Frequency and outcomes of severe hyperlactatemia after elective cardiac surgery

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ABSTRACT

Background: Hyperlactatemia is relatively common in the cardiac surgical patient and is usually considered a marker of illness severity. The frequency and impact of severe hyperlactatemia after elective cardiac surgery has not been described, and prognosis may be different compared with that for other surgical or medical critically ill patient populations.

Methods: We conducted a retrospective study to evaluate the hospital course and outcomes of patients who developed severe postoperative hyperlactatemia (SPHL; lactate >10 mmol/L) after elective cardiac surgery, from January 1, 2008 to December 31, 2012, at a large, academic, tertiary referral center.

Results: Of 9580 cardiac surgical patients who met inclusion criteria, 121 (1.26%) developed SPHL. The most common cause was cardiogenic shock (53.8%). In-hospital mortality was 40.5% but varied widely based on the cause of the SPHL. All patients with definite mesenteric ischemia (n = 5) or extremity compartment syndrome (n = 6) at the time of SPHL died in the hospital. Forty patients (33.1%) were discharged to home, whereas 32 (26.4%) were discharged to a skilled-care facility.

Conclusions: Severe postoperative hyperlactatemia is rare after elective cardiac surgery. Although this phenomenon continues to be associated with mortality, >50% of patients survived to hospital discharge, a more favorable prognosis, compared with other patient populations based on lactate levels alone. Important exceptions were patients who had extremity compartment syndrome or mesenteric ischemia, which were associated with in-hospital death in all cases. In all other etiologic groups, a substantial proportion of patients were discharged to home. (J Thorac Cardiovasc Surg 2016;151:825-30)

Hyperlactatemia in the cardiac surgical population is a well described and relatively common phenomenon.1-5 These patients may undergo substantial hemodynamic perturbations associated with cardiopulmonary bypass (CPB), vasoactive medications, and ischemic injury. Although lactic acidosis can have various etiologies, the presence of an elevated serum lactate level after cardiac surgery has been associated with an increased incidence of postoperative infection, cardiopulmonary dysfunction, renal impairment, prolonged hospital stay, and increased mortality.2,3,6-8 Furthermore, striving to achieve normal lactate values in the postoperative setting has been shown to decrease hospital length of stay after cardiac surgery.9 The normal plasma lactate concentration10 is 0.5 to 1.5 mmol/L. Previous studies have used lactate thresholds of 2 to 5 mmol/L to describe hyperlactatemia and its impact on postoperative outcomes in cardiac surgical patients.11,13,14 No clear consensus has been reached on the cutoff value determining severe hyperlactatemia. However, evidence has been found that at lactate levels >10 mEq/L, the liver and kidney become saturated for lactic acid uptake.10 The frequency and impact of severe postoperative hyperlactatemia (SPHL) after cardiac surgery, defined as plasma lactate levels >10 mEq/L, have not been reported.

The purpose of our investigation was to determine the frequency, clinical impact, and outcomes of SPHL after...
elective cardiac surgery. We evaluated etiology, perioperative management, implications, mortality, and discharge disposition.

METHODS
This study was approved by the Institutional Review Board of Mayo Clinic, and all patients provided written informed consent for the use of their records for research purposes. A computerized search of the medical records database, of records from January 1, 2008 to December 31, 2012, was conducted. The DataMart, a near–real-time electronic database that was developed and validated at Mayo Clinic, imports data from electronic medical records; this system was used to identify patients who developed SPHL after elective cardiac surgery involving CPB. Patients were excluded from analysis if they were aged <18 years, needed emergency and/or urgent surgery, underwent left ventricular assist device implantation, heart or lung transplantation, preoperative mechanical ventilation, or a preoperative need for extracorporeal membrane oxygenation. Once all patients who had SPHL were identified, electronic records were manually reviewed to retrieve baseline characteristics, intraoperative variables, and postoperative events.

Patient Data
Documented postoperative variables included: peak plasma lactate value; use and maximum doses of vasopressors or inotropes; development of severe acute kidney injury; performance of exploratory laparotomy for suspected ischemic bowel and associated intraoperative findings; performance of fasciotomy for extremity compartment syndrome; lowest postoperative hemoglobin; presence of a sepsis diagnosis; days of mechanical ventilation; intensive care unit length of stay; and hospital length of stay. Acute kidney injury was defined according to the Kidney Disease/Improving Global Outcomes guidelines, and was included if the serum creatinine level increased by 2 to 2.9 times the baseline level, or if renal replacement therapy (stages 2 and 3) was initiated. Sepsis and liver failure were included when they had been documented in the electronic medical record as being a possible diagnosis.

Definition of Severe Postoperative Hyperlactatemia
Severe postoperative hyperlactatemia was defined as a peak plasma lactate value >10 mEq/L at any time after arrival to the intensive care unit, regardless of pH or base deficit because buffer administration is common in cardiac surgery. The primary exposure was presence of SPHL after elective cardiac surgery. The causes of hyperlactatemia were recorded, as well as their detailed perioperative management, including surgical interventions required to treat the underlying cause of hyperlactatemia (eg, exploratory laparotomy, compartment release).

The etiology of SPHL was determined via review of all electronic medical records by 1 of the investigators. Most SPHL etiologies were documented in the record by the surgical team, the intensive care team, or the consultation service (gastroenterology, infectious diseases, pulmonaryology). If no etiology had been documented, the clinical context, hemodynamic profile, and laboratory analysis were examined in detail. Cardiogenic shock was defined as a cardiac index <2.2 L/minute/m², with need of inotropic support (epinephrine, milrinone, dopamine, dobutamine, isoproterenol), with or without the assistance of an intra-aortic balloon pump at the time of peak lactate value.

Vasoplegic shock was defined as a cardiac index >3.0 L/minute/m², systemic vascular resistance <700 dynes-second/cm², and the absence of sepsis, liver failure, or mesenteric ischemia. Cardiac index was determined with the use of a pulmonary artery catheter or monitors utilizing arterial pressure waveform analysis. If both were available and discrepant, clinical context determined the etiology. Hemorrhagic shock was identified through manual chart reviews that revealed acute blood loss that required surgical re-exploration. Obstructive shock was defined as evidence or strong suspicion of pulmonary embolus, as determined using computed tomography and/or echocardiography; or as the presence of cardiac tamponade, determined via echocardiography or during surgical re-exploration. The etiology of SPHL was documented as “indeterminate” if review of the chart demonstrated a normal cardiac index or no documented cardiac index, and the clinical context and laboratory data did not suggest any specific cause.

Outcomes
Endpoints were in-hospital mortality and discharge disposition. Categoric variables are reported as frequencies and percentages. Continuous variables are reported as mean (SD), or median (interquartile range), as appropriate.

RESULTS
The final study population included 9580 patients, of whom 121 (1.26%) experienced SPHL (Figure 1). Patients who developed SPHL commonly had chronic hypertension, preoperative anemia, a history of prior cardiac surgery, and a preoperative ejection fraction <55% (Table 1). Some patients had >1 cause of SPHL. Cardiogenic shock was the most frequent contributing etiology, accounting for 78 of the 145 (53.8%) causes of SPHL. The second most common known contributing etiology was septic shock, accounting for 16 patients (11.0%) (Tables 1 and 2).

A total of 49 (40.5%) patients died during the index hospital admission; 40 (33.1%) were discharged to home. The remaining 32 (26.4%) were discharged to a skilled-care facility that included nursing facilities, home health care, inpatient rehabilitation, and long-term acute-care hospitals (Table 2).

Nine patients underwent laparotomy to explore for mesenteric ischemia, and 5 of 9 (55.6%) were found to have nonviable bowel. Of these, 1 patient had diffuse bowel ischemia, and 4 had localized ischemia amenable for bowel resection. All patients with SPHL who went for exploratory laparotomy died during the hospital stay. Six patients underwent fasciotomy for lower-extremity compartment syndrome, and all died in the hospital.

Of the 121 patients with SPHL, the average peak lactate value was 15.2 ± 5.4 mmol/dL. Patients with mesenteric ischemia had the highest average peak lactate value (22.8 ± 8.7 mmol/dL), followed by patients with extremity compartment syndrome (17.5 ± 3.9 mmol/dL) (Figure 2).

Most lactate values peaked within the first 24 hours after arrival to the intensive care unit (ie, postoperative day 0). Patients with mesenteric ischemia had lactate values that tended to peak later in the hospital stay, either on postoperative day 2 or after postoperative day 10. Patients with
abdominal compartment syndrome had lactate values that peaked more frequently after postoperative day 10 (Figure 3).

**DISCUSSION**

The present study is the largest of a series of patients who had SPHL after cardiac surgery. We found that SPHL was uncommon in patients undergoing elective cardiac surgery (1.26%); this percentage is much lower than the previously reported frequencies of mild intraoperative (11.4%-18%) and postoperative (20.6%) hyperlactemia. Postcardiotomy cardiogenic shock was the most common etiology of SPHL and carried a more favorable prognosis, whereas mesenteric ischemia or lower-extremity compartment syndrome were associated with 100% mortality.

Lactic acid levels often guide hemodynamic resuscitation, because this value is considered a reflection of deficient oxygen delivery, a marker of illness severity, and is associated with high mortality. Thirty-day mortality for mild postoperative hyperlactatemia after cardiac surgery, with serum lactate levels peaking between 2 and 4 mmol/L, has been reported to be 5.2%. The overall survival to hospital discharge of 59.5% in our series, although lower, represents a cohort of patients who have an inherently more severe degree of lactic acidosis.

The clinical context and etiology must be taken into consideration for determining management and prognosis. For instance, trending lactates in the setting of septic shock is a well established practice, for monitoring tissue oxygenation and guiding hemodynamic resuscitation, that correlates with improved patient outcomes. However, in contrast to the postoperative setting, patients with sepsis-related hyperlactatemia experience much higher mortality rates (62%), despite having similar absolute serum lactate values.

Twenty patients (13.8%) had no discernable etiology of SPHL. This fact highlights the diagnostic challenge that the elevated lactate values may present. Multiple factors can lead to lactic acidosis, including increased lactic acid production, and decreased uptake and clearance. Type B lactic acidosis is defined as the presence of lactatemia

![Total number of patients undergoing cardiac surgery (n = 12,925)

Total surgical patients included (n = 9580)

SPHL (n = 121)

Patients excluded:
- Age < 18 years (n = 987)
- Repeat procedures (n = 1331)
- No research authorization (n = 322)
- Emergency surgery (n = 252)
- ECMO (n = 75)
- Other, including pre-existing bilateral pulmonary infiltrates, preoperative ventilator dependence, not expected to survive 48 hours, low-risk procedure (n = 378)

**FIGURE 1.** Methods flow diagram. ECMO, Extracorporeal membrane oxygenation; SPHL, severe postoperative hyperlactatemia.

**TABLE 1.** Demographics and surgical characteristics of patients with severe postoperative hyperlactatemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>63.1 ± 15.6</td>
</tr>
<tr>
<td>Gender, female</td>
<td>44 (36.4)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>30.1 ± 7.1</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>69 (57.0)</td>
</tr>
<tr>
<td>Preoperative anemia*</td>
<td>44 (36.4)</td>
</tr>
<tr>
<td>Prior cardiac surgery</td>
<td>58 (47.9)</td>
</tr>
<tr>
<td>Preoperative LVEF &lt;55%</td>
<td>46 (38.0)</td>
</tr>
<tr>
<td>History of smoking</td>
<td>52 (43.0)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>46 (38.0)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>36 (29.8)</td>
</tr>
<tr>
<td>Preoperative metformin</td>
<td>13 (10.7)</td>
</tr>
<tr>
<td>Preoperative dialysis</td>
<td>6 (4.96)</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>170.8 ± 124.0</td>
</tr>
<tr>
<td>Aortic crossclamp time (min)</td>
<td>97.9 ± 59.0</td>
</tr>
<tr>
<td>No. DHCA (mean time in min)</td>
<td>9 (32)</td>
</tr>
<tr>
<td>No. of pressors ± SD</td>
<td>3.5 ± 1.1</td>
</tr>
<tr>
<td>No. of IABP</td>
<td>25 (20.7)</td>
</tr>
</tbody>
</table>

Values are n (%), mean ± SD, unless otherwise indicated. LVEF, Left ventricular ejection fraction; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest; SD, standard deviation; IABP, intra-aortic balloon pump. *Hemoglobin <11.9 g/dL.
with adequate oxygen delivery, and it can be seen with medications such as steroids, epinephrine, and other inotropic agents.\textsuperscript{11,16} Although discernment and quantification of its contribution to hyperlactatemia are difficult, type B lactic acidosis can correlate with a more favorable prognosis.\textsuperscript{11,17} Presumably, patients that develop lactate values >10 mmol/L after cardiac surgery would require prolonged hospitalizations, develop numerous complications, and have poor functional status upon discharge. However, in this series, the overall survival was 59.5\%, and one third of the patients experiencing SPHL were discharged to home. This finding is encouraging and can help guide decision making and prognostication.

Another important finding was the high mortality rate for patients who developed mesenteric ischemia or extremity compartment syndrome despite aggressive perioperative critical care. The decision to perform exploratory laparotomy for resection of suspected ischemic bowel in the critically ill, postcardiotomy patient is extremely challenging to make appropriately. These patients are typically sedated, decreasing the utility of physical examination. Radiographic evidence may be inconclusive. Numerous clinical and experimental studies have demonstrated that serum lactate level is a nonspecific finding and does not accurately reflect early acute mesenteric ischemia.\textsuperscript{18-20} Nonetheless, the presence of persistent severe hyperlactatemia may be suggestive of nonviable intestine. Given that occurrence of this problem is exceedingly rare, little evidence is available within the cardiac surgical literature to assist in deciding whether to take an unstable patient back to the operating room for an invasive procedure such as laparotomy or compartment release.

Of the 9 post–cardiac surgery patients in our study who underwent exploratory laparotomy for suspected mesenteric ischemia, 6 (44.4\%) had normal bowel on surgical inspection, and all of these patients died. The average peak lactate value of the 5 patients who had confirmed mesenteric ischemia was indeed the highest (22.8 ± 8.7 mmol/dL) of the average peak lactate values by etiology, with extremity compartment syndrome ranking second (17.5 ± 3.9 mmol/dL). (Figure 2). These 2 occult etiologies may be further differentiated, from a temporal standpoint, because the lactate value tended to peak later in the hospital course (Figure 3).

### TABLE 2. Postoperative outcomes of patients with severe postoperative hyperlactatemia

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Patients</th>
<th>Discharged to home</th>
<th>Discharged to SCF</th>
<th>Patients who died</th>
<th>ICU LOS (d)</th>
<th>Hospital LOS (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogenic</td>
<td>78 (53.8)</td>
<td>16 (20.5)</td>
<td>23 (29.5)</td>
<td>39 (50.0)</td>
<td>9.1 ± 10.1</td>
<td>15.9 ± 13.8</td>
</tr>
<tr>
<td>Septic</td>
<td>16 (11.0)</td>
<td>3 (18.8)</td>
<td>3 (18.8)</td>
<td>10 (62.5)</td>
<td>12.2 ± 10.0</td>
<td>28.7 ± 21.4</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>20 (13.8)</td>
<td>15 (75.0)</td>
<td>3 (15.0)</td>
<td>2 (10.0)</td>
<td>3.8 ± 4.0</td>
<td>11.9 ± 9.9</td>
</tr>
<tr>
<td>Compartment syndrome</td>
<td>6 (4.1)</td>
<td>0</td>
<td>0</td>
<td>6 (100.0)</td>
<td>16.4 ± 14.3</td>
<td>22.1 ± 11.5</td>
</tr>
<tr>
<td>Mesenteric ischemia</td>
<td>5 (3.4)</td>
<td>0</td>
<td>0</td>
<td>5 (100.0)</td>
<td>4.6 ± 5.6</td>
<td>17.4 ± 27.9</td>
</tr>
<tr>
<td>Other*</td>
<td>20 (13.8)</td>
<td>7 (35.0)</td>
<td>6 (30.0)</td>
<td>7 (35.0)</td>
<td>13.0 ± 10.1</td>
<td>34.8 ± 21.5</td>
</tr>
<tr>
<td>Overall</td>
<td>145</td>
<td>40 (33.1)</td>
<td>32 (26.4)</td>
<td>49 (40.5)</td>
<td>8.1 ± 9.4</td>
<td>16.3 ± 14.8</td>
</tr>
</tbody>
</table>

Values are n (\%), or mean ± SD. SCF, Skilled-care facility, including nursing home, home health care, inpatient rehabilitation center, long-term acute-care hospital; ICU, intensive care unit; LOS, length of stay. \*Other causes of severe postoperative hyperlactatemia accounted for <5\% and include: vasoplegia (n = 7); liver failure (n = 6); obstructive (n = 4); and hemorrhagic (n = 3).

FIGURE 2. Average peak lactate values, by etiology of severe postoperative hyperlactatemia. Comp., Compartment.
Limitations
This study has several limitations. Our efforts were retrospective and involved a single, large-volume tertiary care center. Due to inherent constraints, with lack of standardization of lactate checks, we considered only peak lactic acid levels, possibly underestimating the impact of persistent lactic acidosis as a more important outcome predictor. Medical record omissions or inaccuracies may have made discernment of SPHL etiology difficult.

Furthermore, limited information on baseline liver function tests and the lack of definitive diagnostic criteria for type B lactic acidosis leaves this etiology an underrepresented source of severe hyperlactatemia. Although this study accurately described the frequency of SPHL and its outcomes for patients, it was not sufficiently powered to determine the frequency of acute mesenteric ischemia that required laparotomy in the setting of persistent hyperlactatemia. Further studies are warranted to investigate such scenarios.

CONCLUSIONS
Severe postoperative hyperlactatemia is rare after elective cardiac surgery and may carry a more favorable prognosis compared with other critical illnesses.Postcardiomyotomy cardiogenic shock was the most common etiology of SPHL, and up to 30% of patients recovered with enough functionality to consider having them be discharged to home. However, acute mesenteric ischemia and lower-extremity compartment syndrome in patients with SPHL was associated with a 100% mortality. These findings deserve further evaluation, including the impact of persistent hyperlactatemia on decision making in this complex patient population.

Conflict of Interest Statement
Authors have nothing to disclose with regard to commercial support.

References
15. Park M, Azevedo LC, Maciel AT, Pizzo VR, Noritomi DT, Cruz Neto LM. Evolutive standard base excess and serum lactate level in severe sepsis and septic
The “typical” patient population that is being referred for cardiac surgery continues to evolve. The performance of complex cardiac surgical procedures in octo- and nona-genarians, once deemed borderline, is becoming commonplace.1-6 With this changing demographic, heightened vigilance is needed in perioperative care, to preserve organ perfusion and function in these patients, who often have a greater comorbidity burden and frailty.7,8 These patients have increased vulnerability to perioperative complications that may result in prolonged length of stay in the intensive care unit, and increased morbidity and mortality.9-11

A desirable goal, therefore, is to identify biomarkers that detect when a postoperative patient has “gone off the tracks” at the earliest time point, to permit the healthcare team to intervene prior to the point at which irreversible organ injury has occurred. Perhaps the most commonly used biomarker to determine inadequate oxygen delivery to meet the metabolic demands of the body’s tissues and organs is the measurement of serum lactate. Serial measurements of lactate kinetics to guide adequacy of therapy have been associated with alterations in mortality rates in critical illness.12-14

In patients undergoing cardiac surgery, early hyperlactatemia (<6 hours) has been associated with a >3-fold increase in negative outcomes.15 Similarly, blood lactate measurements have been proposed as a useful tool in prognostication for patients who require extracorporeal life support.16,17 Indeed, a previous report attempted to highlight the “indispensability” of a blood lactate-based scale to complement existing risk prediction scores.18 However, the use of this biomarker remains controversial, as alteration of glucose metabolism in acute illness may result in elevation of serum lactate levels, independent of tissue hypoxia.19 Ultimately, although many groups are very interested in the use of