Surg Today (2004) 34:24–31
DOI 10.1007/s00595-003-2642-z

SURGERY TODAY

Effects of Intestinal Surgery on Pulmonary, Glomerular, and Intestinal Permeability, and its Relation to the Hemodynamics and Oxidative Stress

MARTIN MATEJOVIC[1], ALES KROUZECKY[1], RICHARD ROKYTA JR.[1], VLADISLAV TRESKA[2], VLADIMIR SPIDLEN[2], and IVAN NOVAK[1]

[1] ICU, First Medical Department, and [2] Department of Surgery, Charles University Hospital Plzen, Alej svobody 80, 304 60 Plzen, Czech Republic

Abstract

Purpose. To investigate the pattern of changes of gut mucosal, glomerular, and pulmonary permeability in response to major resectional intestinal surgery, and to evaluate whether these changes are related to oxidative stress.

Methods. Eight patients undergoing elective intestinal surgery. Lactulose/mannitol ratio (LMR), urinary albumin/creatinine ratio (MACR), and extravascular lung water and its ratio to intrathoracic blood volume (EVLW/ITBV) were measured preoperatively and at different time points postsurgery. The oxidant/antioxidant balance was assessed by measuring thiobarbituric acid-reactive species, reduced glutathione, plasma total antioxidant capacity, superoxide dismutase, and glutathione peroxidase.

Results. Uncomplicated intestinal surgery was associated with early increase in LMR and MACR. The EVLW/ITBV ratio increased, but still remained within the normal range. The amount of EVLW was not affected. While renal permeability changes resolved rapidly, increased intestinal permeability persisted longer postoperatively. There was no evidence for any marked disturbances in the oxidant/antioxidant balance.

Conclusions. This pilot study indicated that a moderate increase in gut and renal permeability, even in the absence of clinical sequelae, is an early feature of uncomplicated intestinal surgical trauma. These alterations are not accompanied by any clinically detectable changes in pulmonary permeability.

Key words Surgery · Intestinal permeability · Extravascular lung water · Gastric tonometry · Microalbuminuria

Introduction

Surgical trauma provokes both local and systemic responses that affect inflammation, metabolism, coagulation, and microcirculation. The magnitude of these responses is proportionate to the extent of injury. Particularly cardiac surgery involving cardiopulmonary bypass induces complex inflammatory changes, which may further lead to postoperative complications, and ultimately, multiple organ dysfunction. Both the rise in capillary permeability, increasing the risk of acute lung injury and the altered intestinal permeability, suggesting a dysfunction of the gut mucosal barrier, have been reported in this group of patients.[1–5] Little information, however, exists regarding the distribution and the sequence of permeability alterations in different organs in patients undergoing major intestinal surgery. In this context, the long-lasting manipulation of the gut and/or traction on the mesenteric root may provoke a substantial release of a variety of mediators with both local and systemic effects.[6,7] Furthermore, this concept is underscored by well-recognized susceptibility of the gut to derangements in O_2 and energy availability and its crucial role in producing remote organ injury.[8]

Therefore, we studied patients undergoing elective major intestinal surgery with the aim to investigate the pattern of permeability changes in three different organs that are considered to be particularly sensitive: the gut, the lung, and the kidney. Pulmonary permeability was measured using transpulmonary double indicator dilution technique, intestinal permeability was assessed by dual sugar absorption, and glomerular injury was determined by the measurement of microalbuminuria.

Reprint requests to: M. Matejovic
Presented in part at the 14th Annual Congress of the European Society of Intensive Care Medicine, Geneva, October 2001
Received: August 26, 2002 / Accepted: May 27, 2003

Gastric tonometry was used to detect gut hypoperfusion, which could be involved in the pathophysiology of a postoperative gut barrier dysfunction.[9] Moreover, as oxidative stress has been shown to increase pulmonary endothelial permeability in postcardiac surgery patients,[10] we also evaluated the pro-oxidant/antioxidant balance.

Patients and Methods

This study was approved by the local University Hospital Ethical Committee, conducted according to the principles established in the Helsinki Declaration, and written informed consent was obtained from each patient. Eight patients scheduled for elective resectional intestinal surgery under general anesthesia were prospectively studied. Table 1 summarizes the demographic and clinical data. Patients were excluded if there were a contraindication for the placement of tonometric nasogastric tube, a history of diabetes mellitus, severe hypertension, chronic nephropathy, a history of inflammatory bowel disease, and the use of nonsteroidal anti-inflammatory and immunosuppressive medication.

Study Procedures and Measurements

For hemodynamic monitoring, a 4-F fiberoptic catheter with an integrated thermistor (Pulsiocath PV 2024; Pulsion, Munich, Germany) was introduced to the descending aorta via the femoral artery on the morning of surgery. The transpulmonary double indicator dilution technique (COLD Z021; Pulsion, Munich, Germany) was used to measure the cardiac output, intrathoracic blood volume (ITBV), and extravascular lung water (EVLW).[11] Measurements were performed by injecting 12 ml of ice-cold indocyanine green at a concentration of 2 mg/ml (ICG; Pulsion) into the right atrium via the central venous catheter. All values were based on the average of three consecutive measurements. The ratio EVLW/ITBV, which relates a given value of lung water to the degree of filling volume thereby reflecting pulmonary permeability,[12] was calculated. Ratio values between 0.20 and 0.32 ± 0.16 were considered normal.[12]

Intestinal permeability (GP) was assessed in a standardized fashion by measuring the urinary recovery of lactulose and mannitol administered by oral or nasogastric routes.[13] The test solution consisted of 10 g lactulose, 5 g mannitol, and 22 g glucose diluted in 150 ml of sterile water. After administering the test solution, urine was collected for 5 h, and a 10-ml aliquot was immediately frozen and stored at −70°C until analyzed. Urinary saccharide analysis was performed using capillary gas chromatography, and urinary excretion was expressed as percentage of the ingested dose. Using

Table 1. Patient characteristics

Patient	Age (years)	Diagnosis	Type of operation	Time of surgery (min)	LN dissection	Blood loss (ml)	Crystalloids (ml)	Colloids (ml)	PRBC
1	46	Cancer	Left hemicolectomy	240	D3	400	2600	1000	2
2	77	Diverticulosis	Subtotal colectomy	180		300	2000	—	1
3	67	Cancer	Right hemicolectomy	110	D3	150	1000	—	2
4	71	Cancer	Right hemicolectomy	100	D3	100	200	1000	—
5	43	Cancer	Sigmoideoproctectomy	280	D3	400	2500	500	1
6	54	Cancer	Sigmoidectomy	110	D3	100	1500	—	—
7	42	Polyposis	Proctectomy, pouch	300		750	3600	1500	4
8	57	Cancer	Proctectomy	150	D3	250	1000	—	—
Mean (±SD)	51 (15)			184 (80)		306 (216)	1800 (1100)	1000 (400)	2 (4)

PRBC, units of packed red blood cells; *LN dissection*, degree of lymph node dissection; *D3*, para-aortic lymph node dissection

these results, the lactulose-mannitol ratio (LMR) was calculated to provide a specific index of GP. An increased GP was defined by LMR > 0.03.[13]

Glomerular capillary permeability was determined by measuring microalbuminuria.[14] Urine albumin was detected by immunonephelometry, and the results were expressed as the albumin/urinary creatinine ratio (MACR) to correct for any possible errors arising from changes in the urine volume. The reference value range for MACR is <2.8 mg/mmol.

A gastric tonometry tube (TRIP Catheter; Tonometrics, Worcester, MA, USA) was inserted after the induction of anesthesia, and its position was confirmed by direct palpation after opening of the abdomen. Gastric mucosal PCO_2 ($P_{gm}CO_2$) was measured semicontinuously (time equilibration 10 min) by automated air tonometry (Tonocap; Datex-Ohmeda Instrumentarium, Helsinki, Finland), and $P_{gm}CO_2$ — arterial CO_2 gradient (ΔPCO_2) was calculated. ΔPCO_2 represents a marker of intestinal tissue perfusion, oxygenation and/or cellular energy balance.[15]

Systemic O_2 consumption (VO_2) and CO_2 production (VCO_2) was measured by open-circuit indirect calorimetry (Deltatrac; Datex, Helsinki, Finland) to monitor an acute metabolic response to surgical trauma. Arterial blood gases were measured using a blood gas analyzer (ABL 520; Radiometer, Copenhagen, Denmark), and arterial lactate was measured enzymatically (Hitachi 717; Boehringer-Mannheim, Mannheim, Germany). As a surrogate for systemic inflammatory response, leukocyte count (hemocytometry Coulter Counter; Coulter Electronics, Luton, UK) and C-reactive protein (CRP; nephelometry using Latex CRP, Mono Behring, Vienna, Austria) were measured. The serum CRP/albumin ratio was calculated as a capillary leakage index.[16]

To determine the pro-oxidant/antioxidant balance, arterial blood samples were taken, the serum separated, and stored at at $-70°C$ until assayed. The free radical activity was measured by an assay for thiobarbituric acid-reactive species (TBARS),[17] and by determining the reduced glutathione (GSH) level in erythrocytes (Bioxytech GSH-400; Oxis, Portland, OR, USA). The reference ranges in our laboratory for healthy subjects were 1.75–3.0 μmol/l and 1.90–2.40 mmol/l Ery for TBARS and GSH, respectively. The plasma total antioxidant capacity (AOC) was measured using an ultraviolet spectrophotometric technique (Randox; Randox Laboratories, Crumlin, UK).[18] The reference range for healthy subjects was 1.30–1.77 mmol/l. In erythrocytes measured activity of superoxide dismutase (SOD; Ransod, Randox Laboratories) as described by Werthsond and Gould,[19] as well as glutathione peroxidase (GSH-Px; Ransel, Randox Laboratories) as described by Paglia and Valentine,[20] were used to analyze the enzymatic defenses against free radicals. The reference ranges in our laboratory for healthy subjects are 1092–1817 U/g Hb and 42–65 U/g Hb for SOD and GSH-Px, respectively.

Protocol

All patients were admitted to the intensive care unit (ICU) on the day before the surgery. On this day, a preoperative GP test and indirect calorimetry were performed. The first set of all remaining variables (transpulmonary dilution, gastric tonometry, MACR, the serum level of albumin, CRP, the leukocyte count, and oxidative stress) was completed on the day of the operation, but before surgery (T0). After the operation, the patients continued to be mechanically ventilated and were transferred to the ICU. Immediately upon arrival, the postsurgery data (T1) were collected, except for the GP test, indirect calorimetry, CRP, and serum albumin. Once the second set of data was taken, the lactulose/mannitol solution was given via a nasogastric probe. After another 5 h the third set of measurements was performed (T2), except for oxidative stress, CRP, and serum albumin. Thereafter, the patients were extubated. The last set of measurements (except for indirect calorimetry) was done on the first postoperative day (approximately 20 h after abdominal surgery) (T3).

Statistical Analysis

All values shown are median and interquartile range, unless otherwise stated. After exclusion of the normal distribution the differences between the periods were analyzed by the Friedman rank sign analysis of variance and a subsequent Dunn's test for multiple comparisons. Correlations between variables were calculated using a linear regression analysis. Statistical significance was considered at $P < 0.05$.

Results

All patients underwent uncomplicated operations as well as a smooth postoperative recovery.

Hemodynamics and Gastric Tonometry

Table 2 summarizes the hemodynamic data. All patients remained stable over the whole study and none required vasoactive therapy. Although there was a trend toward a lower ITBV, mainly by the end of operation, the central venous pressure (CVP) increased significantly compared to baseline value [$P = 0.012$; repeated-measures analysis of variance (RM ANOVA)]. The cardiac output decreased only transiently at T1, but this change did not reach statistical significance. No changes

Table 2. Hemodynamic response to surgery

	T0	T1	T2	T3
MAP (mmHg)	104 (91; 109)	96 (82; 104)	87 (75; 97)	99 (93; 105)
CVP (mmHg)	5 (5; 8)	11 (8; 12)*	8 (7; 11)*	8 (7; 10)*
ITBVI ($ml\,m^{-2}$)	876 (777; 986)	695 (602; 906)	755 (726; 913)	775 (728; 868)
CI ($l\,min^{-1}m^{-2}$)	3.3 (3.1; 3.6)	2.6 (2.1; 2.9)	3.3 (2.6; 3.7)	3.4 (3.1; 4.1)
HR (beats min^{-1})	70 (60; 84)	63 (60; 77)	69 (65; 70)	77 (73; 93)
EVLWI ($ml\,kg^{-1}$)	4.0 (2.9; 4.7)	4.0 (3.1; 5.9)	4.7 (3.6; 5.4)	3.6 (3.3; 4.7)
EVLW/ITBV	0.19 (0.16; 0.21)	0.25 (0.19; 0.30)*	0.25 (0.22; 0.26)*	0.20 (0.17; 0.22)
PaO_2/FiO_2	355 (331; 407)	360 (290; 441)	382 (365; 456)	344 (312; 427)
ΔPCO_2 (kPa)	0.7 (0.3; 0.9)	0.8 (0.4; 1.3)	1.0 (0.6; 1.3)	1.0 (0.8; 1.3)

MAP, mean arterial pressure; *CVP*, central venous pressure; *ITBVI*, intrathoracic blood volume; *CI*, cardiac index; *HR*, heart rate; *EVLWI*, extravascular lung water; ΔPCO_2, gastric mucosal — arterial PCO_2 gradient
* $P < 0.05$ *vs* T0

in ΔPCO_2 occurred throughout the study and the values were in a physiological range.

Pulmonary Permeability

EVLW/ITBV ratio increased significantly at T1 and T2 ($P = 0.009$; RM ANOVA), but still remained within the normal range (Table 2). The amount of extravascular lung water was not affected by surgical trauma. Similarly, the PaO_2/FiO_2 ratio did not demonstrate any changes (Table 2).

Intestinal Permeability

The median LMR exceeded the normal value range for GP (<0.03) both at T2 (0.037, range 0.025–0.072) and T3 (0.072, range 0.045–0.120). These changes reached statistical significance ($P < 0.001$; RM ANOVA). The individual changes in GP are shown in Fig. 1.

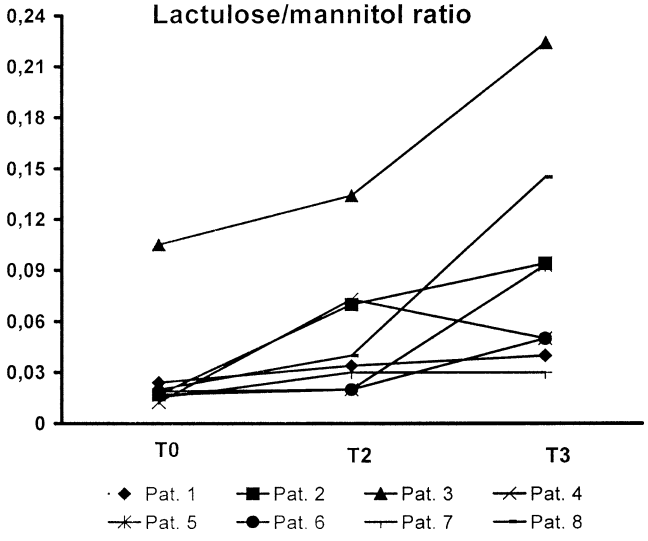

Fig. 1. Individual changes of intestinal permeability in response to surgery. *T0*, before surgery; *T2*, 5 h postsurgery; *T3*, 20 h postsurgery; *Pat.*, patient

Glomerular Permeability

Surgical trauma induced a marked and significant ($P < 0.001$; RM ANOVA), but transient increase in MACR (Fig. 2). The peak values were reached at the end of surgery (T1), while MACR returned to the preoperative values 20 h after surgery (T3). The time course of MACR (median and range) at the respective time points were: T0, 2.2 (1.7–2.7); T1, 9.0 (7.0–29.0); T2, 4.0 (3.4–13.0); T3, 1.3 (1.2–1.8) mg/mmol. No correlations developed between markers of permeability in the gut, kidney, and lung.

Inflammation and Metabolism

Inflammatory and metabolic changes in response to surgery are shown in Table 3. A substantial increase in leukocyte count was already observed by the end of the operation and remained elevated throught the whole course of the study. The median concentration of CRP largely increased from 3.5 g/l at T0 to 97 g/l at T3. An increased immunoinflammatory activity was associated with moderate hypermetabolism as documented by a rising body temperature and a tendency of systemic oxygen consumption (VO_2) to increase. The elevation of median VO_2 from 239 ml/min at T0 to 262 ml/min at T2 was, however, not statistically significant. The CO_2 production (VCO_2) remained stable. Despite stable hemodynamics, the base excess declined postoperatively, reaching a maximum by the end of surgery, whereas the arterial lactate level increased significantly only at T2. The serum level of albumin significantly fell on the first postoperative day in comparison to the baseline. Both the increase in CRP and drop in the serum albumin level caused the CRP/albumin ratio (a surrogate for systemic capillary leak) to significantly increase.

Oxidative Stress

Antioxidant capacity progressively decreased at T1 and T3 compared with the baseline (Table 4). However, there were no concomitant changes in the plasma levels of TBARS and GSH. Similarly, regarding the antioxidant enzymes, no decline in SOD and GSH-Px occurred.

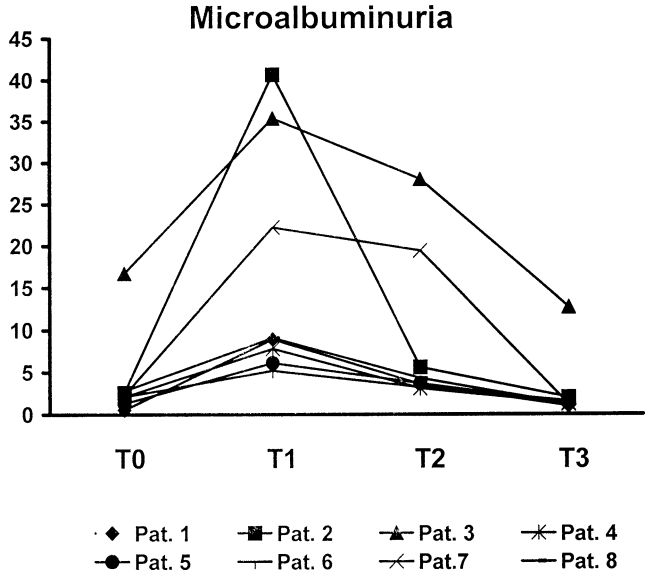

Fig. 2. Individual changes of glomerular permeability in response to surgery. *T0*, before surgery; *T1*, immediately after surgery; *T2*, 5 h postsurgery; *T3*, 20 h postsurgery; *Pat.*, patient

Discussion

This study was designed to evaluate the effects of major resectional intestinal surgery on the permeability changes in three different organ systems, and to analyze the degree and sequence of their alterations. Furthermore, the role of systemic and regional hemodynamic changes and possible implication of alterations in oxidant/antioxidant balance to the pathophysiology of surgical trauma were investigated. We found that (1) intestinal surgery induced a moderate systemic inflammatory and hypermetabolic response; (2) this response was associated with an early increase in intestinal and glomerular permeability, whereas no significant alterations in pulmonary permeability were detected; (3) while renal permeability injury resolved rapidly, the increased intestinal permeability persisted still at least 20 h after the surgery; (4) stable hemodynamics and no evidence for marked disturbances in oxidant/antioxidant balance preclude their significant contribution to the observed permeability changes; and (5) since all patients had an uneventful recovery, it is likely that the magnitude of these alterations represents a physiologi-

Table 3. Inflammatory and metabolic response to surgery

	T0	T1	T2	T3
Leukocyte ($\times 10^9$ l^{-1})	5.1 (4.4; 6.2)	11.0 (8.7; 12.1)*	11.6 (7.1; 14.0)*	11.0 (8.6; 11.2)*
CRP (mg l^{-1})	4 (1; 7)	—	—	97 (59; 114)*
Core temperature (°C)	36.7 (36.5; 37.1)	35.7 (35.1; 36.3)*	37.7 (36.9; 38.4)*	37.2 (37.0; 37.3)*
VO_2 (ml min^{-1})	239 (203; 271)	—	262 (240; 319)	—
VCO_2 (ml min^{-1})	178 (150; 204)	—	163 (136; 206)	—
Base excess (mmol l^{-1})	0.5 (−0.3; 1.5)	−3.3 (−4.2; −2.1)*	−2.6 (−3.5; −2.1)*	−1.4 (−2.0; −0.1)*
Lactate (mmol l^{-1})	1.0 (0.8; 1.5)	1.0 (0.8; 2.5)	2.2 (1.3; 3.1)*	1.5 (1.1; 1.9)
Hb (g l^{-1})	122 (107; 128)	120 (108; 125)	109 (106; 121)	111 (103; 114)
Albumin (g l^{-1})	40 (37; 43)	—	—	29 (27; 31)*
CRP/Albumin	0.09 (0.03; 0.17)	—	—	3.0 (1.4; 4.0)*

CRP, C-reactive protein; *VO_2*, systemic oxygen consumption; *VCO_2*, systemic carbon dioxide production; *Hb*, hemoglobin
* $P < 0.05$ *vs* T0

Table 4. Oxidant/antioxidant balance in response to surgery

	T0	T1	T3
AOC	1.36 (1.21; 1.47)	1.17 (1.13; 1.27)*	1.13 (1.11; 1.23)*
TBARS	2.91 (2.5; 3.5)	2.59 (2.23; 3.68)	2.42 (2.32; 2.84)
GSH	1.89 (1.58; 2.31)	1.95 (1.66; 2.11)	1.84 (1.52; 2.11)
SOD	1374 (1128; 1476)	1311 (1148; 1427)	1238 (1167; 1400)
GSH-Px	63 (53; 79)	58 (57; 70)	61 (57; 77)

AOC, plasma total antioxidant capacity; *TBARS*, thiobarbituric acid-reactive species; *GSH*, reduced glutathione; *SOD*, superoxide dismutase; *GSH-Px*, glutathione peroxidase
* $P < 0.05$ *vs* T0

cal response to surgical trauma without any serious clinical implications.

There were two main reasons why we chose elective intestinal surgery for this physiological study. First, patients undergoing radical resectional intestinal surgery may be at risk for systemic inflammatory response (SIRS), sepsis, and organ dysfunction. Second, the majority of clinical studies demonstrating increased pulmonary and intestinal permeability were performed in surgery involving cardiopulmonary bypass or in patients undergoing major vascular surgery.[2–4,10,21,22] Extracorporal circulation-induced systemic inflammation and ischemia-reperfusion injury are principal mechanisms of impaired endothelial permeability in these types of surgery.[5] In contrast, little is known about the distribution, sequence, and the magnitude of permeability alterations in different organs in patients undergoing major intestinal surgery. Finally, the manipulation and retraction of the bowel and intestine may alter the barrier function, thus leading to bacterial or endotoxin translocation into the systemic circulation, and thereby initiating SIRS and permeability changes in distant organs.[7,23,24] In a recent experimental study in rats, any abdominal surgery associated with the mechanical manipulation of the gut resulted in alterations in the intestinal integrity, reaching a maximum as early as 1 h postsurgery.[24] Moreover, perioperative endotoxemia and bacterial translocation have been documented during major vascular and cardiac operations and an elective pancreatoduodenectomy.[7,21,25] Furthermore, since the gut is highly sensitive to a low blood flow and is among the first to be subject to early tissue injury, it is plausible that peri- and postoperative inadequate tissue perfusion and oxygenation of the gut may precipitate and/or exacerbate the above-mentioned consequences.[9]

The present study, for the first time to our knowledge, simultaneously quantified the changes of both the gut mucosal, glomerular, and pulmonary barrier in response to resectional intestinal surgery. The lactulose-mannitol assay has been previously used in the trauma and surgery setting, where an increase in the LMR indicated loss of the gut barrier function.[21,26] In contrast to these previous studies, where GP tests were performed only from the first postoperative day, we assessed LMR within 5 h after the end of surgery. In four of six patients, in whom the GP test could be achieved at this postoperative phase, LMR significantly increased above the normal value range (>0.03), thus suggesting that an alteration in gut permeability may occur very early after clinical surgical insult. At 20 h after the operation we recorded an approximately 2–3-fold increase in LMR as compared to the 4–10-fold increases in LMR observed in patients having major resectional surgery for upper gastrointestinal tract and major vascular surgery, respectively.[21,27] The different magnitude of surgical trauma could account for the lower degree of LMR changes in our patients. Regarding the methodology, one could argue that the interpretation of the results of sugar absorption may be confounded by several factors other than gut barrier failure. However, by expressing the results as a ratio of urinary recovery of the two saccharides, it is possible to factor out confounding effects related to alterations in gastric emptying, small intestinal peristalsis, or changes in renal clearance.[28]

Simultaneously with GP measurements, gastric tonometry was used to assess changes in gut mucosal O_2 availability. Although systemic markers of tissue perfusion, base deficit, and arterial lactate transiently increased after the operation, ΔPCO_2 remained within the normal range. This supports the results of previous studies,[3,22] thus suggesting that increased intestinal permeability is not attributable to gut hypoperfusion in uncomplicated surgery. On the other hand, one cannot rule out the possibility that gastric tonometry failed to detect microcirculatory changes in other parts of the intestinal tract.

The rapid increase in MACR, observed already by the end of operation, indicated that surgical stress was associated with early renal permeability injury. The transient time course of the variations in MACR with the normalization within 24 h postsurgery correlated with those described in previous studies.[29,30] Although there was a relatively wide interindividual variability in the degree of MACR among our patients, the median MACR was lower than that seen in patients undergoing aortic aneurysma surgery. This is in line with observations that the magnitude of MACR is proportionate to the severity of the surgical insult.[21,30,31] Moreover, a considerable body of evidence in humans indicates that a low-level urinary albumin excretion is associated with a generalized endothelial vascular dysfunction.[14,32] In other words, it is possible that changes in renal permeability during surgery may simply reflect the glomerular component of the systemic capillary leak.[30] This assumption is further supported by the markedly increased CRP/albumin ratio observed in our study, which was recently demonstrated to be a novel index of capillary leakage.[16]

Another major organ system that could be a target of the acute phase response induced by surgical trauma is the lung. Sinclair et al. previously demonstrated a transient increase in both the pulmonary and gut permeability after surgery requiring cardiopulmonary bypass.[4] Likewise, in a recent study by Hachenberg et al., EVLW increased transiently by 52% after cardiopulmonary bypass surgery.[2] These results are in contrast with those observed in our study. Although the EVLW/ITBV ratio significantly increased in our patients, the median EVLW remained normal throughout, thus suggesting that changes in the EVLW/ITBV ratio were not clini-

cally significant. A marked increase in EVLW was only recorded in one patient (from 4.9 ml/kg preoperatively to 8.1 ml/kg postoperatively). This patient exhibited signs of subclinical sepsis as judged by an increased MACR, CRP, leukocytes, and GP just before the operation. Hence, it is tempting to speculate that not only the extent and duration of surgery, but also the degree of preoperative systemic inflammation may determine the magnitude of surgical trauma-induced permeability changes. This may have important clinical implications in septic patients subjected to surgical insult.

The link between oxidative stress and an increased pulmonary permeability has been established in cardiac surgery patients.[10] In the current study this relationship was not apparent, and no significant imbalance between oxidants and antioxidants was observed. This may be a reflection of the moderate extent of surgical stress in this population, in that all of these patients studied made an uncomplicated recovery.

The major limitation of our study is the low number of patients, which limits the inferences that could be drawn, but nonetheless there was a significant increase in the recorded permeability changes and these results were produced in a prospective manner. One could also argue that a longer time period would be interesting to observe the time course of permeability changes. We stopped our measurements within 24 h postoperatively from a clinical point of view, in order to minimize the prolonged use of the femoral artery catheter in patients.

In conclusion, increased gut and renal permeability, even in the absence of demonstrable clinical sequelae, is an early feature of the acute complex inflammatory response in elective resectional intestinal surgery. This response occurs very early in the kidney, and then disappears rapidly provided that the recovery is uncomplicated, while the gut permeability changes persist longer after the surgical insult. No clinically detectable alterations in pulmonary permeability were observed. Furthermore, our data do not support any link between increased permeability and the presence of oxidative stress in this type of surgical stress. The important implication for clinicians is the reaffirmation that major intestinal surgery may be accompanied by widespread microvascular and barrier changes, although they do not reach the magnitude induced by cardiac or major vascular surgery. The careful optimization of a patient's hemodynamic status pre- and postoperatively is therefore essential, since factors such as hypovolemia, even if occult, could be expected to amplify these changes.

Acknowledgments. Supported by a research grant, IGA MZ CR 5649-3. We thank L. Trefil and P. Stehlik for their skillful technical assistance.

References

1. Butler J, Rocker GM, Westaby S. Inflammatory response to cardiopulmonary bypass. Ann Thorac Surg 1993;55:552–9.
2. Hachenberg T, Tenling A, Rothen HU, Nystrom SO, Tyden H, Hedenstierna G. Thoracic intravascular and extravascular fluid volumes in cardiac surgical patients. Anesthesiology 1993;79:876–904.
3. Riddington DW, Venkatesh B, Boivin CM, Bonser RS, Elliot TS, Marshall T, et al. Intestinal permeability, gastric intramucosal pH, and systemic endotoxemia in patients undergoing cardiopulmonary bypass. JAMA 1996;275:1007–12.
4. Sinclair DG, Haslam PL, Quinlan GL, Pepper JR, Evans TW. The effects of cardiopulmonary bypass on intestinal and pulmonary endothelial permeability. Chest 1995;108:718–24.
5. Wan S, LeClerc JL, Vincent JL. Cytokine responses during clinical cardiopulmonary bypass. In: Vincent JL, editor. Yearbook of intensive care and emergency medicine. Berlin: Springer; 2000. p. 868–74.
6. Brinkmann A, wolf CF, Berger D, Kneitinger E, Neumeister B, Buchler M, et al. Perioperative endotoxemia and bacterial translocation during major abdominal surgery. Evidence for the protective effect of endogenous prostacyclin? Crit Care Med 1996;24:1293–301.
7. Lau LL, Halliday MI, Lee B, Hannon RJ, Gardiner KR, Soong CV. Intestinal manipulation during elective aortic aneurysm surgery leads to portal endotoxemia and mucosal barrier dysfunction. Eur J Vasc Endovasc Surg 2000;19:619–24.
8. Pastores SC, Katz DP, Kvetan V. Splanchnic ischemia and gut mucosal dysfunction in sepsis and multiple organ dysfunction syndrome. Am J Gastroenterol 1996;91:1691–710.
9. Mythen M, Webb AR. The role or gut mucosal hypoperfusion in the pathogenesis of post-operative organ dysfunction. Intensive Care Med 1994;20:203–9.
10. Messent M, Sinclair DG, Quinlan GJ, Mumby SE, Gutteridge JM, Evans TW. Pulmonary vascular permeability after cardiopulmonary bypass and its relationship to oxidative stress. Crit Care Med 1997;25:425–9.
11. Hoeft A. Transpulmonary indicator dilution: an alternative approach for hemodynamic monitoring. In: Vincent JL, editor. Yearbook of intensive care and emergency medicine. Berlin: Springer; 1995. p. 593–605.
12. Honore PM, Jacquet LM, Beale RJ, Renauld JC, Valadi D, Noirhomme P, et al. Effects of normothermia versus hypothermia on extravascular lung water and serum cytokines during cardiopulmonary bypass: a randomized, controlled trial. Crit Care Med 2001;29:1903–9.
13. Wyatt J, Vogelsang H, Huebl W, Waldhoeer T, Lochs H. Intestinal permeability and the prediction of elapse in Crohn's disease. Lancet 1993;341:1437–9.
14. Gosling P. Microalbuminuria: a marker of systemic disease. Br J Hosp Med 1995;54:285–9.
15. Brinkmann A, Calzia E, Träger K, Radermacher P. Monitoring the hepato-splanchnic region in the critically ill patient. Measurement techniques and clinical relevance. Intensive Care Med 1998;24:542–56.
16. Malbrain ML, Debaveye Y, De Coninck J, Delmarcelle D. Capillary leakage index as outcome predictor? Intensive Care Med 2001;27(suppl 2):S229.
17. Moore K, Roberts LJ. Measurement of lipid peroxidation. Free Radic Res 1998;28:659–71.
18. Miller NJ, Rice-Evans C, Davies MJ, Gopinathan V, Milner A. A novel method for measuring antioxidant capacity and its application to monitoring antioxidant status in premature neonates. Clin Sci 1993;84:407–12.
19. Werthsond ED, Gould MN. Relationship between cellular superoxide dismutase and susceptibility to chemically induced cancer in rat mammary gland. Carcinogenesis 1986;7:1197–201.

20. Paglia DE, Valentine WN. Studies on the quantitative and qualitative characterization of erythrocyte glutathione peroxidase. J Lab Clin Med 1967;70:158–69.
21. Roumen RM, van der Vliet JA, Wevers RA, Goris RJ. Intestinal permeability is increased after major vascular surgery. J Vasc Surg 1993;17:734–7.
22. Sinclair DG, Houldsworth PE, Keogh B, Pepper J, Evans TW. Intestinal permeability following cardiopulmonary bypass: a randomized study comparing the effects of dopamine and dopexamine. Intensive Care Med 1997;23:510–6.
23. Schemmer P, Enomoto N, Bradford BU, Bunzendahl H, Raleigh JA, Thurman RG. Autonomic nervous system and gut-derived endotoxin: involvement in activation of Kupffer cells after in situ organ manipulation. World J Surg 2001;25:399–406.
24. Simmy T, Anup R, Prabhu R, Balasubramanian KA. Effect of surgical manipulation of the rat intestine on enterocyte populations. Surgery 2001;130:479–88.
25. Naito Y, Tamai S, Shingu K, Shindo K, Matsui T, Segawa H, et al. Responses of plasma adrenocorticotropic hormone, cortisol, and cytokines during and after upper abdominal surgery. Anesthesiology 1992;77:623–5.
26. Faries PL, Simon RJ, Martella AT, Lee MJ, Machiedo GW. Intestinal permeability correlates with severity of injury in trauma patients. J Trauma 1998;44:1031–5.
27. Brooks AD, Hochwald SN, Heslin MJ, Harrison LE, Burt M, Brennan MF. Intestinal permeability after early postoperative enteral nutrition in patients with upper intestinal malignancy. J Parenteral Enteral Nutr 1999;23:75–9.
28. Fink MP. Interpreting dual-sugar absorbtion studies in critically ill patients: what are the implications of apparent increases in intestinal permeability to hydrophilic solutes. Intensive Care Med 1997;23:489–92.
29. DeGaudio AR, Barneschi MG, Ginanny R, Martinelli P, Novelli GP. Perioperative assessment of glomerular permeability. Anesthesia 1995;50:810–2.
30. Sarti A, DeGaudio AR, Messieno A, Cuttini M, Ventura A. Glomerular permeability after surgical trauma in children. Relationship between microalbuminuria and surgical stress score. Crit Care Med 2001;29:1626–9.
31. Smith FC, Gosling P, Path MRC, Sanghera K, Green MA, Paterson IS, et al. Microproteinuria predicts the severity of systemic effects of reperfusion injury following infrarenal aortic aneurysm surgery. Ann Vasc Surg 1994;8:1–5.
32. Pedrinelli R, Giampietro O, Carmassi F, Melillo E, Dell'Omo G, Catapano G, et al. Microalbuminuria and endothelial dysfunction in essential hypertension. Lancet 1994;344:14–8.