Tech Coloproctol (2014) 18:65–71
DOI 10.1007/s10151-013-1020-0

ORIGINAL ARTICLE

Identification of anastomotic leakage after colorectal surgery using microdialysis of the peritoneal cavity

F. Daams · Z. Wu · H. Cakir · T. M. Karsten · J. F. Lange

Received: 5 December 2012 / Accepted: 15 April 2013 / Published online: 30 April 2013

Abstract

Background Early detection of colorectal anastomotic leakage (AL) may lead to better outcome. AL may be preceded by change in local metabolism and local ischaemia. Microdialysis of the peritoneal cavity is able to measure these changes in real-time and is minimally invasive. The aim of this prospective cohort study was to compare values of intraperitoneal microdialysis in patients with AL to patients without AL after open and laparoscopic colorectal surgery.

Methods Twenty-four patients underwent surgery for left-sided, sigmoid and rectal carcinoma with creation of an anastomosis. Intraoperatively a juxta-anastomotical intraperitoneal and subcutaneous microdialysis catheter was placed. The levels of lactate, pyruvate, glucose and glycerol in the dialysate were measured every 4 h during the first 5 post-operative days, and mean values and area under the curve (AUC) were calculated.

Results Mortality was 0 % and morbidity 38 %. In 3 patients (17 %), AL occurred. In patients with AL, post-operative peritoneal lactate level was 3.2 mmol/l (standard deviation (SD) 0.9) for patients without AL, compared to 4.4 mmol/l (SD 1.5) in case of AL ($p = 0.03$ for AUC). Intraperitoneal glucose levels were 8.1 mmol/l (SD 1.3), compared to 7.8 mmol/l (SD 2.2) in the complicated course (ns for AUC). Mean intraperitoneal lactate/pyruvate-ratio was 19.2 (SD 3) after colorectal surgery without AL compared to 25 (SD 4.7) in case of AL (non-significant (ns) for AUC). No significant differences were observed between patients who underwent laparoscopic resection and those who underwent open resection.

Conclusions Anastomotic leakage was preceded by a significantly higher AUC and mean value of lactate levels during the first 5 post-operative days. To identify cut-off values for clinical use, pooling of data is necessary.

Keywords Colorectal surgery · Anastomotic leakage · Early detection · Microdialysis

Introduction

Anastomotic leakage (AL) is a major complication after colorectal surgery, which occurs in 3–13 % of patients [1, 2]. AL after rectal surgery leads to increased morbidity and mortality, many surgical and non-surgical interventions and longer hospitalisation [3–5]. Several studies have identified risk factors for AL after rectal surgery including male sex, low colorectal anastomosis (<6 cm), multiple blood transfusions and long operating time [5, 6], and a colon leakage score has been proposed [7].

The preventive role of routine draining is the subject of ongoing investigation, along with other interventions [8]. Still, apart from the possible beneficial effect of draining fluid, the fluid itself has a role in the early detection of AL. Where, in some recent studies, analysis of cytokines in drain fluid seems to help in the early detection of this dreaded complication [9–11], routine measurement of TNF-alpha nor IL-6 in drain fluid enabled a quick diagnosis of AL in a study by Bertram

F. Daams · H. Cakir
Department of Surgery, Reinier de Graaf Gasthuis, Delft, The Netherlands

F. Daams (✉) · Z. Wu · J. F. Lange
Department of Surgery, Erasmus Medical Centre, PO box 2040, 3000 CA Rotterdam, The Netherlands
e-mail: freekdaams@gmail.com

T. M. Karsten
Department of Surgery, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

et al. [12]. Intraperitoneal bacterial colonisation can be measured by quantitative cultures or real-time-polymerase chain reaction (RT-PCR) of drain fluid and is positively related with the occurrence of AL [9, 13].

Clinical scoring systems, as described by den Dulk et al. [14], use clinical features such as presence or absence of fever, ileus and pain to score patients objectively. These are easily applicable to daily practice and reduce delay in diagnosis by 2.5 days. Instruments like these prevent doctor-dependent delay and decrease false-negative results of diagnostic imaging, which are key causes of delay in diagnosis [15]. A study by Bellows using non-standardised clinical examination showed that pulmonary and neurological events occur prior to AL and should warn the treating physician [16].

Another method for early detection of AL is routine post-operative measurement of serum levels of C-reactive protein (CRP). In a study by Ortega-Deballon et al. [17] a cut-off of 125 mg/l on post-operative day (POD) 4 resulted in a sensitivity of 82 % and a negative predictive value of 96 % for AL. Welsch et al. [18] showed similar predictive value of 91 % for a complicated post-operative course, not just AL, when CRP levels were 140 mg/l on POD 4. Another study showed correlation of AL with a prolonged post-operative elevation of CRP [19].

The drawback of all these parameters is that they are only useful as indications of the presence of overt systemic disturbances and are not helpful in detecting preceding local ischaemia, disintegration of cells and confined peritonitis. Furthermore, large indwelling intraperitoneal drains are considered to impair independent mobilisation and leave scars. Daily clinical scoring has the disadvantage of a low probability of detection resulting in decreased motivation. Therefore, the minimally invasive method of intraperitoneal microdialysis seems promising, since it measures ischaemia and changes in metabolism locally and in real-time [20, 21], by the use of a small 0.9-mm-double lumen catheter. At the tip of this catheter, a semipermeable membrane enables diffusion of small molecules such as lactate, glucose and glycerol (cut-off 20 kDa) intraperitoneally. It has been used extensively in the fields of neurosurgery, pharmacology and plastic surgery, and the above mentioned parameters have been thoroughly validated. In a few small studies, intraperitoneal microdialysis has shown promising results in detecting post-operative complications after colorectal surgery [22–25]. Our prospective study was designed to compare values of intraperitoneal microdialysis in patients with AL to patients without AL after open and laparoscopic colorectal surgery.

Materials and methods

Patients who underwent elective open or laparoscopic left-sided hemicolectomy, sigmoid or rectal resection for resectable colorectal carcinoma, or stenosing diverticulitis were included. All patients were >18 years old, had an American Association of Anaesthesiologists (ASA) score <4 and gave informed consent prior to the operation. The local ethical committee approved this study.

In microdialysis of the peritoneal cavity and subcutaneous fat, a physiological salt solution (NaCl 147 mmol/L, KCl 4 mmol/L, $CaCl_2$ 2.3 mmol/L, T1 perfusion fluid, CMA, Solna Sweden) was pumped (CMA 106 MD Pump, CMA, Solna, Sweden) with a constant speed of 0.3 L/min through a semipermeable membrane. The solution was equilibrated with the surrounding tissue fluid. The intraperitoneal catheter (Fig. 1a, CMA 62 Gastrointestinal MD Catheter, CMA, Solna, Sweden) was placed transabdominally during the last stage of the operation in the direct proximity of the anastomosis. For open and laparoscopic surgery, this was performed by introducing a splittable tunnelling needle to transduce the microdialysis catheter. In laparoscopic surgery extra care was taken not to touch the distal membrane. A second catheter (Fig. 1b, CMA60 MD Catheter, CMA, Solna, Sweden) was placed in the subcutaneous fat of the abdominal wall serving as a reference. Before placement, each catheter was flushed with perfusate so that no air was trapped in the catheter lumen. The subcutaneous catheter was placed at least 5 cm from the laparotomy or laparoscopy wounds. All catheters were fixed with a single non-resorbable suture. A sterile dressing protected both catheters. The outgoing dialysate was stored in a small airtight receptacle that was removed from the catheter every 4 h, starting at 0000 hours of POD 1 for a period of 96 h. Samples were processed in a batch using a CMA 600-analyser (CMA 600 MD Analyser, CMA, Solna, Sweden) directly after the patient was discharged.

In the sample, levels of lactate, pyruvate, glycerol and glucose were measured. The lactate/pyruvate-ratio (L/P-ratio) is an indicator for hypoxia, whereas decreased glucose levels indicate increase in metabolism. When local ischaemia progresses, cells are broken down, and due to lipolysis, glycerol is released.

Patients were treated according to the standard post-operative protocol of enhanced recovery, and microdialysis values were not used clinically. Every day, patients underwent physical examination which included temperature, heart rate, mean arterial blood pressure and haemoglobin saturation. According to our local post-operative protocol, during POD 1-3 plasma CRP levels were determined. In case of a suspected abdominal complication, diagnostic and/or therapeutical steps were undertaken according to current local standards. If an AL was diagnosed, the time of diagnosis was recorded as well as findings during reoperation. AL was defined according to the grading system of Rahbari et al. [26].

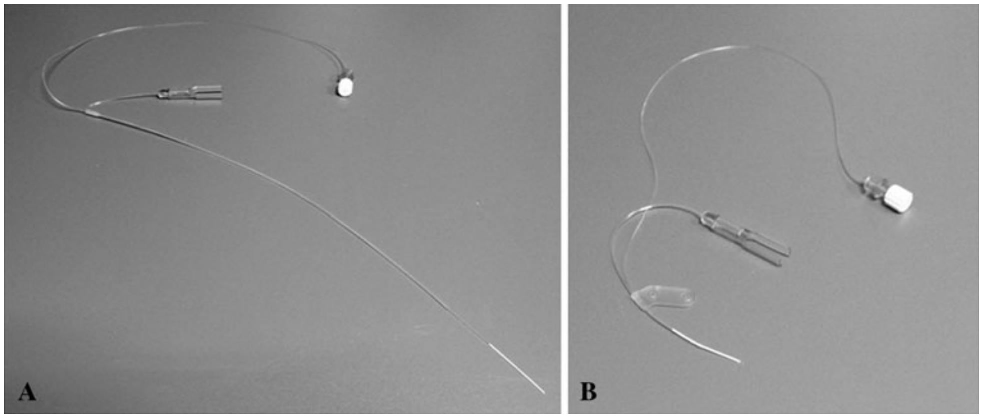

Fig. 1 **a** CMA 62 catheter for intraperinoneal application. **b** CMA 60 for subcutaneous use. Both catheters have a double-lumen shaft, a connector to the CMA 106 pump (not shown) and a connector for the sample tubes. Note the 3-cm-long semipermeable tip at the end of both catheters

Statistical analysis

For glucose, lactate, pyruvate, glycerol and L/P-ratios, the area under the curve (AUC) was calculated for POD 1–4 and used for statistical analysis. The Mann–Whitney test for unpaired samples was used. $p < 0.05$ was considered statistically significant.

Results

Forty-five patients met the inclusion criteria during the study period. Data of 24 patients could finally be used for evaluation, since 12 refused to participate, and in 9 patients technical failure was encountered. Eighteen patients were operated on laparoscopically. Four of them underwent conversion to open surgery, 6 had open resection. Conversions occurred in an early phase of the operation in all 4 patients, therefore, for analysis, these were considered as open procedures.

In 21 patients, no AL occurred, but in 5 of them, other complications were observed, including pneumonia, superficial wound infection, prolonged post-operative ileus, delirium and congestive heart failure. Three patients (3/24, 12 %) were diagnosed with AL on POD 4, 5, 42, respectively. Patient characteristics are shown in Table 1. All AL were demonstrated by abdominal computed tomography (CT) scan and confirmed by reoperation or endoscopy. The severity of AL was grade 3 according to Rahbari et al. in all patients, and mortality was 0 % [26].

Clinically, patient 1 developed tachycardia on POD 2 and had a CRP level of 298 mg/l, but no abdominal pain or tenderness. On POD 4, the patient developed sepsis and a CT-scan showed AL, which necessitated reoperation and

Table 1 Patient characteristics

	No. ($n = 21$)	Leakage ($n = 3$)
Sex		
Male	15	1
Female	6	2
Age		
Years	68	69
ASA classification		
I	7	–
II	10	2
III	4	1
Indication		
Malignancy	18	1
Benign	3	2
Type of operation		
Left-sided colectomy	3	–
Sigmoid resection	9	2
LAR	8	1
HR	1	–
Type of procedure		
Laparoscopic	14	–
Open	4	2
Converted	3	1
Hospital admission		
Days	7.1	21.7
Other complications		
Pneumonia	1	–
Wound infection	1	–
Prolonged post-operative ileus	1	–
Evisceration	–	1

LAR low anterior resection, *HR* restoration of continuity after Hartmann's procedure, *ASA* American Society of Anesthesiologists admission to the intensive care unit (ICU). At reoperation, an abscess was found at the site of the anastomosis, showing a small leak. No signs of anastomotical ischaemia were present. Patient 2 developed fever 48 h after the primary operation and had an acute abdominal evisceration on POD 3. During reoperation, no signs of AL were observed. Two days later (POD 5), the patient developed fever again, while the CRP level was 235 mg/l, and the abdomen was distended and tender. A CT-scan demonstrated AL, which was confirmed during reoperation the same day. The anastomosis did not appear ischaemic. Patient 3 was discharged from the hospital on POD 12 after reversal of a colostomy that was placed previously due to perforated diverticulitis. Intraoperatively, iatrogenic bladder injury occurred. On POD 27, the patient was readmitted with fever and signs of colovaginal fistula. This was confirmed by CT and endoscopy, which showed a large pelvic abscess partially draining through the dorsal vaginal wall. After conservative treatment failed, reoperation followed on POD 94 and confirmed the aforementioned findings. Partial dehiscence of the anastomosis was observed. The anastomosis was broken down and did not show macroscopic signs of ischaemia.

Patients with an uncomplicated course after colorectal surgery had mean intraperitoneal glucose levels were 8.1 mmol/l (standard deviation (SD) 1.3), compared to 7.8 mmol/l (SD 2.2) in those with a complicated postoperative course. The AUC for patients with AL was not significantly different from that for patients without AL ($p = 0.6$). For the subcutaneous samples, glucose levels were 7.4 (SD 1.5), and 7.4 (SD 1.5) for patients without and with a AL, respectively. Mean intraperitoneal lactate levels were 3.2 mmol/l (SD 0.9) for patients without AL, compared to 4.4 mmol/l (SD 1.5) for patients who developed AL, showing significantly different AUCs for patient with and without AL ($p = 0.03$) (Fig. 2a, b). Subcutaneous microdialysis showed a mean lactate level in patients without AL of 2 mmol/l (SD 0.6), compared to a level of 3 mmol/l (SD 1.2) in patients without AL. The mean intraperitoneal lactate/pyruvate-ratio was 19.2 (SD 3) after colorectal surgery without AL compared to 25 (SD 4.7) in case of AL. The AUC for patients with AL, however, was not significantly different from that for patients without AL (Fig. 3). The mean subcutaneous LP-ratio was 14 (SD 3.9) and 17.7 (SD 4.2) for patients without and with AL. In the group of patients that was operated on laparoscopically and did not develop AL, mean intraperitoneal glucose levels were 7.2 mmol/l (SD 2.7 mmol/l) compared to 9.1 mmol (SD 3.1 mmol/l) for open surgery patients. AUCs were not significantly different between these groups ($p = 2.4$). Mean intraperitoneal lactate levels were higher in laparoscopic patients (laparoscopic: 3.5 mmol/l, SD 1.8; open: 2.7 mmol/l, SD 1.2) but the difference in AUCs was not significant ($p = 0.5$). Intraperitoneal pyruvate (laparoscopic: 165.5 µmol/l, SD 67.8 µmol/l, open: 151.1 µmol/l, SD 47.9 µmol/l, AUC $p = 1.0$), glycerol (laparoscopic: 179 µmol/l, SD 64.2 µmol/l, open: 153.6 µmol/l, SD 53.7 µmol/l, AUC $p = 1.0$) and LP-ratio (laparoscopic: 21.4, open: 18, AUC $p = 0.35$) were not significantly different after laparoscopic and open surgery. None of the parameters for subcutaneous microdialysis showed any difference between open and laparoscopic surgery.

Two patients developed an early AL after 4 days (patient 1) and 5 days (patient 2), respectively. Figure 4 shows curves for the intraperitoneal L/P-ratio in during the first 4 days for these individual patients. A clear peak can be seen for both patients at 48 and 32 h, respectively. Patient 3, who had a late leak, did not have L/P-ratio abnormalities in the immediate post-operative period resulting in comparable values to the patients without AL.

C-reactive protein levels were measured daily during POD 1-3. Differences were observed in mean daily values (day 0: CRP uncomplicated course (uc) 5.3 mg/l, CRP anastomotic leakage (al): 45 mg/l; day 1 CRPuc 81 mg/l, CRPal 88 mg/l; day 2 CRPuc 154 mg/l, CRPal 206 mg/l;

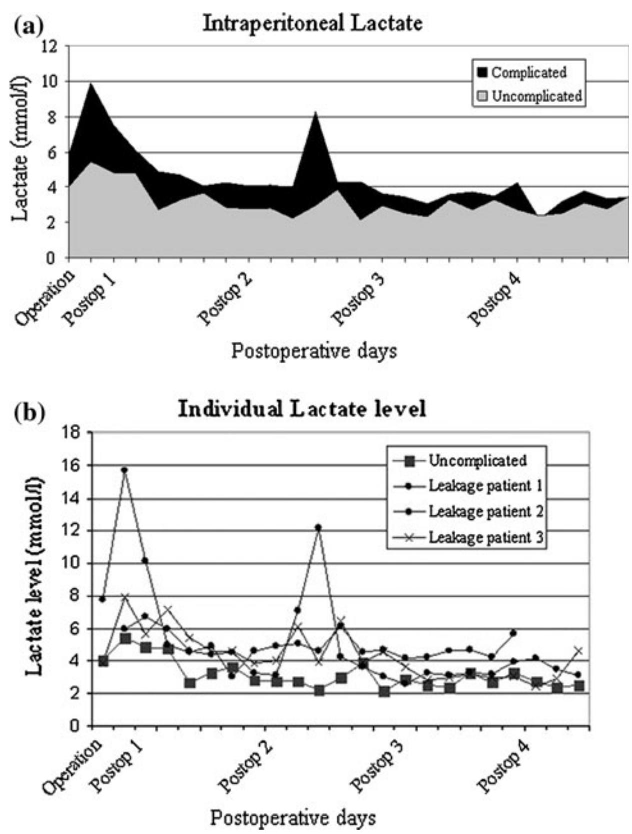

Fig. 2 **a** Mean intraperitoneal lactate levels for patients with and without leakage. The area under the *curve* was significantly different ($p = 0.03$) for the first 4 post-operative days. **b** Individual intraperitoneal lactate levels for patients with anastomotic leakage compared with the mean value of patients without leakage

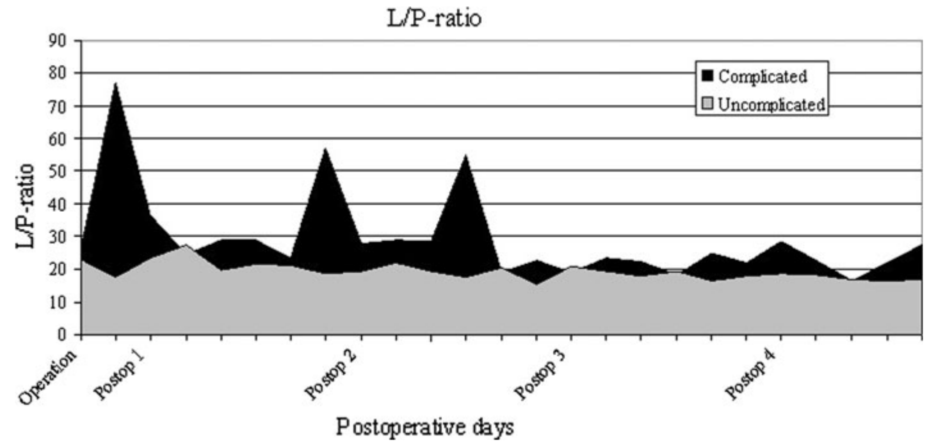

Fig. 3 Mean lactate/pyruvate-ratios for patients with and without leakage. The area under the *curve* was not significantly different

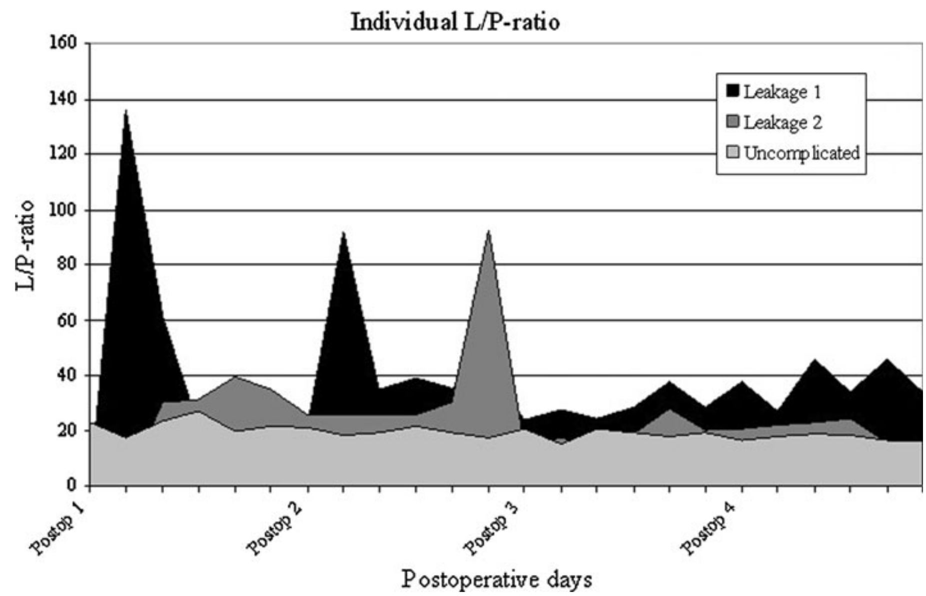

Fig. 4 Individual lactate/pyruvate-ratios for leakage (patients 1 and 2) compared with the mean of lactate/pyruvate-ratio of the uncomplicated group

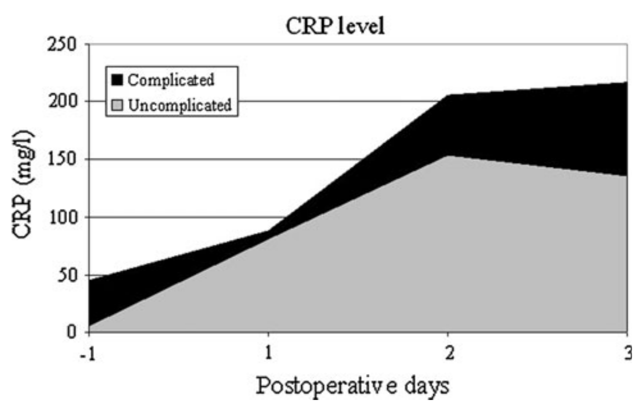

Fig. 5 C-reactive protein levels pre-operatively and 3 days post-operatively of patients with and without a leakage. The area under the *curve* was not significantly different

day 3 CRPuc 136 mg/l, CRP al 217 mg/l), but the difference in AUC ($p = 0.12$) did not reach significance (Fig. 5). Pre-operatively, the CRP level in patient 2 was 127 mg/l. This patient underwent elective surgery for a diverticular stricture, and intraoperatively, an abscess in the subcutaneous fat, which was the only focus of infection, was drained.

Discussion

Anastomotic leakage is the most feared complication after colorectal surgery, occurring after a mean of 12 days postoperatively [27]. Since early detection of AL might lead to a better outcome, many authors have focussed on risk estimation of leakage. One risk factor, which is objectively measurable, is local ischaemia and is detectable endoluminally. Nonetheless, tissue hypoperfusion is not always present in AL, and when ischaemia occurs, this does not always lead to AL. Therefore, we chose to investigate extraluminal local metabolic and ischaemic changes. Microdialysis is a minimally invasive method to detect changes in carbohydrate metabolism in the tissue directly surrounding the tip of the catheter and has been described for intraperitoneal use in just a few publications. Our study shows that lactate levels in patients who develop AL after left-sided colectomies, sigmoid and rectal resections are significantly higher during the first days after surgery, compared to patient levels in patients who had an uncomplicated course. This finding corresponds with previous research by Ellebaek et al. [22] who found elevated levels of lactate prior to AL after rectal resections. In this study, AL was also related to a decrease in intraperitoneal glucose levels, which in our study was not observed. A reason for this could be the small sample of patients with AL and the variations in clinical presentation. Another study, by Horer et al. [25], showed an elevated intraperitoneal L/P-ratio and decreased intraperitoneal glycerol levels in patients developing AL. In our study, both patients with an early AL showed a peak in L/P-ratio prior to the diagnosis of AL. Lactate levels increase in case of hypoxia because of fermentation of pyruvate and hypermetabolism due to inflammation, thus, an elevated L/P-ratio can be observed under these circumstances. In AL, both of these processes might be present, although there is no consensus regarding the underlying pathophysiology [10, 26, 28]. Our findings support the hypothesis that ischaemia of the anastomosis compromises its healing in most cases of AL. However, the anastomosis did not appear ischaemic during reoperation in our patients.

C-reactive protein level is increased in the presence of inflammation and reaches a peak after 48 h. In this study, uncomplicated surgery caused an elevation in CRP precisely according to this pattern. One patient with an early AL had a subcutaneous abscess during the primary operation, so it was difficult to interpret the post-operative samples. Other studies with larger sample size have investigated the value of CRP measurement in the detection on AL and found that a failure of decreasing plasma levels after POD 2 or a level of >125 mg/l on POD 4 are indicative of inflammatory complications [17, 18]. Since the routine CRP measurement was terminated after POD 3, all the patients with AL met the first criterion.

In a study by Gianotti et al. [29] on the influence of pneumoperitoneum in laparoscopic resections on the pO_2 of the colon wall, an increased pO_2 in laparoscopic patients was found. Another study by Pascual et al. [30] showed that the inflammatory response, measured by levels of interleukins in the peritoneal fluid post-operatively after laparoscopic or open colectomy, is higher in patients after open surgery. In our study, there were no differences in the intraperitoneal microdialysis results of patients who were operated on laparoscopically compared to patients in the open surgery group. Since the intraperitoneal catheter was placed right next to the anastomosis, samples reflect the local metabolism of this area. Our findings suggest that local metabolism is not influenced by the operative technique. The conversion rate in this study was 22 %, which we consider rather high although this percentage is comparable with the national conversion rate in the Netherlands of 15 %.

Intraperitoneal microdialysis is a costly technique and requires full cooperation from nursing staff and patients. Often, technical failure cause early cessation of sampling. In this study, this occurred in 9 patients and ranged from iatrogenic damage to the catheter or air entrapment in the catheter to erroneous preliminary removal of the catheter by either the patient or nursing staff. In our study and in a comparable study by Ellebaek et al. [22], no differences between local and systemic changes in metabolism and/or ischaemia could be identified using a subcutaneous reference catheter. Hence, in our opinion, the routine placement of a subcutaneous reference catheter should be omitted in the future. Although other techniques for early detection of AL—like clinical scoring systems and plasma CRP measurement also have their drawbacks, these methods can be applied easily, being cheap and superior in terms of higher sensitivity and specificity. In our study, microdialysis samples were batch-analysed, but samples can also be analysed bedside at any preferred frequency.

A drawback of the current study is its small sample size, due to this, no cut-off values could yet be established for intraperitoneal microdialysis for the earliest possible detection of AL. Since our findings correspond with the limited prior research reported in the literature, the next step for further development of microdialysis as a method for early detection of AL is a meta-analysis of all available data.

Acknowledgments The authors thank DSW-health insurance, Schiedam, The Netherlands and the Scientific Activity Committee of the Reinier de Graaf Groep, Delft, The Netherlands and Stichting BG, Delft, The Netherlands for their financial contribution to this study.

Conflict of interest None.

References

1. Krarup PM, Jorgensen LN, Andreasen AH, Harling H (2012) A nationwide study on anastomotic leakage after colonic cancer surgery. Colorectal Dis 14:e661–e667
2. Yeh CY, Changchien CR, Wang JY et al (2005) Pelvic drainage and other risk factors for leakage after elective anterior resection in rectal cancer patients: a prospective study of 978 patients. Ann Surg 241:9–13
3. Eckmann C, Kujath P, Schiedeck TH, Shekarriz H, Bruch HP (2004) Anastomotic leakage following low anterior resection: results of a standardized diagnostic and therapeutic approach. Int J Colorectal Dis 19:128–133
4. Eriksen MT, Wibe A, Norstein J, Haffner J, Wiig JN (2005) Anastomotic leakage following routine mesorectal excision for rectal cancer in a national cohort of patients. Colorectal Dis 7:51–57

5. Matthiessen P, Hallbook O, Andersson M, Rutegard J, Sjodahl R (2004) Risk factors for anastomotic leakage after anterior resection of the rectum. Colorectal Dis 6:462–469
6. Alberts JC, Parvaiz A, Moran BJ (2003) Predicting risk and diminishing the consequences of anastomotic dehiscence following rectal resection. Colorectal Dis 5:478–482
7. Dekker JW, Liefers GJ, de Mol van Otterloo JC, Putter H, Tollenaar RA (2011) Predicting the risk of anastomotic leakage in left-sided colorectal surgery using a colon leakage score. J Surg Res 166:27–34
8. Karliczek A, Jesus EC, Matos D, Castro AA, Atallah AN, Wiggers T (2006) Drainage or nondrainage in elective colorectal anastomosis: a systematic review and meta-analysis. Colorectal Dis 8:259–265
9. Fouda E, El Nakeeb A, Magdy A, Hammad EA, Othman G, Farid M (2011) Early detection of anastomotic leakage after elective low anterior resection. J Gastrointest Surg 15:137–144
10. Komen N, de Bruin RW, Kleinrensink GJ, Jeekel J, Lange JF (2008) Anastomotic leakage, the search for a reliable biomarker. A review of the literature. Colorectal Dis 10:109–115
11. Uğras B, Giris M, Erbil Y et al (2008) Early prediction of anastomotic leakage after colorectal surgery by measuring peritoneal cytokines: prospective study. Int J Surg 6:28–35
12. Bertram P, Junge K, Schachtrupp A, Gotze C, Kunz D, Schumpelick V (2003) Peritoneal release of TNFalpha and IL-6 after elective colorectal surgery and anastomotic leakage. J Invest Surg 16:65–69
13. Komen N, Morsink MC, Beiboer S et al (2009) Detection of colon flora in peritoneal drain fluid after colorectal surgery: can RT-PCR play a role in diagnosing anastomotic leakage? J Microbiol Methods 79:67–70
14. den Dulk M, Noter SL, Hendriks ER et al (2009) Improved diagnosis and treatment of anastomotic leakage after colorectal surgery. Eur J Surg Oncol 35:420–426
15. Doeksen A, Tanis PJ, Vrouenraets BC, van Lanschot JJ, van Tets WF (2007) Factors determining delay in relaparotomy for anastomotic leakage after colorectal resection. World J Gastroenterol 13:3721–3725
16. Bellows CF, Webber LS, Albo D, Awad S, Berger DH (2009) Early predictors of anastomotic leaks after colectomy. Tech Coloproctol 13:41–47
17. Ortega-Deballon P, Radais F, Facy O et al (2010) C-reactive protein is an early predictor of septic complications after elective colorectal surgery. World J Surg 34:808–814
18. Welsch T, Müller SA, Ulrich A et al (2007) C-reactive protein as early predictor for infectious postoperative complications in rectal surgery. Int J Colorectal Dis 22:1499–1507
19. Woeste G, Muller C, Bechstein WO, Wullstein C (2010) Increased serum levels of C-reactive protein precede anastomotic leakage in colorectal surgery. World J Surg 34:140–146
20. Jansson K, Ungerstedt J, Jonsson T et al (2003) Human intraperitoneal microdialysis: increased lactate/pyruvate ratio suggests early visceral ischaemia. A pilot study. Scand J Gastroenterol 38:1007–1011
21. Ungerstedt J, Nowak G, Ericzon BG, Ungerstedt U (2003) Intraperitoneal microdialysis (IPM): a new technique for monitoring intestinal ischemia studied in a porcine model. Shock 20:91–96
22. Ellebaek Pedersen M, Qvist N, Bisgaard C, Kelly U, Bernhard A, Møller Pedersen S (2009) Peritoneal microdialysis. Early diagnosis of anastomotic leakage after low anterior resection for rectosigmoid cancer. Scand J Surg 98:148–154
23. Jansson K, Redler B, Truedsson L, Magnuson A, Ungerstedt U, Norgren L (2004) Postoperative on-line monitoring with intraperitoneal microdialysis is a sensitive clinical method for measuring increased anaerobic metabolism that correlates to the cytokine response. Scand J Gastroenterol 39:434–439
24. Matthiessen P, Strand I, Jansson K et al (2007) Is early detection of anastomotic leakage possible by intraperitoneal microdialysis and intraperitoneal cytokines after anterior resection of the rectum for cancer? Dis Colon Rectum 50:1918–1927
25. Horer TM, Norgren L, Jansson K (2011) Intraperitoneal glycerol levels and lactate/pyruvate ratio: early markers of postoperative complications. Scand J Gastroenterol 46:913–919
26. Rahbari NN, Weitz J, Hohenberger W et al (2010) Definition and grading of anastomotic leakage following anterior resection of the rectum: a proposal by the International Study Group of Rectal Cancer. Surgery 147:339–351
27. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA (2007) Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg 245:254–258
28. Macarthur DC, Nixon SJ, Aitken RJ (1998) Avoidable deaths still occur after large bowel surgery. Scottish Audit of Surgical Mortality, Royal College of Surgeons of Edinburgh. Br J Surg 85:80–83
29. Gianotti L, Nespoli L, Rocchetti S, Vignali A, Nespoli A, Braga M (2011) Gut oxygenation and oxidative damage during and after laparoscopic and open left-sided colon resection: a prospective, randomized, controlled clinical trial. Surg Endosc 25:1835–1843
30. Pascual M, Alonso S, Pares D et al (2011) Randomized clinical trial comparing inflammatory and angiogenic response after open versus laparoscopic curative resection for colonic cancer. Br J Surg 98:50–59