Intraperitoneal microdialysis - after hemicolectomy and rectal resections as a method for early postoperative complications detection

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ABSTRACT

Background: Intraperitoneal microdialysis and measurements of the lactate/pyruvate ratio had recently been presented as a promising method in detecting intraperitoneal ischemia preceding postoperative complications.
Aim: To investigate if the magnitude of the surgical procedure influence the postoperative microdialysis response and define different patterns in several pathological conditions.
Patients and methods: During the two first postoperative days after noncomplicated surgery sixteen patients operated on due to cancer recti with anterior resection and primary anastomosis were compared to twelve patients operated due to cancer in the right colon with right sided hemicolectomy. They were investigated regarding intraperitoneal postoperative metabolic response with measurements of lacate/pyruvate ratio, glucose and glycerol,
Results: Intraperitoneal lactate/pyruvate ratio was initially about 15 in hemicolectomy patients. After rectal resections it was higher the first 31 hours of the study and started at about 18, both groups showed parallel decreasing values. Glucose levels increased 9-11 hours postoperatively in both groups to levels around 9 mmol/l and were thereafter stable during the study. Intraperitoneal glycerol levels were stable initially, around 100 μmol/l, but after 20 hours the levels in the rectal resection group had a tendency to increase. Two patients with postoperative complications and increasing lactate/pyruvate ratio and decreasing glucose presents separately.
Conclusions: Different magnitudes of the surgical procedure do not significant affect the metabolic intraperitoneal response measured by microdialysis. Different patterns and trends early in the postoperative period characterize the patient who developing a serious postoperative complication, it is of high importance to have metabolic knowledge and recognize those changes.

Key Words: Intraperitoneal microdialysis, lactate/pyruvate ratio, intraperitoneal metabolism, intraperitoneal glucose, intraperitoneal glycerol

INTRODUCTION

Intraperitoneal microdialysis (IPM) has been introduced as a promising method for prediction of surgical complications after gastrointestinal surgery [1-5]. IPM studies have been presented in both animals and humans [6-12]. An increasing intraperitoneal lactate/pyruvate ratio and decreasing glucose are signs of an increased anaerobe metabolism that may develop due to splanchnic hypoxia and ischemia. Such changes have been presented prior to appearance of postoperative complications [1, 13]. Subcutaneous and intraperitoneal locations of measurements have been compared [14] and only changes in the intraperitoneal measurements have been registered before the appearance of clinical signes[1, 13]. It is suggested that major surgical complications are preceded by splanchnic hypoxia/ischemia and the changes are possible to measure by IPM [15]. We have investigated obese and diabetic patients and did not find difference in the postoperative intraperitoneal lactate/pyruvate ratio compared to control patients[16]. A correlation between intraperitoneal lactate/pyruvate ratio measured by microdialysis and intraperitoneal TNF-α has been found suggesting on-line measurements with IPM as a possible method for detecting an increased postoperative intraperitoneal inflammatory reaction [17].

Splanchnic ischemia and proinflammatory cytokine activation have been described as early events in the stepwise development of shock and organ failure [18]. Studies in postoperative cytokine response have presented higher intraperitoneal inflammatory response suggesting the gastrointestinal tract as the major source of the postoperative inflammatory response [17, 19]. Uninhibited the inflammatory reaction might spread systemically and several cascade systems could be activated resulting in shock and organ failure [20].

The aim of this study was to investigate how the magnitude of two different surgical procedures will influence the intraperitoneal postoperative metabolic response and define different pathological patterns in the microdialysis results.

MATERIALS AND METHODS

Sixteen patients, mean age 71.9 years (range 58-80 years), which had an open rectal resection (anterior resection with primary anastomosis) due to cancer recti were compared with twelve patients, mean age 77.2 years (range 60-86 years) operated on with open right sided hemicolectomy and primary anastomosis due to colonic cancer in the right colon. Two patients (operated on with hemicolectomy and rectal resection) developed surgical complications, these two patients presents separately. Before closing the abdomen a microdialysis catheter M-dialysis 62 or 70 (M-dialysis AB, Stockholm, Sweden) was introduced intraperitoneally through a small incision in the abdominal wall with a M-dialysis needle (M-dialysis AB, Stockholm, Sweden) and placed free-floating in the intraperitoneal cavity. The catheter was fixed to the skin with a suture to minimize the risk of unintentional extraction. Samples were continuously collected every second hour from 1-45 hours postoperatively in microvials from the microdialysis catheters and immediate analysis was performed in the analyzer (M-dialysis AB, Stockholm, Sweden). The study was approved of the Ethic Committee at the University Hospital of Örebro.

Microdialysis: The microdialysis catheter is a 0.9 mm thin, double lumen concentric plastic tube with a 30 mm semi-permeable tubular membrane (cut off at 20.000 Dalton) at its distal end. A M-dialysis 62 gastrointestinal catheter with 210 mm shaft and 30 mm membrane or M-dialysis 70 with 80 mm shaft and 30 mm semi-permeable tubular membrane (M-dialysis AB, Stockholm, Sweden) were used in the peritoneal cavity. Physiologic perfusion fluid T1 (M-dialysis AB, Stockholm, Sweden) was pumped at a rate of 0.3 μl/min from a M-dialysis 106 microdialysis pump (M-dialysis AB, Stockholm, Sweden) through the outer tube of the catheter and flowed underneath the membrane, where the exchange between the intraperitoneal fluid and the perfusion fluid took place. At the tip the fluid entered the inner tube through a small hole, flowed backwards and was finally collected in a microvial. The perfusate equilibrates with molecules in the intraperitoneal fluid. In this way microdialysis monitors substances supplied from the blood (e.g. glucose) as well as substances originating from cell metabolism (e.g. pyruvate, lactate and glycerol). Glucose is converted to pyruvate in the intracellular lmetabolism of carbohydrates, if oxygen is not present (anaerobic metabolism) pyruvate is converted to lactate, but in the presence of oxygen pyruvate will be utilized as energy in the Kreb’s cycle (aerobic metabolism). The ratio between lactate and pyruvate is describing the current relationship between anaerobic and aerobic metabolism. A microvial with the microdialysis sample takes 7 minutes to be analyzed for glucose, pyruvate, lactate and glycerol. And the lactate/pyruvate ratio will be calculated in the analyzer (M-dialysis AB, Stockholm, Sweden).

Using the Wilcoxon rank sum test the statistical analysis was performed in Statistix® 8. P values<0.05 were considered significant.

RESULTS

Lactate/pyruvate ratio: Postoperative median levels were initially about 18 in patients operated with rectal resection and about 15 in patients after hemicolectomy, both groups showed parallel decreasing values to 31 hours postoperatively but the difference between groups was not significant (rectal resection 12.9 and hemicolectomy 10.9, p=0,15,) during this time. After 31 to 45 hours the difference between groups was equalized and values of the lactate/pyruvate ratio settled around 12 in both groups (fig. I).

Glucose: Values around 7 mmol/l one hour postoperatively, an increase was thereafter seen to values around 9 mmol/l after 9-11 hours postoperatively in both groups. Levels remind stable during the rest of the study (fig. II).

Glycerol: Median values were initially around 100 μmol/l. After 20 hours slightly increasing values were seen in the rectal resection group while the levels in the hemicolectomy group remained stable (the difference 29-45 hours was not significant) (fig. III).

Postoperative complication patient no 1: The patient was operated with left sided hemicolectomy due to perforated diverticulitis four days earlier (before time 0), intraperitoneal microdialysis was started at time zero. The patient was suffering of lung and kidney failure and treated by ventilator and dialysis. During the next 48 hours the patient improved clinically, better circulatory and respiratory response but during this time the lactate/pyruvate ratio increased rapidly. Suddenly after 48 hours a fast worsening of the patient´s clinical status appeared with increasing respiratory and circulatory failure. Reoperation was performed and findings were stomanecrosis, peritonitis, ceacal ischemia and ileum hypoxia. Colectomy of the remaining colon and distal-ileum resection was performed and the IPM after the operation had normalized values. Increasing levels later precede an intraperitoneal abscess (fig. IX)(picture 1).

Postoperative complication patient no 2: The patient was operated with rectal resection, primary anastomosis and loop ileostomy due to cancer recti. Intraperitoneal microdialysis was started immediate postoperatively. After 20 hours the lactate/pyruvate ratio started to increase and intraperitoneal glucose decreased but at that time the patient had a normal postoperative status, 80 hours postoperatively the patient respond with fever and lower abdominal pain, a normal CT scanning was performed and the patient was treated with imipenem due to sepsis and improved. A new CT scanning was performed after nine postoperative days and this second CT showed an anastomotic leakage (fig. X).

DISCUSSION

Increasing intraperitoneal metabolism and inflammation postoperatively are early signs in patients in risk developing surgical complications. Promising results have been presented there an increasing lactate/pyruvate ratio and decreasing glucose can be interpreted as ischemia in patients who later develop surgical complications[1, 4, 5, 13]. It has been shown that neither diabetes nor obesitas affect the postoperative intraperitoneal response.

Laparotomy and rectal resection implies a larger operative trauma than right sided hemikolectomy, which in our study is demonstrated by more excessive bleeding and a longer operation time (table I). A larger operative trauma should imply a larger metabolic demand. The lactate/pyruvate ratio has been considered as normal when below 20[27]. In this study comparing surgical procedures with different magnitude we can observe small changes in lactate/pyruvate ratio, there a larger intervention like rectal resection appear to have slightly higher levels of the lactate/pyruvate ratio the first 31 postopertive hours. Intraperitoneal glycerol showed small differences between the groups in this study, but it did show a tendency to increase in the rectal resection group after 20 hours. This may be explained by the increased intraperitoneal metabolic demand and a regional lipolysis being more pronounced in the rectal resection group. This increase of glycerol was however smaller than the increase of subcutaneous glycerol described in a previous study [14]. That study's interpretation was that the increasing postoperative metabolic demand intraperitoneally is mostly compensated of an increased lipolysis subcutaneously. Glucose levels increased initially, almost equal in both groups, as a response to the surgical trauma and remained stable and high intraperitoneally, such difference can be a result of a higher metabolic demand postoperatively, a secondary insulin resistance or intravenous glucose given but in this study no significant difference in glucose infusions the first 48 hours was noted (233 vs 196 g/L). The increase in glucose is interpreted as a probable response to increased metabolic demand intraperitoneally.

These changes presented in this study are small compared to these changes seen in patients developing postoperative complications, like patient no one and two presented in this study separately. Our experience after performance of 170 patients, monitored with postoperative intraperitoneal microdialysis is that several patterns in lactate/pyruvate ratio, glycerol and glucose can be seen and we suggest that following metabolic disturbances can be recognized in the microdialysis response:

Hypermetabolism (fig. IV), lactate is increasing while the lactate/pyruvate ratio and glucose do not show changing values. In **increasing anaerobic metabolism** (fig.V) the lactate/pyruvate ratio increase and glucose remain stable. **Hypoxia** (fig.VI) is characterized of increasing lactate/pyruvate ratio and decreasing glucose. **Ischemia** (fig. VII), produces increasing lactate/pyruvate ratio and low glucose values close to zero while **intestinal necrosis** (fig. VIII) is characterized of an initial pattern of ischemia followed by normalized values, in clinical praxis this pattern in combination with signs of peritonitis is highly suspect for intestinal gangrene and leakage.

In patients developing serious postoperative complications the increase of the lactate/pyruvate ratio usually show high values but in the interpretation of the IPM results it is more the trend of the curves, rather than the values of the analysis, which is important.

It is difficult to present the pathological intraperitoneal results in a group of patients due to the fact that complications appear at different time for each patient in the postoperative period. A better view and understanding of the intraperitoneal microdialysis result is to present the results separately for each patient. Probably are these changes seen in hypermetabolism, increased anaerobic metabolism and hypoxia reversible changes and can be normalized with a good supply of oxygen and glucose to the cell. Changes presented as ischemia and intestinal necrosis is often irreversible changes leading to intestinal gangrene and leakage. From this study and from our earlier investigations we do not declare if it is an effect of mitochondrial dysfunction or lack of substrates (glucose and oxygen) as an explaination to the changes of reversible nature described. IPM has been suggested and discussed as a monitoring device in clinical practice [21, 22] for early detection of major postoperative complications [4, 5, 23-26].Further investigations in this subject and learning however this method is useful for treatment of early metabolic disturbances postoperatively is necessarily for better avoiding postoperative complications.

CONCLUSION

Intraperitoneal microdialysis seems to be a reliable method for prediction of threatening hypoxia/ischemia, which may precede postoperative complications. It is of importance to recognize the different patterns in the microdialysis respond for early diagnosis of intraperitoneal ischemia and a threatening complication. Repeated measurements of the lactate/pyruvate ratio, glucose and glycerol by the microdialysis technique can early detect metabolic disturbances intraperitoneally which may develop to serious complications like anastomotic leakage.

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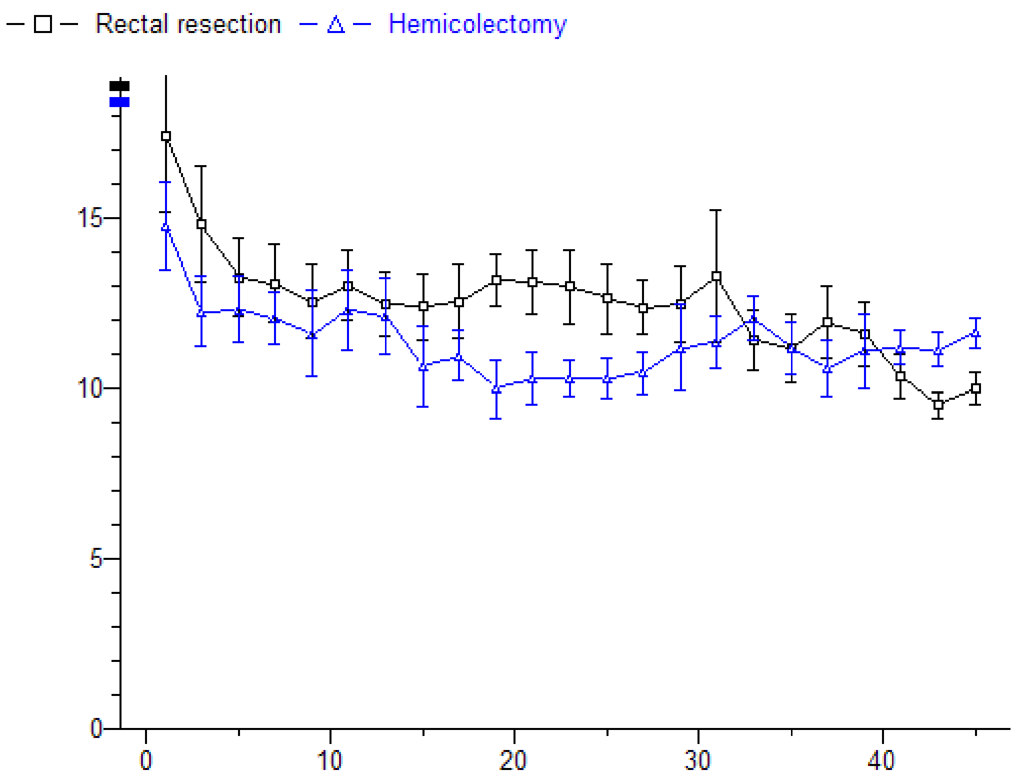

Fig. I
The intraperitoneal lactate/pyruvate ratio during the first two postoperative days after rectal resections (open squares) and right sided hemicolectomy (open triangles). Lactate/pyruvate ratio SEM (y), time (x).

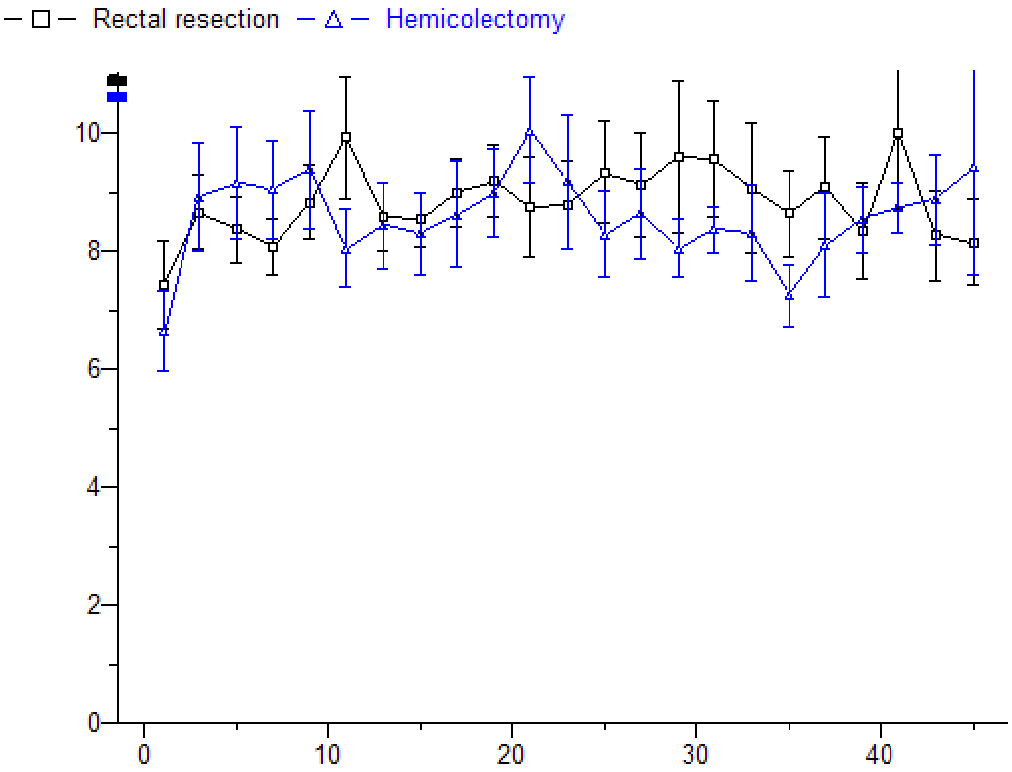

Fig. II
The intraperitoneal glucose mmol/l SEM (y) and time (x) during the first two postoperative days after rectal resections (open squares) and right sided hemicolectomy (open triangles).

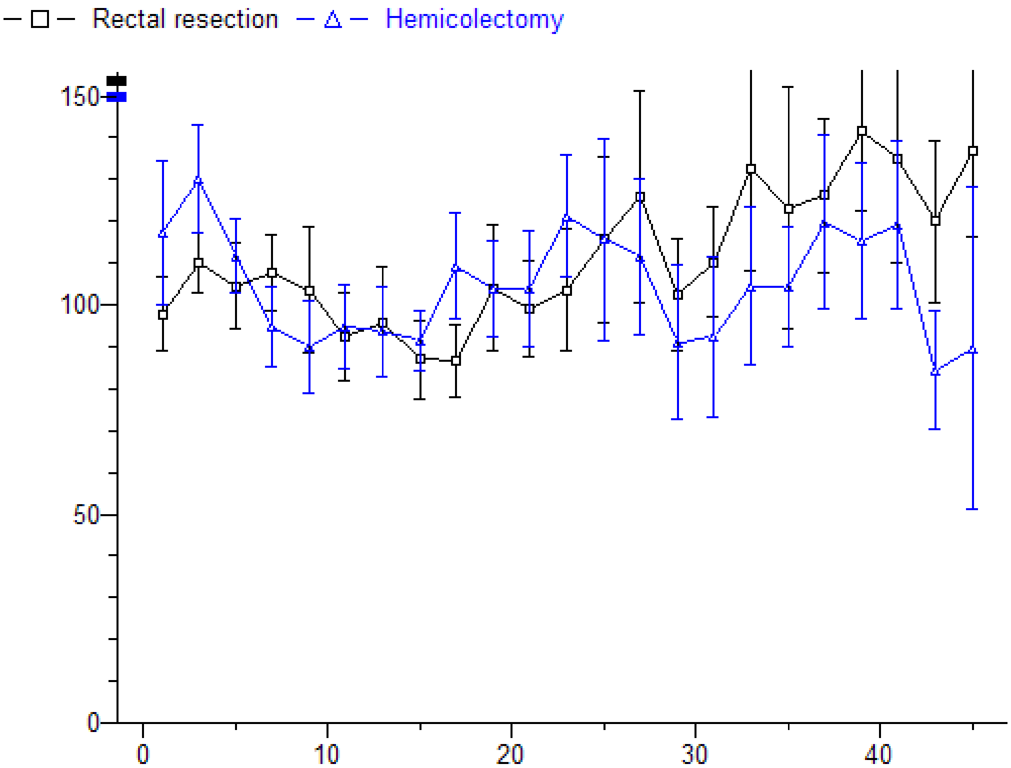

Fig. III
The intraperitoneal glycerol μmol/l SEM (y) and time (x) during the first 45 postoperative hours after rectal resections (open squares) and right sided hemicolectomy (open triangles).

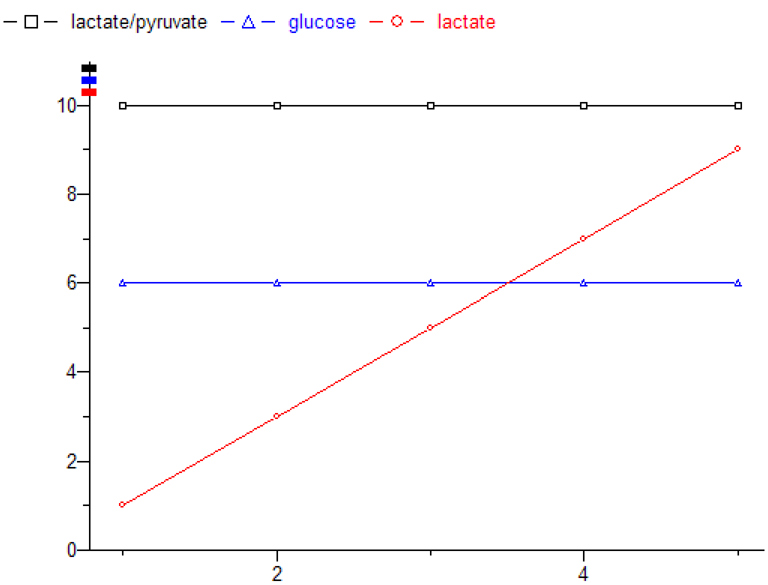

Fig. IV
Hypermetabolism. Increasing lactate while the lactate/pyruvate ratio and glucose are constant.

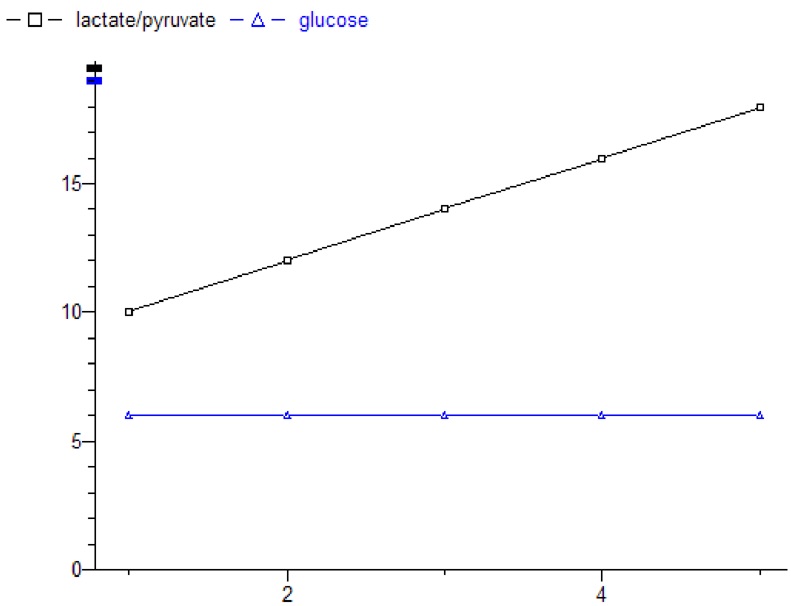

Fig. V
Anaerobic metabolism. Increasing lactate/pyruvate ratio and glucose show constant values.

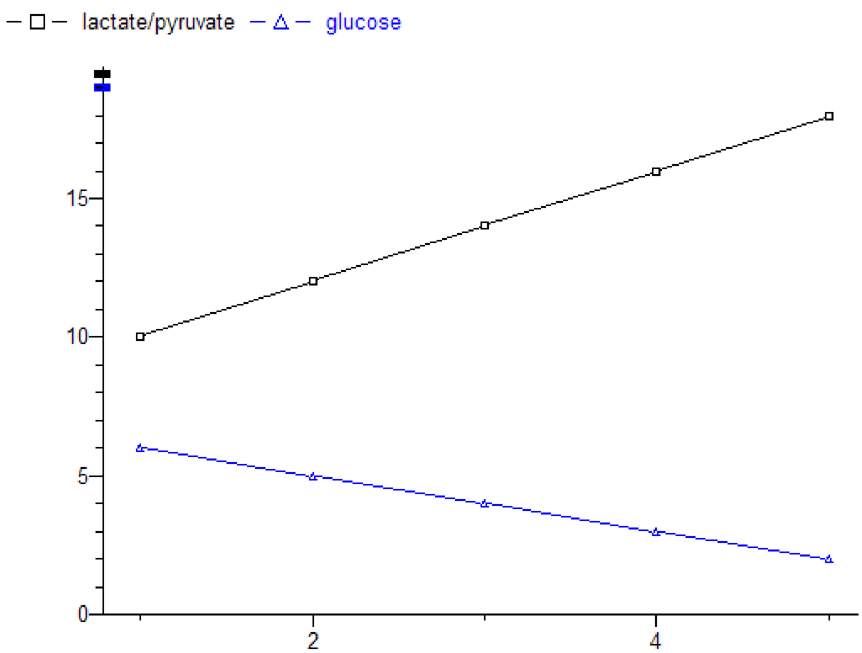

Fig. VI
Hypoxia. Increase of the lactate/pyruvate ratio and decreasing glucose.

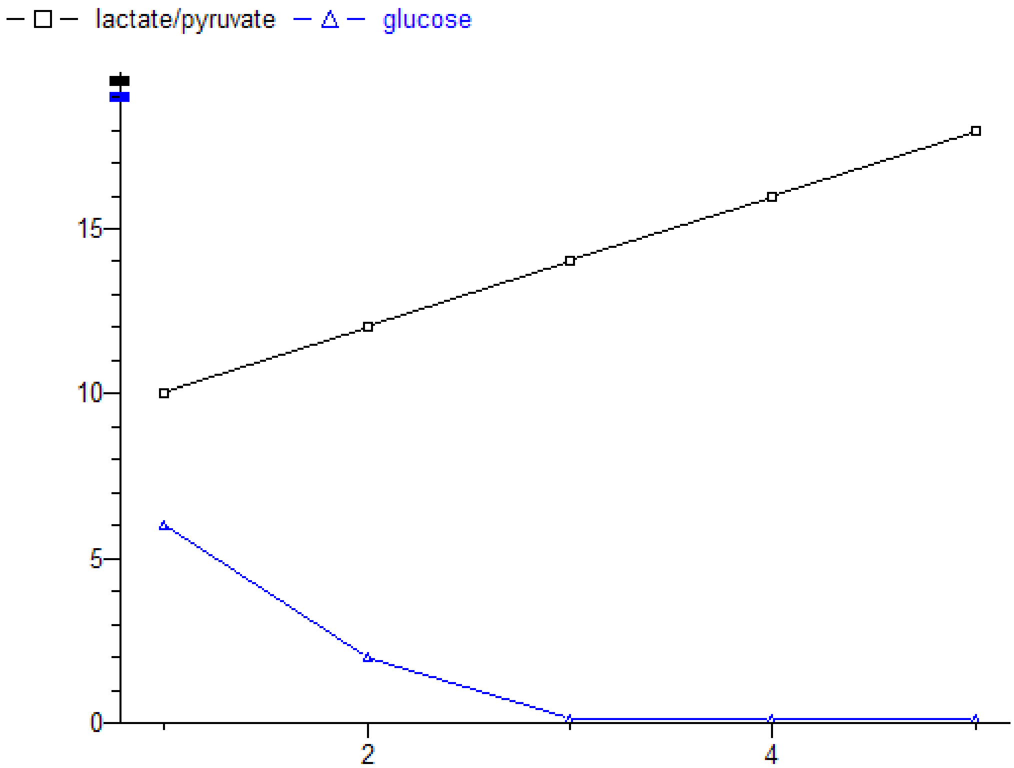

Fig.VII
Ischemia. Increasing lactate/pyruvate ratio and glucose close to zero.

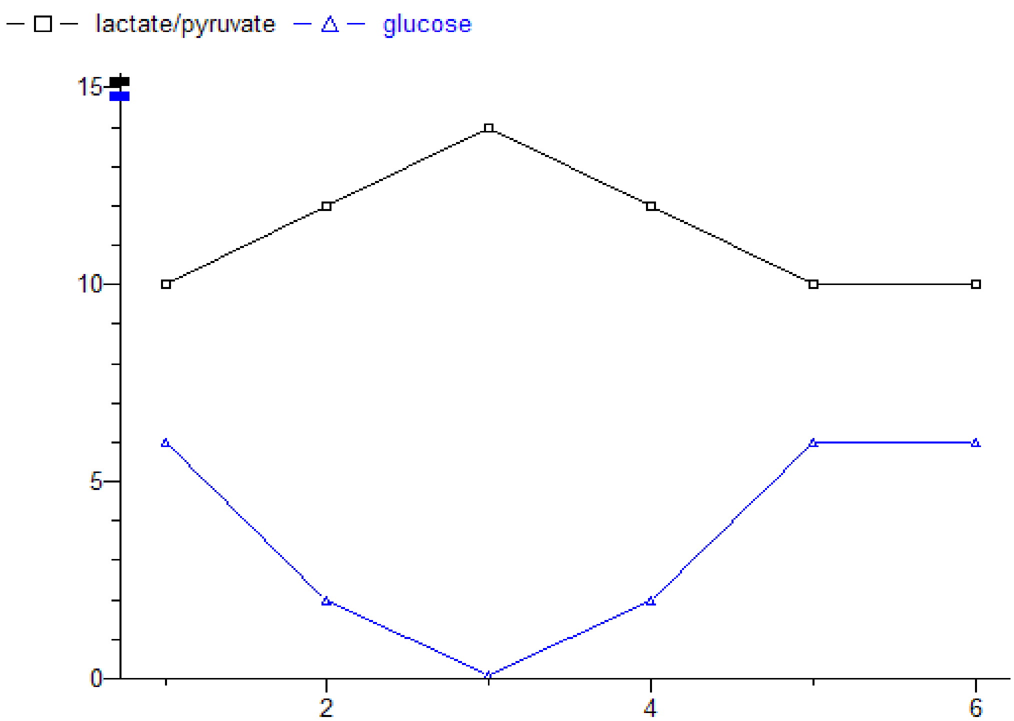

Fig. VIII
Necrosis, after ischemia, normalized lactate/pyruvate ratio and glucose while the patient develops clinical signs of peritonitis.

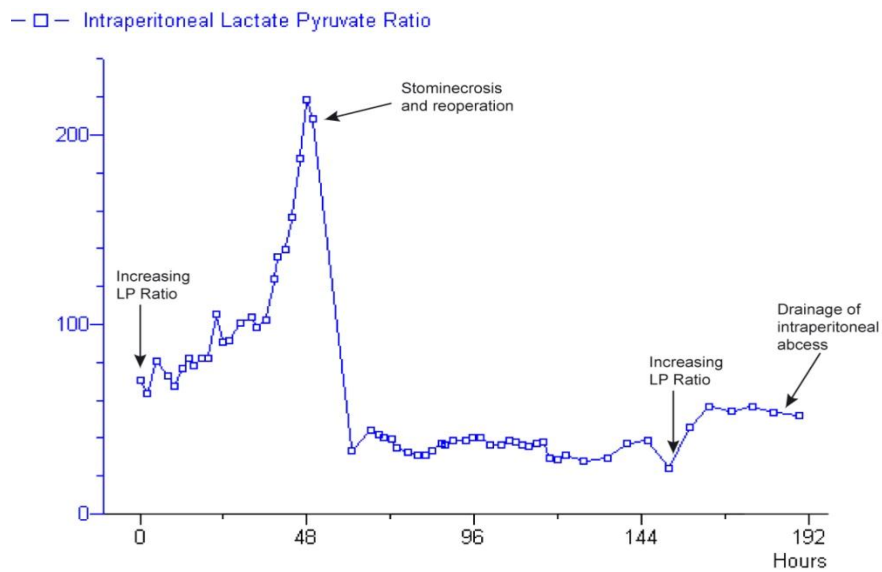

Fig. IX

Patient n:o 1, operated on with left sided hemicolectomy and transversostomy due to acute perforated diverticulitis. Postoperative developing increasing lactate/pyruvate ratio while she was clinically better. Suddenly clinical worse and the lactate/pyruvate ratio increase over 200. Reoperation and operative findings are caecal ischemia, peritonitis and stomal necrosis.

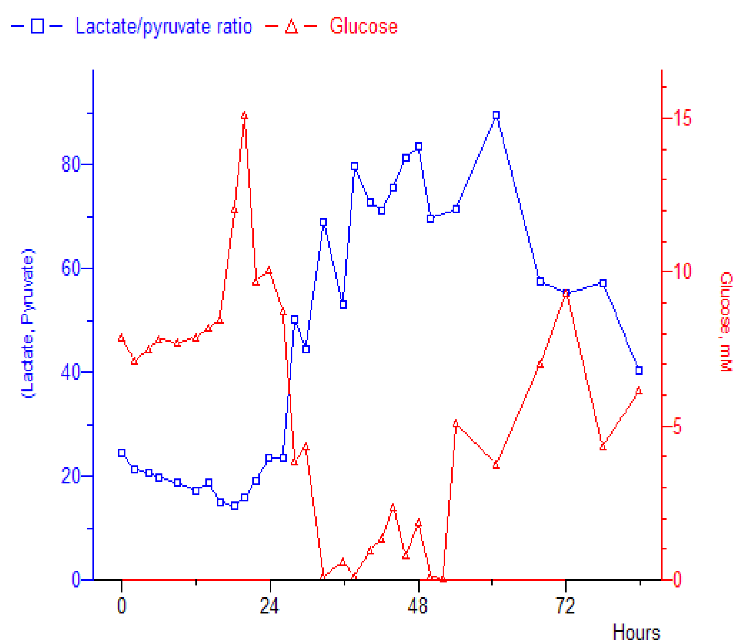

Fig. X

Patient n:o 2, operated on with rectal resection due to cancer recti. Initially clinically normal postoperative course and the lactate/pyruvate ratio increased. After 48 hours postoperatively septic symptoms with fever, lower abdominal pain and takycardia. CT scanning at that time was normal but a new CT scanning after 9 days showed an anastomotic leakage.

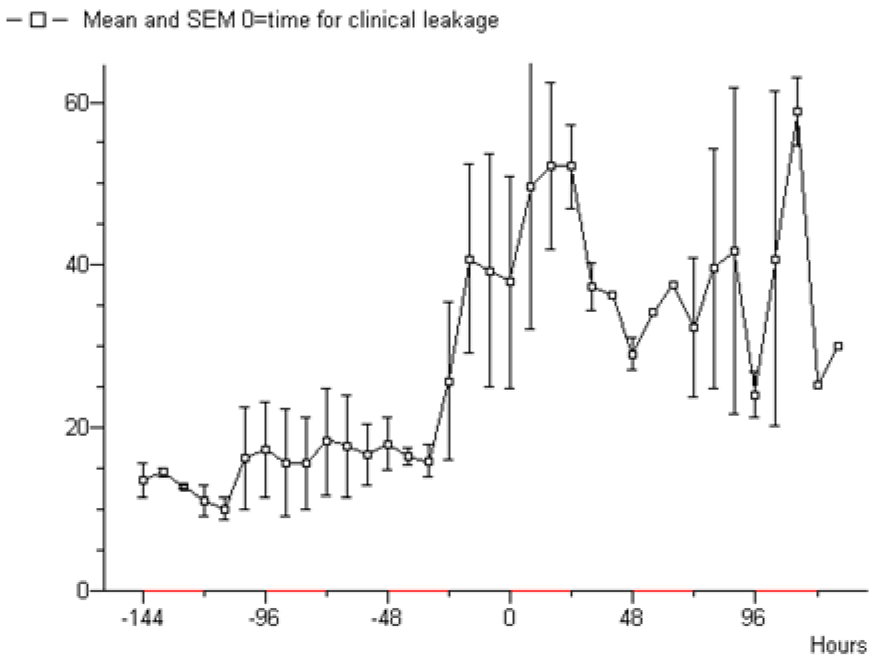

Fig. XI
4 patients with anastomotic leaks. Time 0 represent the time for clinical diagnosis.

		Hemicolectomy	Rectal resection	p-value
Age	mean	77.2	71.9	0.061
	SD	7.96	6.81	
Bleeding (ml)	mean	206	1130	<0.001
	SD	251	606	
Length of operation (min)	mean	140	261	<0.001
	SD	66.9	64.6	

Table I
Age in year, bleeding in ml, length of operation in minutes and p-values in patients after rectal resections and right sided hemicolectomy.

Picture I
Peroperative picture pat no.1. Reoperation and operative findings are caecal ischemia, peritonitis and stomal necrosis.