Comparison of On-demand vs Planned Relaparotomy for Treatment of Severe Intra-abdominal Infections

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Aim
To compare morbidity and mortality of patients with severe intra-abdominal infections after two types of surgical treatment, on-demand (“wait and see”) relaparotomy and modified planned relaparotomy.

Methods
We prospectively analyzed the outcomes of 65 patients with severe peritonitis surgically treated in two Croatian hospitals. In one hospital, 34 patients were treated on-demand, and in another hospital 31 patients were treated by planned relaparatomy. We compared severe postoperative complications, mortality, and length of hospital stay in the two groups of patients.

Results
Severity of patient’s disease, as measured from preoperative group-average Acute Physiology and Chronic Health Evaluation (APACHE) II scores, was comparable in both on-demand and planned relaparotomy groups. The mortality rate was higher in patients operated on-demand (59% vs 29%, \( P = 0.024 \)). In nonadjusted model, the relative risk of dying was 2.5-fold higher for patients treated by on-demand operation in comparison with planned relaparatomy (\( P = 0.030 \)). However, after the adjustment of the survival data for individual patient’s sex and APACHE II scores, the difference in the relative risk became non-significant (\( P = 0.178 \)). The patients who died had higher APACHE II scores (26.1±8.9 vs 19.7±5.9, \( P = 0.009 \)). Relative risk of dying per 5-point increase in APACHE II score was 1.24 (95% confidence interval, 1.01-1.51; \( P = 0.039 \)), irrespective of the surgical technique.

Conclusions
Patients with severe peritonitis treated with planned relaparotomy seemed to have lower mortality. However, the relative risk of dying was not statistically different between the on-demand and planned relaparotomy groups after adjustment for preoperative APACHE II scores. The severity of disease rather than surgical approach plays more important role in survival of these patients.

Despite advances in antimicrobial therapy, surgical techniques, and intensive care, the mortality of patients with severe intra-abdominal infection remains between 22% and 70% (1-6), or even higher in patients who have multiple organ failure at the time of initial surgery (7). Current therapy for severe peritonitis is founded on several principles, which include early administration of antibiotics, effective surgical control of infection, and supportive care to maintain organ function and limit the development of multiple organ failure (8,9). When surgery is considered, two factors should be taken into account. First, single initial operation is frequently insufficient to control the infection and reexplorations are often needed. Second, patients with severe abdominal infections may develop intra-abdominal hypertension leading to abdominal compartment syndrome.

Over the last several decades, different surgical approaches have been developed to im-
prove the outcome of patients with severe abdomi-
nal infections. The most frequently used tech-
niques have been relaparotomy on-demand ("wait
and see" approach), continuous postoperative
peritoneal lavage, open drainage (laparostomy),
and planned relaparotomy. Surgical approach that
leaves the abdomen open may both facilitate fre-
quent reexploration and prevent deleterious ef-
fects of increased intra-abdominal pressure. How-
ever, current surgical opinion does not favor lib-
eral use of an "open-abdomen" technique (10).

A comparison of outcomes of different
surgical approaches used for treatment of peritoni-
tis is difficult because various studies compare pa-
tients with different severity of the disease. Treat-
ment of patients with different stages of abdominal
infections may require individualized surgical ap-
proach. This was best illustrated by Holzheimer et
al (3), who found that the overall mortality in pa-
tients with diffuse peritonitis was nearly 30%.
When closure of the abdomen was achieved at the
termination of the planned relaparotomy, mortal-
ity was 18%, but when closure was not feasible,
mortality was 100%. After initial closure of the ab-
domen, some patients continued to show signs of
abdominal sepsis; mortality was 38% in patients
who were reexplored, and 67% in those without
reexploration (3).

In the present study, we prospectively
compared morbidity and mortality in patients with
severe abdominal infections who underwent treat-
ment with one of two following surgical tech-
niques: on-demand reoperations and modified
prescheduled individually planned relaparotomy
via laparostomy. Our hypothesis was that by using
an approach that leaves the abdominal incision open
between reexplorations, both the morbidity and
mortality would be reduced. The improved outcome
might be achieved because more fre-
quent reexploration would result in more efficient
eradication of infection, and/or because by pre-
venting development of abdominal compartment
syndrome, these patients would have lower inci-
dence of multiple organ failure.

**Patients and Methods**

**Study Design**

This prospective study included 68 con-
secutive patients with severe peritonitis admitted
to the Split University Hospital and Sisak General
Hospital. The patients were treated by two experi-
enced surgical teams using two different surgical
approaches. All surgeries were performed be-
The surgical techniques compared are well-es-
stablished standardized treatments for abdominal
infections, and no aspect of these treatments was
modified for this study. The standards of surgical
management of peritonitis differ between the two
institutions, and we took advantage of this varia-
tion in practice to design this study. In Split Uni-
versity Hospital, the standard surgery is on-de-
mand reoperation, ie, after primary laparotomy,
consecutive interventions are done only if the sur-
gical team assesses on the basis of clinical, radi-
ological, and ultrasound or computed tomography
findings that the condition of the patient is deterio-
rating due to reaccumulation of infectious material
or occurrence of abdominal compartment syn-
drome. Between the two surgeries, the abdominal
wound is suture-closed and abdominal drains are
placed. In Sisak General Hospital, the standard
surgical practice is individually planned relaparo-
tomy via laparostomy, ie, after the initial interven-
tion the abdominal wall is left open if the surgeon
assesses that the severity of abdominal infection is
such that will require second exploration. The ab-
dominal content is then covered with a protective
plastic sheet (modified technique), and the time of
relaparotomy is prescheduled at regular 24 to 48
hour intervals. The decision on the timing of
reoperation is made during the primary interventi-
on, and is based on the surgeon’s subjective assess-
ment of severity of the individual patient’s disease.

In both hospitals, the surgeons treated the
source of infection during the initial operation, ie,
repaired the ruptured internal organ and removed
both devitalized tissues and purulent material
from the abdomen. With each subsequent opera-
tion, necrotic and infected material was removed
and lavage of the abdominal cavity was per-
formed.

The Ethics Committee in both Split Uni-
versity Hospital and Sisak General Hospital ap-
proved this study.

**Inclusion Criteria and Surgical
Management**

The main inclusion criterion was the
presence of severe and diffuse peritonitis requiring
surgical intervention. Computed tomography scan,
abdominal ultrasound, and abdominal x-ray were
performed before surgery to confirm both the diag-
nosis and need for laparotomy. During laparotomy, samples of infectious and/or necrotic material and peritoneal exudate were collected for microbiologic analyses. Parenteral antibiotic therapy was immediately initiated with empiric broad-spectrum coverage against gram-negative microorganisms and anaerobes (11), and this therapy was subsequently adjusted after culture and sensitivity results were obtained. All patients received fluid therapy, hemodynamic support, and correction of both electrolyte and coagulation abnormalities. All conservative treatments, requirement for mechanical ventilation, timing for tracheal extubation, and invasive hemodynamic monitoring were performed according to current intensive care standards, and no aspect of management was affected by the study protocol. Every day, intra-abdominal pressure was assessed indirectly from pressures recorded in urinary bladder (intravesical route) through the urinary catheter, as described elsewhere (12).

Data Collection and Outcome Measures

We recorded patients’ age, sex, infection source (infected primary organ as a cause of peritonitis), and Acute Physiology and Chronic Health Evaluation (APACHE II) scores before initial operation, and on the third and ninth postoperative days. APACHE II scoring system, a severity of disease classification system, uses basic physiologic principles to stratify acutely ill patients and calculates probability of in-hospital mortality. The basis of APACHE score development was the hypothesis that the severity of acute disease can be measured by quantifying the degree of abnormality of multiple physiologic variables (http://www.vh.org/adult/provider/pharmacieservices/PTNews/2002/APACHEII.pdf). APACHE II has been used for many years to calculate a patient’s risk score based on the most abnormal data at the intensive care admission and helped to compare the efficacy of intensive care treatments in different hospitals over time (13), which is what we did in the present study. In addition to APACHE II scores, we daily recorded the intravesical pressure (the highest value measured in a respective day was recorded for the purpose of analysis), the number of reoperations, severe postoperative complications (myocardial infarction, pneumonia, multiple organ failure, adult respiratory distress syndrome [ARDS], wound dehiscence, and anastomosis leak), need for mechanical ventilation (for more than 24 hours postoperatively), duration of mechanical ventilation (in days), length of hospital stay (from initial operation until hospital discharge or death), and mortality rates.

Statistical Analysis

The primary endpoint in this analysis was the number of days from hospital admission to either death or hospital discharge. Differences in survival between on-demand and planned relaparotomy patient groups were compared by a log rank test. A Cox proportional hazards model was developed to estimate the relative risk of death for the on-demand vs the planned relaparotomy group. An adjusted relative risk was estimated after including sex and APACHE II score in the Cox model. Baseline characteristics were reported across study groups as mean±standard deviation for continuous variables, and median with range or interquartile range for categorical variables. Differences in the baseline characteristics across study groups were compared by rank sum test for continuous variables and Fisher’s exact test for categorical variables. Analyses were completed in either SAS (version 6.12 SAS, Cary, NC, USA) or Stat-View statistical packages (Stat-View, Abacus Concepts, Berkeley, CA, USA).

Results

Sixty-eight patients with severe peritonitis, 36 in Split, and 32 in Sisak, were enrolled in this study. Two patients from Split and one from Sisak were excluded from the analyses because of an intraoperative finding of localized peritonitis. Therefore, 65 patients were included in the final analysis. There was a similar number of men and women in each group, but the patients in the on-demand group were older (Table 1). The average preoperative APACHE II score in on-demand group was 3-point higher than in planned relaparotomy group, but this difference was not statistically significant (P=0.255). The distribution of infection sources (infected primary organ as a source of peritonitis) in the two study groups were not different (P=0.560). In both groups, the predominant pathogen isolated was methicillin resistant Staphylococcus aureus (Table 2). Pneumonia, multiple organ failure, and ARDS were the most frequent severe complications that occurred during hospitalization.
There was no difference in length of hospital stay for patients who survived to discharge between the two centers (Table 1). The average number of reoperations was 1.8 ± 1.3 in on-demand group and 4.8 ± 2.6 in planned relaparotomy (P = 0.002). Death occurred in 59% of on-demand patients, and in 29% of patients who had planned relaparotomy (Table 1, P = 0.024). When we compared hospital survival in nonadjusted model, the relative risk (RR) of dying was almost 2.5-fold higher when surgical approach was on-demand (Table 3, Fig. 1; P = 0.030). However, after adjustment for APACHE II scores and sex, the difference in relative risk became nonsignificant (RR, 1.79; P = 0.178). In either hospital, the patients who died had higher preoperative APACHE II scores than survivors (Table 4). Averaged across all patients in both centers, the nonsurvivors had significantly higher preoperative APACHE II scores (26.1 ± 8.9 vs 19.7 ± 5.9, P = 0.009), and relative risk of dying increased for 24% per 5-point increase in APACHE II score (RR, 1.24; 95% CI, 1.01-1.51; P = 0.039), irrespective of the type of surgery performed.

Discussion

In this study we compared two surgical approaches, on-demand relaparotomy vs modified planned relaparotomy, for treatment of patients with severe diffuse abdominal infections. We found that patients who underwent scheduled reexplorations had a lower mortality. Relative risk of dying for patients who were treated with on-demand relaparotomy was almost 2.5-fold higher than that for patients treated with planned relapa-
rotomy. Preoperative APACHE II scores were not significantly higher (3-points) in on-demand patients. However, when this criterion was used to calculate the adjusted risk of dying, the comparison of risk of dying between two groups became statistically nonsignificant. Therefore, the severity of disease, as represented by preoperative APACHE II scores, plays the most important role in the outcome of patients with severe peritonitis.

The single major event resulting in the reduction of abdominal infection mortality from 90% to 40% was the introduction of surgical treatment 70 years ago (14). Despite the advancements in the field of intensive care medicine and surgery, severe abdominal infections still remain associated with a very high mortality (1,15,16). The concurrent development of systemic sepsis, systemic inflammatory response syndrome, and multiple organ failure maintains mortality of severe abdominal infections between 70% and 93% (5-7). The outcome of severe peritonitis is dependent upon prompt diagnosis, and decisive antimicrobial and surgical treatment (17). Different surgical techniques, such as planned relaparotomy, relaparotomy on-demand, or continuous closed peritoneal lavage, have been used to improve outcomes but no significant difference in clinical outcomes in patients with severe intra-abdominal infections have been reported (7,15,18). However, Mulier et al (1) reported no mortality in the planned relaparotomy group vs 64% mortality in the on-demand group. In another report, the interval between the initial operation and reexploration was the most significant factor influencing outcome, and reexploration performed more than 48 hours after the initial operation resulted in a higher mortality (77%) than reexploration done within 48 hours (28%) (7). Presumably, this may be interpreted that early and more frequent relaparotomy achieved better infection control, and hence increased survival. However, this is not universally true because the severity of the patient’s general condition, as evidenced by the number of failed organs, plays an important role in the outcome (1,5,7,19). In some patients with very severe abdominal infections even the best surgical technique and its appropriate timing cannot prevent mortality. For example, Koperna and Schulz (7) demonstrated that the timing of reoperation had no impact on survival in patients with an APACHE II score ≥26. Physiologic derangements in these patients are so severe that only a few patients could benefit from reoperation (7). It has been repeatedly shown that the severity of patient’s disease directly correlates with outcome. Koperna and Schulz (20) demonstrated no mortality in patients with peritonitis without organ failure, <5% if the APACHE II score was <15, 47% if the APACHE II score was >15, and over 93% with quadruple organ failure. The significance of high preoperative APACHE II scores in predicting mortality was also confirmed in our study. The majority of patients who died, in both study hospitals, had preoperative APACHE II scores above 20. Furthermore, for each increase in 5-points in APACHE II score, the relative risk of dying increased for 24%. Therefore, the severity of disease at the time of initial surgery is an important predictor of mortality.

An important aspect of surgical therapy of peritonitis is the prevention of intra-abdominal

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**Table 4.** Perioperative distribution of APACHE II scores in patients with severe intra-abdominal infection. Broken line – planned relaparotomy, full line – on-demand relaparotomy, \( P=0.019 \).
hypertension and abdominal compartment syndrome (21). Because intra-abdominal hypertension has an adverse impact on function of numerous organs (kidney, heart, lungs, and liver), its prevention is critical for improving survival (21,22). Primary closure of abdominal fascia under tension has been associated with an increased incidence of multiple organ failure and mortality (3,23). There is no agreement upon the upper limit of intra-abdominal pressure when it becomes deleterious, and although a pressure of 25 mm Hg was cited as critical (9,21), no single intra-abdominal pressure threshold can be applied universally (19,24). However, when intra-abdominal pressure exceeds 25 mm Hg, decompressive laparotomy may be considered (25). Since it represents the only treatment available for established abdominal compartment syndrome, the prevention of abdominal compartment syndrome by adoption of an “open-abdomen” approach (laparostomy) may be preferable in those at significant risk for developing intra-abdominal hypertension. Despite this sound theoretical consideration, a survey of American trauma surgeons showed that only a minority would leave the abdomen open and only when there was a risk of developing abdominal compartment syndrome (10). Most surgeons prefer to adopt a “wait and see” (on-demand) approach, ie, only intervening when clinical deterioration is associated with a significant increase in the intra-abdominal pressure (10,26,27). A large number of patients in our on-demand group had some degree of intra-abdominal hypertension, but no comparison of the abdominal pressure in laparostomy group could be made because the abdominal wall was left open. An open-abdomen technique, such as that used routinely in Sisak General Hospital, could theoretically minimize secondary adverse effects related to increased intra-abdominal pressure. Surprisingly, we did not find any difference in the incidence of multiple organ failure between the two patient groups.

From a theoretical standpoint, laparostomy techniques could be more effective in controlling abdominal infection because they facilitate early recognition of abscess formation or intestinal necrosis. This is important because of the established association between delayed treatment, organ failure, and mortality (3). Since early recognition of deterioration of abdominal infection may be difficult, a planned re-intervention may be an option whenever successful eradication of infection is uncertain. In the present study, number of surgical reinterventions in either surgical group could not be correlated with mortality. This is surprising, at least for patients in the on-demand group, as re-exploration in these patients represents an index of disease deterioration. Indeed, Koperna and Schulz (20) found that the need for re-interventions resulted in a substantially higher mortality.

In comparing the outcomes of two surgical techniques in treating severe intra-abdominal sepsis, we took advantage of the fact that surgeons in two different institutions used different surgical approach. Performing this study in a single institution was found unacceptable as neither the Ethical Committees nor individual surgeons in respective hospitals would agree to randomize the patients into a group against individual surgeon’s belief what was the best approach for the patient. Therefore, this study describes standards of surgical care in the respective hospitals, which may represent a limitation to our findings. By the same token, a form of “natural randomization” was utilized to compare the outcomes. Another limitation arises from a relatively small number of patients included in our study. After the adjustment for severity of disease, a relative risk of dying was 80% higher in on-demand group than in planned relaparotomy patients. Despite the fact that this difference was not statistically significant, a possibility exists that our study did not have sufficient power, ie. that we needed larger sample size to establish a more definitive association between the surgical approach and outcome.

In conclusion, after adjusting for the severity of disease, our patients treated with individually planned relaparotomy had similar mortality compared to those who were operated on-demand. “Open-abdomen” surgical approach did not reduce the incidence of multiple organ failure, which, when present, resulted in 100% mortality. Fatality in either group was associated with higher preoperative APACHE II scores, and the risk of dying increased by 24% for 5-point increase in APACHE II scores irrespective of the surgical technique used. Therefore, the severity of disease before initial surgical intervention was an important factor influencing survival of patients with peritonitis.
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