Evaluation of Serial Arterial Lactate Levels as a Predictor of Hospital and Long-Term Mortality in Patients After Cardiac Surgery

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Objectives: **Although hyperlactatemia is common after cardiac surgery, its value as a prognostic marker is unclear. The aim of the present study was to determine whether postoperative serial arterial lactate (AL) measurements after cardiac surgery could predict outcome.**

Design: **Prospective, observational study.**

Setting: **Surgical intensive care unit in a tertiary-level university hospital.**

Participants: **Participants included 2,935 consecutive patients.**

Interventions: **AL was measured on admission to the intensive care unit and 6, 12, and 24 hours after surgery, and evaluated together with clinical data and outcomes including in-hospital and long-term mortality.**

Measurements and Main Results: **In-hospital and long-term mortality (mean follow-up 6.3 ± 1.7 years) were 5.9% and 8.7%, respectively. Compared with survivors, nonsurvivors showed higher mean AL values in all measurements ($p < 0.001$). Hyperlactatemia (AL >3.0 mmol/L) was a predictor for in-hospital mortality (odds ratio = 1.468; 95% confidence interval = 1.239-1.739; $p < 0.001$) and long-term mortality (hazard ratio = 1.511; 95% confidence interval = 1.251-1.825; $p < 0.001$). Recent myocardial infarction and longer cardiopulmonary bypass time were predictors of hyperlactatemia. The pattern of AL dynamics was similar in both groups, but nonsurvivors showed higher AL values, as confirmed by repeated measures analysis of variance ($p < 0.001$). The area under the curve also showed higher levels of AL in nonsurvivors (80.9 ± 68.2 *v* 49.71 ± 25.8 mmol/L/h; $p = 0.038$). Patients with hyperlactatemia were divided according to their timing of peak AL, with higher mortality and worse survival in patients in whom AL peaked at 24 hours compared with other groups (79.1% *v* 86.7%-89.2%; $p = 0.03$).**

Conclusions: **The dynamics of the postoperative AL curve in patients undergoing cardiac surgery suggests a similar mechanism of hyperlactatemia in survivors and nonsurvivors, albeit with a higher production or lower clearance of AL in nonsurvivors. The presence of a peak of hyperlactatemia at 24 hours is associated with higher in-hospital and long-term mortality.**

KEY WORDS: cardiac surgery, hyperlactatemia, area under the curve, postoperative care, in-hospital, long-term mortality

HYPERLACTATEMIA HAS BEEN ASSOCIATED with worse outcomes during circulatory failure, regardless of the presence of acidosis or anion gap disturbances.[1,2] Hyperlactatemia is common after cardiac surgery and is associated with poorer outcomes.[3–7] It mainly appears to be related to an imbalance between oxygen delivery and needs (type A hyperlactatemia) during cardiopulmonary bypass (CPB) or after cardiac surgery.[6] Lactate production increases in cells as a result of anaerobic glycolysis. Organ dysoxia mainly occurs in peripheral and nonvital tissues during CPB, becoming more severe as a result of inadequate cardiac output.[4] However, a considerable body of evidence has shown that hyperlactatemia may be due to increased aerobic lactate production.[8] Confounding variables such as the presence of liver cirrhosis may lower lactate clearance rates, and the presence of hyperlactatemia should be interpreted with caution and on a case-by-case basis.

Preoperative stratifications such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE)[9] and the Parsonnet score[10] do not take into account the morbidity and mortality produced by intraoperative and postoperative factors,[11] and other models that evaluate the postoperative period in the intensive care unit (ICU) do not take into account intraoperative factors, such as CPB time.[12] Patient prognosis during the initial postoperative period may differ significantly from the preoperative estimation. Hyperlactatemia, defined based on a threshold of 3 mmol/L,[5,6] is associated with intraoperative complications and with postoperative outcome.[3,6] Serial arterial lactate (AL) levels in the blood also have been evaluated in pediatric and adult patients undergoing cardiac surgery, with similar results in terms of outcomes.[7,13] However, the dynamics of the AL curve and the impact of the timing of hyperlactatemia on postoperative outcome and late mortality after discharge have not been evaluated. Furthermore, the incremental area under the curve (AUC), which has been used to evaluate endocrinologic factors such as glucose[14] and cortisol levels[15] and is a reflection of changes over time in the intensity of a measured factor, has not been used to date to assess AL levels in adult patients undergoing cardiac surgery.

The aim of the present study was to determine whether serial AL measurements after cardiac surgery could predict postoperative outcome. For this purpose, the authors evaluated the dynamics (level changes over time), intensity (estimation of AL production), and timing of AL levels during the first 24 hours of the postoperative period to determine whether they

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1053-0770/2601-0001$36.00/0

http://dx.doi.org/10.1053/j.jvca.2015.04.024

could serve as tools for postoperative assessment including the long-term outcome. Predictors of hyperlactatemia (AL levels >3 mmol/L) also were studied.

METHODS

This study was a prospective study of 2,935 consecutive patients undergoing different types of cardiac surgery between January 2004 and December 2009 at a university hospital. Patients undergoing heart transplant (n = 134), patients undergoing off-pump coronary artery bypass (n = 185), and patients with liver dysfunction (n = 62) were excluded because of the different pathophysiology of AL production under these conditions.[3] The study was approved by the Institutional Ethics Committee of the hospital (Comité d'Ètica i Assajos Clínics, Hospital Universitari de Bellvitge). Owing to the observational nature of the study, the need for consent was waived. The follow-up was conducted using the Catalan Health Central Registry. The hospital records data were deidentified and analyzed anonymously. A complete follow-up to May 2013 was available for 2,837 patients (mean follow-up 6.3 ± 1.7 years).

AL was measured on ICU admission and 6, 12, and 24 hours after cardiac surgery and evaluated together with clinical data and outcomes. AL measurements were performed in the local laboratory using amperometric measuring principles with a range measurement of 0.0 to 30.0 mmol/L (reference range, 0.5-2.2 mmol/L). Data on and during ICU admission were extracted from the medical registry of each patient in real time using a standardized questionnaire and recorded in the local database for analysis. Recent acute myocardial infarction (AMI) was defined as an AMI that required admission to the hospital during the month before cardiac surgery or an AMI that did not allow discharge from the hospital before cardiac surgery. Long-term mortality was defined as late mortality after discharge and excluded in-hospital mortality. Major bleeding was defined as an output from chest drains >300 mL during 3 hours the first 24 hours after cardiac surgery. The other definitions used for this study were based on the Society of Thoracic Surgeons national cardiac surgery database definitions.[16] Preoperative data (demographic data, comorbidities, and treatment before cardiac surgery), operative data, and postoperative variables usually were measured on and during admission and included main outcomes. Cardiac surgery scores (Parsonnet, EuroSCORE) and ICU scores (APACHE II and III, SAPS II and III) were recorded for risk assessment.

Hyperlactatemia was defined as an AL concentration >3.0 mmol/L, in accordance with the previous literature.[3–6] Patients

Table 1. Preoperative Variables in In-Hospital Survivors and Nonsurvivors

	All patients (n = 2,935)	Survivors (n = 2,761; 94.1%)	Nonsurvivors (n = 174; 5.9%)	p Value
Sex (male)	63.9% (1,876)	64% (1,768)	62% (108)	0.63
Sex (female)	36.1% (1,059)	36% (993)	38% (66)	
Age (y)	64.5 ± 11.6	64.2 ± 11.6	69.9 ± 9.7	<**0.001**
BMI (kg/m^2)	28 ± 4.3	27.9 ± 4.2	27.9 ± 4.6	0.93
Hypertension	62.8% (1,844)	62.0% (1,713)	75.3% (131)	<**0.001**
Diabetes mellitus	25.5% (748)	24.9% (689)	33.9% (59)	**0.01**
Dyslipidemia	50.5% (1,483)	50.3% (1,388)	54.6% (95)	0.27
Peripheral vascular disease	8.9% (262)	8.3% (230)	18.4% (32)	<**0.001**
Chronic renal insufficiency	5.3% (156)	4.7% (129)	15.5% (27)	<**0.001**
Renal failure (on dialysis)	0.8% (24)	0.8% (21)	1.7% (3)	0.16
Creatinine before surgery (mmol/L)	96 ± 60	95 ± 59	119 ± 66	<**0.001**
Previous stroke	5.7% (166)	5.5% (152)	8.0% (14)	0.17
COPD	11.0% (352)	11.6% (321)	17.8% (31)	**0.021**
Active smokers	23.1% (678)	23% (636)	24.1% (42)	0.46
Previous atrial fibrillation	23.9% (701)	23.4% (646)	25.8% (45)	0.35
Previous myocardial infarction	15.5% (454)	15.2% (420)	19.5% (34)	0.13
Recent myocardial infarction	11.1% (325)	10.6% (292)	19.0% (33)	**0.002**
NYHA class III-IV	41.7% (1,225)	41.7% (1,152)	41.9% (73)	0.92
On β-blockers	41% (1,204)	41.1% (1,134)	40.2% (70)	0.87
On statins	41.3% (1,212)	41.3% (1,141)	40.8% (71)	0.93
On aspirin	44.5% (1,306)	44.5% (1,230)	43.7% (76)	0.87
On diuretics	47.6% (1,396)	46.6% (1,286)	63.2% (110)	0.001
Hypertrophic cardiomyopathy	31% (909)	30.6% (847)	35.6% (62)	0.26
Dilated cardiomyopathy	20.4% (600)	20.2% (558)	24.1% (42)	0.29
LVEF (%)	60 ± 12	59 ± 13	60 ± 11	0.31
PAP (mmHg)	46 ± 16	45 ± 16	49 ± 16	0.05
Hemoglobin before surgery (g/dL)	13 ± 1.7	13 ± 1.7	12 ± 1.9	**0.01**
Platelet count before surgery (×10^9/nl)	215 ± 68	216 ± 68	206 ± 74	0.07
Emergent surgery	5.0% (148)	4.5% (124)	13.8% (24)	<**0.001**
Past cardiac surgery	9.4% (276)	9.2% (253)	13.2% (23)	0.08
EuroSCORE	6.3 ± 3.5	5.7 ± 2.8	8.5 ± 3.7	<**0.001**
Parsonnet score	11.5 ± 4.4	11.2 ± 7.1	15.3 ± 9.6	<**0.001**

NOTE. Results are expressed as mean ± SD or percentage.

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PAP, pulmonary arterial pressure.