Peripheral venoarterial extracorporeal membrane oxygenation for severe hyperlactataemia after cardiac surgery: a pilot study

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ABSTRACT

Background: Severe hyperlactataemia in patients after cardiac surgery is associated with poor prognosis and implies possible splanchnic hypoperfusion. Peripheral venoarterial extracorporeal membrane oxygenation (splanchnic ECMO) may be more effective at reducing lactic acidosis for these patients.

Objective: To investigate whether splanchnic ECMO attenuates hyperlactataemia and liver enzyme release in these patients, despite them having a cardiac index > 2 L/min/m^2 and a mixed venous oxygen saturation > 55%.

Design and participants: Retrospective matched case–control study of patients treated with splanchnic ECMO for hyperlactataemia. Seven patients who had had cardiac surgery were treated with splanchnic ECMO compared with seven matched control patients.

Results: We observed a mean decrease in lactate levels from 9.9 mmol/L (SD, 2.9 mmol/L) to 1.4 mmol/L (SD, 0.6 mmol/L) in patients receiving 48 hours of splanchnic ECMO, compared with a mean of 10.4 mmol/L (SD, 2.8 mmol/L) to 4.4 mmol/L (SD, 5 mmol/L) during 48 hours in control patients ($P < 0.0001$). Normalisation of lactate levels (to < 2 mmol/L) was achieved within a mean of 16.3 hours (SD, 14.6 hours) with splanchnic ECMO, compared with 38.3 hours (SD, 23.8 hours) in the control group ($P = 0.029$). The median increase in alanine aminotransferase level with splanchnic ECMO was 68% (range, –84% to 2015%) compared with 158% (range: 0%–6024%) (not significant) in control patients.

Conclusion: In a selected cohort of patients who had had cardiac surgery with severe post-operative hyperlactataemia, despite an acceptable cardiac index and a mixed venous oxygen saturation, splanchnic ECMO appeared to reduce overall lactate levels and time to normalisation of lactataemia.

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Hyperlactataemia of ≥ 3 mmol/L occurs in about 50% of patients undergoing cardiac surgery,[1,2] and severe hyperlactataemia (≥ 10 mmol/L) occurs in about 1.25%.[3] Lactate levels are associated with poor outcome and an eight-fold increase in the risk of mortality with each 1 mmol/L increment increase for these patients.[1,4-11] Greater mortality rates are also found in patients with slower normalisation of lactate levels,[1,12] and a lactate level > 10 mmol/L in patients receiving combined intra-aortic balloon counter-pulsation (IABP) and inotropic and vasoactive support has a 100% mortality.[13]

It is likely that splanchnic lactate release contributes to this hyperlactataemia. The associated gastric mucosal acidosis, lactic acidosis and oxygen desaturation of hepatic venous blood all suggest insufficient oxygen delivery to abdominal organs.[14-17] Splanchnic hypoxia may also occur despite an apparently clinically acceptable cardiac output.[18,19] Finally, hyperlactataemia after cardiac surgery not only suggests splanchnic hypoxia[18,20] but, when severe, typically precedes ischaemic hepatitis, liver enzyme release and coagulopathy by 12 to 24 hours.[21]

We therefore applied a strategy of limited-flow, peripheral, venoarterial extracorporeal membrane oxygenation (splanchnic ECMO) for a cohort of patients with severe hyperlactataemia. We compared our findings with those seen in a contemporaneous control cohort of patients, matched for severity of hyperlactataemia but not treated with ECMO.

Methods

Study population

We studied patients admitted to the intensive care units of two adjoining hospitals in Melbourne, Australia, from January 2010 to December 2015. First, we identified all patients treated with splanchnic ECMO for hyperlactataemia. Inclusion criteria were:

- elective coronary artery bypass graft and/or valve surgery
- severe hyperlactataemia of ≥ 7 mmol/L
- cardiac index before splanchnic ECMO ≥ 2 L/min/m^2 body surface area
- preserved mixed venous oxygen saturation
- ongoing treatment with inotropes and vasopressors.

From a contemporaneous cohort of ICU patients, we identified a control cohort, matched according to the same inclusion criteria, and with patient selection blinded to subsequent course, management and outcome.

Principles of treatment and monitoring

Norepinephrine and epinephrine were titrated to maintain a mean arterial pressure (MAP) of ≥ 65 mmHg and milrinone and/or epinephrine were used to maintain a cardiac index > 2 L/min/m^2. Cardiac output was measured with a pulmonary artery catheter (Edwards Lifesciences) aiming to ensure a cardiac index of ≥ 2 L/min/m^2 body surface area. Serum creatinine levels were measured twice a day, and hourly urine output was monitored for assessment of acute kidney injury, as defined by the risk, injury, failure, loss and end-stage (RIFLE) criteria.[22] We measured glucose levels every 2–4 hours. We treated hyperglycaemia > 10 mmol/L with insulin infusion aiming to maintain blood glucose levels within a 6–10 mmol/L target range.

Data collection

We obtained baseline characteristics, comorbidities and post-operative data from the scanned medical record database. Post-operative data collection was restricted to the ICU stay or to 7 days, whichever was the shorter period. We obtained biochemical, urine output, haemodynamic, liver enzyme, serum creatinine, vasopressor dose, inotropic drug dose, arterial blood gas, splanchnic ECMO-related and patient outcome data.

Statistical methods

Statistical analyses were performed using Stata, version 11.2 (StataCorp). Continuous variables are expressed as medians with IQRs and compared using the Mann–Whitney *U* test. Categorical variables are expressed as frequencies with percentages. The difference in repeated measurements between cases and controls during the 48-hour assessment period was explored using repeated-measures (RM) analysis of variance (ANOVA) after including an interaction variable between group and time in the ANOVA model. A two-sided $P < 0.05$ was considered statistically significant.

Results

Patients

Baseline characteristics of the seven splanchnic ECMO and the seven control patients are shown in Table 1. In the patients treated with splanchnic ECMO, the median cardiac index before intervention was 2.4 L/min/m^2 (IQR, 2.2–3.1 L/min/m^2) and the mixed venous oxygen

Table 1. Baseline characteristics

Characteristic	Splanchnic ECMO (*n* = 7)	Control (*n* = 7)
Median age, years (range)	71 (70–77)	75 (65–81)
Women, *n* (%)	2 (29%)	2 (29%)
Median bodyweight, kg (range)	72 (64–90)	70 (68–72)
Type of surgery, *n* (%)		
Coronary bypass	0	4 (57%)
Emergency bypass	2 (29%)	1 (14%)
Valve replacement	3 (43%)	1 (14%)
Valve and bypass combined	1 (14%)	0
Aortic arch replacement	1 (14%)	1 (14%)
Comorbidity, *n* (%)		
Hypertension	6 (86%)	4 (57%)
Hyperlipidaemia	5 (71%)	5 (71%)
Chronic heart failure	1 (14%)	1 (14%)
Ischaemic heart disease	3 (43%)	4 (57%)
Diabetes mellitus	1 (14%)	2 (29%)
Organ support, *n* (%)		
Mechanical ventilation	7 (100%)	7 (100%)
IABP	5 (71%)	4 (57%)
CRRT	5 (71%)	6 (86%)
Inhaled nitric oxide	4 (57%)	1 (14%)
Norepinephrine, *n* (%)	6 (86%)	7 (100%)
Median dose, pts treated, μg/min (range)	20 (20–26)	14 (13–18)
Epinephrine, *n* (%)	4 (57%)	3 (43%)
Median dose, pts treated, μg/min (range)	7 (3–10)	2 (2–3)
Milrinone, *n* (%)	7 (100%)	7 (100%)
Median dose, pts treated, μg/min (range)	0.3 (0.25–0.44)	0.25 (0.25–0.39)
Baseline haemodynamic data, median (range)		
Mean arterial pressure, mmHg	72 (66–81)	67 (64–75)
Heart rate, bpm	99 (80–112)	96 (72–109)
Cardiac index	2.4 (2.2–3.1)	2.5 (2.4–2.9)
Central venous pressure, mmHg	11 (11–14)	11 (9–16)
Mixed venous saturation,%	63% (58%–68%)	59% (55%–62%)
ECMO flow rate, L/min	3.9 (3.8–4)	0
Baseline biochemical levels, median (range)		
Lactate, mmol/L	9.6 (8–12.1)	11.2 (7.9–12.5)
Creatinine, μmol/L	122 (97–144)	93 (72–118)
Haemoglobin, g/L	8.6 (8.1–8.8)	9.2 (8.3–9.6)
ALT, IU/L	37 (36–48)	25 (25–42)
pH	7.23 (7.21–7.26)	7.27 (7.23–7.3)
Base excess, mEq/L	–12 (–9.6 to –13.6)	–9.3 (–7.1 to –12.6)
Bicarbonate, mmol/L	14 (13–17.2)	16.2 (13.4–19.5)
$Paco_2$, mmHg	40 (35–42)	33 (30–41)
Glucose, mmol/L	11.8 (8.7–12.8)	10.5 (8.8–12.4)

ECMO = extracorporeal membrane oxygenation. IABP = intra-aortic balloon pump. CRRT = continuous renal replacement therapy.
pts = patients. bpm = beats per minute. ALT = alanine aminotransferase.

saturation was 63% (IQR, 58–68%) (see supplementary Figure 1 in the Appendix, online at cicm.org.au/Resources/Publications/Journal). Splanchnic ECMO patients required more cardiovascular support at baseline; more were being treated with IABP (five v four patients), inhaled nitric oxide (four patients v one patient) and epinephrine (four v three patients). Baseline median blood lactate was 9.6 mmol/L (IQR, 8–12.1 mmol/L) in the splanchnic ECMO group and 11.2 mmol/L (IQR, 7.9–12.5 mmol/L) in the control group. However, metabolic acidosis was more pronounced in the splanchnic ECMO patients and baseline creatinine levels were higher (Table 1).

Intervention

In all splanchnic ECMO patients, ECMO cannulation was performed via the femoral route (median venous cannula, size 21 Fr and median arterial cannula, size 16 Fr). Splanchnic ECMO was initiated at a median flow of 3.9 L/min (IQR, 3.8–4 L/min), followed by 3.7 L/min (IQR, 3.5–4 L/min) and 3.4 L/min (IQR, 3–4 L/min) at 24 and 48 hours, respectively. Splanchnic ECMO was performed for a median of 4.5 days (IQR, 2.8–5.6 days). A single episode of bleeding around the femoral cannulation site was successfully managed conservatively.

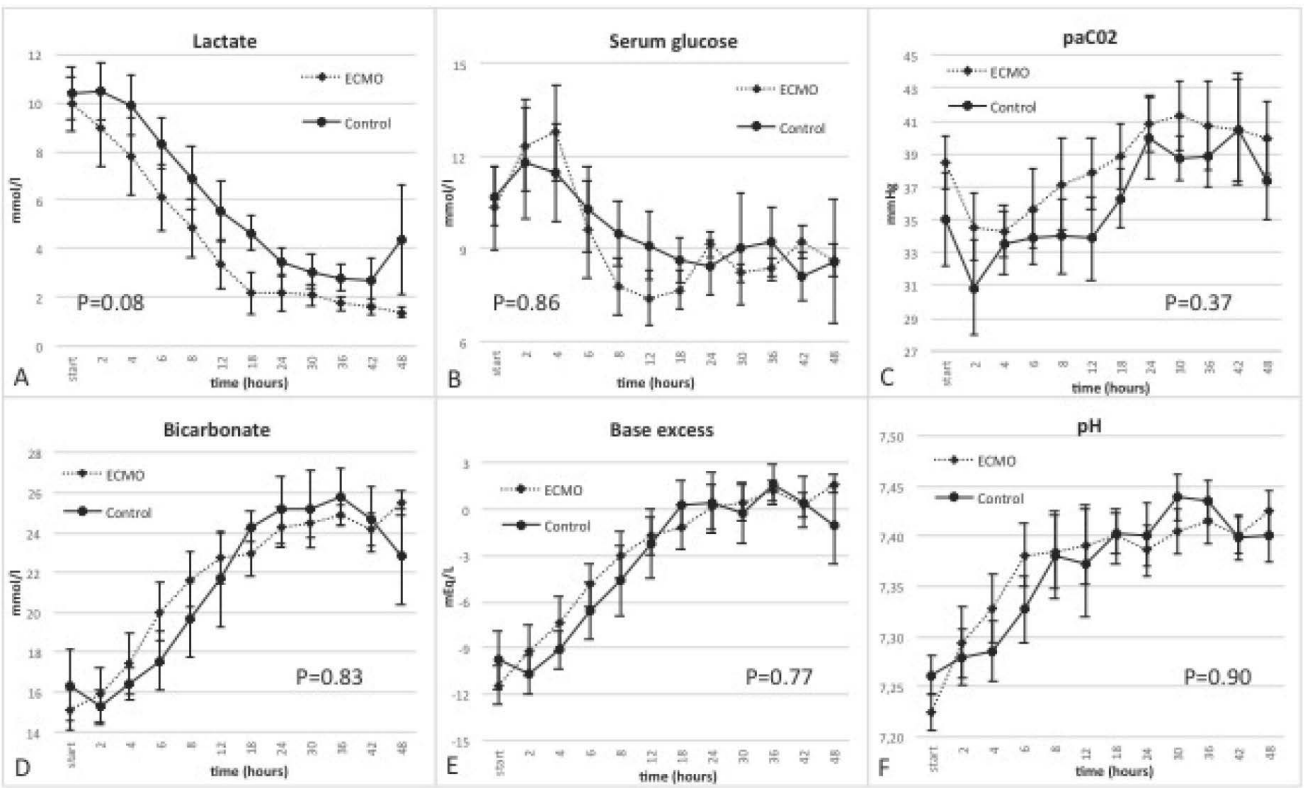
Biochemical, physiological and clinical outcomes

The blood lactate level decreased significantly in both groups during the 48-hour study period (Figure 1). However, it normalised (< 2 mmol/L) faster in patients treated with splanchnic ECMO ($P = 0.047$) (Figure 2), and the bicarbonate level, base excess and pH improved to a similar extent in both groups (Figure 1).

Several additional non-statistical changes were seen. For example, the median percentage 48-hour increase in ALT was less pronounced in the splanchnic ECMO group (68% v 158%). In addition, a more pronounced relative decline in serum creatinine (9% v 2%) and a greater relative increase in urine output (169% v 15%) were seen in the splanchnic ECMO group. Finally, fewer patients required vasoactive or inotropic support in the control group after 48 hours (Table 2).

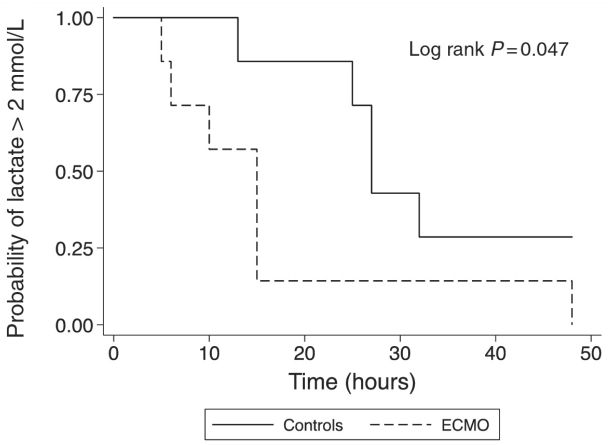
Patient-centred outcomes are shown in Table 3. Ventilation-free days after 1 week and hospital-free days after 1 month were similar in both groups. We observed a non-significant but striking difference in median ICU-

Figure 1. Mean lactate, serum glucose, $Paco_2$, bicarbonate, base excess and pH levels during initial 48 hours on ECMO, or since hyperlactataemia in controls*



ECMO = extracorporeal membrane oxygenation. * Control patients (solid line); patients undergoing ECMO (dotted line); data are shown as means with SEMs, shown as H bars. *P* is a measure of between-group differences on repeated-measures analysis of variance.

Figure 2. Kaplan–Meier estimates for probability of having a lactate level > 2 mmol/L*



ECMO = extracorporeal membrane oxygenation. * Control patients (solid line); patients undergoing ECMO (dashed line).

free days after 30 days between splanchnic (15.3 days) and control patients (0 days). Furthermore, five splanchnic ECMO patients survived to hospital discharge, compared with three controls (Table 3).

Discussion

Key findings

Our study provides the first evaluation of the physiological effect of splanchnic ECMO treatment for severe hyperlactataemia in patients who have had cardiac surgery, with a preserved cardiac index > 2 L/m²/min and mixed venous oxygen saturation > 55%. Our results show that such treatment is associated with significantly faster normalisation of lactate level, greater non-significant attenuation of liver enzyme release and more hospital-free days despite greater illness severity at baseline.

Relationship to previous studies

Clinical studies have consistently shown the poor prognosis associated with severe and sustained hyperlactataemia.[12,23,24] A decrease in lactate level in the first 24 hours after ICU admission is also considered the best predictor of 28-day mortality,[25] suggesting that early resolution of hyperlactataemia may be a clinically important marker of improving perfusion or decreasing cellular stress.[26] Nevertheless, apart from optimal haemodynamic support, there are no specific treatment options. However, such measures do not address the likely underlying pathophysiology. Other treatment options have been investigated but with limited success; blood pressure goals above 65 mmHg MAP did not improve lactate levels,[27] and dexamethasone therapy increased lactate and glucose levels.[28] Further, an altered pattern of mesenteric vasomotor regulation after cardiac surgery may contribute to reduced efficacy of inotropic drugs.[29] In contrast, splanchnic ECMO appears to be an effective and relatively safe treatment option as shown in our study.

Table 3. Outcomes

Outcome	ECMO group (*n* = 7)	Control group (*n* = 7)
Median ventilation-free time at Day 7, days (IQR)	0 (0–0.7)	0 (0–4.8)
Median ICU-free time at Day 30, days (IQR)	15.3 (5.5–17.7)	0 (0–27.2)
Median hospital-free time at Day 30, days (IQR)	0 (0–11.3)	0 (0–17.7)
Survived to hospital discharge, *n* (%)	5 (71%)	3 (43%)
Cause of death, *n* (%)		
Refractory cardiogenic shock	1 (14%)	2 (29%)
Arrhythmia	1 (14%)	2 (29%)

ECMO = extracorporeal membrane oxygenation. IQR = interquartile range.

Table 2. Organ function and vasoactive support after intervention

	ECMO group			Control group			
Variable	Baseline	48 h	Change, %	Baseline	48 h	Change, %	*P*
Median ALT, IU/L (IQR)	37 (25–48)	62 (8–695)	68 (–84 to 2025)	25 (25–42)	93 (55–875)	158 (0–6024)	0.48
Median creatinine, µmol/L (IQR)	179 (161–220)	164 (138–186)	–9 (–27 to 4)	106 (99–138)	120 (117–129)	–2 (–19 to 18)	0.48
Median urine output, mL/h (IQR)	35 (19–66)	115 (103–165)	169 (34–900)	75 (50–95)	75 (51–80)	15 (–9 to 54)	0.38
Norepinephrine, *n* (%)	6 (86%)	5 (71%)	–	7 (100%)	3 (43%)	–	–
Epinephrine, *n* (%)	4 (57%)	3 (43%)	–	3 (43%)	1 (14%)	–	–
Milrinone, *n* (%)	7 (100%)	6 (86%)	–	7 (100%)	4 (57%)	–	–

ECMO = extracorporeal membrane oxygenation. ALT = alanine aminotransferase. IQR = interquartile range.

Implications of study findings

Our findings imply that splanchnic ECMO as described in this study may be a safe and effective option for the correction of severe hyperlactataemia and the attenuation of splanchnic hypoperfusion after cardiac surgery. This may be the case even at flows of < 4 L/min, and even in patients with a cardiac index > 2 L/m²/min and preserved mixed venous oxygen saturation. Faster resolution was achieved in ECMO patients despite higher creatinine levels, greater inotropic requirements and increased use of inhaled nitric oxide and IABP before intervention, which suggested a greater severity of disease at baseline and further corroborating the the robustness of the physiological effect.

Strengths and limitations

To our knowledge, this is the first report of the use of ECMO in the management of severe hyperlactataemia after cardiac surgery in patients with a cardiac index above 2 L/m²/min and a mixed venous oxygen saturation > 55%. The demonstration that such intervention achieved more rapid resolution of hyperlactataemia is robust. The notion that such resolution implies improved splanchnic perfusion is supported by the diminished release of liver enzymes and the resolution of acute kidney injury. Finally, the achievement of such biochemical improvements in a cohort, which appeared more acutely ill than the lactate-matched control patients, lends further support to their validity.

Our study, however, carries several limitations. First, it is not a randomised controlled study, but before conducting such a study, preliminary evidence of potential benefit from such an invasive intervention needs to be shown. Our report provides such preliminary evidence. Second, this is a retrospective study, which carries the potential for several biases. For example, more patients in the control group underwent coronary bypass surgery and more valvular procedures were performed in the intervention group. However, patients were matched according to inclusion criteria by investigators who were blinded to biochemical and clinical outcomes. Moreover, patients in both cohorts were treated by the same team of clinicians in the same setting. Third, this is a study in two adjacent institutions and its external validity is unclear. However, severe hyperlactataemia in cardiac surgery has been repeatedly found to carry a high risk of poor outcomes. Patient management was with standard drugs, monitoring and other widely used supportive interventions, such as IABP, CRRT and nitric oxide, which suggested a degree of relevance to similar patients in similar institutions. Fourth, small cohort studies expose investigators to a high risk of both type I and type II error. Thus larger studies are desirable in the future.

Conclusion

We have shown that peripheral venoarterial splanchnic ECMO at flows < 4 L/min may be an effective and safe technique to treat severe hyperlactataemia in patients who have had cardiac surgery and have preserved cardiac index and mixed venous oxygen saturation. Further prospective studies of this intervention are now needed to confirm or refute these preliminary findings.

Competing interests

None declared.

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References

1 Mak NT, Iqbal S, de Varennes B, Khwaja K. Outcomes of post-cardiac surgery patients with persistent hyperlactatemia in the intensive care unit: a matched cohort study. *J Cardiothorac Surg* 2016; 11: 33.

2 Maillet JM, Le Besnerais P, Cantoni M, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. *Chest* 2003; 123: 1361-6.

3 Renew JR, Barbara DW, Hyder JA, et al. Frequency and outcomes of severe hyperlactatemia after elective cardiac surgery. *J Thorac Cardiovasc Surg* 2016; 151: 825-30.

4 Park SJ, Kim SP, Kim JB, et al. Blood lactate level during extracorporeal life support as a surrogate marker for survival. *J Thorac Cardiovasc Surg* 2014; 148: 714-20.

5 Toraman F, Evrenkaya S, Yuce M, et al. Lactic acidosis after cardiac surgery is associated with adverse outcome. *Heart Surg Forum* 2004; 7: E155-9.

6 Demers P, Elkouri S, Martineau R, et al. Outcome with high blood lactate levels during cardiopulmonary bypass in adult cardiac operation. *Ann Thorac Surg* 2000; 70: 2082-6.

7 Kogan A, Preisman S, Bar A, et al. The impact of hyperlactatemia on postoperative outcome after adult cardiac surgery. *J Anesth* 2012; 26: 174-8.

8 Laine GA, Hu BY, Wang S, et al. Isolated high lactate or low central venous oxygen saturation after cardiac surgery and association with outcome. *J Cardiothorac Vasc Anesth* 2013; 27: 1271-6.

9 Maarslet L, Møller MB, Dall R, et al. Lactate levels predict mortality and need for peritoneal dialysis in children undergoing congenital heart surgery. *Acta Anaesthesiol Scand* 2012; 56: 459-64.

10 Ranucci M, Isgrò G, Carlucci C, et al. Central venous oxygen saturation and blood lactate levels during cardiopulmonary bypass are associated with outcome after pediatric cardiac surgery. *Crit Care* 2010; 14: R149.

11 Ranucci M, De Toffol B, Isgrò G, et al. Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome. *Crit Care* 2006; 10: R167.

12 McNelis J, Marini CP, Jurkiewicz A, et al. Prolonged lactate clearance is associated with increased mortality in the surgical intensive care unit. *Am J Surg* 2001; 182: 481-5.

13 Davies AR, Bellomo R, Raman JS, et al. High lactate predicts the failure of intraaortic balloon pumping after cardiac surgery. *Ann Thorac Surg* 2001; 71: 1415-20.

14 Landow L. Splanchnic lactate production in cardiac surgery patients. *Crit Care Med.* 1993; 21(2 Suppl): S84-91.

15 Karhausen J, Stafford-Smith M. The role of nonocclusive sources of acute gut injury in cardiac surgery. *J Cardiothorac Vasc Anesth* 2014; 28: 379-91.

16 Fiore G, Brienza N, Cicala P, et al. Superior mesenteric artery blood flow modifications during off-pump coronary surgery. *Ann Thorac Surg* 2006; 82: 62-7.

17 McNicol L, Lipcsey M, Bellomo R, et al. Pilot alternating treatment design study of the splanchnic metabolic effects of two mean arterial pressure targets during cardiopulmonary bypass. *Br J Anaesth* 2013; 110: 721-8.

18 O'Connor E, Fraser JF. The interpretation of perioperative lactate abnormalities in patients undergoing cardiac surgery. *Anaesth Intensive Care* 2012; 40: 598-603.

19 Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. *Crit Care* 2004; 8: R60-5.

20 Okorie ON, Dellinger P. Lactate: biomarker and potential therapeutic target. *Crit Care Clin* 2011; 27: 299-326.

21 Raman JS, Kochi K, Morimatsu H, et al. Severe ischemic early liver injury after cardiac surgery. *Ann Thorac Surg* 2002; 74: 1601-6.

22 Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure — definition, outcome measures, animal models, fluid therapy and information technology needs: the second international consensus conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 2004; 8: R204-12.

23 Attanà P, Lazzeri C, Picariello C, et al. Lactate and lactate clearance in acute cardiac care patients. *Eur Heart J Acute Cardiovasc Care* 2012; 1: 115-21.

24 Bakker J, Gris P, Coffernils M, et al. Serial blood lactate levels can predict the development of multiple organ failure following septic shock. *Am J Surg* 1996; 171: 221-6.

25 Marty P, Roquilly A, Vallée F, et al. Lactate clearance for death prediction in severe sepsis or septic shock patients during the first 24 hours in Intensive Care Unit: an observational study. *Ann Intensive Care* 2013; 3: 3.

26 Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med* 2004; 32: 1637-42.

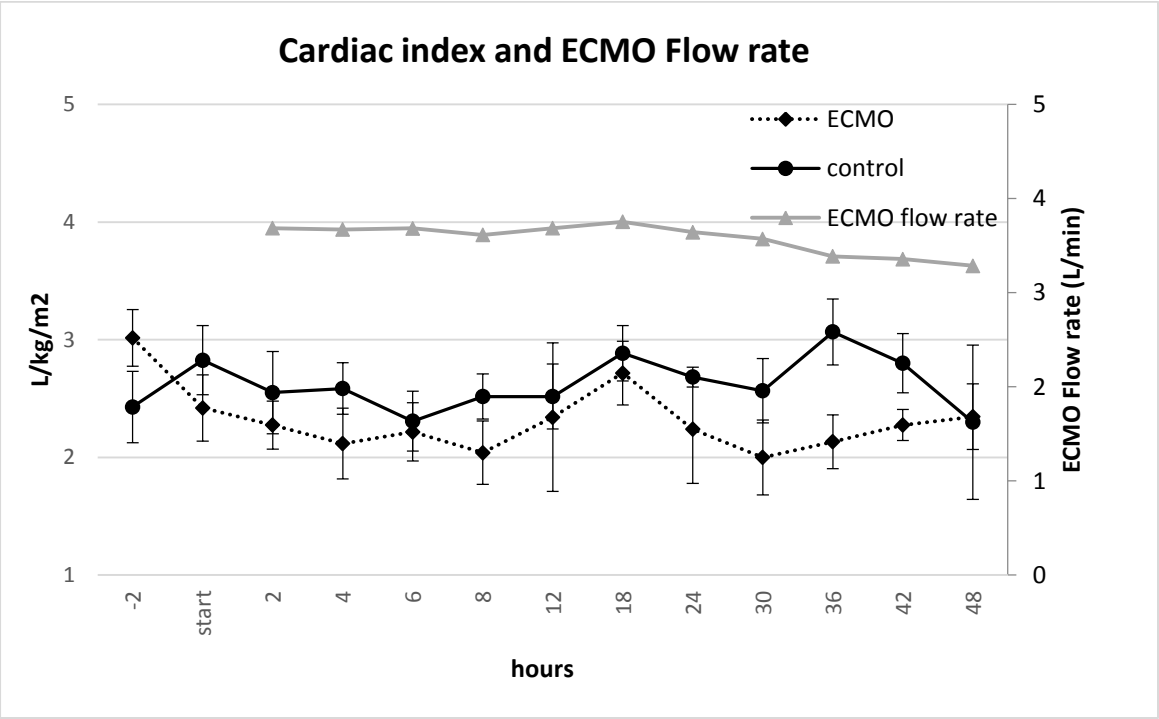
27 Lipcsey M, McNicol L, Parker F, et al. Effect of perfusion pressure on the splanchnic circulation after CPB: a pilot study. *Minerva Anestesiol* 2015; 81: 752-64.

28 Ottens TH, Nijsten MW, Hofland J, et al. Effect of high-dose dexamethasone on perioperative lactate levels and glucose control: a randomized controlled trial. *Crit Care* 2015; 19: 41.

29 Khan TA, Bianchi C, Ruel M, et al. Differential effects on the mesenteric microcirculatory response to vasopressin and phenylephrine after cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 2007; 133: 682-8. ❑

Appendix

This appendix was part of the submitted manuscript and has been peer reviewed. It is posted as supplied by the authors.



Suppl. Figure 1. Mean (SEM) cardiac index levels during the initial 48 hours on ECMO (dotted line) or since hyperlactatemia in controls (solid line). Mean flow rate of ECMO during the initial 48 hours of observation (grey line).