Commentary

Lactate: the "Black Peter" in high-risk gastrointestinal surgery patients

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Lactate arises from metabolisation of glucose to pyruvate. Pyruvate either is transformed to or from lactate in the cytosol or converted by pyruvate dehydrogenase in mitochondria to acetyl coenzyme A which enters the Krebs cycle to produce energy for cellular metabolism. Any switch to anaerobic metabolism will reduce activity of the highly oxygen-dependent Krebs cycle and shunt "redundant" pyruvate towards lactate (1).

Why is this seemingly trifle lactate molecule so important in the intensive care unit (ICU)? Increased blood lactate concentrations are dreaded by ICU physicians since they are almost invariably linked to the presence or persistence of inadequate tissue perfusion and oxygenation. Hyperlactatemia at a cut-off value between 2 and 4 mmol/L is associated with worse outcome in all types of shock. As such, the blood lactate level has become a powerful "biomarker" to predict morbidity and mortality as well as a tool to guide resuscitation in hemodynamically compromised critically ill patients (2). However, lactate may also be produced independently from tissue hypoxia in conditions characterized by decreased pyruvate dehydrogenase activity (e.g., thiamine deficiency), modification of the cellular redox potential (e.g., ketoacidosis, ethanol abuse), or accelerated glycolytic flux (e.g., induced by drugs such as catecholamines and biguanides) (3).

Monitoring lactate has been progressively introduced in the postoperative setting. Blood lactate concentration proved to be an indispensable and accurate marker of mortality at both individual patient and patient cohort level after cardiac surgery (4). An early lactate increase was also found to predict complications after elective pancreatic (5) and extensive liver surgery (6). However, the association between lactate concentrations and mortality with regard to type of gastrointestinal (GI) surgery (emergency *vs*. elective) remained unexplored. Hyperlactatemia following elective GI surgery was intuitively accepted as a relatively "physiological" reaction to surgical stress. Indeed, a GI surgical intervention itself will cause activation of coagulation and inflammatory pathways which can be further accentuated by procedure-related gut manipulation, temporary ischemia, and eventual bacterial translocation and shedding. In contrast, elevated lactate during emergency GI surgery was traditionally linked to a more frequent occurrence of peri-operative hemodynamic instability and resuscitation-associated ischemia-reperfusion disorders.

Li *et al*. studied dynamic postoperative changes in blood lactate levels during the first 24 h after elective major abdominal surgery. They found that time-weighted average lactate at a cut-off level as low as 1.5 mmol/L was independently predictive of both overall and major postoperative complications observed in nearly half of the patients (7). These findings have now been corroborated and expanded by the recently published study of Creagh-Brown *et al*. in *Critical Care Medicine*. These investigators showed that the highest lactate level obtained on the first day after ICU admission in patients who underwent major GI surgery was independently associated with increased morbidity and in-hospital mortality. This association was not related to the type of intervention (emergency *vs*. elective) and also continued down into the "normal lactate concentration" range (8). The key message of Creagh-Brown *et al*. is that any increase in postoperative lactate after high-risk GI surgery is a "bad" prognostic sign. It can be assumed that

the increase in lactate after major GI surgery is related either to an overt imbalance between oxygen delivery and consumption (as in shock accompanying emergency surgery) or to a systemically occult deficit in tissue oxygen handling (as in elective surgery). Microcirculatory alterations that hamper gut oxygen extraction have been incriminated as the main culprit to explain insidious tissue oxygen debt during elective surgery. Increased blood lactate levels have indeed been shown to reflect microcirculatory dysfunction after general or thoracic surgery (9). However, changes in microcirculation during abdominal surgery were found to be rather modest and not correlated with perioperative lactate levels (10).

The findings of Creagh-Brown *et al*. do have important clinical implications. Interventions aimed at increasing gut perfusion or altering glycolytic flux during GI surgery should be promptly implemented in an attempt to lower deleterious lactate levels. The question is how this can be adequately and safely achieved. Glycolytic flux could be modulated by insulin administration but such treatment is controversial and may have significant and often unwarranted effects on glucose homeostasis (11). Lactate elimination in GI surgery patients could be enhanced by boosting oxygen delivery with a combination of intravenous fluids and inotropes. However, results of such "goal-directed" therapy after major surgery are conflicting (12,13) and probably benefit only those patients with the highest risk profile (14). Also, pursuing lactate normalization at all costs in the absence of other signs of tissue hypoperfusion may expose patients to the toxicity of over-resuscitation without any clear benefit. Nevertheless, lactate-driven adjustment of intravenous fluid administration intraoperatively and in the early postoperative period allowed early detection and correction of inadequate tissue perfusion and significantly decreased the overall complication rate after elective surgery for GI malignancy (15).

The study of Creagh-Brown *et al*. has some important limitations. First, the authors measured peak lactate levels within 24 h after ICU admission. Lactate levels result from a dynamic balance between lactate production and clearance. Therefore, serial lactate sampling is preferable to a single value since changes in lactate concentration may significantly lag behind clinical interventions, a transient increase in blood lactate does not necessarily predict poor clinical outcome, and sustained hyperlactatemia is associated with an even worse prognosis (16). Second, resuscitation policy (in emergency surgery) and routine surgical and anesthesiology procedures (in elective surgery) may have differed substantially between hospitals, hence introducing potential bias into the lactate/outcome relationship. For instance, artificial colloids can augment the risk of perioperative hemorrhage by more than 50% (17) while a sustained positive fluid balance in the early postsurgical period may significantly increase infectious complications and mortality in critically ill surgical patients (18). Also, the grade of intestinal mucosal damage and corresponding high lactate concentrations have been found to be directly correlated with the duration of surgery (19). Third, the study results were adjusted for age, severity of illness, and cardiopulmonary resuscitation status. However, in-hospital mortality may be determined by other variables that were not registered such as co-morbidity and complications either related (e.g., suture detachment or leakage necessitating revision), or unrelated to surgery (e.g., ICU-acquired infection or organ failure).

Despite these shortcomings, the study of Creagh-Brown *et al*. underscores that occurrence of increased blood lactate in the immediate postoperative period after major GI surgery is an ominous sign that requires close monitoring and adequate therapeutic anticipation. Future research must determine which intervention(s) best counteract hyperlactatemia after planned or acute GI surgery without harming the patient.

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Footnote

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