	73.9 ± 27.4	75.4 ± 27.2	0.352
Red blood cell transfusion, n (%)	168 (23.5)	170 (28.9)	0.031
Postoperative characteristics			
Vasoactive drugs use, n (%)			
Dobutamine	652 (91.2)	511 (86.8)	0.012
Dopamine	11 (1.5)	21 (3.6)	0.020
Norepinephrine	159 (22.2)	215 (36.5)	<0.001
Epinephrine	30 (4.2)	87 (14.8)	<0.001

NL: normal lactate; HL: high lactate; SD: standard deviation; IQR: interquartile range; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; CKD: chronic kidney disease; CABG: coronary artery bypass graft.

The outcomes are summarized in table 2. There was a statistically significant difference between the groups regarding the primary outcome occurred in 13.6% of the HL group compared to 3.9% of the NL group ($p < 0.001$). Among the NL group and HL group, the incidence of acute kidney injury, need for mechanical ventilation support in 24h and 48h and length of SICU stay, patients from HL group had poorer outcomes, having a longer SICU stay (4 days [3 – 6] vs. 5 days [3 – 7]; $p<0.001$), patients from HL group needed mechanical ventilation for more time, being this outcome evaluated in 24 hours (9.4% vs. 18.1%; $p<0.001$) and 48 hours (7.7% vs. 15.1%; $p<0.001$) after admission in SICU. In 24h hours after admission in the SICU, the use of IABP was more frequently employed in the HL group (8.1%), when compared to the NL group (8.1% vs. 5.5%; $p=0.034$). No differences were found in the length of hospital stay or the frequency of return to the operation room for re-exploration.

Table 2 - Comparison of postoperative outcomes between NL group and HL group

Outcomes	NL Group (n=715)	HL Group (n=589)	p-value
Mortality, n (%)	28 (3.9)	80 (13.6)	<0.001
Acute Kidney Injury, n (%)	261 (36.8)	302(52.6)	<0.001
Mechanical Ventilation (24h), n (%)	67 (9.4)	106 (18.1)	<0.001
Mechanical Ventilation (48h), n (%)	55 (7.7)	87 (15.1)	<0.001
Length of SICU stay (days)	4 [3 – 6]	5 [3 – 7]	0.019
Length of hospital stay (days), median [IQR]	14 [9 – 20]	14 [10 – 23.5]	0.066
IABP (24h), n (%)	39 (5.5)	48 (8.1)	0.034
Return to operation room, n (%)	32 (4.5)	33 (5.6)	0.373

SICU: surgical intensive care unit; IABP: intra-aortic balloon pump; IQR: interquartile range

Patients with hyperlactatemia were 3.85 (95% CI 2.47 – 6.02) times more likely to die. Patients in the HL group had 1.90 (95% CI 1.52 – 2.38) times the chance of developing acute kidney injury in the postoperative period as compared to those from the NL group. Similarly, the requirement for mechanical ventilation supports was 2.14 (95% CI 1.54 – 2.97) times greater in the HL group 24 hours and 2.13 (95% CI 1.44 – 3.05) times greater than 48 hours after admission in the SICU. Concerning the requirement of IABP, patients in the HL group had a 2.09 times more chance of using this type of support (Table 3).

Table 3 - Logistic regression analysis for adverse outcomes in patients with hyperlactatemia (HL group).

Variable	p-value	OR	(95% CI)
Mortality	<0.001	3.85	(2.47 – 6.02)
Acute Kidney Injury	<0.001	1.90	(1.52 – 2.38)
Mechanical Ventilation (24h)	<0.001	2.14	(1.54 – 2.97)
Mechanical Ventilation (48h)	<0.001	2.13	(1.44 – 3.05)
Intra-aortic balloon pump	0.021	2.09	(1.12 – 3.93)

OR: odds ratio; CI: confidence interval

Survival curves show that overall survival was better in the patients from the NL group as presented in figure 2.

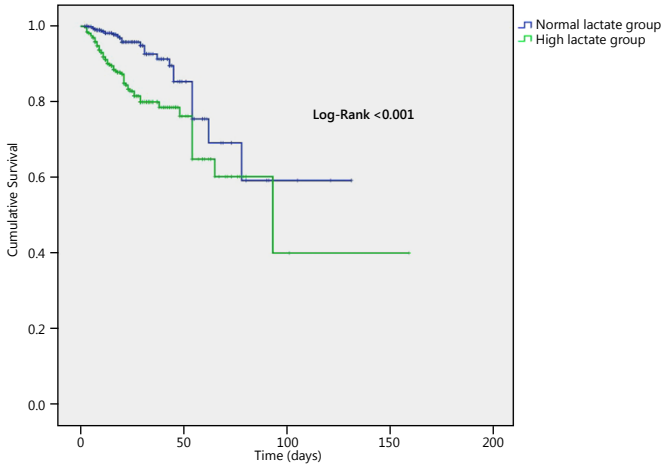

Figure 2 - Kaplan-Meier plot showing relationship between development of mortality and lactate levels

DISCUSSION

The incidence of hyperlactatemia in our cohort was 45.2 %e with a mortality rate of approximately 14%, values close to those found in the literature[4,10]. We also found that hyperlactatemia defined by lactate levels higher than 3 mmol/L was independently associated with a 3.85 times chance of in-hospital mortality. Besides, it was observed that the use of vasoactive drugs in the perioperative period was more frequent among patients of the HL group, but we found no statistical significance in the logistic regression model, as shown in other studies[5, 8].

The association between serum lactate concentration above 2mmol/L in cardiac surgery patients and a higher risk of postoperative hospital morbidity and mortality has also been reported in other studies[6,7,10,11]. The study by Yang et al. showed that increased lactate levels were associated with tissue hypoperfusion, the release of glycogenesis catecholamine and glycolysis, systemic inflammation reaction, and lactate load from a blood transfusion. It also reported the association between high lactate levels and negative outcomes in the postoperative period, highlighting the importance of professionals adopting serum lactate measurement during cardiac surgery and use of CPB[4].

The authors of some clinical studies found an association between vasoactive drugs and hyperlactatemia[12]. After cardiac surgery, vasopressor use was identified by Totaro et al.[13] as a factor frequently associated with a high lactate concentration, but no statistical analysis was performed. The authors demonstrated that increased circulating catecholamines secondary to the stress response to the anesthetic-surgical process, in combination with the use of vasoactive drugs in the perioperative period, have been reported to result in increased blood lactate levels[13]. Moreover, the association between the increase of lactate and the use of vasoactive drugs can be related to a greater presence of cardiogenic shock in the HL group[13].

In the study by Lenkin et al. [14], patients with postoperative complications had a higher peak of lactate concentrations than in the group without complications and draw the attention of the team to the need to reassess the patient's condition. Our study also demonstrated a higher mean value of EuroSCORE for patients in the HL group. In a large cohort of post-cardiosurgical patients, it was observed that lactate levels at ICU admission were positively correlated with CPB time and EuroSCORE, which reaffirms a higher prediction of 30-day mortality in patients with hyperlactatemia undergoing cardiac surgery[15].The importance of blood lactate levels measurement has been demonstrated in general ICU patients[2, 16] and in children patients[8].

Some worse outcomes, including AKI, need for mechanical ventilation support in 24 and 48 hours, and need for IABP support were also increased in patients from HL group. A study conducted by Hoshino et al. [10] showed that the time of mechanical ventilation was significantly longer in the HL group and pulmonary complications were more frequent. In parallel, in a retrospective observational study conducted on adult patients (>18 years old) who underwent cardiac surgery under CPB, Matteucci et al. [16] observed that patients with hyperlactatemia made greater postoperative use of intra-aortic balloon pump (IABP), needed more inotropic support after surgery, had a prolonged time of mechanical ventilation and hospitalization, in addition to higher rates of postoperative renal dysfunction.

We also observed a statistically significant difference in the duration of SICU stay, but not in the hospital stay in patients of the HL group. Patients with lactate ≥ 3 mmol/L were associated with a significantly longer SICU stay (P = 0.019) compared to patients with lactate < 3, as reported by other studies4-6, 17. However, we found no statistical significance in the logistic regression model. Also, we observed a statistically significant difference in the need for mechanical ventilation support in 24 and 48 hours between the two groups. Patients from the HL

group were associated with the need for mechanical ventilation support in 24h (P < 0.001) and 48 h (P < 0.001). Our results were similar to those presented by Mak et al. [17], they showed that hyperlactatemia patients had greater time on mechanical ventilation.

Interestingly, in our study, AKI in the postoperative period, defined by KDIGO criterion at any stage, was strongly associated with hyperlactatemia, as demonstrated in a matched cohort study[17]. From this, we learn that this is not just a hyperlactatemia result of decreased oxygen delivery, but which is also affected by end-organ dysfunction. Interpretation of lactate trends must therefore take into account non-cardiogenic factors. From this, we understand that this phenomenon is not only a result of inadequate oxygen supply to the tissues, but it is also affected by organic dysfunction.

Our study has some limitations. First, it was a retrospective single-center study and therefore potentially subject to systematic errors and omissions or inaccuracies of medical letters. Second, it represents 1 year of experience in a tertiary-level cardiac surgery center. Third, this study evaluated a heterogeneous study population submitted to different surgical procedures. Fourth, hemodynamic data, such as blood pressure, heart rate, and central venous oxygen saturation, were not analyzed along with lactate levels.

Anyway, these findings are very important in cardiac surgery scenario, the additional role of hyperlactatemia as a risk factor for increased morbidity and mortality suggests that in the clinical setting, it might help the multidisciplinary team in the perioperative planning to conduct patients' monitoring and therapy.

CONCLUSION

Conclusions: In the postoperative period of cardiac surgery, the prevalence of hyperlactatemia was 45.2% with worse outcomes for this group. Patients in the HL group had higher mortality, higher frequency of mechanical ventilation in the first 24 and 48 hours, higher incidence of acute kidney injury, more need for the use of IABP, and longer length of SICU stay.

COMPETING INTERESTS

The authors declare that there are no competing interests regarding the publication of this paper.

REFERENCES

1. Garcia-Camacho C. Continuous ultrafiltration during extracorporeal circulation and its effect on lactatemia: a randomized controlled trial. PLOS ONE. 2020;15(11). https://doi.org/10.1371/journal.pone.0242411
2. Minton J, Sidebotham DA. Hyperlactatemia and Cardiac Surgery. J Extra Corpor Technol [Internet]. 2017[cited 2021 Apr 01];49(1):7-15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5347225/
3. Couto-Mallón D, González-Vílchez F, Almenar-Bonet L, et al. Prognostic value of serum lactate levels in patients undergoing urgent heart transplant: a subanalysis of the ASIS-TC Spanish Multicenter Study. Rev Esp Cardiol (Engl Ed). 2019;72(3):208-14. https://doi.org/10.1016/j.rec.2018.02.021
4. Yang HH, Chang JC, Jhan JY. Prognostic value of peak lactate during cardiopulmonary bypass in adult cardiac surgeries: a retrospective cohort study. Tzu Chi Med J. 2020;32(4):386-91. https://doi.org/10.4103/tcmj.tcmj_215_19
5. Kędziora A, Wierzbicki K, Piątek J. Postoperative hyperlactatemia and serum lactate level trends among heart transplant recipients. PeerJ. 2020;8:e8334. https://doi.org/10.7717/peerj.8334

6. Piot J, Hébrard A, Durand M, Payen JF, Albaladejo P. An elevated respiratory quotient predicts complications after cardiac surgery under extracorporeal circulation: an observational pilot study. J Clin Monit Comput. 2019;33(1):145-53. https://doi.org/10.1007/s10877-018-0137-0

7. Draben L. Hyperlactatemia and Patient Outcomes After Pediatric Cardiac Surgery. Crit Care Nurse. 2018;38(5):e1-e6. https://doi.org/10.4037/ccn2018910

8. Şahutoğlu C, Yaşar A, Kocabaş S, Aşkar FZ, Ayık MF, Atay Y. Correlation between serum lactate levels and outcome in pediatric patients undergoing congenital heart surgery. Turk Gogus Kalp Damar Cerrahisi Derg. 2018;26(3):375-85. https://doi.org/10.5606/tgkdc.dergisi.2018.15791

9. Group KDIGO KBPW. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int. 03 2021;99(3S):S1-S87. https://doi.org/10.1016/j.kint.2020.11.003

10. Hoshino Y, Kinoshita O, Ono M. The Incidence, Risk Factors, and Outcomes of Hyperlactatemia after Heart Transplantation. Int Heart J. Jan 2018;59(1):81-6. https://doi.org/10.1536/ihj.17-146

11. Ferreruela M, Raurich JM, Ayestarán I, Llompart-Pou JA. Hyperlactatemia in ICU patients: incidence, causes and associated mortality. J Crit Care. 12 2017;42:200-205. https://doi.org/10.1016/j.jcrc.2017.07.039

12. Boldt J, Piper S, Murray P, Lehmann A. Case 2-1999. Severe lactic acidosis after cardiac surgery: sign of perfusion deficits? J Cardiothorac Vasc Anesth. Apr 1999;13(2):220-4. https://doi.org/10.1016/s1053-0770(99)90093-9

13. Totaro RJ, Raper RF. Epinephrine-induced lactic acidosis following cardiopulmonary bypass. Crit Care Med. 1997;25(10):1693-9. https://doi.org/10.1097/00003246-199710000-00019

14. Lenkin PI, Smetkin AA, Hussain A, et al. Continuous monitoring of lactate using intravascular microdialysis in high-risk cardiac surgery: a prospective observational study. J Cardiothorac Vasc Anesth. 2017;31(1):37-44. https://doi.org/10.1053/j.jvca.2016.04.013

15. Zante B, Reichenspurner H, Kubik M, Kluge S, Schefold JC, Pfortmueller CA. Base excess is superior to lactate-levels in prediction of ICU mortality after cardiac surgery. PLoS One. 2018;13(10):e0205309. https://doi.org/10.1371/journal.pone.0205309

16. Matteucci M, Ferrarese S, Cantore C. Hyperlactatemia during cardiopulmonary bypass: risk factors and impact on surgical results with a focus on the long-term outcome. Perfusion. 2020;35(8):756-62. https://doi.org/10.1177/0267659120907440

17. Mak NT, Iqbal S, de Varennes B, Khwaja K. Outcomes of post-cardiac surgery patients with persistent hyperlactatemia in the intensive care unit: a matched cohort study. J Cardiothorac Surg. 2016;11:33. https://doi.org/10.1186/s13019-016-0411-5