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CASE REPORT

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Mediastinal microdialysis: early diagnosis of anastomotic leakage after resection for esophageal cancer

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Abstract The aim of the present study was to evaluate the safety of mediastinal microdialysis and its efficacy regarding the early diagnosis of anastomotic leakage after gastroesophageal resection for esophageal cancer. Eight consecutive patients were included; one patient was excluded for reasons of catheter malfunction. The tip of the mediastinal microdialysis catheter was placed close to the anastomosis and held by a 4-0 absorbable suture. A subcutaneous microdialysis catheter placed in the pectoral region served as a reference. Samples collected every 4 h in the first 8 postoperative days were analyzed for lactate, glucose, pyruvate, and glycerol and the lactate/pyruvate ratio (L/P ratio) was calculated. There were no procedure-related complications. Six patients had an uncomplicated postoperative course. In one patient, the L/P ratio was within normal range during the first 20 h postoperatively, but a steady and significant increase in L/P ratio then occurred, reaching a maximum of 105 after 124 h. The patient developed leakage symptoms on day 3, but endoscopy was unable to demonstrate any leakage. On the sixth postoperative day, blue dye administered through the nasogastric tube was recovered in the pleural drain. The leakage was treated with a covered self-expanding metal stent; an immediate and significant drop in the L/P ratio occurred. Mediastinal microdialysis seems to be a safe and promising tool in the early diagnosis of anastomotic leakage in patients undergoing gastroesophageal resection for cancer.

Key words Microdialysis · Anastomotic leakage · Esophageal cancer · Lactate/pyruvate ratio

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Introduction

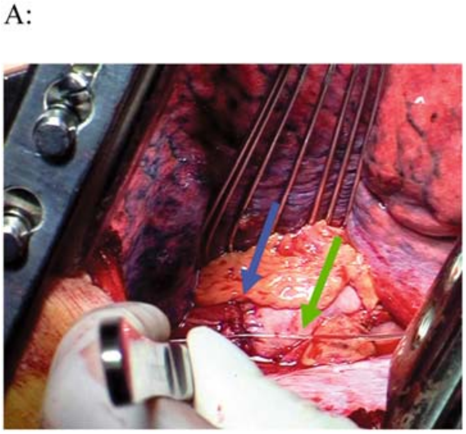
Anastomotic leakage after gastroesophageal resection for cancer is a serious complication with high morbidity and mortality. The reported incidence of anastomotic leakage is between 4% and 9%, and it is responsible for approximately 35% of postoperative deaths [1–6]. Early diagnosis and intervention are critical to improve outcome. Diagnosis is primarily based on clinical symptoms and increased inflammatory parameters in the peripheral blood. However, diagnostic specificity and accuracy are low and have a significant delay [7]. Invasive procedures such as endoscopy and fluoroscopy have a higher specificity and accuracy, but both procedures carry a potential risk.

Microdialysis is a semiinvasive method to monitor local metabolism of the gastrointestinal tract after surgery. So far, the principle has been evaluated for intraperitoneal use. In animal studies and a few human studies, intraperitoneal microdialysis has been able to detect anastomotic bowel leakage before the development of significant clinical symptoms [8–15]. The lactate/pyruvate ratio (L/P ratio) is the parameter with the highest sensitivity [15,16]. The principle of the microdialysis technique has been described in detail elsewhere [17].

The aim of the present study was to evaluate the safety of mediastinal microdialysis in patients undergoing gastroesophageal resection and to investigate if anastomotic leakage could provide significant changes in the microdialysis results.

Methods and materials

A 300-mm-long microdialysis catheter (CMA 61; CMA Microdialysis, Sweden) was placed in the right pleural cavity in patients undergoing gastroesophageal resection for cancer. The catheter was anchored to the pleura with a 4-0 absorbable suture near the anastomosis to ensure a fixed position (Fig. 1). A 20-mm-long subcutaneous microdialysis



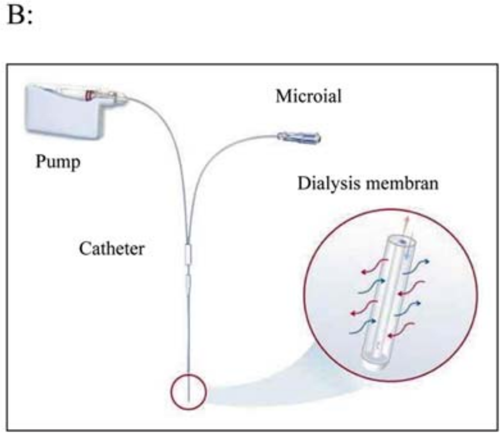


Fig. 1. **A** Mediastinal microdialysis catheter (*green arrow*) placed near the gastroesophageal anastomosis line (*blue arrow*). B Clinical instrumentation setup. Perfusion fluid is pumped from the Microdialysis Pump through the Microdialysis Catheter into the Microvial. (Courtesy of CMA Microdialysis)

catheter (CMA 60; CMA Microdialysis) was placed in the pectoral region and served as a reference.

Both catheters consisted of a 1-mm-thick, double-lumen plastic tube with a 30-mm semipermeable tubular membrane at the distal end. The membrane has a cut-off at 20 kDa. Fluid (Perfusion fluid T1; CMA Microdialysis) was infused via a portable minipump (CMA Microdialysis) through each catheter. Samples were collected every 4 h for 8 consecutive days postoperatively and stored at –20°C. Samples were analyzed within 5 days for lactate, pyruvate, glucose, and glycerol concentrations (CMA 600 Microdialysis Analyser; CMA Microdialysis), and the L/P ratio was calculated.

Eight consecutive patients who underwent surgery for esophageal or cardia cancer were included. Average age was 61 years (range, 49–71), and all patients were men. All patients were operated on using a three-step procedure, including laparoscopy and laparoscopic ultrasound, abdominal laparotomy, and right-side thoracotomy (Ivor–Lewis resection). One patient had a colonic interposition; the other patients had a standard gastric pull-up. One patient was excluded because of catheter malfunction.

The local Committee of Ethics approved the study. All patients gave informed consent before inclusion.

Results

Uncomplicated postoperative course

Six patients had an uneventful postoperative recovery. The overall results of the mediastinal as well as subcutaneous microdialysis are listed in Table 1. The difference in L/P ratio and the concentration of glycerol between mediastinal and subcutaneous microdialysis were statistically significant ($P < 0.001$), whereas the difference in glucose concentration was not significant ($P = 0.335$) (Student's t test).

Table 1. Ratio between lactate (L) and pyruvate (P) concentration and mean values (range) in glucose and glycerol concentration from mediastinal and subcutaneous microdialysis in six patients with uncomplicated postoperative course

	Mediastinum	Subcutaneous
L/P ratio	20.7 (11.1–53.8)	12.4 (8.2–23.6)
Glucose (mmol/l)	6.5 (1.9–11.8)	7.2 (1.6–12.2)
Glycerol (μmol/l)	52.1 (7.1–21.3)	231 (26–602)

Anastomotic leakage: case report

A 49-year-old man with a stage III adenocarcinoma (UICC, 5th edition) of the cardia (37–47 cm from the incisor teeth) underwent a combined gastric and esophageal resection. The right colon half was used as an interponate with an esophago-colonic anastomosis between the cecum and the distal esophagus. During the first 4 postoperative days the patient received intermittent artificial ventilation because his respiratory function was impaired. A plain X-ray of the thorax showed accumulation of fluid in the pleural cavity and segmentary pulmonary atelectasis on the right side. An endoscopy performed on the third postoperative day revealed normal findings and no sign of anastomotic dehiscence. However, the respiratory problems, pleural effusion, and fever continued. On the sixth postoperative day, blue dye administered through the nasogastric tube was recovered in the pleural drain. Leakage in the esophago-colonic anastomosis was confirmed by endoscopy and treated with a covered self-expanding metal stent, continuous aspiration, intravenous antibiotics, enteral bacterial decontamination, and parenteral nutrition. The patient recovered uneventfully and was discharged from the intensive care unit after 11 days.

Results from mediastinal microdialysis during the first 20 h in the postoperative period showed a L/P ratio within the mean value (± SEM) for the group of patients with an uncomplicated course (Fig. 2). After this period, a steady and significant increase in the L/P ratio occurred, reaching a maximum of 105 after 124 h. After stent placement, an immediate and significant drop in L/P ratio to a level of 30–35 was observed. Compared to patients with an uncomplicated course, a significant drop in mediastinal glucose concentration to values below 4.0 mmol/l was observed in the period from 20 to 84 h postoperatively (Fig. 3). No significant change in mediastinal glycerol concentration was

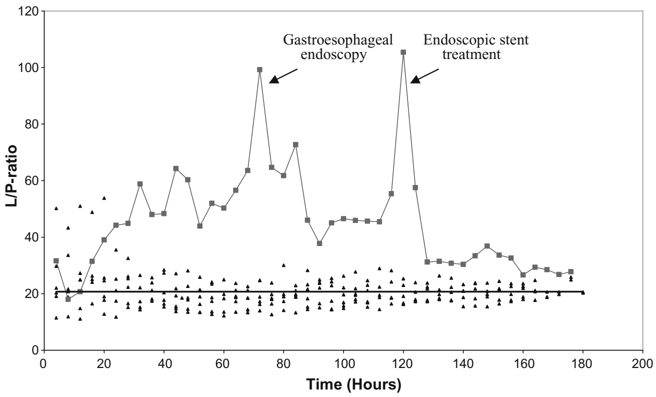


Fig. 2. The ratio of lactate and pyruvate concentration (L/P ratio) in microdialysis from mediastinum in a patient with anastomotic leakage (*squares*) compared to the values from six patients with an uncomplicated course (*triangles*)

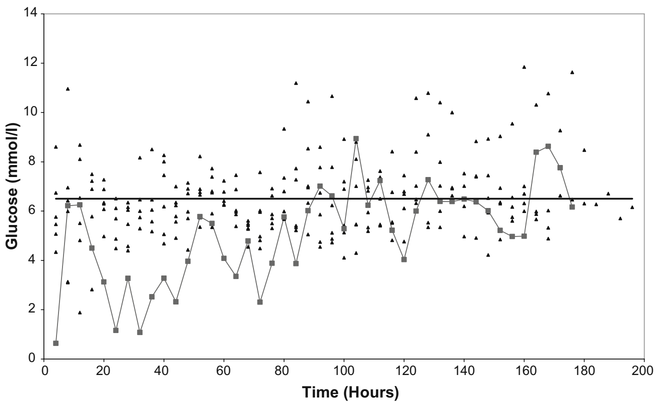


Fig. 3. Mediastinal glucose concentration in the patient with anastomotic leakage (*squares*) and values from six uncomplicated patients (*triangles*)

observed. The results from subcutaneous microdialysis showed L/P ratio and concentration of glucose and glycerol within the ranges of uncomplicated patients throughout the whole observation period. No significant changes in pH and lactate concentration in peripheral blood were observed.

There were no complications related to the microdialysis procedure or the removal of catheters in any of the patients.

Discussion

These preliminary results show, that mediastinal microdialysis is a safe procedure and a promising method to detect anastomotic leakage before the development of significant clinical symptoms.

In the present case, the L/P ratio from mediastinal microdialysis was significantly increased from 20 h postoperatively and onward until sufficient treatment of the anastomotic leakage was performed. A corresponding intermittent drop in glucose concentration was found. The highest values of L/P ratio were observed from 20 to 84 h, and at the same time a corresponding significant reduction in glucose level was observed. The same phenomenon between L/P ratio and glucose concentration was seen at the second peak of L/P ratio at 120 h. The reason for the fluctuation in L/P ratio is unknown, but fluctuation in blood supply, increased mediastinal contamination, and increased inflammation may be important factors. In addition, whether procedures such as endoscopy, stent placement, desaturation, and the use of inotropic drugs may have influenced the measurements is still unknown. However, the most interesting observation is not the fluctuation but the changes in average L/P ratio before and after stent treatment (average, 51.5 and 32.7, respectively) (Fig. 2).

The early increase in L/P ratio several days before the final diagnosis of leakage by conventional investigation was another and important finding. The increase in L/P ratio and the reduced glucose level may reflect anaerobe metabolism caused by contamination of the mediastinal cavity with microorganisms and digestive enzymes.

The drop in L/P ratio to a lower elevated level of 30–35 after stent placement indicates that an ongoing inflammation/anaerobic metabolism is still taking place in the mediastinum, but at a significantly lower level than before treatment. Although the anastomotic leakage occurred in the patient with colonic interposition, there is no reason to believe that this method itself would have had any influence on the results compared to the patients with a gastroesophageal anastomosis.

The use of inotropic drugs is common in the postoperative period after gastroesophageal resection, and this may be an important factor in the development of anastomotic leakage caused by the induction of ischemia. Studies have demonstrated that the splanchnic blood flow is reduced as much as 20% when using inotropic drugs [18,19]. Continuous mediastinal microdialysis could perhaps be used in the titration of this treatment, thereby reducing the risk of ischemia. However, further clinical studies are needed to evaluate the method of mediastinal microdialysis in this aspect, as well as regarding the aspect of early diagnosis of anastomotic leakage and the potential impact of this in a routine clinical setting.

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