Journal of Cardiothoracic and Vascular Anesthesia 31 (2017) 45–53

Contents lists available at ScienceDirect

ScienceDirect

journal homepage: www.jcvaonline.com

Use of Postoperative Peak Arterial Lactate Level to Predict Outcome After Cardiac Surgery

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Objectives: In the present study, the authors investigated the predictive value of postoperative peak arterial lactate levels for early and late mortality after cardiac surgery.
Design: Retrospective analysis of prospectively collected data.
Setting: Single-center study in an academic hospital.
Participants: Adult patients who underwent cardiac surgery between 2004 and 2014 (n = 16,376).
Interventions: Different cardiac surgical procedures.
Measurements and Results: Patients were classified according to the peak arterial lactate level (PALL) within 3 days postoperatively. Logistic regression analysis and Cox regression analysis were performed to identify postoperative peak arterial lactate level as a predictor for early and late mortality respectively.

In 8460 patients (51.7%), lactate was not measured postoperatively because these patients were managed according to the fast-track protocol. These patients constituted group 1 in our population but were excluded from the regression analysis. The remaining patients (n = 7,916; 48.3%) were divided according to the postoperative peak arterial lactate level (PALL): PALL $<$ 5 mmol/L (group 2), PALL 5 to 10 mmol/L (group 3), and PALL of $>$ 10 mmol/L (group 4). Early mortality was 3.7%, 20.4%, and 62.9% in groups 2, 3, and 4 respectively ($p < 0.0001$). This mortality rate was significantly higher than that of group 1 (1.6%); $p < 0.0001$. Multivariate regression analyses revealed postoperative peak arterial lactate as a significant predictor of 30-day mortality (odds ratio = 1.44 [1.39-1.48], $p < 0.001$) as well as for late mortality (hazard ratio = 1.05 [1.01-1.10], $p < 0.025$).
Conclusions: Postoperative peak arterial lactate level in patients undergoing cardiac surgery is an independent predictor for both early and late mortality.

Key Words: cardiac surgery, hyperlactatemia, mortality; survival analysis; outcomes

INCREASED LACTATE LEVELS during and following cardiac surgery frequently are encountered and the clinical impact has been the subject of considerable discussion in the literature.[1-8] Although the exact mechanism for hyperlactatemia during cardiac surgery is not known, the role of lactate levels in detecting the severity of perioperative circulatory failure in patients recovering from cardiac surgery has been advocated.[5-7] Several reports substantiated that increased perioperative lactate levels were associated with postoperative complications, including mortality.[8-10] It has been demonstrated that multiple factors contribute to lactate metabolism

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http://dx.doi.org/10.1053/j.jvca.2016.04.017
1053-0770/

after cardiac surgery. For example, pre-existing liver and kidney function, splanchnic circulation during cardiopulmonary bypass, and intraoperative anesthetic management of hemodynamics during cardiac surgery might contribute to postoperative hyperlactatemia. On the other hand, postoperative cardiac performance and reduced oxygen delivery to critical organs substantially contribute to lactate production.[1,7] It generally is accepted that the clinical impact of postoperative hyperlactatemia because of tissue hypoxia is worse compared with nonhypoxic causes. However, both mechanisms are reported to occur in cardiac surgery and this may call into question the predictive reliability of postoperative lactate levels with regard to outcome.[2] Furthermore, most reports focused on early complications and mortality after cardiac surgery, while previous evidence suggested that perioperative factors and management also influenced the long-term outcome.[11] Preoperative stratification models such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE) do not consider these perioperative factors.[11] Postoperative monitoring of cardiac surgical patients using serial blood markers such as arterial lactate also could be used to predict the prognosis. However, timing and frequency of blood sampling for lactate monitoring during and after cardiac surgery are controversial.[1,7,9] In this study, the authors investigated the hypothesis that postoperative peak arterial lactate level (PALL) within 3 days postoperatively could predict early and late mortality in patients undergoing cardiac surgery.

Patients and Methods

In this study, data for all patients undergoing cardiac surgery at the Catharina Hospital in Eindhoven, the Netherlands, between January 2004 and April 2014 were analyzed. The institutional database contains prospectively collected data, including all clinical data, demographic data, risk factors, and laboratory data of all patients undergoing cardiac surgery at the facility. The institutional review board approved the study and waived the need for informed consent.

For the present analysis, postoperative PALL within the first 3 days postoperatively was considered. In 8,460 (51.6%) patients, PALL was not collected because most of these patients were managed according to the fast-track protocol, which did not include arterial lactate measurement. All of these patients were transferred to the ward within 24 hours after surgery. Although these patients were not considered in the regression analysis of the present study, the authors chose to address the data regarding their baseline characteristics, operative information, and outcomes. These patients were presented as group 1 but were not included in the analysis because their arterial lactate was not measured postoperatively. The rest of the patient population (n = 7,916; 48.4%) stayed longer than 24 hours in the intensive care unit (ICU). Serial measurements of arterial lactate are performed as standard care for all patients in the ICU. The time-based protocol is to measure lactate at least twice daily. Repeated lactate measurements are guided by the degree of hyperlactatemia with or without hemodynamic instability. These patients were classified into 3 groups according to PALL within the first 3 days postoperatively: group 2 (PALL $<$ 5 mmol/L), group 3 (PALL = 5-10 mmol/L), and group 4 (PALL $>$ 10 mmol/L).

The primary endpoints of the study were early mortality, defined as all-cause mortality within 30 days after surgery; and late mortality, defined as all-cause mortality later than 30 days postoperatively. Follow-up data concerning late mortality were gathered using the database of the authors' institution, which includes information from healthcare insurance companies, general practitioners, and databases of local government authorities. Mortality data are checked regularly through a direct link with the local government authority.

Anesthetic and Operative Techniques

All patients were treated according to the cardiac anesthesia protocol at the authors' institution, with the standard preoperative medication and a routine ventilation protocol. In brief, anesthesia was induced with fentanyl, etomidate, midazolam, and rocuronium and maintained with continuous administration of propofol and alfentanil. All patients received a central venous catheter and a radial artery catheter. Depth of anesthesia was monitored with a bispectral index monitor (Philips Medical System, Best, The Netherlands). Ventilation parameters were set to achieve tidal volumes between 6 and 10 mL/kg, positive end-expiratory pressure of 5 cmH_2O and end-tidal CO_2 levels between 4% and 5%.

After institution of cardiopulmonary bypass (CPB) using normothermic nonpulsatile flow, cardiac arrest was induced with cold antegrade crystalloid cardioplegia (St Thomas solution) or warm intermittent antegrade blood cardioplegia, according to the surgeon's preference.

Patients were weaned from CPB only when the nasal temperature was $\geq$ 37.0°C and the rectal temperature was $\geq$ 36.0°C. If necessary, dobutamine, norepinephrine or milrinone was used for hemodynamic support to facilitate weaning. The operative mean aortic pressure was maintained at $\geq$ 60 mmHg during CPB.

ICU Management

In the authors' institution, postoperative care for patients after cardiac surgery is standardized and carried out according to an institutional postcardiac surgery protocol. In the ICU, a daily standard time-based protocol is used for blood sampling and laboratory diagnostics, including arterial lactate measurement. Additional sampling of arterial lactate is performed in cases of initial hyperlactatemia or when one of the following criteria of hemodynamic instability and decreased organ flow is present: low blood pressure (mean under 60 mmHg), low peripheral temperature ($<$ 30°C), low urine output ($<$ 30 mL/h), low venous saturation ($SvO_2 < 60$ mmHg) or the use of inotropic agents. Hypovolemia is treated with infusion of