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# Rectal lactate levels in endoluminal microdialysate during routine coronary surgery*

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## Summary

The aim of this prospective study was to determine the feasibility of intestinal endoluminal microdialysis as a new method for clinical monitoring of the adequacy of splanchnic perfusion in the large bowel. A microdialysis catheter for continuous lactate, glycerol, glucose and pyruvate measurements attached to a tonometric catheter was placed into the lumen of the recto-sigmoid junction prior to surgery in 13 patients undergoing elective cardiac surgery with cardiopulmonary bypass (CPB). Lactate was also measured in blood and muscle. CPB was associated with a 10-fold increase in luminal lactate from 0.16 (0.01) to 1.67 (0.38) mmol.l$^{-1}$ ($p < 0.001$). Muscular lactate increased from baseline levels 1.20 (0.21) to 1.77 (0.36) mmol.l$^{-1}$ during CPB ($p = 0.01$), but the muscular lactate–pyruvate ratio remained unchanged. Arterial lactate increased only slightly from 0.9 (0.05) to 1.1 (0.06) mmol.l$^{-1}$ ($p = 0.027$) during CPB. Increased lactate concentrations in the large bowel during CPB are suggestive of local lactate production consistent with impaired oxygen delivery. Intestinal endoluminal microdialysis is a potential clinically applicable method for monitoring intestinal metabolism. Combined with tonometry, microdialysis provides the opportunity to monitor both circulation and metabolism in the rectal mucosa.

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Patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) are at risk of developing intestinal mucosal ischaemia, leading to disturbed mucosal integrity and increased intestinal permeability [1]. The latter may result in leakage of endotoxins into the circulation contributing to systemic inflammation observed during CPB [2]. The most likely cause of increased intestinal vascular permeability is imbalance between splanchnic oxygen supply and demand [3].

There are currently few reliable methods available for monitoring adequacy of splanchnic perfusion during CPB. If available, these data could lead to strategies being developed to reduce intestinal ischaemia and the resulting increased mucosal permeability. Gastric tonometry is the only clinically available method that allows monitoring of gastro-intestinal perfusion. Even though in cardiac [4, 5] and high-risk surgical patients [6] peri-operative tonometry-derived variables are predictive

of postoperative complications, therapeutics using tonometry variables as a goal have yielded controversial results [7, 8].

Microdialysis is increasingly recognised as a means of detecting biochemical markers in the interstitial fluid of many organs [9, 10], and brain microdialysis has recently been used in monitoring the effects of hypertonic saline therapy for reduction of cerebral ischaemia following subarachnoid haemorrhage [11]. The technique is based on the principle of diffusion of substances through a semipermeable membrane along a concentration gradient [12]. In abdominal aortic surgery, elevated levels of lactate in the portal venous blood predicts organ failure [13], and microdialysis catheters placed intraperitoneally during surgery have been evaluated for monitoring intestinal ischaemia in surgical patients [9, 14, 15]. In animal studies using gut luminal microdialysis, we have shown that there is a correlation between lactate released into the jejunal lumen and alterations in the permeability of the intestine [16]. Intraluminal glycerol is a marker of intestinal injury. When possible, the gut lumen is to be preferred as a site for placement of microdialysis catheters [17]. As the colon is at risk, following both aortic surgery [18] and cardiac surgery [19], and in experimental septic shock [20], microdialysis probes placed in the rectum may be a potential minimally invasive tool for the detection of increased levels of lactate and glycerol in the gut lumen. However, as high systemic levels of lactate (> 5–10 mmol.l$^{-1}$) may contribute to increased luminal levels in pigs [21], it is important to measure lactate both in the blood and in muscle.

The aim of the present study was to evaluate the feasibility of intestinal luminal microdialysis as a method for clinical monitoring of the adequacy of splanchnic metabolism in patients undergoing coronary artery bypass grafting (CABG) with CPB.

As tonometry has also been used for monitoring the colonic mucosa during aortic surgery [13] and during CPB [22], we also sought to compare that method with endoluminal microdialysis.

## Methods

### Patients

Thirteen male patients scheduled for elective CABG surgery were included in the study. Exclusion criteria included: a history of gastro-intestinal disease including gastritis, ulcers, inflammatory bowel disease or malignancy; emergency surgery; planned combined valvular surgery, and re-operative surgery. The study protocol was approved by the Regional Ethics Committee, and written informed consent was obtained from each patient.

### Anaesthesia, CPB and peri-operative care

All patients were treated with $\beta_1$-selective adrenergic receptor blockers until the day of surgery. Premedication was with diazepam 10 mg p.o. Anaesthesia was induced using fentanyl 400 μg, thiopental 200 mg, and neuromuscular blockade was produced using pancuronium 7 mg. Anaesthesia was maintained using isoflurane and fentanyl. Propofol (2–5 mg.kg$^{-1}$.h$^{-1}$) was started during CPB and continued until extubation 2–6 h after CPB. The patients' lungs were mechanically ventilated to produce normocapnia and $F_{IO_2}$ adjusted to keep $P_{O_2}$ > 14 kPa. Standard monitoring was performed, which included direct arterial pressure monitoring and pulmonary artery catheter monitoring (CCOmbo V, 7.5F, Edwards Lifesciences LLC, Irvine, CA).

The cardiopulmonary bypass equipment included non-pulsatile roller pumps and coated membrane oxygenators (Maxima Medtronic Inc., Minneapolis, MN). The pump was primed with 1800 ml of Ringer's acetate containing 7500 IU of heparin. Heparin (300 IU.kg$^{-1}$) was administered prior to vascular cannulation to maintain activated clotting time (ACT) > 480 s during CPB. Following the institution of cardiopulmonary bypass at a flow rate of 2.4 l.min$^{-1}$.m$^{-2}$, the aorta was cross-clamped and a cold crystalloid cardioplegic solution was injected. The arterial perfusion pressure was kept between 50 and 70 mmHg using phenylephrine if necessary. The CPB perfusate temperature was maintained at 34 °C with active rewarming at the end of CPB. Following CPB, protamine was infused to achieve baseline ACT.

The patients received routine institutional postoperative care including blood glucose control with target values between 4.5 and 8 mmol.l$^{-1}$. The patients were extubated in the ICU when clinically appropriate.

### Microdialysis and tonometry

We manufactured our own rectal catheter combining two commercially available devices – a microdialysis catheter (CMA 62, membrane length 30 mm, OD 0.6 mm, membrane cut-off 20 kDa, inlet and outlet lines of 50 cm, CMA Microdialysis AB, Stockholm, Sweden) for sampling of interstitial fluid for measurements of lactate, glucose, pyruvate and glycerol, and a 16F tonometric catheter (Tonometrics$^{TM}$, Datex-Ohmeda, Finland) for measurements of regional carbon dioxide production in the intestinal wall. To ascertain contact between the catheter and the intestinal mucosa, the microdialysis catheter was attached to the tonometry catheter with tape so that the membrane was at the level of the tonometric balloon (Fig. 1). The microdialysis catheter was perfused to ascertain patency prior to use. To reduce the amount of faeces in the ampulla recti, the patients defecated 1 h prior to the insertion of the rectal

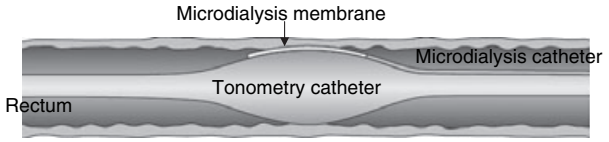


**Figure 1** Rectal device. Schematic drawing of the combined rectal device with microdialysis- and tonometry catheter.

catheters. The use of enema and lubricating gel was avoided due to its glycerol content. Two hours prior to surgery, the patients were placed in the left lateral recumbent position and sedated using propofol. The microdialysis/tonometric catheter was inserted into the rectum and advanced to the rectosigmoid junction (15–20 cm proximal to the anus) using a rectoscope. In case of faeces in the ampulla recti, saline and a suctioning catheter were gently used. The rectoscope was withdrawn over the catheter and the catheter left in situ. The catheter was secured to the skin using tape just outside the anus, and inspected regularly for bleeding and to check whether it was in situ. An additional microdialysis catheter (CMA 60, membrane length 20 mm, OD 0.6 mm, membrane cut-off 20 kDa, CMA Microdialysis AB) was inserted deep intramuscularly into the ventral aspect of the thigh in nine patients.

An isotonic sterile fluid (Perfusion Fluid T1 ($Na^+$ 147 mmol, $K^+$ 4 mmol, $Ca^{2+}$ 2.3 mmol, $Cl^-$ 156 mmol); CMA Microdialysis AB) was perfused into the microdialysis catheters at a rate of 1 $\mu l.min^{-1}$ using microdialysis pumps (CMA 107, CMA Microdialysis AB). During passage through the catheter, the perfusion fluid equilibrated with the tissue surrounding the membrane of the catheter, and it was passively drained into microvials. Following insertion, the catheters were perfused for at least 60 min before any measurements were made, and all deadspace perfusion was discarded. Baseline measurements were obtained from two fractions sampled prior to induction of anaesthesia (pre op) and from induction of anaesthesia to the start of CPB (pre CPB), respectively. One sample was collected during 30 min from the start of CPB (CPB 30) and one fraction to the end of CPB (End CPB). Post bypass, the microdialysate was sampled in 60-min fractions for the first 6 h postoperatively, and then every 2 h. Microdialysate samples were immediately analysed to determine the concentrations of glycerol, lactate, pyruvate, and glucose using an enzymatic fluorometric assay using an automated analyser (CMA 600 Microdialysis analyser, CMA Microdialysis AB). Mean (SD) in vitro recovery (i.e. percentage uptake of the true concentration) for the microdialysis catheters with a flow rate of 1 $\mu l.min^{-1}$ was tested for lactate 64% (5), glycerol 37% (3), pyruvate 28% (6) and glucose 32% (4).

Following insertion of the catheters into the rectum, the tonometer sampling line was connected to the automated air tonometry system (Tonocap™, TC-200; Datex-Ohmeda). After the tonometer balloon was filled with air and allowed to equilibrate for 10 min, the gas was automatically sampled and measured for mucosal $P_iCO_2$ using infrared spectroscopy at the same time intervals as those used for microdialysis and blood gas measurements. The mucosal ($P_iCO_2$) and arterial ($P_aCO_2$) gap ($P_{(i-a)}CO_2$) was calculated at each time point. $PaCO_2$ was temperature corrected [23, 24]. The combined microdialysis/tonometry catheter was removed 16 h after surgery. The patients and nurses were interviewed about any discomfort or complications related to the rectal device.

### Haemodynamic measurements

Haemodynamic variables, haematocrit, $P_aCO_2$ and $P_aO_2$ (ABL 330 radiometer, Copenhagen, Denmark) were measured at the same time points as the microdialysate. Systemic vascular resistance (SVR), systemic oxygen delivery ($DO_2$), and uptake ($VO_2$), and oxygen extraction were calculated using standard formulae. Blood was analysed for white blood cell count, haemoglobin, platelet count, serum aspartate aminotransferase (ASAT), serum alanine aminotransferase (ALAT), troponin T and CK-MB pre-operatively and postoperatively on days 1 and 2.

### Statistical analysis

Systemic haemodynamic data, systemic oxygen transport and uptake, and haematology during the observational period were evaluated using ANOVA for repeated measures (SPSS, Chicago, IL). In addition, pairwise comparisons were done with the Bonferroni correction. Enzyme, microdialysate and tonometry measurements obtained at different time points were analysed using the non-parametric Friedman and Wilcoxon tests. Descriptive data is reported as mean (SD), or median, with 25 and 75 percentiles or range as appropriate. We considered $p < 0.05$ to represent a statistically significant difference.

## Results

### Demographic data, postoperative course and haemodynamic data (Tables 1–3)

Demographic data are summarised in Table 1. All patients made an uncomplicated recovery. No blood products were given during the measurement period. During the first 2 postoperative days there was an increase in white blood cell count, Troponin T and CK-MB, and decreased haemoglobin levels and platelet count (Table 2). After completion of the study, one patient had a myocardial infarction and one a pneumothorax diagnosed on the second postoperative day. None had

**Table 1** Demographic and clinical data. Values are presented as median or number of patients and 25–75 percentile or range.

| Variable | Median | 25–75 percentile or range |
|---|---|---|
| Age; years | 71 | (64, 74) |
| Height; cm | 175 | range (162, 188) |
| Weight; kg | 79 | range (70,91) |
| Ejection Fraction pre-op; % | 69 | (55, 70) |
| Diseased vessels; *n* | 3 | range (1, 3) |
| Bypasses; *n* | 4 | range (2,5) |
| CPB duration; min | 56 | (41, 82) |
| Aortic cross-clamping duration; min | 30 | (27, 44) |
| Intubation time; min postop | 218 | (174, 258) |
| Postop ICU stay; days | 1 | range (1, 1) |
| Postop in-hospital stay; days | 6.5 | range (4, 10) |
| Postop blood loss; ml | 610 | (409, 775) |
| | | **No. of patients** |
| Pre-op morbidity | | |
| Diabetes mellitus | | 1/12 |
| Renal failure | | 0/12 |
| Cardiac failure | | 0/12 |
| Hypertension | | 3/12 |
| Pre-op medication | | |
| β-blockers | | 12/12 |
| Ca-antagonists | | 2/12 |
| Diuretics | | 0/12 |
| Nitro | | 9/12 |
| Digitalis | | 0/12 |
| Intra-operative vasopressors (phenylephrine) | | 9/12 |
| Postoperative vasopressors | | 0/12 |
| Postoperative α/β blockade | | 5/12 |

CPB, cardiopulmonary bypass; ICU, intensive care unit.

any abdominal complications or stroke, and all patients survived the first 30 postoperative days.

Mean arterial pressure (MAP) and systemic vascular resistance (SVR) decreased during CPB, and returned to pre-CPB levels in the postoperative phase (Table 3). Haematocrit decreased during CPB and remained reduced postoperatively. Except for a short-lived reduction in oxygen delivery 2 h postoperatively, both delivery and uptake remained unchanged in the peri-operative period. Mixed venous oxygen saturation or systemic oxygen extraction also remained unchanged. Arterial oxygen tension did not change during CPB, but was reduced 16 h after CPB.

## Regional and systemic metabolic variables (Figs 2–4)

Baseline levels of luminal lactate were $< 0.25$ mmol.l$^{-1}$ both before induction of anaesthesia and prior to institution of CPB. After 30 min of CPB, luminal lactate increased fivefold, and it increased further until the end of CPB. Following CPB, gut luminal lactate gradually decreased, but was still elevated 16 h after surgery ($p < 0.001$) (Fig. 2). Intramuscular lactate nearly doubled during CPB and remained significantly elevated until 6 h postoperatively (Fig. 3a) ($p = 0.01$). Intramuscular pyruvate increased gradually from baseline levels of 55 (SD 13) to 123 (SD 12) μmol.l$^{-1}$ 16 h postoperatively ($p = 0.05$). The intramuscular lactate pyruvate ratio (LP-ratio) remained unchanged throughout the observational period (Fig. 3b). Arterial lactate was slightly increased (from 0.9 to 1.1 mmol.l$^{-1}$) only at the end of CPB compared with baseline levels ($p = 0.027$) (Fig. 3c). Arterial carbon dioxide tension was unchanged during CPB, but increased following tracheal extubation and remained 20% elevated compared to baseline levels between 4 and 16 h postoperatively ($p < 0.001$). Intestinal carbon dioxide tension was unchanged both during CPB and postoperatively (Fig. 4a). The intestinal–arterial carbon dioxide gap ($P_iCO_2$–$P_aCO_2$) did not increase relative to baseline at any time, but showed a decrease in the late postoperative period ($p = 0.004$) (Fig. 4b). Neither glycerol nor glucose was detected in the gut lumen.

Insertion of the rectal catheters was uncomplicated, and all but one catheter functioned properly during the investigation. The defective catheter (damaged microdialysis membrane) was not identified until after the start of surgery, and could not be changed, therefore the

**Table 2** Laboratory data.

| Variable | Preoperative | Postop Day 1 | Postop Day 2 | *p*-value |
|---|---|---|---|---|
| White cell count; × 10$^9$.l$^{-1}$ | 5.9 (1.1) | 8.4 (2.3)* | 9.7 (2.5)*# | < 0.0001 |
| Haemoglobin; g.dl$^{-1}$ | 14.8 (0.9) | 10.3 (0.7)* | 9.8 (1.0)* | < 0.0001 |
| Platelet count; × 10$^9$.l$^{-1}$ | 204 (34) | 119 (23)* | 113 (22)* | < 0.0001 |
| Serum ASAT; U.l$^{-1}$ | 31 (17–65) | 66 (24–140)* | | 0.039 |
| Serum ALAT; U.l$^{-1}$ | 32 (15–72) | 25 (16–47) | | NS |
| Troponin T; ng.ml$^{-1}$ | 0.01 (0.01–0.03) | 0.20 (0.06–1.94)* | 0.12 (0.04–1.46)*# | < 0.0001 |
| CK-MB; μg.l$^{-1}$ | 2.7 (1.2–3.9) | 15 (5.6–61.4)* | 4.8 (2.8–10.1)*# | < 0.0001 |

Values given as mean (SD) or median (range).
*$p < 0.05$ compared with pre-operative values. #$p < 0.05$ compared with postoperative day 1.
ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase; CK-MB, creatine kinase-MB. NS, nonsignificant.

**Table 3** Systemic haemodynamics, systemic oxygen transport, and uptake.

| Variable | Pre CPB | CPB 30 | End CPB | Postop 2 h | Postop 4 h | Postop 6 h | Postop 16 h | p value |
|---|---|---|---|---|---|---|---|---|
| MAP (mmHg) | 74 (5) | 61 (8)# | 61 (7)# | 77 (7) | 79 (10) | 78 (7) | 79 (7)# | < 0.0001 |
| CI/pump flow; $l.min^{-1}.m^{-2}$ | 2.20 (0.45) | 2.67 (0.24)# | 2.60 (0.17)# | 2.22 (0.56) | 2.39 (1.03) | 2.68 (0.56)# | 3.04 (0.65)# | < 0.0001 |
| SVRI; $dynes.s^{-1}.cm^{-5}.m^{-2}$ | 2341 (863) | 2054 (467) | 1911 (456)# | 2614 (533) | 2319 (656) | 2132 (551) | 1944 (602)# | 0.003 |
| $S_VO_2$; % | 77 (5) | 76 (4) | 77 (4) | 71 (8) | 75 (9) | 75 (9) | 75 (5) | NS |
| $DO_2I$; $ml.min^{-1}.m^{-2}$ | 395 (27) | 345 (25) | 366 (28) | 306 (24)# | 392 (36) | 419 (36) | 417 (28) | 0.007 |
| $VO_2I$; $ml.min^{-1}.m^{-2}$ | 84 (7) | 73 (8) | 79 (7) | 81 (5) | 79 (10) | 103 (11) | 104 (10) | 0.008 |
| $O_2$-extraction$_{syst}$; % | 22.4 (4.8) | 22.6 (5.0) | 22.3 (3.5) | 26.9 (6.4) | 23.0 (8.6) | 24.7 (7.7) | 24.6 (5.3) | NS |
| $P_aO_2$; kPa | 21.0 (7.4) | 16.7 (4.9) | 17.7 (9.4) | 18.4 (4.6) | 18.5 (7.2) | 18.1 (6.3) | 13.1 (2.8)# | 0.05 |
| Haematocrit$_{syst;}$ % | 39 (3) | 31 (3)# | 31 (3)# | 34 (3)# | 35 (3)# | 34 (3)# | 31 (3)# | < 0.0001 |
| Central blood temperature | 35.5 (0.8) | 35.4 (1.2) | 35.9 (0.9) | 36.6 (0.6)# | 37.2 (0.7)# | 37.3 (0.6)# | 37.0 (0.4)#°C | < 0.0001 |

Values given as mean (SD). #$p < 0.05$ compared with Pre CPB value.
Pre CPB, before cardiopulmonary bypass; CPB 30, after 30 min of CPB; End CPB, during rewarming; Postop 2 h, 4 h, 6 h, 16 h, 2–16 h after termination of CPB; MAP, mean arterial pressure; CI, cardiac index; SVRI, systemic vascular resistance index; $S_VO_2$, mixed venous oxygen saturation; $DO_2I$, systemic oxygen delivery index; $VO_2I$, systemic oxygen uptake index; $O_2$-extraction$_{syst}$, systemic oxygen extraction.

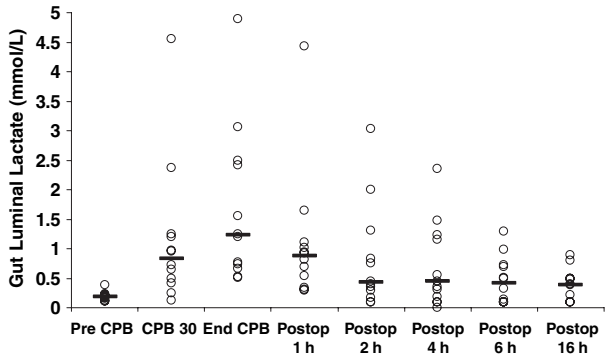


**Figure 2** Rectal lactate. Gut luminal levels of lactate in the 12 patients subjected to coronary surgery during baseline, cardiopulmonary bypass and postoperatively. Values are individual observations from each patient (open circles) with median (bars). Pre CPB, before cardiopulmonary bypass; CPB 30, the first 30 min of cardiopulmonary bypass; End CPB, after 30 min on CPB to termination of CPB; postop 1 h, 2 h, 4 h, 6 h, 16 h: 1–16 h after end of CPB.

patient was not included in the study. There were no visible signs of intestinal bleeding or lacerations in any of the patients when the catheters were removed. Neither patients or nurses reported any complaints or complications attributed to the catheters on the first postoperative day.

## Discussion

This study demonstrates that uncomplicated CPB is associated with an increase in lactate level in the rectal lumen as measured using the microdialysis technique during and after cardiac surgery. The current study also shows that microdialysis can detect changes that occur within 30 min, making rapid interventions possible. This suggests that microdialysis might be a potentially valuable tool for clinical monitoring the adequacy of splanchnic perfusion. The method is reasonably minimally invasive, causes little patient discomfort, and the success rate was high.

Lactate in the rectal lumen increased concomitantly with the CPB. The precise mechanism behind this phenomenon is not fully understood. Splanchnic oxygen delivery is reduced during hypothermic CPB partly due to a decrease in arterial oxygen content, in turn caused by haemodilution, and a decreased [25, 26] or unchanged [27–29] splanchnic blood flow has been shown. However, total blood flow rate in the intestinal wall of the jejunum has recently been reported to be well preserved or even elevated during mild hypothermic CPB when measured using the laser-Doppler technique [3, 30]. These findings are supported by our tonometric data showing an overall unchanged carbon dioxide tension of the rectal mucosa during and after CPB, and even a decrease in the mucosal–arterial $CO_2$ gap, at least in the relatively late postoperative course, indicating preserved blood flow also in the rectal mucosa.

These observations point to mechanisms other than reduced total blood flow in the gut mucosa as an explanation for the elevated rectal luminal lactate during and after CPB surgery.

### Can lactate in the gut lumen be a result of spill over from the systemic circulation?

Tenhunen et al. demonstrated that gut luminal lactate concentration in anaesthetised pigs, as measured by microdialysis, increased substantially during gut ischaemia when the intestinal permeability was altered, but did not increase from moderate systemic hyperlactataemia in control animals without gut ischaemia [21]. In that study, spill-over from the systemic circulation to the intestinal lumen occurred only when blood levels of lactate

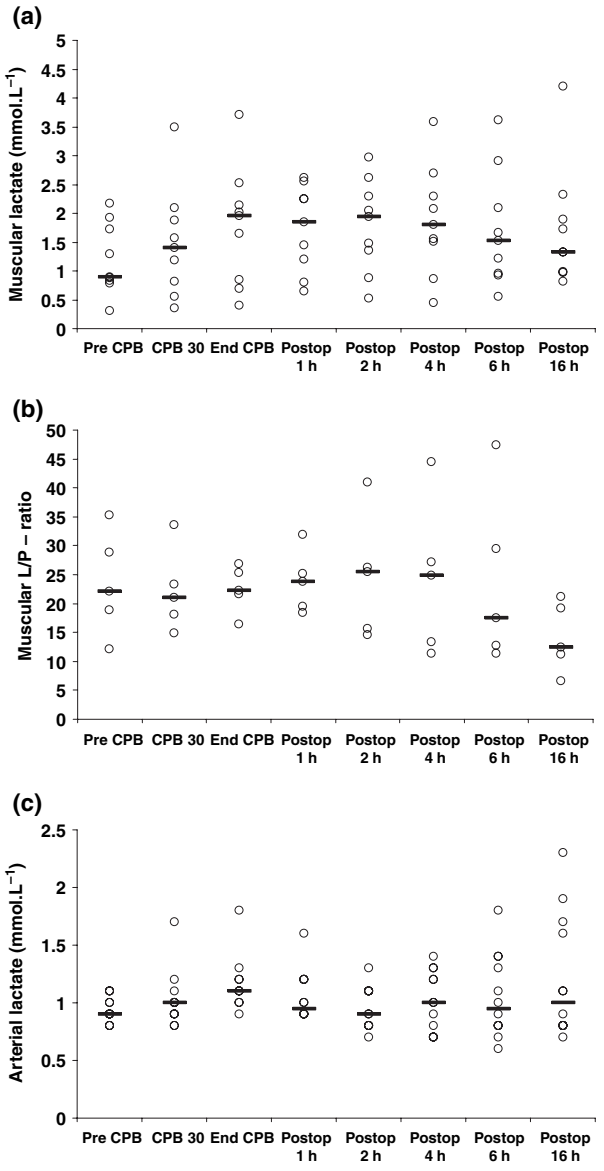


**Figure 3** Muscular lactate, lactate–pyruvate ratio, and arterial lactate. (a) Muscular lactate levels in eight patients subjected to coronary surgery during baseline, cardiopulmonary bypass and postoperatively. (b) Muscular lactate–pyruvate ratio (L/P ratio) in five patients subjected to coronary surgery during baseline, cardiopulmonary bypass and postoperatively. (c) Arterial lactate levels in 12 patients subjected to coronary surgery during baseline, cardiopulmonary bypass and postoperatively. Values are presented as individual points from each patient (open circles) with median (bars). Pre CPB, before cardiopulmonary bypass; CPB 30, the first 30 min of cardiopulmonary bypass; End CPB, after 30 min on CPB to termination of CPB; postop 1 h, 2 h, 4 h, 6 h, 16 h: 1–16 h after end of CPB.

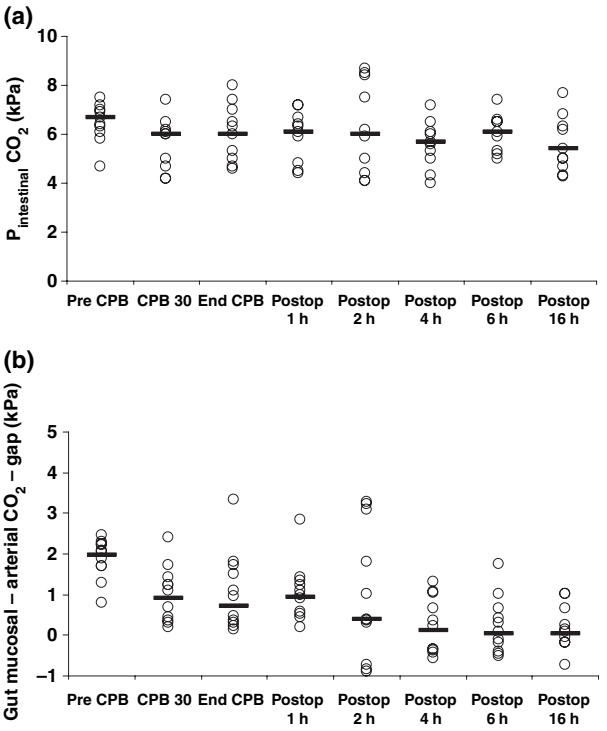


**Figure 4** Regional gut mucosal carbon dioxide and gut mucosal–arterial carbon dioxide gap. (a) Gut mucosal $P_{CO_2}$ ($P_iCO_2$) and (b) gut mucosal–arterial carbon dioxide gap ($P_{(i-a)}CO_2$) in 12 patients subjected to coronary surgery. Values are presented as individual points from each patient (closed circles) and median (bars). Pre CPB, before cardiopulmonary bypass; CPB 30, the first 30 min of cardiopulmonary bypass; End CPB, after 30 min on CPB to termination of CPB; postop 1 h, 2 h, 4 h, 6 h, 16 h: 1–16 h after end of CPB.

exceeded 5 mmol.l$^{-1}$. In the present study, only three of 12 patients had a moderately elevated blood lactate (maximum 2.0, 2.3 and 2.8 mmol.l$^{-1}$, respectively). Of these three patients, only one had a luminal lactate concentration above the median lactate level for all patients at any time of the observational period. The rest of those patients with highly elevated gut luminal lactate had normal blood levels of lactate. This suggests that the spill-over is sparse, although it is not possible to exclude some contribution from the systemic circulation due to the altered permeability of the intestinal mucosa seen during CPB [1].

All of our patients received beta-blockade perioperatively, and no patients were hyperglycaemic. This precludes these factors in causing hyperlactataemia, which has been observed in other studies [31]. Hypotension resulting from haemodilution on CPB is often treated using vasopressors. The only vasopressor used in this study was phenylephrine, which has been shown to redirect blood flow from the bowel and muscle to the brain and liver in pigs [32], and can therefore theoretically explain the increased luminal lactate. In this study, nine of the patients received phenylephrine: six of them 0.1 mg, and

three 0.8–1.0 mg. We could not find any correlation between the levels of gut luminal lactate and phenylephrine administration.

Hyperlactataemia in cardiac surgical patients may be a manifestation of inflammation induced by excess cytokine production [33, 34]. Therefore, the excess systemic and gut mucosal lactate production seen during CPB may result from an inflammatory effect causing mitochondrial dysfunction. Regional impairment and redistribution of blood flow within the layers of the gut wall during CPB may also be a contributing factor to local lactate production [35]. Others have suggested that increased production of lactate in the gut tissue contributes to increased systemic lactate concentrations in CPB patients [36]. However, the increased muscular lactate levels found in our study suggest that, in fact, muscle may be a more important source for increased systemic levels of lactate than the gut. This may resemble the situation seen in sepsis, where endogenous epinephrine release stimulates sarcolemmal $Na^+$-$K^+$-ATPase-coupled lactate production [37]. Further, we found increased muscular pyruvate levels without an increased lactate–pyruvate ratio.

This may reflect a decreased peripheral metabolism of pyruvate as seen when the activity of the enzyme pyruvate dehydrogenase is impaired by tumour necrosis factor, for example in septic patients [38], also indicating that this increased lactate should not necessarily be taken as an indication of oxygen debt either in the skeletal muscle nor in the gut lumen, but rather altered lactate homeostasis.

Although the data with regard to lactate in the rectal lumen point to a clear dysfunction of the gut mucosa, glycerol was not detected at this site. This is not surprising as glycerol is a marker of cellular membrane disintegration following cellular necrosis [39], whereas apoptosis has been shown to be the predominant mode of cell death in the gut mucosa during CABG surgery [40]. A key difference between the two forms of cell death is that during necrosis, the membrane integrity breaks down and cytosolic and membrane constituents as glycerol are released into the extracellular space, whereas during apoptosis, cells shrink and their nuclei condense, resulting in their encapsulation into well-enclosed apoptotic bodies followed by consumption by macrophages and no 'free' glycerol is detected [41].

Tonometry is used to measure the partial pressure of carbon dioxide within the lumen of the gastrointestinal tract ($PgCO_2$). Under stable haemodynamic circumstances, $PgCO_2$ reflects the balance between carbon dioxide production and carbon dioxide elimination by the gastric mucosal blood flow. $PgCO_2$ increase is predominantly due to reduced washout of carbon dioxide, and can be taken as an alarm of a situation at risk of circulatory failure and a low flow state [42]. Tonometry has also been used to monitor the colonic mucosa during aortic surgery [13] and during CPB [22]. The normal value of the mucosal–arterial carbon dioxide gap has not yet been established, however, a baseline level around 1 kPa found in our own study concurs with data obtained from other studies on cardiac and aortic surgery patients [13, 22]. During and after aortic surgery, mucosal–arterial carbon dioxide gap as measured by tonometry appears to be increased [43]. The preserved or even decreased mucosal–arterial carbon dioxide gap detected in our patients agrees with data reported by Fisher et al. [22], who found decreased regional rectal carbon dioxide during CPB and no correlation between regional carbon dioxide production in the rectal and gastric mucosa.

In hypoxic hypoxia models, as opposed to low flow states, the lactate levels increase much earlier and to a greater degree than the carbon dioxide gap [44]. This suggests that tissue carbon dioxide monitoring may be useful in low flow states (compensated or uncompensated shock), and lactate levels may be more useful in hypoxic hypoxia (septic shock or CPB).

Major limitations of this study are that the sample size was very small, the study was not designed as an outcome study and all patients did well. How therefore can, the elevated levels of gut luminal lactate be of clinical relevance? Lactate in the gut lumen is a marker of altered intestinal permeability [16], and in abdominal aortic surgery, elevated levels of lactate in the splanchnic circulation predict organ failure [13]. Our patients were chosen due to the known occurrence of altered permeability during CPB [1], and therefore we expected to detect increased levels of lactate in the gut lumen. They were not chosen from expectations of detecting serious intestinal ischaemia, which is very rare.

The technique of using a rectal device combining a microdialysis and a tonometric catheter has several advantages. When combining these two methods we have the opportunity to compare both methods at the same place in the intestine, and the tonometric balloon assures contact between the microdialysis catheter and the intestinal mucosa. The principle of sampling mediators from the intestinal mucosa by means of the microdialysis technique seems promising, but more studies are needed to evaluate the clinical relevance as a prognostic/therapy guiding tool and to evaluate the sensitivity of the method for the detection of intestinal ischaemia and dysfunction (aortic surgery, septic shock, etc.).

The method is not yet routine for use in all at-risk patients. The membrane of the microdialysis catheter is vulnerable, so a very gentle technique and visual guidance

through a rectoscope have to be used for insertion. The catheters need to be reinforced so they can be inserted blindly without the use of a rectoscope. The rectal device can then be introduced without sedating the patients, thereby expanding the potential for clinical applicability of the technique.

In conclusion, this study has demonstrated that endoluminal rectal microdialysis can be used clinically to help in monitoring intestinal metabolism. However, the ability to evaluate fully the use of gut luminal microdialysis in the rectum was limited due to the fact that none of the patients developed serious alterations in intestinal ischaemia. Combined with tonometry, microdialysis provides the opportunity to monitor both circulatory and metabolic parameters in the rectal mucosa. Increased lactate concentrations in the rectum detected by gut luminal microdialysis during CPB indicate local lactate production.

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