The early dynamic behavior of lactate is linked to mortality in postcardiotomy patients with extracorporeal membrane oxygenation support: A retrospective observational study

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Objective: Extracorporeal membrane oxygenation (ECMO) is used to support postcardiotomy cardiogenic shock patients. Elevated serum lactate levels might reflect hypoxia in the tissues, which is associated with mortality in critically ill patients. This study examined the association between the early dynamic behavior of lactate and mortality after ECMO support.

Methods: We included 123 adult patients who had undergone cardiac surgery and received venous-arterial ECMO implantation to treat refractory postcardiotomy cardiogenic shock. The dynamic behaviors of lactate within 6 hours and 12 hours after the beginning of the ECMO support were incorporated into 2 regression models.

Results: A total of 56% of the patients were successfully weaned from ECMO support. The in-hospital mortality was 65.9% overall. Univariate and multivariate analyses indicated that age (odds ratio [OR]: 1.1 in the 6-hour model; 1.1 in the 12-hour model), gender (female; OR: 5.6 in the 6-hour model; 7.7 in the 12-hour model), mean lactate concentration (OR: 1.1 in the 6-hour model; 1.2 in the 12-hour model) and lactate clearance (OR: 0.5 in the 6-hour model; 0.1 in the 12-hour model) were reliable predictors ($P < .05$) of in-hospital mortality. The mean lactate concentration (C statistic: 0.71) and lactate clearance (C statistic: 0.72) 12 hours after the initiation of ECMO support provided better prognostic guidance. The mean lactate concentration (OR: 1.2) and lactate clearance (OR: 0.3) were able to predict successful weaning from ECMO in the 12-hour model only.

Conclusions: In addition to age and gender (female), early lactate behaviors, particularly lactate clearance, after ECMO support are highly associated with in-hospital mortality in postcardiotomy patients. Additionally, early lactate behavior is also predictive of successful weaning from ECMO. (J Thorac Cardiovasc Surg 2015;149:1445-50)

See related commentary pages 1451-2.

Cardiac surgery is an important procedure for patients with heart disease. Postcardiotomy cardiogenic shock (PCS) is a life-threatening complication with an incidence that ranges from 0.5% to 1.5% in adult cardiac surgery patients.[1] Because left ventricular assist devices are not registered in People's Republic of China, extracorporeal membrane oxygenation (ECMO) is our major alternative for temporary mechanical circulatory support. This technique facilitates cardiac and pulmonary recovery, despite the use of inotropic agents and optimal medical management in PCS patients.[2] In-hospital mortality ranges from 60% to 80%,[1,3-5] with successful ECMO weaning rates ranging from 30% to 60%, as reported.[6]

Lactate is a metabolic end product of anaerobic glycolysis that is produced by the reduction of pyruvate and primarily removed by the liver.[7,8] Lactate has been proposed as a marker of tissue perfusion that is influenced by not only macrocirculation but also microcirculation (ie, the network of arterioles, capillaries, and venules), whereas traditional hemodynamic parameters have been suggested to be unreliable.[9] Lactate has been proven to be associated with increased risks of death in infection,[10] sepsis,[11] trauma,[12] and operations,[13] including cardiac surgery.[14,15] In addition, the lactate levels of intra-aortic balloon pump (IABP)[16] and ECMO-supported[17,18] patients might be predictors of mortality. However, the dynamic behavior of lactate is rarely referenced. The primary aim of this investigation was to examine the association between the dynamic behavior of lactate and mortality in postcardiotomy patients under ECMO support.

METHODS

Patients

With the approval of the Institutional Review Board of Beijing Anzhen Hospital, Capital Medical University, Beijing, People's Republic of China,

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This work was supported by grants from the National Natural Science Foundation of China (No. 81270327, 81470528 to X-T. H.), the Research Fund of Capital Medical Development (2014-1-1051 to X-T. H.), and the Beijing Municipal Science and Technology Commission-Funded Project (Z111107067311038 to N.M.).

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Aug 27, 2014; revisions received Oct 31, 2014; accepted for publication Nov 19, 2014; available ahead of print Dec 19, 2014.

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0022-5223/$36.00

http://dx.doi.org/10.1016/j.jtcvs.2014.11.052

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Abbreviations and Acronyms

CABG = (on-pump) coronary artery bypass graft
ECMO = extracorporeal membrane oxygenation
IABP = intra-aortic balloon pump
MAP = mean artery pressure
OR = odds ratio
PCS = postcardiotomy cardiogenic shock

a retrospective analysis was performed at a university-affiliated cardiac surgical intensive-care unit over a 2-year period from January 2011 to December 2012. The requirement for individual patient consent was waived because this study was based on anonymized data from routine care. A total of 123 of 13,538 (0.9%) adult patients undergoing cardiac surgery received venous-arterial ECMO implantation to treat refractory PCS. ECMO was initiated intraoperatively in the operating room for circulatory instability during or immediately after weaning from the cardiopulmonary bypass in the primary cardiac procedure. The capability to institute ECMO secondarily in the intensive-care unit, for delayed PCS, was available. The secondary indications included intractable ventricular arrhythmia or fibrillation, progressive univentricular or biventricular failure, or sudden idiopathic heart failure. The clinical criteria for PCS include systolic arterial hypotension (<80 mm Hg), increased central venous pressure exceeding 12 mm Hg, signs of end-organ failure (urinary flow rate <0.5 mL/kg), and metabolic acidosis (pH < 7.3, lactate level >3.0 mmol/L) despite optimized supportive measures, such as an IABP, inotropes, nitric oxide, and phosphodiesterase inhibitors.

Extracorporeal Membrane Oxygenation Circuit

The ECMO circuit was completely implanted via peripheral cannulation through the femoral route with the cut-down method. A distal leg perfusion cannula was introduced to prevent lower-extremity ischemia. Before cannulation, a bolus of heparin (100 units/kg) was given intravenously, and the activated clotting time was measured at >180 seconds. The ECMO circuit was primed with normal saline containing heparin at a concentration of 2 IU/ml. The ECMO circuit consisted of a centrifugal pump console (Bio-Pump PB-80, Medtronic BioMedicus, Eden Prairie, Minn; or Jostra RotaFlow centrifugal pump, Maquet, Hirrlingen, Germany) in conjunction with an inline plasma-tight hollow-fiber microporous membrane oxygenator (Affinity NTTM, Medtronic, Anaheim, Calif; or Hilite 7000 LTTM, Medos Medizintechnik AG, Stolberg, Germany) with an integrated heat exchanger.

Management Strategy

The mixed venous oxygen saturation was kept at 60% by adjusting the ECMO pump flow. Oxygen flow was titrated to maintain a postoxygenator partial oxygen pressure of ≥300 mm Hg. Carbon dioxide was maintained within the normal range by adjusting the sweep flow. The heat exchanger temperature was set to maintain the patient's normal temperature. Inotropic agents were minimized to allow for optimal myocardial recovery, and the left ventricular ejection was simultaneously maintained to avoid thrombus formation inside the left ventricle. Support with an IABP was employed in some cases to decrease afterload and to increase coronary perfusion and pulsatility. The activated clotting time was measured every 4 hours to achieve levels of 160-180 seconds via continuous intravenous heparin administration. The hematocrit was maintained at 30% to 35% by packed red blood cell transfusion. Platelets were transfused when the patient's platelet count decreased to $<50 \times 10^3/mm^3$. Midazolam and fentanyl were routinely used to sedate the patients.

All of the patients were ventilated on the volume-controlled ventilation mode at 10 breaths/min. The ventilator was commonly set at a tidal volume of 6-8 ml/kg with a positive end-expiration pressure of 6-8 mm Hg to prevent alveolar collapse, and the inspired oxygen fraction was 40%.

The circuit was checked daily and changed if hemolysis or thrombocythemia occurred, if significant fibrin depositions or clots accumulated on the membrane, or if the blood oxygenation ability faltered. Weaning was cautiously initiated only under stable hemodynamic and metabolic conditions. The full flow was decreased gradually to 1 L/min over 36-48 hours while observing the echocardiograph, metabolic status, venous saturation, and end-organ perfusion. The medicine was adjusted when necessary. The ECMO was removed at the patient's bedside under intravenous anesthesia, and the patient's vessels were primarily repaired. Successful weaning was defined by the lack of obvious hemodynamic deterioration for at least 48 hours after the removal of the ECMO support.

The adverse outcomes were defined as follows: leg ischemia (pallor, pulselessness, gangrene), multiple organ dysfunction syndrome (failure of >2 organs including renal failure, hepatic failure, neurologic dysfunction, and disseminated intravascular coagulation), infection (as proven by blood or sputum cultures obtained during ECMO support), stroke (cerebrovascular accident with neurologic impairment), and ''re-do surgeries'' (cardiac surgery of any cause after any previous cardiac surgical procedure).

Setting of the Parameters

The first arterial blood gas that contained arterial serum lactate concentrations was taken 0.5 to 1 hours after the ECMO support had commenced. Next, the arterial blood gas was measured approximately every 4 hours. In addition, the blood pressures and the times at which the blood samples were taken were recorded. The arterial lactate concentrations obtained during the first 6 hours and 12 hours after the ECMO support had commenced were averaged. The mean lactate concentration was useful but did not suggest directional information or indicate whether a patient was improving or worsening.

Lactate clearance was calculated by linear regression of the lactate concentrations over time, and the unit of lactate clearance was mmol/L · hour. Lactate clearance was positive when the lactate concentration went down, and this measure represented the dynamic behavior of lactate. The mean lactate concentrations and the lactate clearances after 6 hours (ie, the 6-hour model) and 12 hours (ie, the 12-hour model) from the initiation of ECMO support were individually incorporated into 2 regression models. The inotrope score was calculated when the inotrope agent adequately maintained a relatively stable hemodynamic status according to the following formula[19]: dosages of dopamine (in μg/kg · min) + dosages of dobutamine (in μg/kg · min) + [dosages of epinephrine (in μg/kg · min) + norepinephrine (in μg/kg · min)] × 100 + dosages of pituitrin (in u/min) × 100 + dosages of milrinone (in μg/kg · min) × 15.

Statistical Methods

Continuous variables are expressed as mean ± SD. The categoric data are given as numbers or proportions. Independent continuous variables were compared with 2-tailed Student *t* tests or Mann-Whitney *U* tests, as appropriate. Categoric variables were compared with the Pearson χ^2 statistic. Univariate and stepwise multivariate logistic regressions were used to analyze the predictors of in-hospital mortality. C statistics are reported and were used in this investigation to help determine the accuracy of the selected measures in the predictions of the selected outcomes. Linear correlations were used to analyze the relationships between the continuous variables. All statistical calculations were performed with SPSS 19.0 (SPSS, Inc, Chicago, Ill).

RESULTS

Over the 2-year period, 123 patients received ECMO support during their ICU admissions for cardiac surgery. The

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