

RE-OPERATION FOR COMPLICATED SECONDARY PERITONITIS – HOW TO IDENTIFY PATIENTS AT RISK FOR PERSISTENT SEPSIS

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Abstract:

Introduction: There is an ongoing dispute on the benefit of planned relaparotomy for patients with diffuse peritonitis.

Setting: Surgery Department, university hospital
Patients: 145 patients with diffuse peritonitis treated with planned relaparotomy were analysed for APACHE II, MOF- and MODS-score (Goris and Marshall), complications, outcome and clinical/laboratory factors indicating intra-abdominal compartment syndrome (positive endexpiratory pressure (PEEP), central venous pressure (CVP), creatinine, blood urea nitrogen (BUN)) after termination of planned relaparotomy. Statistical analysis of data (mean and standard deviation) was performed using Mann-Whitney, chi-square, ANOVA and multiple regression analysis.

Results: The overall mortality was 29.7% and APACHE II score on admission 16.7 ± 8.3 . In 107 patients (mortality 17.8%) closure of the abdomen was achieved at termination of planned relaparotomy. 20 patients (mortality 30%) were treated with mesh closure and in 18 patients (mortality 100%) closure of the abdomen was not feasible. After closure of the abdomen 39 patients showed signs of persistent sepsis. Patients who were explored had a mortality of 37.5% and without re-exploration a mortality of 67%. BUN, PEEP and CVP were significantly different in survivors and non-survivors. Independent predictors of outcome were closure of the abdomen, complications, APACHE II and MOF scores.

Conclusion: Patients with planned relaparotomy for diffuse peritonitis are not a uniform group and differ in mortality depending on source control and closure of the abdomen. Patients with persistent sepsis after termination of planned relaparotomy may be recognized by clinical and laboratory parameters and benefit from a timely reexploration. The decision when to close the abdomen may not only be based on intraperitoneal findings but also on the existence and level of organ failure.

Key words: Peritonitis; intra-abdominal infection; planned relaparotomy; multi-organ-failure; intra-abdominal compartment syndrome; closure of the abdomen; mesh; immune response; laparotomy on demand; risk factors

INTRODUCTION

Therapeutic success in the management of intra-abdominal infection translates into mortality. Most patients die from infection if not operated upon in a timely fashion. Standard treatment includes source control and intra-abdominal lavage. (Kirschner 1926) Adhering exclusively to standard principles may not adequately treat a subset of patients with advanced disease. In advanced peritonitis, the source of infection may be difficult to eliminate with one single operation, and there may be excessive pus, necroses, and spoilage of the peritoneum. Adequate cleansing may not be achieved with the classical single operation standard in these cases. Additionally, peritonitis may have produced inflammatory oedema that increases intra-abdominal pressure, and closure of the abdominal incision over the commonly dilated bowels will not be possible without creating undue tension to the fasciae and increasing intra-abdominal pressure upon forced closure (Holzheimer and Dralle 2001). For such conditions, planned relaparotomies (Teichmann et al. 1986) or STaged Abdominal Repair (STAR) (Wittmann et al. 1990) have been proposed. It has been suggested that these strategies allow a better elimination of the source of infection, decompress the intra-abdominal pressure, offsetting the liabilities (adverse pathological consequences) of the abdominal compartment syndrome on renal, hepatic, cardiovascular, and intestinal perfusion (Schein et al. 1995). Other options are leaving the abdomen open or covering the gap with a mesh (Steinberg 1979; Hedderich et al. 1986). However, in recent years the dispute on which technique is better – planned relaparotomy or laparotomy on demand – has been taken up again without solving the problem (Hau et al. 1995). Some of the problems reported with planned relaparotomy may be associated with technical errors or human factor, which are always difficult to discuss. In this study an analysis of the patients with complicated secondary peritonitis treated with planned relaparotomy was performed with regard to clinical and laboratory parameters indicating increased intra-abdominal pressure after closure of the abdomen. To our knowledge this is the first time that a sub-group of

patients with complicated secondary peritonitis who failed after termination of planned relaparotomy is presented and further analysed.

PATIENTS AND METHODS

A total of 145 patients treated with planned relaparotomy for severe intra-abdominal infection at a University Surgery Department (1992-1997) were included in the analysis. In all patients, the abdomen was not closed at the end of the initial operation and subsequent abdominal exploration (planned relaparotomy) was planned when source control was not secured, the patient was not hemodynamically stable to close the abdomen, or the abdomen could not be closed due to increased intra-abdominal pressure. The abdomen was then temporarily closed, bridging the gap between the fascial edges with an artificial burr. Once the fascial gap had become sufficiently narrow to allow for final closure without leaving undue abdominal pressure, the abdominal wall was closed fascia to fascia, whenever possible with closure of the skin. If sepsis persisted or had progressed to tertiary peritonitis, and further abdominal intervention appeared to do harm, no further re-entries were done, and the abdomen was closed either with a Vicryl™ mesh or by leaving it totally open, in the presence of increased intra-abdominal pressure. Re-exploration in patients with closed abdomen was necessary when signs of persistent intra-abdominal sepsis were present. Patient demographics were recorded and analysed with regard to operative technique (planned relaparotomy with closure of the abdomen, mesh closure, no closure) and post-operative complication and mortality. The APACHE II severity of diseases score (Knaus et al. 1985), the Goris multi-organ failure (MOF) score (Goris et al. 1985) and the Marshall multi-organ dysfunction (MODS) score (Marshall et al. 1995) were assessed on admission, during the planned relaparotomy procedure, and after closure of the abdomen. At the day of closure of the abdomen and the two consecutive days data were collected, which were considered to correlate with increased intra-abdominal pressure, e.g., positive end-expiratory pressure (PEEP), urine output, blood urea nitrogen (BUN), creatinine, central venous pressure (VCP) (Sugerman et al. 1999). Statistical evaluation of the data and distribution pattern was performed with the InStat statistical package (Santa Monica Ca USA) and with the Mann-Whitney and ANOVA test for quantitative analysis. Multi regression analysis was performed to identify risk factors for death using the SPSS program.

RESULTS

A total of 145 patients (75 men and 70 women, age 57 ± 18 years) were entered into the study. 43 (29.7%) of the patients died 2 to 179 days after the first operation for peritonitis, either from sepsis or tertiary peritonitis. All patients underwent an ab-

dominal operation for intra-abdominal infection (index operation) followed by 4 ± 5.8 abdominal re-entries. The median age of all 145 patients was 61 years and the mean APACHE II score was 16.7 ± 8.3 , median 16 (1-26). The source of peritonitis was located in the following organs: stomach $n = 9$, duodenum $n = 8$, biliary tree $n = 10$, small bowel $n = 45$, appendix $n = 17$, large bowel $n = 48$. 11 patients were treated with cortisol. 9 patients received chemotherapy and radiation for malignant tumour, and 26 patients had diabetes. 40 patients had a malignant tumour as underlying disease. Patients stayed for 20 ± 27 days (mean; range 0-176) in the intensive care unit and for 42 ± 47 days (mean; range 2-280) in the hospital.

There are three types of patients in this study: patients with primary abdominal closure after presumed source control ($n = 107$), patients with mesh secondary closure ($n = 20$), and patients where no abdominal closure could be performed ($n = 18$). (Table 1)

After the index operation, the abdomen was explored daily for a total of 508 days in all 145 patients. The final abdominal closure was performed after 4 days (mean; median 2.0; range 0-37). During the index operation, the source of infection was resected in 84 cases (58%) or closed by suture in 37 (26%) cases. 9 cholecystectomies were performed and 15 cases required simple drainage only. During planned relaparotomy, additional problems and complications were observed in 36 (25%) patients. Problems encountered and treated during planned relaparotomy included intra-abdominal haemorrhage ($n = 16$), intra-abdominal abscess formation ($n = 6$), persistent intestinal leak ($n = 3$) and anastomotic leakage ($n = 1$). Abdominal wall infection ($n = 7$), the burr sheet torn out of the abdominal wall fascia ($n = 2$) and surgical haemorrhage ($n = 1$) were considered complications of the operative technique. Ongoing sepsis that could not be controlled perpetuated multi-organ failure in $n = 16$ cases, and led to pneumonia in 9 cases during planned relaparotomy. Source control was thought to be achieved by resection of the diseased bowel in 83, suture closure of the perforated bowel in 42 cases. 46 colostomies were thought to be necessary to exteriorise the infectious source or as protective colostomy.

The abdomen was closed primarily at the termination of planned relaparotomy in 107 (74%) of patients. 19 (17.8%) patients in this group died from tertiary peritonitis (ongoing inflammatory response) without any further re-exploration ($n = 10$), and from sepsis after a re-exploration has been performed despite termination of the planned relaparotomy ($n = 9$). These 19 patients were further analysed. In 20 patients, after a mean of 11.2 ± 8.1 re-entries, the abdominal wall could not be closed because of persisting inflammatory oedema. The abdominal fascial gap was bridged by Vicryl mesh when planned relaparotomy was terminated. These patients spent 51 ± 40 days in the intensive care unit; six (30%) of them died.

Table 1. Patients with primary closure after termination of planned relaparotomy, mesh closure and no abdominal closure in peritonitis treatment.

Clinical parameters	A) Primary abdominal closure * n = 107	B) Mesh closure * n = 20	C) No abdominal closure * n = 18	p-value by ANOVA	
APACHE II	15.43 ± 7.56	17.95 ± 7.75	23.11 ± 10.20	0.001	A vs C
Goris-Score	3.36 ± 2.91	6.35 ± 3.28	8.11 ± 2.37	0.000	A vs B vs C
MODS-Score	5.11 ± 4.93	5.80 ± 6.06	13.27 ± 3.17	0.000	A vs B vs C
Age ± years)	57.68 ± 18.35	53.75 ± 16.40	57.66 ± 16.74	0.661	A vs B vs C
Duration of symptoms ± days)	3.83 ± 4.21	3.65 ± 2.20	4.50 ± 3.16	0.763	A vs B vs C
Goris-Score at admission	1.50 ± 1.49	2.50 ± 2.41	2.88 ± 2.74	0.003	A vs B vs C
Intensive care stay ± days)	15.48 ± 22.49	50.75 ± 39.54	14.88 ± 12.84	0.000	A vs B
Hospitalization period ± days)	40.48 ± 45.68	77.00 ± 57.01	14.88 ± 12.84	0.000	A vs B vs C
Time until closure of the abdomen ± days)	2.66 ± 4.17	11.20 ± 8.06		0.000	A vs B

* Data are given as mean and standard deviation

Table 2. Severity of disease scores and indicators of increased abdominal pressure at the completion of planned re-laparotomies ± after fascial closure comparing patients with recovery versus ongoing sepsis/SIRS.

Parameter	Unit	Recovery group	Ongoing sepsis or SIRS group	Difference at p < 0.05
Number of cases		N = 68	N = 39	
Age ± years)	mean ± SD	55.1 ± 19.2	62.2 ± 15.9	No
APACHE II	mean ± SD	13.3 ± 7	19.3 ± 7.1	Yes
Number of abdominal reentries		2.7 ± 4.4	2.5 ± 3.8	No
CVP after closure	CmH ₂ O	12.5	10.3	Yes
Serum creatinine after closure	mg/dl	1.5	1.8	Yes
BUN after closure	mg/dl	16.7	33	Yes
PEEP after closure	Torr	8.8	11.5	Yes
MOF score after closure	mean ± SD	2.2 ± 2.3	5.4 ± 2.8	Yes
MODS score after closure	mean ± SD	3.3 ± 4	8.2 ± 4.8	Yes
Mortality		0 (0%)	19 (48.7%)	Yes
ICU stay	Days	8.9 ± 12	27 ± 30.7	Yes

MOF = Multi-Organ Failure score (Goris)

MODS = Multi-Organ-Dysfunction (Marshall) score

APACHE II = acute physiology and chronic health evaluation (APACHE) II score

CVP = central venous pressure

BUN = blood urea nitrogen

PEEP = positive end expiratory pressure

Table 3. Severity of disease and outcome of patients with ongoing sepsis and SIRS stratified for post-planned re-laparotomy re-explorations.

	Without reexploration n = 15	With re-exploration n = 24	Difference significant
Mortality	n = 10 (66.7%)	n = 9 (37.5%)	P < 0.001
Age (years)	66.7 ± 15.9	59.4 ± 15.6	ns
Lag-phase (days)	3.4 ± 4	5.4 ± 5.6	Ns
APACHE II	18.9 ± 7.3	19.5 ± 7.2	Ns
PR time until closure	1.7 ± 3.1	3.1 ± 4.2	Ns
MOF score	5.2 ± 2.6	5.5 ± 2.9	Ns
MODS score	8.4 ± 3.8	8.1 ± 2.9	Ns
ICU stay (days)	10.6 ± 9.6	37.2 ± 34.9	P < 0.05

MOF = Multi-Organ Failure score (Goris)

MODS = Multi-Organ-Dysfunction (Marshall) score

APACHE II = acute physiology and chronic health evaluation (APACHE) II score

PR = planned re-laparotomy

data indicated as mean ± standard deviation

Hemodynamic parameters and organ failure scores of 14 patients indicated ongoing inflammatory reaction or sepsis, requiring a significantly prolonged intensive care treatment (60 versus 30 days; $p < 0.05$ when compared to patients without ongoing sepsis/inflammation). In 18 patients the abdomen was never closed because of ongoing sepsis; all patients died after 16 ± 12 days (mean). All patients in this group presented with advanced disease at the time of the index operation indicated by significantly higher APACHE II scores (average 23; $p < 0.05$) when compared to patients with primary closure of the abdomen (average 15) or mesh closure (average 18).

39 patients in the first group with closure of the abdomen who demonstrated signs of ongoing sepsis/inflammation after closure of the abdomen were analysed in comparison to the 68 patients who were cured. Patients with ongoing sepsis/inflammation had significantly higher APACHE II scores (average 19 ± 7) versus patients who were cured (average 13 ± 7 ; $p < 0.001$). These patients also had significantly higher organ failure scores and stayed longer in the intensive care unit (27 ± 30.7 days versus $8.9(12$ days; $p < 0.01$). The length of surgical treatment (planned relaparotomy) was not different in both groups (3 days). (Table 2)

Patients with presumed successful termination of planned relaparotomy and abdominal closure (n = 107 total) had to be re-explored due to symptoms of abdominal compartment syndrome and/or ongoing sepsis in n = 24 cases of whom n = 9 (37.5%) died and 15 patients survived. The mortality rate of patients with ongoing sepsis/inflammation who were not re-explored was 67% and significantly higher (10/15) (Chi-square = 3.1431; $p < 0.05$). This difference in outcome was not indicated by a difference in the APACHE II score at the index operation nor did the number of explorations before closure of the abdomen (n = 5

in patients with re-exploration after closure of the abdomen versus n = 3 in patients without re-exploration; n.s.) reveal a possible association with the disease severity or ongoing sepsis/inflammation. Non-surviving patients who were re-explored after closure of the abdomen for ongoing sepsis/inflammation had significantly higher APACHE II scores (23.88 ± 26), MOF scores (7.67 ± 7) and MODS scores (12.4 ± 11) than survivors (17.13 ± 17 ; 4.2 ± 5 ; 5.53 ± 7 , respectively). However, the scores were not different in patients who were re-explored when compared to patients without re-exploration after closure of the abdomen and ongoing sepsis/inflammation. (Table 3)

Blood urea nitrogen (BUN), creatinine, and central venous pressure (CVP) were significantly different in surviving patients after termination of planned relaparotomy and closure of the abdomen when compared to non-survivors. (Table 4) An increase of 20% in creatinine levels (positive prediction 91.6%, sensitivity 83.4%, specificity 56.3%) as well as increased creatinine levels at the second day after closure of the abdomen and increased blood urea nitrogen levels at the first day after closure of the abdomen were associated with detrimental outcome. (Table 5)

The closure of the abdomen (positive predictive value 100%, sensitivity 80.3%, specificity 66.7%), complications during surgical treatment, e.g., bleeding or pneumonia, (positive predictive value 95.1%, sensitivity 84.2%, specificity 83.2%), anastomotic leakage and translocation (positive predictive value 93.1%, sensitivity 74%, specificity 58.7%) were associated with poor outcome. Isolation of pathogens, the classification of the exudate, the origin of peritonitis, pre-treatment, pre-existing malignancy did not seem to have an influence on the outcome. Co-existing liver disease (positive predictive value 97.1%, sensitivity 75%, specificity 76.8%), organ failure at the time of the index oper-

Table 4. Blood urea nitrogen (BUN), creatinine (CR), positive end expiratory pressure (PEEP), and central venous pressure (CVP) of survivors and non-survivors at the day of abdominal closure and termination of the planned relaparotomy, first and second postoperative day (ANOVA analysis). mean \pm standard deviation

		n	Survivors	n	Non-survivors	p-value
BUN 0	mg/dl	96	16.97 \pm 20.19	24	43.38 \pm 42.74	0.000
BUN 1	mg/dl	96	17.47 \pm 21.40	24	45.25 \pm 40.27	0.000
BUN 2	mg/dl	96	17.87 \pm 22.40	22	43.42 \pm 38.52	0.000
CR 0	mg/dl	101	1.47 \pm 1.98	24	2.57 \pm 1.75	0.015
CR 1	mg/dl	102	1.36 \pm 1.39	24	3.03 \pm 2.08	0.000
CR 2	mg/dl	102	1.31 \pm 1.56	22	3.16 \pm 1.79	0.000
PEEP 0	Torr	86	9.19 \pm 1.99	24	9.75 \pm 2.38	0.253
PEEP 1	Torr	82	8.86 \pm 1.93	22	9.83 \pm 2.18	0.039
PEEP 2	Torr	81	8.19 \pm 2.25	22	9.59 \pm 2.34	0.012
CVP 0	cm H ₂ O	95	10.65 \pm 3.67	24	13.20 \pm 2.99	0.002
CVP 1	cm H ₂ O	94	9.85 \pm 3.72	24	13.62 \pm 3.10	0.000
CVP 2	cm H ₂ O	94	8.96 \pm 3.91	22	13.22 \pm 3.89	0.000

Table 5. Creatinine (CR) and blood urea nitrogen (BUN) after abdominal closure and termination of planned relaparotomy (Multivariate analysis).

Parameter	β	S.E.	Wald	Df	Sig	R	Exp (β)
CR (20%)	2.2422	0.6100	13.5087	1	0.0002	0.3179	9.4139
CR 2	3.0162	1.1230	7.2141	1	0.0072	0.2230	20.4128
BUN 1	0.1794	0.0805	4.9684	1	0.0258	0.1682	1.1965

CR 20% : 20% increase of creatinine

CR 2 : creatinine level on day 2 after closure of the abdomen

BUN 1: blood urea nitrogen on day 1 after closure of the abdomen

Table 6. Multivariate analysis of risk factors in peritonitis for death.

	β	S.E.	Wald	df	Sig	R	Exp (β)
Abdominal closure	-1.9474	0.4828	16.2709	1	0.0001	-.2845	0.1426
Hemorrhage	2.5717	0.8664	8.8107	1	0.0030	0.1966	13.0884
Pneumonia	1.7413	0.7135	5.955	1	0.0147	0.1498	5.7046
Insufficiency	1.4538	0.6653	4.7754	1	0.0289	0.1257	4.2798
Translocation	1.4018	0.6948	4.0706	1	0.0436	0.1086	4.0626
Liver	2.6674	1.2371	4.6492	1	0.0311	0.1226	14.4020
MOF score	0.4896	0.0831	34.7278	1	0.0000	0.4317	1.6317
APACHE II	0.1182	0.0272	18.8591	1	0.0000	0.3092	1.1255
MODS score	0.3575	0.0585	37.3931	1	0.0000	0.4490	1.4297

ation (MOF score: positive predictive value 90.1%, sensitivity 85.7%, specificity 73.7%; MODS score: positive predictive value 91.1%, sensitivity 88.5%, specificity 77.5%) and severity of disease at

the time of the index operation (APACHE II score: positive predictive value 93.0%, sensitivity 86.4%, specificity 68.2%) were identified as significant predictors for outcome in peritonitis (Table 6).

DISCUSSION

In our study 145 patients with severe peritonitis and treated with planned relaparotomy were analysed with regard to closure of the abdomen – primary closure after planned relaparotomy, secondary closure with mesh, and no closure at all – and complications after termination of planned relaparotomy and closure of the abdomen. The mean mortality of 29.7% in all patients is comparable to the mortality rate reported in other studies. (Schein et al. 1988). Patients in whom closure of the abdomen was successfully done had a similar severity of disease score (APACHE II) and mortality rate compared to results in recent studies. (Wacha et al. 1999; Koperna and Schulz 2000)

PLANNED RELAPAROTOMY VERSUS LAPAROTOMY ON DEMAND AND SOURCE CONTROL

Yet, there is an unresolved dispute over the benefit of planned relaparotomy. Several reports have demonstrated that planned relaparotomy may help to control the intra-abdominal infection (Teichmann et al. 1986; Wittmann et al. 1990; Penninckx et al. 1990; Hubens et al. 1994). Open management of the septic abdomen with mesh has been advocated by others (Hedderich et al. 1986; Bose et al. 1991; Hakkiuoto and Hannukainen 1992). It has been stated that planned relaparotomy is associated with increased frequency of infectious complications, e.g. suture leaks, recurrent intra-abdominal sepsis, septicaemia and that more patients with a Goris score above 5 are in this group when compared to laparotomy on demand (Hau et al. 1995). The authors of this study have compared 38 patients in each group. The study protocol did not include a clear definition of successful source control. This decision was left to the personal discretion of each participating and/or operating surgeon. The missing definition of source control is not just a problem of this study but of most published studies on peritonitis (Holzheimer and Dralle 2001). In other studies the patients treated with planned relaparotomy had more complications due to primary disease or sepsis which may reflect a different patient group (Demmel et al. 1993). In large studies there was no significant difference detectable in mortality in patients treated with planned relaparotomy or laparotomy on demand (Christou et al. 1993; Gotzinger et al. 1996; Koperna and Schulz 2000) The dilemma is obviously also not resolved by meta-analysis (Lamme et al. 2002).

COMPARABILITY OF STUDIES – WHAT IS THE REASON FOR THE DIFFERENCES IN OUTCOME: HUMAN FACTOR, OPERATIVE TECHNIQUE OR DIFFERENT PATIENTS?

Despite the introduction of disease severity and multi-organ failure/dysfunction scores into clinical studies in order to make studies comparable (Dellinger et al. 1985; Bohnen et al. 1988;

Ohmann et al. 1993) we still have a problem when we analyse clinical studies with regard to complications and outcome. It is well accepted that none of the existing scores can be trusted enough for individual therapeutic decisions in peritonitis patients (Ohmann et al. 1997). It has been suggested to combine several scores (Bosscha et al. 1997) or to measure inflammatory cytokines as surrogate parameters (Holzheimer et al. 1991). Despite promising results of a recently published European multi-centre trial with regard to the combination of scores and cytokine analysis in critically ill surgical patients, the measurement of scores and cytokines does not relieve the surgeons dilemma to re-explore or not a patient with suspected persistent sepsis nor does it characterize the individual patient perfectly (Holzheimer et al. 2000) The benefit of doing sophisticated analysis in critically ill surgical patients remains to be clarified with regard to the high cost in intensive care treatment (Welcker et al. 2002).

There are obvious differences between some studies on peritonitis. A conservative surgical treatment concept supplemented with extensive intraoperative lavage in just one surgical intervention in almost 90% of patients was said to reduce the reoperation rate and to translate into a low mortality rate of just 14% in patients with diffuse peritonitis (Seiler et al. 2000). What is responsible for differences in peritonitis studies: is it the human factor, the operative technique or do we investigate different patients? The surgeon may have positive as well as negative effects on outcome, which may not be recognized precisely and with validity in studies (de Leval et al. 2000; Bruce et al. 2001; Healey et al. 2002).

There is an argument that the surgical technique treating peritonitis is responsible for outcome. Planned relaparotomy has been criticized to cause intra-operative complications and to be unable to reverse organ dysfunction (van Goor et al. 1997). Intra-abdominal complications were more common among the non-survivors than the survivors, but the non-survivors had higher MOF scores than the survivors at the beginning of treatment. Patients with advanced disease may have in reality more complications no matter what kind of treatment is started. We, in contrast, observed no significant increase in intra-abdominal complications during planned relaparotomy.

HOST RESPONSE IN PERITONITIS – IS IT INCREASED OR DECREASED BY THE SURGICAL TREATMENT?

Peritonitis can cause an increased intra-peritoneal inflammatory response, which may lead to organ failure and death (Holzheimer et al. 1995). Planned relaparotomy has been accused to further increase the inflammatory response causing a need for more blood products and to harm the patients (Sautner et al. 1997; Zugel et al. 2002). However, other factors, e.g., source control, circadian rhythm, antibiotic-induced endotoxin release, may be involved (Holzheimer 2001; Holzheimer

et al. 2002). Another recent study demonstrated the significant dominance of host-related factors over type, source of infection and other factors on the prognosis of patients with intra-abdominal infection (Pacelli et al. 1996), but this has been challenged by others (Burger et al. 1995).

ORGAN FAILURE AND SOURCE CONTROL – DECISIVE FACTORS AT THE START OF TREATMENT

Organ failure and failure in source control may have implications early in the treatment process and this may not be recognized at the index operation. In our study 39 patients who were diagnosed to have ongoing sepsis/inflammation after termination of planned relaparotomy had significantly higher APACHE II scores at the index operation and higher MOF scores after closure of the abdomen pointing into the direction of a failure in source control. Preoperative organ impairment has been identified as independent predictor of death in intra-abdominal infection (Pacelli et al. 1996). Koperna and Schulz observed in 105 patients in whom standard surgical treatment of secondary peritonitis failed and who had to undergo relaparotomy for persisting abdominal sepsis that aggressive surgical treatment has reached its limit in patients whose source of infection could not be controlled at the initial operation (Koperna and Schulz 2000) Gotzinger et al. stated that regardless of the type of operation – planned relaparotomy or laparotomy on demand – the crucial point is that the elimination of the infectious source is achieved as soon as possible (Gotzinger et al. 1996).

CAN WE IDENTIFY PATIENTS THAT WILL FAIL OR WHO WILL DEVELOP PERSISTENT SEPSIS?

Can we recognize patients who do not profit from standard treatment or who may develop tertiary peritonitis/ persistent sepsis after closure of the abdomen? Poorly localized intra-abdominal infection, altered microbial flora, progressive organ dysfunction and significantly higher mortality have been associated with tertiary peritonitis (Rotstein and Meakins 1990), which describes the clinical situation of most patients with ongoing sepsis after termination of planned relaparotomy in this study. The type of surgery may not have a relationship to tertiary peritonitis and it may not be possible to predict the development of tertiary peritonitis by scores (Nathens et al. 1998). A recent retrospective study revealed that while increasing APACHE II score independently predicted progression from secondary to tertiary peritonitis but tertiary peritonitis was not an independent predictor of mortality. The authors concluded that the high mortality associated with tertiary peritonitis is more a function of the patient population in which it occurs than the severity of the pathological process itself (Evans et al. 2001). The evaluation of scores may not be of help since it does not provide any therapeutic alternative to

the surgeon who has to perform a relaparotomy as soon as possible and the impossibility of definitive operative resolution of the intra-abdominal pathologic findings at initial operation may have no significant effect on mortality (Koperna and Schulz 1996). In our study we found some evidence that organ failure, clinical and laboratory parameters reflecting the development of intra-abdominal compartment syndrome may be clinically useful to identify patients at risk. This is also supported by others who investigated the scores in patients with or without persistent sepsis (Paugam-Burtz et al. 2002).

WHEN TO CLOSE THE ABDOMEN AND STOP THE PLANNED RELAPAROTOMY?

When to close the abdomen and to stop planned laparotomy is another important aspect of peritonitis treatment. It is not yet clear which clinical parameters do definitely allow us to decide on the termination of planned relaparotomy. The colonization of the upper gastrointestinal tract with *Pseudomonas*, *Staphylococcus epidermidis* and *Candida* has been associated with the development of invasive infection and may progress into organ failure (Marshall et al. 1993). Intra-abdominal cultures have been advocated by some authors and rejected by others (Sawyer et al. 1992; Schoeffel et al. 1995; van Goor et al. 1997) The isolation of *Candida* in peritoneal fluid has been associated with mortality (Dupont et al. 2002).

DOES RELAPAROTOMY AFFECT THE OUTCOME?

Re-operation in peritonitis has been considered to be harmful (Sautner et al. 1997) and to have no benefit for the clinical course of disease (van Goor et al. 1997). A higher mortality rate (42%) in patients with reoperation versus 27% without reoperation has been observed (Christou et al. 1993). Others have reported a 27% reduction of mortality in patients with persisting or relapsing sepsis (Billing et al. 1992) In several studies organ failure was not reversed by relaparotomy even when adequate therapy has been accomplished (Norton 1985; Marshall et al. 1988). However, the development of tertiary peritonitis or persistent intra-abdominal sepsis may reflect inadequate therapy of peritonitis leading to multi organ failure which then may be considered to be an indication for re-exploration of the abdomen (Fry et al. 1980; Ferraris et al. 1983; Hinsdale and Jaffe 1984; Polk and Shields 1977; Nathens et al. 1998). In difference to most of these studies we have analysed patients with ongoing sepsis after termination of planned relaparotomy. We observed that clinical and laboratory signs of abdominal compartment syndrome and organ failure may be present at the time of closure of the abdomen. An increased compartmentalized intraperitoneal inflammatory response may be followed by an increase in intra-abdominal pressure with consecutive renal failure (BUN, creatinine), ventilatory disturbances re-

flected by high peak inspiratory pressure and impaired gas exchange, and increased central venous pressure (Burch et al. 1996; Sugerman et al. 1999). The role of abdominal compartment syndrome in trauma victims is well recognized (Meldrum et al. 1997; Ivatury et al. 1998; Maxwell et al. 1999). Peritonitis patients, especially patients after cessation of planned relaparotomy, have not been studied comparably. In our study we observed significant alterations in the renal function, which have been observed as consequence of increased intra-abdominal pressure and predictor of fatal outcome in patients undergoing reoperation for sepsis (Sugrue et al. 1999; Machiedo et al. 1985). Re-exploration of some of these patients resulted in a better survival rate (37.5% versus 67%) when compared to the survival rate of patients who were not re-explored again. Intra-abdominal compartment syndrome is not in any case the reason for increased mortality – at least in this study. Despite leaving the abdomen open or secondary closure with mesh, which is known to avoid abdominal compartment syndrome in trauma patients (Ciresi et al. 1999; Mayberry et al. 1997), the mortality rate was unacceptable high (30% and 100%, respectively) in this group of patients and mostly the failure in source control accounted for this mortality. The concept of timely re-exploration is supported by several other studies, although they have not investigated the subgroup of patients after cessation of planned relaparotomy (Hinsdale and Jaffe 1984; Koperna and Schulz 2000).

In conclusion, we observed a different mortality in sub-groups of patients treated with planned relaparotomy with regard to closure of the abdomen. Patients in whom organ failure is present at the index operation or where source control is impossible are at risk for death. Sub-group analysis of patients with ongoing sepsis after cessation of planned relaparotomy revealed that most of these patients had indicators (MOF scores, renal failure) of intra-abdominal compartment syndrome mostly due to failure in source control and that re-exploration reduced the mortality when compared to patients who were not re-explored. There is still a problem to compare clinical studies despite powerful scores. Especially in subgroups of patients who may benefit from early detection of complications the characterization of these patients could be improved. The decision to close the abdomen may not only be influenced by the intra-abdominal findings, but also by the existence and level of organ failure.

Acknowledgment: I thank Jeanine von Holleben, who has collected the data from patient charts.

Furthermore I would like to express my gratitude to Dietmar Wittmann, Professor of Surgery at the Medical College of Wisconsin, Milwaukee, USA. He has helped to analyse and discuss the results.

Karsten Sekulla, Department of Surgery, University Halle-Wittenberg, has contributed to the statistical analysis of the data.

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Received: February 26, 2003 / Accepted: March 14, 2003

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