Increased concentrations of L-lactate in the rectal lumen in patients undergoing cardiopulmonary bypass

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Background. Gut ischaemia may contribute to morbidity in patients after cardiopulmonary bypass (CPB), but little is known about the metabolic state of the large bowel in such patients. Therefore we estimated the concentrations of L-lactate and P\textsubscript{CO2} in rectal mucosa in patients undergoing cardiac surgery with or without the use of CPB.

Methods. Patients undergoing coronary artery bypass grafting (CABG) (n=12) or off-pump CABG (n=10) were subjected to equilibrium dialysis of the rectal lumen during the procedure and in the first 4 h afterwards. Dialysate concentrations of L-lactate and P\textsubscript{CO2} were measured using an auto-analyser and compared with values obtained in healthy subjects (n=10).

Results. During CPB, a 2- to 3-fold increase in luminal concentrations of L-lactate was observed (CABG vs off-pump CABG, P<0.05; CABG vs healthy subjects, P<0.01). The dialysate concentrations of L-lactate were higher than the mean systemic values (luminal–arterial gradient mean (SD) 0.9 (1.0) mmol litre\textsuperscript{−1}, P<0.05), and the two values were positively correlated (P<0.05). Luminal L-lactate concentrations remained elevated 4 h after the operation. In contrast, dialysate P\textsubscript{CO2} was equally high in patient and control groups and substantially higher than values observed in arterial blood.

Conclusions. Uncomplicated CPB is associated with moderate but sustained increases in luminal concentrations of L-lactate in the rectum, indicating metabolic dysfunction of the mucosa in the large bowel.
decided whether or not CPB was to be used based on the anatomy of the coronary lesions. In the off-pump CABG group, only patients expected to have two or more grafts were included in an attempt to match the time of anaesthesia in the two groups of patients. We did not include patients in whom a complicated perioperative course was expected (Euroscore >6 or left ventricular ejection fraction <30%) or patients with abnormal rectum or colon, inflammatory bowel disease or any gastrointestinal symptoms within the preceding month. Patients who had taken non-steroidal anti-inflammatory drugs within the previous week or had excessive alcohol consumption were also excluded. Ten healthy volunteers from a previous study served as controls.5

**Anaesthesia**

Patients received diazepam 10–15 mg orally 1 h prior to induction. Anaesthesia was induced with fentanyl 10 μg kg⁻¹ and midazolam 2–5 mg. Tracheal intubation was facilitated by pancuronium 0.1 mg kg⁻¹, and anaesthesia was maintained with isoflurane (0.5–1.0%) and fentanyl 2.5–5 μg kg⁻¹ h⁻¹. The patients in the CPB group received 500 ml isotonic saline. The off-pump CABG group received isotonic saline and 6% dextran 70 in saline (Macrodex®, Pharmacia-Upjohn, Uppsala, Sweden). In the intensive care unit (ICU), all patients were sedated with an infusion of propofol (100–250 mg h⁻¹) during the study.

**Treatment with vasoactive drugs**

Hypotension prior to CPB (mean arterial pressure [MAP] <60 mm Hg) was treated with i.v. ephedrine 5 mg or i.v. phenylephrine 0.1 mg depending on the heart rate. Hypotension during CPB (MAP <50 mm Hg) was treated with increased flow; if this was ineffective, phenylephrine was administered in i.v. boluses of 0.1 mg. Post-CPB hypotension (MAP <60 mm Hg) was treated with infusion of 500 ml dextran 70 and dopamine 2–10 μg kg⁻¹ min⁻¹.

In the off-pump CABG group, hypotension (MAP <60 mm Hg) was treated with 500 ml dextran 70; if this was ineffective, phenylephrine was administered in i.v. boluses of 0.1 mg. The latter was supplemented by dopamine 2–10 μg kg⁻¹ min⁻¹ if several doses had to be given.

Perioperative hypertension (MAP >90 mm Hg) was treated by either increasing the depth of anaesthesia or infusion of nitroglycerin.

**Cardiopulmonary bypass**

Normothermic non-pulsatile CPB, using a membrane oxygenator and flow of 2.4 litre min⁻¹ m⁻², was provided by a heart–lung machine primed with Ringer’s lactate, which contains L-lactate 28 mmol litre⁻¹. Cardiac arrest was induced by antegrade blood cardioplegia and distal grafting was performed during complete aortic clamping.

**Study protocol**

L-lactate concentrations and Pco₂ in the rectal lumen were measured by equilibrium dialysis as previously described.5 After the induction of anaesthesia, a 12 cm long bag of dialysis tubing (semipermeable cellulose, cut-off 12 kDa) (Sigma, St Louis, MO, USA) was placed in the rectal lumen. The bag was filled with 4 ml of 10% dextran 40 in isotonic saline (Rheomacrodex®, MEDA, Solna, Sweden) and closed over 5 cm of Tygon® tube (Cole-Parmer Instruments Company, Vernon Hills, IL, USA) with a three-way stopcock at the distal end to allow airtight sampling. At the end of the procedure the dialysate was sampled and the bag was removed. Dialysis for 4 h is required to ensure full equilibrium in the rectal lumen.4 In two CABG and three off-pump CABG patients, the procedure lasted <4 h, and so 10–20 min of the postoperative period was included in the time of equilibration in these patients. Upon arrival in the ICU, a new bag was placed and another full equilibrium dialysis was performed during the first 4 h after the operation. Arterial blood samples were taken before anaesthesia and every hour during the study. L-lactate concentrations and Pco₂ in dialysates and arterial blood were measured by autoanalyzer (ABL 725, Radiometer, Copenhagen, Denmark). The healthy subjects were subjected to a single rectal equilibrium dialysis of 4 h.

**In vitro equilibration**

Dialysis bags were incubated for 0.5–4 h in saline baths containing 1 mmol litre⁻¹ L-lactate (Sigma) or 5% carbon dioxide (AGA, Copenhagen, Denmark) at 37°C (n=5). Dialysates were analysed as described above. The median (range) dialysate values of L-lactate reached 50 (33–56)%; 78 (54–78)%; 89 (75–100)% and 100 (88–100)% equilibrium at 0.5 h, 1 h, 2 h and 4 h, respectively. The equivalent values for Pco₂ were 91 (89–93)%; 98 (93–101)%; 101 (99–104)% and 105 (103–108)%.

**Statistics**

Data are presented as median (range) and analysed using the Mann–Whitney or Wilcoxon tests or Spearman’s rank correlation test where appropriate (GraphPad Prism v. 4.00, GraphPad Software, San Diego, CA, USA). P-values <0.05 (two-tailed) were considered significant. The sample size was not calculated prior to the study, but we have previously detected clinically relevant differences in sepsis using similar numbers of patients and controls.5

**Results**

The patient characteristics and the procedures undertaken are shown in Table 1. All patients had an uneventful perioperative course. In the CPB group, five patients were treated with phenylephrine 0.1–1.5 mg during CPB and six patients required dopamine 4–6 μg kg⁻¹ min⁻¹ when
The luminal values of L-lactate remained elevated 4 h after the operation (Fig. 1). There were no significant differences in luminal values of L-lactate between patients who were treated with dopamine for post-CPB hypotension (n=6), and those who came off CPB without dopamine (n=6) (during surgery 3.3 (0.7–4.9) vs 1.5 (0.9–3.1) mmol litre\(^{-1}\), \(P=0.13\); in the ICU 1.8 (0.5–6.0) vs 1.0 (0.5–3.0) mmol litre\(^{-1}\), \(P=0.39\)).

In the off-pump CABG patients, the luminal concentrations of L-lactate were also increased during and after the procedure and the luminal L-lactate concentrations were higher than the mean values in arterial blood (Fig. 1).

Luminal \(P_{CO_2}\) was the same in all groups of patients and controls and substantially higher than the mean values observed in arterial blood (Fig. 3). There was no difference in the luminal–arterial \(P_{CO_2}\) gradient between the groups of patients (Fig. 3).

### Discussion

The data obtained show that the use of CPB is associated with increased concentrations of L-lactate in the rectal lumen in patients during and after cardiac surgery, implicating moderate but sustained metabolic dysfunction of the mucosa. The high lumen-to-blood gradient of L-lactate indicates that luminal L-lactate is produced in the mucosa rather than spilled over from the blood. This is substantiated by data from animal studies of systemic lactate clamp, where luminal lactate was minimally affected by severe hyperlactataemia (>6 mmol litre\(^{-1}\)). Priming of the heart–lung machine with Ringer’s lactate has been shown to increase the systemic concentrations of lactate by 35%, which was observed immediately after the establishment of CPB and lasted no more that 40 min. In contrast, we observed a much higher increase in luminal values, which was prolonged into the postoperative period. Therefore it is unlikely that the Ringer’s lactate used for priming contributed to our observation of increased luminal L-lactate.

### Table 1

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<td>50 (30–60)</td>
<td>48 (30–50)</td>
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<td>Duration of anaesthesia (min)</td>
<td>253 (210–350)</td>
<td>240 (220–320)</td>
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<tr>
<td>Duration of CPB (min)</td>
<td>77 (48–138)</td>
<td>—</td>
<td>—</td>
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<td>Duration of clamp (min)</td>
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### Fig 1

(A) Luminal concentrations of L-lactate in the rectum and (B) luminal–arterial difference in patients undergoing CABG or off-pump CABG (OPCABG) and healthy subjects. Rectal values were obtained by luminal equilibrium dialysis, which in patients was performed during surgery and the first 4 h in the postoperative ICU. Dots represent values of individual patients and bars represent group medians. *\(P<0.05\) compared with normal subjects by the Mann–Whitney test; \#\(P<0.05\) compared with OPCABG by the Mann–Whitney test; \$\(P<0.05\) compared with CPB patients by the Wilcoxon’s test.

### Fig 2

Correlation between luminal and mean arterial concentrations of L-lactate in patients during CABG using CPB (n=12). Luminal values were assessed by rectal equilibrium dialysis. \(P=0.02\) and \(r=0.66\) by Spearman’s rank correlation test.

The luminal values of L-lactate were 2- to 3-fold higher in patients undergoing CABG than in patients undergoing off-pump CABG and healthy subjects (Fig. 1). During CPB, the luminal concentrations of L-lactate were higher than the mean concentrations in arterial blood (Fig. 1), and the two values were positively correlated (Fig. 2).
Increased l-lactate in rectal mucosa during CPB

The correlation between the luminal and systemic values in the present study suggests that the production of L-lactate in gut mucosa contributes to the hyperlactataemia observed in these patients. Alternatively, a common cause for the increased concentrations of L-lactate indicates bowel ischaemia. Epinephrine may cause systemic lactic acidosis through aerobic glycolysis, but to our knowledge this has not been shown for phenylephrine or dopamine, which were the sympathomimetics used in the present study. However, systemic concentrations of D-lactate have been suggested to be a marker of metabolic dysfunction of the large bowel in critically ill patients. The elimination kinetics of this isoform in humans, including the influence of critical illness, need to be established before this simple measure can be used to assess the metabolic state of the colonic mucosa.

Luminal dialysis in the rectum has the potential to be used clinically to estimate mucosal concentrations of L-lactate. This is substantiated by observations in patients with septic shock, where luminal values of L-lactate correlated with mucosal permeability in the large bowel. Future studies of patients on CPB should address these matters, as well as the effects of fluid management and different vasoactive drugs.

In summary, uncomplicated normothermic CPB is associated with a moderate but sustained increase in luminal concentrations of L-lactate in the rectum, indicating metabolic dysfunction of the mucosa. In contrast, luminal \( P_{CO_2} \) in the rectum was equally raised in patients and healthy subjects, questioning its use as a marker of metabolism. It can be speculated that this might make a difference to patients with lower cardiovascular reserves.

The high values of \( P_{CO_2} \) in the rectal lumen of patients are within the range previously observed in patients with septic shock. As the values were equally raised in healthy subjects, luminal carbon dioxide in the rectum may originate from bacterial metabolism. Alternatively, acids in faeces may be buffered by bicarbonate ions, which are secreted into the lumen by epithelial cells. Consequently, any change in bacterial metabolism or epithelial secretion of bicarbonate ions could affect \( P_{CO_2} \) and complicate the interpretation of these values. On the other hand, changes in luminal–arterial carbon dioxide difference, as detected by gas tonometry in the sigmoid colon during surgery, may predict complications in patients undergoing repair of abdominal aortic aneurysm. It is currently not known whether \( P_{CO_2} \) values observed in the rectum in our healthy subjects were within the range of those observed in the sigmoid colon during aortic repair. Taken together, it is unlikely that the measurement of luminal \( P_{CO_2} \) in the rectum is a useful marker of regional flow or metabolism. Luminal bacteria may also generate lactate, but these produce the D-isoform, which is not detected by the auto-analyser used in the present study. However, systemic concentrations of D-lactate have been suggested to be a marker of metabolic dysfunction of the large bowel in critically ill patients. The elimination kinetics of this isoform in humans, including the influence of critical illness, need to be established before this simple measure can be used to assess the metabolic state of the colonic mucosa.

**References**


3 Kavarana MN, Frumento RJ, Hirsch AL, Oz MC, Lee DC, Bennett-Guerrero E. Gastric hypercarbia and adverse outcome after cardiac surgery. *Intensive Care Med* 2003; 29: 742–8


