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Postoperative Serum Lactate Levels for In-Hospital Mortality Prediction Among Heart Transplant Recipients

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Background: Hyperlactatemia is a common phenomenon following cardiac surgeries and is associated with prolonged ICU stay and higher morbidity and mortality rates, but such analyses have never focused on patients undergoing heart transplantation (HTX), in whom hyperlactatemia defined with the traditional threshold is observed in nearly every individual. The present study aimed to assess the prognostic value and clinical usefulness of postoperative serum lactate level measurements for in-hospital mortality prediction following HTX.

Material/Methods: Forty-six consecutive patients who underwent HTX in the Department of Cardiovascular Surgery and Transplantology between 2010 and 2015 were enrolled into a retrospective analysis. Serum lactate level measurements within the first 48 h after HTX were obtained from arterial blood gas analyses, that were routinely conducted every 6 h. Lactate clearance was determined for each patient individually throughout 3 different time frames: the first 24-h (Lac clear 0–24) and second 24-h period (Lac clear 24–48), and the first 48 h after surgery (Lac clear 0–48).

Results: The ICU admission serum lactate levels differed between the deceased and survivors (7.6 *vs.* 4.3 mmol/L; p=0.000). Among all tested postoperative lactate level measurements, only the measurement taken upon ICU admission predicted in-hospital mortality (OR 1.94 95% CI [1.09–3.43]; p=0.024). The receiving operating characteristic (ROC) curve for in-hospital mortality was constructed for ICU admission measurement, with the optimal cut-off point estimated at 7.0 mmol/L.

Conclusions: Serum lactate level measurement upon ICU admission can be used as a predictive parameter for in-hospital mortality among heart transplant recipients. Values greater than 7.0 mmol/L can predict in-hospital mortality with 90% accuracy.

MeSH Keywords: **Acidosis, Lactic • Heart Transplantation • Hospital Mortality • Lactic Acid**

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Background

Hyperlactatemia is a common phenomenon following cardiac surgeries. Although it is frequently used as a marker of observed tissue hypoxia, lactate metabolism during the perioperative period is complex and dynamic. Early-onset hyperlactatemia is defined as developing in the operating room or very early following Intensive Care Unit (ICU) admission and it usually does not spontaneously resolve within 24 h after surgery. *De novo* hyperlactatemia, which is not present up to 6 h following ICU admission, is accompanied by normal cardiac output and absence of impaired tissue oxygen delivery and is observed in approximately 15–20% of cardiosurgical patients [1]. Previous studies, comparing survivors *vs.* non-survivors following non-transplant cardiac surgeries, have indicated that higher lactate levels upon ICU admission (2–3 mmol/l), or within early postoperative hours (3–4 mmol/l), are associated with increased perioperative risk and prolonged hospital stay [2–5].

Nevertheless, such analysis, which would define the threshold for increased postoperative risk of major complications, has never been performed in patients undergoing heart transplantation (HTX). Among these individuals, higher postoperative levels are expected, as end-organ hypoperfusion, need for inotropic and vasopressor support, and low cardiac output syndrome are commonly observed, and results from studies of other cardiac surgeries may not be comparable.

Therefore, this study aimed to assess the prognostic value and clinical usefulness of postoperative serum lactate level measurements for in-hospital mortality prediction following HTX.

Material and Methods

Forty-six consecutive patients who underwent HTX in the Department of Cardiovascular Surgery and Transplantology between 2010 and 2015 were enrolled into this retrospective analysis. All patients who underwent HTX within the analyzed period were included into the analysis. The majority of the study group were males (89.1%), with a mean age of 48.7±11.7 years, and were qualified for HTX due to dilated cardiomyopathy (73.9%) (Table 1). Serum lactate level measurements within the first 48 h after HTX were obtained from arterial blood gas analyses routinely assessed every 6 h. The observation made upon ICU admission was defined as the *zero* serum lactate measurement *(Lac 0)*. Lactate clearance was calculated based on the equation: $([lactate_{initial}–lactate_{delayed}]/lactate_{initial}\times100)$ [6], and was determined for each patient individually throughout 3 different time frames: the first 24-h period (Lac_{clear} *0–24*) and the second 24-h period (Lac_{clear} *24–48*), and the first 48 h after surgery (Lac_{clear} *0–48*). The threshold for hyperlactatemia was set at >1.6 mmol/L, based on internal laboratory standardization. The end-point was determined as death during hospitalization following HTX.

Table 1. Baseline characteristics.

Variable	Analyzed population; N=46
Age, years	48.7±11.7
Male sex, n (%)	41 (89.1)
Dilated cardiomyopathy, n (%)	34 (73.9)
Ischemic cardiomyopathy, n (%)	12 (26.1)
Dyslipidemia, n (%)	16 (34.8)
Hypertension, n (%)	21 (45.7)
Diabetes, n (%)	12 (26.1)

Data shown as mean±SD or as median (IQR), or number (percentage).

The study was approved by the Jagiellonian University Bioethics Committee (122.6120.74.2017). Verbal consent was obtained from all living patients. The study was funded by a grant from Jagiellonian University Medical College (K/ZDS/007226).

Statistical analysis

Statistical analysis was performed with IBM® SPSS® Statistics 25. Normality of data distribution was tested using the Shapiro-Wilk test. Continuous variables are presented as means and standard deviation (±SD) or medians and interquartile ranges (IQR). For categorical variables, numbers and proportions are reported. The non-parametric test for independent samples (Mann-Whitney U test) was used to assess differences between groups. Univariate regression analysis followed by multivariate regression were performed to explore the relationship between various serum lactate measurements and in-hospital mortality. All available serum lactate level measurements were included into the univariate analysis. Receiver operating characteristic (ROC) curves and respective areas under the ROC curves (AUC) were constructed to identify the optimal marker and cut-off value.

Results

The ICU admission serum lactate level (*Lac 0*) differed between the deceased and survivors (7.6 *vs.* 4.3 mmol/L; p=0.000), with no differences observed in the lactate clearance parameters throughout the observation (Figure 1). In the multivariate regression model, from all analyzed lactate parameters, only the ICU admission serum lactate level (*Lac 0*) independently

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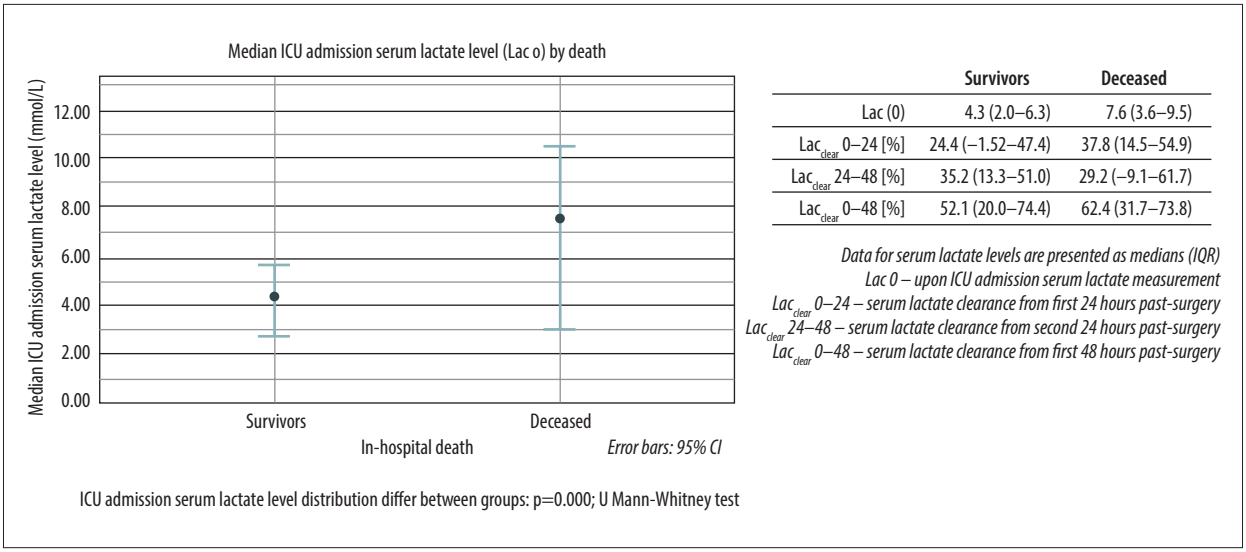

	Survivors	Deceased
Lac (0)	4.3 (2.0–6.3)	7.6 (3.6–9.5)
Lac_{clear} 0–24 [%]	24.4 (–1.52–47.4)	37.8 (14.5–54.9)
Lac_{clear} 24–48 [%]	35.2 (13.3–51.0)	29.2 (–9.1–61.7)
Lac_{clear} 0–48 [%]	52.1 (20.0–74.4)	62.4 (31.7–73.8)

Data for serum lactate levels are presented as medians (IQR)
Lac 0 – upon ICU admission serum lactate measurement
Lac_{clear} 0–24 – serum lactate clearance from first 24 hours past-surgery
Lac_{clear} 24–48 – serum lactate clearance from second 24 hours past-surgery
Lac_{clear} 0–48 – serum lactate clearance from first 48 hours past-surgery

Figure 1. ICU admission serum lactate level (*Lac 0*) by in-hospital death.

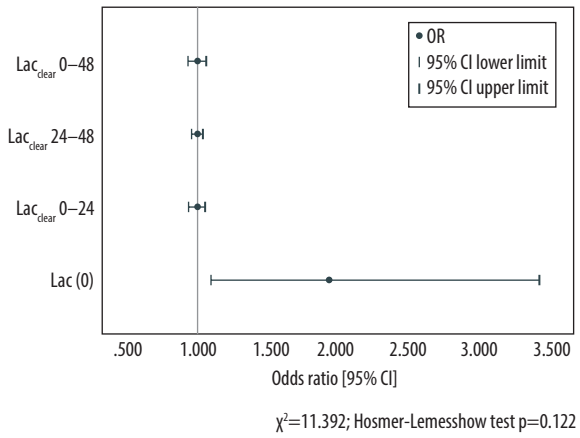

Figure 2. Selected postoperative lactate level measurements for in-hospital mortality prediction. A mutli-variate regression model.

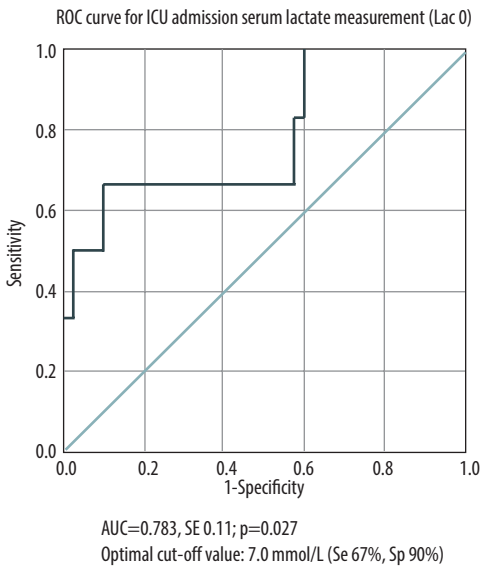

Figure 3. Receiver operating characteristic (ROC) curve for prediction of in-hospital mortality.

predicted in-hospital mortality (OR 1.94 95% CI [1.09–3.43]; p=0.024) (Figure 2). The ROC for in-hospital mortality was constructed for the ICU admission serum lactate level (*Lac 0*), and the optimal cut-off value was estimated to be 7.0 mmol/L (67% sensitivity, 90% specificity) (Figure 3).

Discussion

Early-onset hyperlactatemia is strongly associated with postoperative adverse events, presumably due to the complex pathogenesis, which combines hypoxic (circulatory or microcirculatory shock) and non-hypoxic (accelerated aerobic metabolism) mechanisms [1]. Because it reflects the status of tissue perfusion, it is used to predict early outcome in terms of mortality, morbidity, and ICU length of stay following cardiosurgical procedures [2–5].

Nevertheless, adapting thresholds for serum lactate levels corresponding with higher postoperative risk, established for other cardiac surgeries, will not be clinically efficient, as serum lactate levels observed early after HTX are higher, even among the survivors (Figure 1). However, to date, only 2 studies on postoperative hyperlactatemia among heart transplant recipients have been published. Extreme hyperlactatemia was defined

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by Hsu et al. as the serum lactate level over 15 mmol/L and was reported to have a prevalence rate of 20.7% in patients after HTX. Despite the further serum lactate level decrease below 4 mmol/L, all patients died either while in the hospital (33.3%) or within 5 years after HTX (66.6%) [7]. In another study, the cut-off level for postoperative hyperlactatemia was set according to the guidelines for severe sepsis and septic shock treatment (4 mmol/L). Based on this estimation, postoperative hyperlactatemia was observed among two-thirds of the recipients, but no in-hospital deaths were reported [8]. Both of these studies only evaluated the fact of reaching the predefined threshold, which had never previously been defined for heart transplant recipients. Based on the present study, which sought to define the threshold, the cut-off value of 7 mmol/L should be considered relevant for in-hospital mortality prediction (Figure 3).

Although single serum lactate concentration is potentially useful, it does not contain directional information about the patient's improvement or deterioration. Sequential serum lactate level measurements, which have been assessed for patients undergoing coronary artery bypass-grafting, mitral valve surgery, or Norwood procedure, showed that high lactate concentration is associated with inability to clear blood lactate levels, and have highest predictive value for adverse outcome [9–11]. However, among heart transplant recipients, no such association was found for lactate utilization ability and, unlike other cardiosurgical populations, hyperlactatemia was not combined with low lactate clearance values (Figure 1). Although metabolic pathways that provide lactate resolution are widely described in the literature [1], there is still limited knowledge regarding clinical features that might alter individual ability to clear serum lactate.

The greatest study limitation is the small sample size, which did not allow us to test the applicability of the estimated cut-off value. However, we believe that setting a threshold to be tested and further investigated by other researchers will allow such data to be produced in the future.

Conclusions

Serum lactate level measurement upon ICU admission can be used as a predictive parameter for in-hospital mortality among heart transplant recipients. Values greater than 7.0 mmol/L can determine in-hospital mortality with 90% specificity.

Conflict of interest

None.

References:

1. Minton J, Sidebotham DA: Hyperlactatemia and cardiac surgery. J Extra Corpor Technol, 2017; 49(1): 7–15
2. Renew JR, Barbara DW, Hyder JA et al: Frequency and outcomes of severe hyperlactatemia after elective cardiac surgery. J Thorac Cardiovasc Surg, 2016; 151(3): 825–30
3. Hajjar LA, Almeida JP, Fukushima JT et al: High lactate levels are predictors of major complications after cardiac surgery. J Thorac Cardiovasc Surg, 2013; 146(2): 455–60
4. Andersen LW, Holmberg MJ, Doherty M et al: Postoperative lactate levels and hospital length of stay after cardiac surgery. J Cardiothorac Vasc Anesth, 2015; 29(6): 1454–60
5. Lopez-Delgado JC, Esteve F, Javierre C et al: Evaluation of serial arterial lactate levels as a predictor of hospital and long-term mortality in patients after cardiac surgery. J Cardiothorac Vasc Anesth, 2015; 29(6): 1441–53
6. Zollo AM, Ayoob AL, Prittie JE et al: Utility of admission lactate concentration, lactate variables, and shock index in outcome assessment in dogs diagnosed with shock. J Vet Emerg Crit Care, 2019; 29(5): 505–13
7. Hsu YC, Hsu CH, Huang GS et al: Extreme hyperlactatemia after heart transplantation: One center's experience. Transplant Proc, 2015; 47(6): 1945–48
8. Hoshino Y, Kinoshita O, Ono M: The incidence, risk factors, and outcomes of hyperlactatemia after heart transplantation. Int Heart J, 2018; 59(1): 81–86
9. Lindsay AJ, Xu M, Sessler DI et al: Lactate clearance time and concentration linked to morbidity and death in cardiac surgical patients. Ann Thorac Surg, 2013; 95(2): 486–92
10. Murtuza B, Wall D, Reinhardt Z et al: The importance of blood lactate clearance as a predictor of early mortality following the modified Norwood procedure. Eur J Cardio-Thoracic Surg, 2011; 40(5): 1207–14
11. Evans AS, Levin MA, Lin H-M et al: Prognostic value of hyperlactatemia and lactate clearance after mitral valve surgery. J Cardiothorac Vasc Anesth, 2018; 32(2): 636–43

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