



Original Contribution

NEW POST-OPERATIVE CLINICAL INDEX INFLUENCING THE DECISION FOR RELAPAROTOMY IN PATIENTS WITH INTRA-ABDOMINAL INFECTION

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ABSTRACT

BACKGROUND: The purpose of the study was to analyze clinical parameters related to the development of postoperative complication and the indications for relaparotomy in patients with intra-abdominal infection.

METHODS: For a 15-year period (March 1995 - March 2009) 482 emergency operations of intra abdominal infection have been performed. A retrospective study on medical records of group of 58 patients with oncological disease was performed, taking consideration of all clinical parameters that were supposed to influence the decision making for relaparotomy and to be related to disease outcome. Studied parameters included body temperature, general or local peritoneal reaction, leukocyte count, paresis of gastrointestinal organs and presence of intestinal content in peritoneal drain fluid. A new quantitative index was introduced to evaluate the necessity for emergency relaparotomy.

RESULTS: The average time for anastomosis insufficiency occurrence was 4.5 ± 1.7 days. The onset of the first clinical signs associated with this complication and the evaluation of the need for second operation were determined on the basis of criteria introduced by us. That consequently turned out to be statistically significant in decision making for second laparotomy ($p=0.022$). In this retrospective study, no relationship between empirical antibiotic therapy and either the decision for relaparotomy ($p=0.655$) or clinical outcome ($p=0.431$) was established. There was no statistically significant association between patients with one surgical intervention and those with relaparotomy due to anastomosis leakage ($p=0.34$).

CONCLUSION: The evaluation of the postoperative complication and the condition of every patient that needs relaparotomy is not possible without the active surveillance from the surgical team. Complementary diagnostic methods could assist in decision making for reoperation but could also provide falsely negative information and therefore, to result in considerably delayed relaparotomy. In such conditions, the benefits of antibiotic therapy would be insignificant and the clinical outcome - poor.

Key words: peritonitis; intra-abdominal infection; index; decision making; relaparotomy; evaluation.

INTRODUCTION

Anastomotic leakage is essential for postoperative mortality and the quality of life of patients with colorectal surgery for peritonitis. According to literature data this mortality could attain 30% after the postoperative complication is diagnosed (1-8). The leakage of intestinal content from drains or the abdominal wall is a critical moment in its detection at an earlier stage

(9) and frequently requires one or more operative interventions accompanied by prolonged intensive care and hospitalization. In some patients, the temporary colostoma becomes permanent and in those with restored intestinal passage, functional disturbances are sometimes reported (10).

Many studies have focused on factors, leading to anastomotic leakage, including surgical technique flaws, methods for diagnosing the insufficiency and its prevention in high-risk groups (3-15). Nevertheless, the clinical diagnosis remains atypical and requires active surveillance for several days (16), but when it

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becomes obvious, concomitant organ disorders could be already present. Therefore, the issue for diagnosing an occurring postoperative event and the subsequent surgical intervention is still important today.

The present retrospective study aimed to investigate the time of onset and the causes resulting in postoperative complications of the anastomosis in patients operated for colorectal carcinoma complicated with peritonitis and to evaluate the outcome of performed complex therapy.

MATERIAL AND METHODS

Patients and operative methods

In the period January 1995 – December 2010, a total of 265 patients underwent a planned or emergency resection of the colon or rectum with subsequent ileocolic, colocolic or colorectal anastomosis in the Second Surgical Clinic of the University Hospital in Stara Zagora, Bulgaria.

The planned operative intervention included removal of the neoplasm with restoration of the passage. Preoperatively, 58 (22%) of patients showed clinical and instrumental evidence of diffuse, secondary, purulent peritonitis from perforated carcinoma of the colon or the rectum.

In the group of 58 patients, the time interval from the onset of complaints at home and the operation varied from 6 to 72 hours (mean 49.21 ± 23.60 , median 48 hours). The anastomosis was performed after removal of the neoplasm and the collected pus. All patients were with locally advanced disease.

In 50 out of 58 patients (86%) the oncological disease affected the colon whereas in the other 8 (14%) comprised the upper third of the rectum. The sex distribution of patients in this group was as followed: 39 men (67%) and 19 women (33%) at the age of 21 to 83 years (median 64 years, mean 58.9 ± 16.6 years) (**Table 1**).

Table 1. Demographic and clinical parameters of colorectal cancer patients, included in the survey

| <i>Parameter</i> | <i>Number (%)</i> |
|----------------------------------|-------------------|
| <i>Sex</i> | |
| Men | 39 (67%) |
| Women | 19 (33%) |
| <i>Age</i> | |
| Mean \pm SD (years) | 58.9 \pm 16.6 |
| Range (median) | 21–83 (64.0) |
| <i>Type of surgery</i> | |
| Right resection | 14 (24%) |
| Intermediate resection | 7 (12%) |
| Left colectomy | 19 (33%) |
| Sigmoid resection | 4 (7%) |
| Anterior resection of the rectum | 14 (24%) |

Right resection was performed in 14 (24%), intermediate resection in 7 (12%), left colectomy with anastomosis in 19 (33%), anastomosis after resection of the sigmoid in 4 (7%) and colorectal anastomosis in 14 (24%) patients. The studied group of 58 patients was admitted to the clinic in emergency. Each patient went through a standard preoperative preparation including clinical and laboratory analysis, ECG, chest radiography, abdominal sonography and consultation with an anesthesiologist. Prior to induction in anesthesia, patients received a first intravenous antibiotic dose including cephalosporin and Metronidazole. The anastomosis type (end-to-end or end-to-side) depended on surgeon's preferences. The restoration of the intestinal passage was done

manually observing the commonly accepted rules for simple or continuous suturing. In 34 patients (58.6%) there was no postoperative complication. Thirty-seven operations (64%) were performed by surgeons with two specialties, and the other 21 (36%) – by surgeons with one specialty.

Postoperative feeding of patients was initiated after removal of the gastric tube and categorical evidence for restored flatus. During the first seven postoperative days, the following parameters were recorded: tachycardia, blood pressure, heart rate, temperature > 38 oC, local or diffuse peritoneal reaction throughout the clinical examination by a specialist, leukocytosis

> 14×10³/mL, adynamic ileus (> 2 days) proved by radiography, increased gastric emptying rate (more than 400 mL/24 h) or vomiting. All patients were actively observed by a surgeon during the first 120 post operative hours, including the weekends. Additional instrumental examinations in the early postoperative period such as radiography or computed tomography were performed only if signs of anastomotic leakage were present. Thirty-four (58.6%) patients from the group with severe peritonitis and concomitant oncological disease underwent only one operative intervention according to surgery standards, and in them, no postoperative complication has occurred.

Surgical interventions in patients with severe peritonitis were divided in two groups according to team's qualification: group A – 36 patients were operated by surgeons with one specialty and group B – 22 operated by surgeons with more than one specialty. In the medical records of patients, all mentioned parameters that were then used in the analysis were written down by the surgeon. In 24 patients (41.4%), postoperative complications have occurred due to the following reasons: anastomosis leak in 15 patients (62.4%), postoperative ileus in 7 (29.2%), wound dehiscence in 1 (4.2%) and intestinal wall injury during the first surgery in another one (4.2%). Eighteen patients (75%) underwent emergency emergency laparotomy. In 3/15 patients (20%) a partial insufficiency was present and another 3/7 (29.2%) were treated for postoperative ileus by medication. The mean period between the first operation and the relaparotomy was 16.6±24.1 days (range 2 to 77 days, median 6 days).

Urgent relaparotomy was performed observing the minimum diagnostic and clinical algorithm of examinations (ECG, abdominal radiography, echosonography of abdominal organs and retroperitoneal cavity, complete blood counts and blood biochemistry).

During the operative interventions, the following procedures have been performed: mechanical cleaning of exudate and formed fibrin deposits, removal of devitalized tissues in the region of anastomosis, in cases of anastomosis insufficiency the intestinal passage was restored once again and a protective colostoma was created. By the end of the operation, the peritoneal cavity was drained and the operative wound – sutured.

The overall postoperative mortality rate was 5.2% (3/58). One patient died after the emergency second laparotomy and in another two, the lethal issue occurred without second operations.

Evaluation of the severity of patient's status

The status of each patient was assessed twice: prior to the first operation and prior to emergency second laparotomy. The initial evaluation was scored according the Mannheim peritonitis index (MPI) (15, 16).

Antibiotic therapy

A preoperative empirical antibiotic therapy was prescribed to each patient, including a first generation cephalosporin and Metronidazole.

Microbiological analysis

Specimens from the peritoneal cavity were collected, stored and send for microbiological examination in the Microbiology Lab at the University Hospital, Stara Zagora during the first operation and the emergency second laparotomy.

Statistical analyses

Statistical analyses were performed by means of statistical software, StatView[®] v 4.53 (Abacus Concepts Inc., Berkeley, California, USA). Descriptive statistical parameters included: the mean, median, standard deviation (SD), standard error (SE) and 95% confidence intervals (95% CI). The differences between means were evaluated by unpaired t-test for 2 independent groups and ANOVA for more than 2 independent groups.

The frequency of categorical variables in studied groups was evaluated in 2×3 and 2×2 contingency tables and compared by Pearson Chi-square test (Pearson χ^2 test). When the number of observations was <5, Fisher's Exact test was applied in at least one of the four fields of 2×2 contingency tables.

Survival curves were plotted according to Kaplan-Meier's procedure, and differences were evaluated in the Mantel-Cox (Log-rank) test.

In all analyses, differences were considered statistically significant at the $p < 0.05$ level.

RESULTS

The initial hematological and blood biochemical parameters and deviations from the reference ranges in the studied group of 58 patients are presented in **Table 2**.

Table 2. Initial haematological and blood biochemical parameters in patients with severe purulent peritonitis and a concomitant oncological disease of the colon and the rectum.

| Parameter | Patients median) | Mean ± SD (range, |
|---|---------------------------------------|------------------------------|
| Haemoglobin (g/l) | | 126.3±26.1, (53-175, 130.5) |
| Haemoglobin normal anaemia | 37 (63.8%) 21 (36.2%) | |
| Leukocytes (10 ⁹ /l) | | 11.97±4.15, (1.3-25.1, 11.7) |
| Leukocytes normal counts leukocytosis | 30 (51.7%) 28 (48.3%) | |
| Serum total protein (g/l) | | 64.0±11.9, (35-88, 65) |
| Serum total protein hypoproteinaemia normal values | 31 (53.4%) 27 (46.6%) | |
| Serum Na ⁺ (mmol/l) | | 139.7±5.7, (123-151, 141) |
| Serum Na ⁺ - groups Hyponatraemia Normonatraemia Hypernatraemia | 1 (1.7%) 51 (87.9%) 6 (10.0%) | |
| Serum K ⁺ (mmol/l) | | 4.35±0.67, (3.2-6.0, 4.3) |
| Serum K ⁺ - groups Hypokalaemia Normokalaemia Hyperkalaemia | 8 (13.8%) 29 (50.0%) 21 (36.2%) | |

Although 21 patients exhibited anemic and another 31 hypoproteinaemic syndrome, this did not result in any statistically significant correlation between them and the occurrence of anastomotic leakage, persisting adynamic ileus ($p>0.05$, χ^2 -test) and/or urgent relaparotomy ($p>0.05$, χ^2 -test). Regardless of that, 12 patients were reoperated after evidence of anastomosis insufficiency and one – due to operative wound dehiscence. Injured abdominal wall necessitated the relaparotomy in one patient and in another three the cause was adynamic ileus that could not be overcome with medications. Thus, the overall number of patients with second operation was 17.

The parameters controlled during the early postoperative period correlated neither with the occurrence of early postoperative complication ($p>0.05$, χ^2 -test) nor with the necessity for relaparotomy ($p>0.05$, χ^2 -test).

The body temperature of patients in the early postoperative period was also included in the

database and processed parameters. Although the period of measurement ranged between the 24th and the 120th hour, this clinical parameter was not statistically significant ($p>0.05$).

Using the commonly introduced Mannheim peritonitis index (15, 16) the clinical severity of the disease was evaluated in all 58 patients prior to the first operation and a second evaluation of the same parameters was done in the 17 patients with indications for relaparotomy. The average score in the entire group ranged between 9 and 32 points (mean 20.07 ± 4.9 ; median 19.5). On the basis of this assessment and acknowledged values, it was found out that 4 patients (7.0 %) were with scores ≤ 20 indicating low severity, 44 patients (75.8 %) had medium scores (21-28), and 10 (17.2%) patients had initial high MPI scores (≥ 29). It should be noted that 4/24 patients (16.7%) with initial local inflammation have developed postoperative complications, but yet, the latter predominated in patients with diffuse peritonitis (16/24, 66.7%).

The performed statistical analyses did not establish an association between preoperative scores and the occurrence of postoperative complication ($p=0.309$, χ^2 -test), and/or the need for relaparotomy ($p=0.599$, χ^2 -test).

As to the anastomosis technique (simple or continuous suture) as a cause for postoperative complication, no relationship between these two parameters has been observed ($p=0.684$, χ^2 -test). The complications in the group with continuous suture were however less – 39.5% (15/38), as compared to cases when simple sutures have been used – up to 45% (9/20).

On the basis of clinical observations during the early postoperative period in patients with relaparotomy, we introduced additional parameters for evaluation of disease severity to those already included in the Mannheim peritonitis index. They included: the time from the appearance of the postoperative complication in hours, amount of secreted fluids from drains in ml, persisting blood hemorrhage from drains or from the abdominal wall for more than 48 hours and paresis of abdominal organs. Each parameter was

numerically scored with 1 point and the sum of points for each patient was added to the individual MPI score (15, 16). Thus, the newly obtained thresholds for the severity of patients' state in the postoperative period were as followed: ≤ 24 – I degree; 25-32 – II degree and ≥ 33 – III degree. On the basis of the new scoring system, the severity of the disease was evaluated as first-degree in 34 (58.6%) patients, second degree in 16 (27.6%) and third degree – in 8 (13.8%) patients. The newly introduced score for disease severity allowed a subsequent more precise evaluation of the individual status of patients with relaparotomy due to postoperative complications.

The comparison of both indexes (the standard MPI and the modified index) as criteria for evaluation of the clinical risk in the postoperative period and decision for second operation showed that the values of the commonly used Mannheim peritonitis index were not statistically significant ($p=0.599$, χ^2 -test). The introduction and analysis of the new criteria and the resulting new threshold scores in the early postoperative period were found to be very significant for the need for emergency second operation ($p=0.0006$, χ^2 -test) (**Figure 1**).

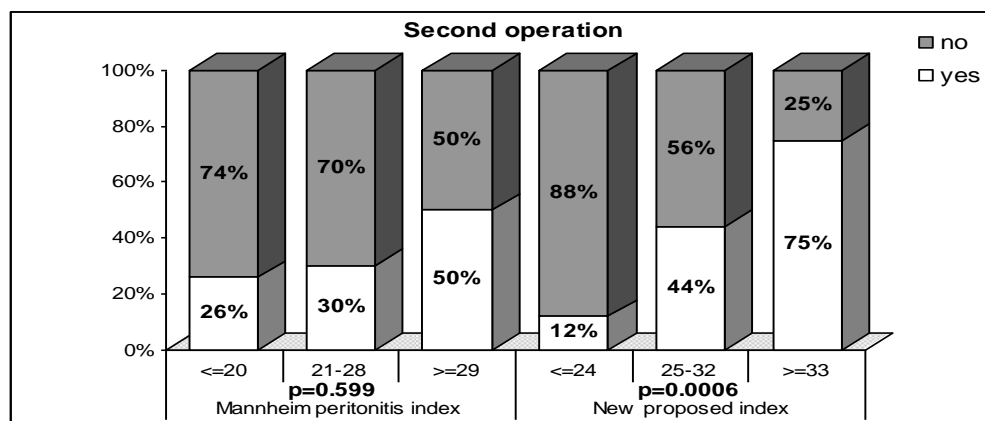


Figure 1. Criteria for clinical relevance and evaluation of the need for emergency emergency second laparotomy according to the commonly used Mannheim peritonitis index and the newly proposed index (χ^2 test)

The mean period of hospitalization of patients with one operation was 17 ± 3 days whereas in the group with occurred complications – slightly longer – 21 ± 4 days. The parameters related to the hospital stay of patients with severe peritonitis did not exhibit statistically significant difference between the group with one operation and the groups with relaparotomy ($p > 0.05$,

ANOVA test). The qualification of the surgeon is directly related to the quality, nature, efficacy and the duration of the hospital treatment. In this

study, a correlation was found between the anastomosis insufficiency and the qualification of surgeons ($p=0.006$). Thus, 11 patients from group A were with anastomotic leaks as compared to only 2 with the same complication in group B (**Figure 2**).

It turned out that 83.33% of all postoperative complications occurred (operative wound dehiscence, anastomotic leakage, cutaneous and subcutaneous inflammations in the region of the operative cicatrix, bronchopneumonia, sepsis, myocardial infarction and hepatorenal

syndrome) were in patients operated by colleagues with one specialty whereas the

respective percentage for teams with two specialties were only 16.66%.

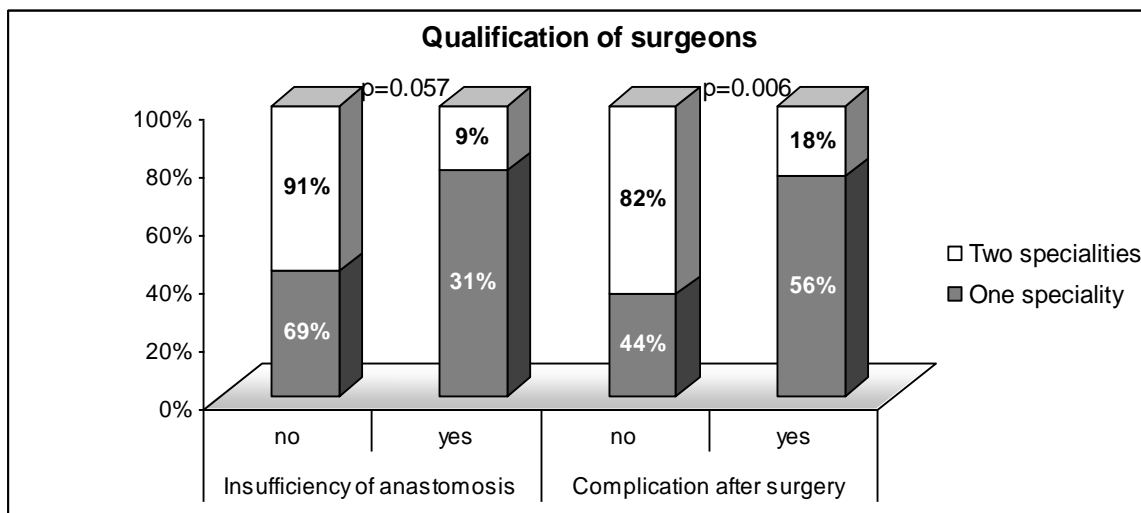


Figure 2. Development of anastomosis leaks in relation to operating surgeon's qualification

During their hospital stay, all patients were treated by intravenous application of antibiotics that, based on the anamnesis and instrumental examinations, consisted of cephalosporin and metronidazole. This way we were able to monitor the efficacy of antibiotic therapy from the very beginning. In 3/58 patients, the applied antibiotic was changed in the early postoperative period as in these cases, resistant Gram-negative aerobes: *Echericia coli* and *Pseudomonas aeruginosa* were involved. Two patients received third-generation and one – a fourth-generation cephalosporin. The therapy was also completed with the second-generation antifungal agent Diflucan. At this stage we could not affirm whether the presence of poly infection in patients with severe peritonitis and oncological disease has influenced the occurrence of postoperative complications. Nevertheless, as seen from this study, the involvement of more than one microbial pathogen did not affect significantly the duration of the hospital stay.

We were able to answer whether the initial antibiotic therapy was effective and whether it was related to the need for second emergency operation and the clinical outcome of the disease. In this study, the empirical antibiotic therapy of patients had a significant effect neither on the decision for emergency laparotomy ($p=0.655$, χ^2 test), nor on the clinical outcome ($p=0.431$, χ^2 test). The duration

and/or change in antibiotic therapy in patients with severe peritonitis was shorter in group B than in patients operated by surgeons with one specialty (group A). Thus, 45% of patients from group B received 5-6 day therapy and only 9% – 7-day therapy. On the contrary, 33% of patients from group A received antibiotics for more than 7 days and in the other 47% the therapy ended between the 5th and the 6th postoperative days ($p=0.039$) (**Figure 3**).

The comparison of Mannheim peritonitis index and the newly proposed index showed that MPI had a higher statistical significance ($p=0.0001$, χ^2 -test) with regard to the need for change in antibiotic therapy than the index proposed by us ($p=0.022$, χ^2 -test). Thus, 17.4 % of studied patients needed change in their antibiotic therapy (**Figure 4**).

As mentioned above, during the first operation it was observed that inflammation has affected 2/3 of the peritoneal cavity in 76% (44/58) patients (diffuse peritonitis); in 10 (17%) all abdominal organs were involved (total peritonitis) and in only 4 cases (6%) the purulent process was local. Regardless of the expectations for a closer relationship between the distribution of inflammation and the probability for subsequent postoperative complication (more specifically, for anastomotic leaks), such correlation was not found out ($p=0.449$, χ^2 -test).

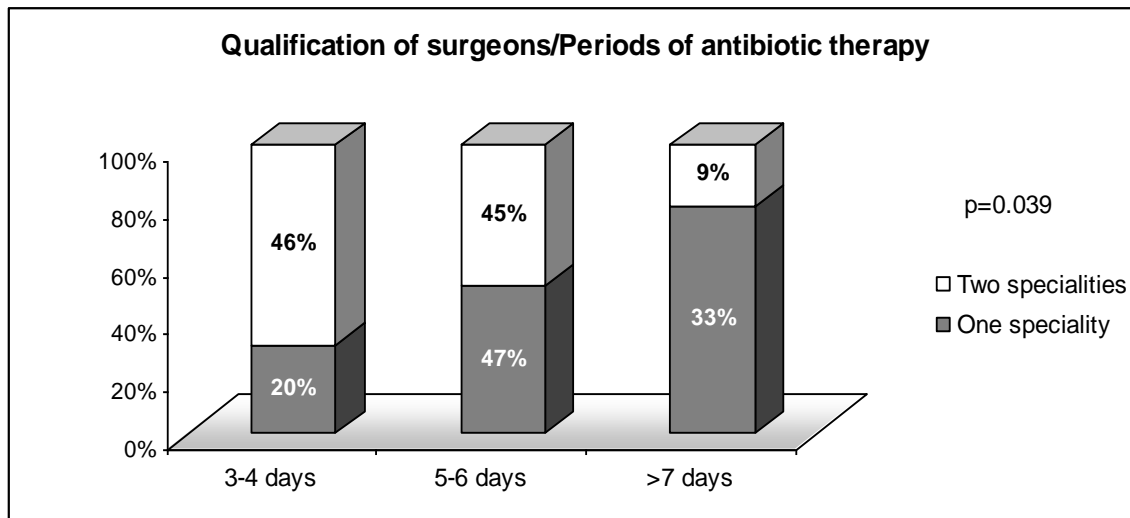
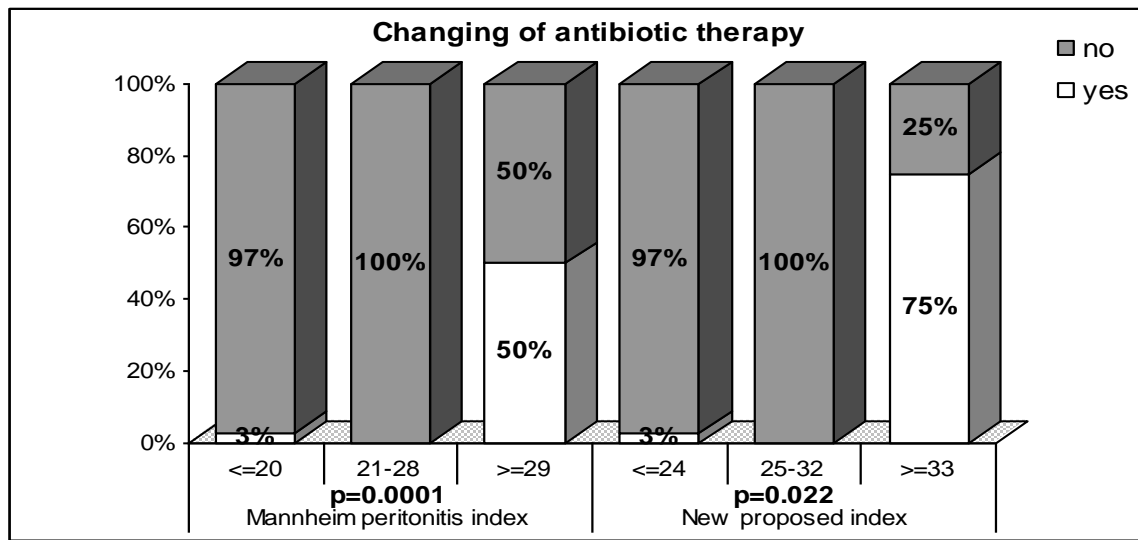


Figure 3. Duration of antibiotic therapy in relation to surgeon's qualification



Change in antibiotic therapy

Figure 4. Evaluation of the need for change of antibiotic therapy with relation to the commonly used Mannheim peritonitis index and the newly proposed index (χ^2 -test)

On the basis of general and local signs, anastomosis leaks was diagnosed in 15 patients (25.86 %). In another 6 (10.34 %) this postoperative complication was established by means of radiography and computed tomography. For the first group of 15 patients, relaparotomy was necessitated in 11, while in the other four the treatment consisted in local lavage and aspiration. Insufficiency was most frequently present in patients with anterior rectal resection and extraperitoneal anastomosis. Ileus paralyticus was diagnosed instrumentally in 7 patients and second laparotomy was done in 2 of them. The other 4 were treated conservatively.

On the basis of all presented data and the results of statistical analyses, it could be concluded that anastomotic leaks remained the primary cause for second laparotomy ($p=0.025$, χ^2 test), and that the newly introduced index was a powerful prognostic factor with a high statistical significance ($p<0.0001$, χ^2 test).

There was no correlation between the time of second emergency laparotomy and the duration of the hospital stay ($p=0.34$). The mortality in the second emergency operation group was 5.88 % (1/17). This way, the time between the two operative interventions was not statistically

significant ($p > 0.05$). The hospital mortality in the entire group of patients with severe peritonitis consequently to complicated colon or rectal carcinoma was 5.17% (3/58 patients).

The survival rates in patients in connection to the primary disease that resulted in development of severe peritonitis, showed a statistically significant difference in survival related to the stage of disease ($p < 0.0001$), as well as, to the

additional prognostic factors included in the new index for evaluation of the postoperative status.

We have categorized two groups of patients: group A with a low score prior to the laparotomy and group B – with a high score. The statistical analysis showed that the survival was more significant in the first group as compared to patients with higher index scores ($p < 0.013$) (Figure 5)

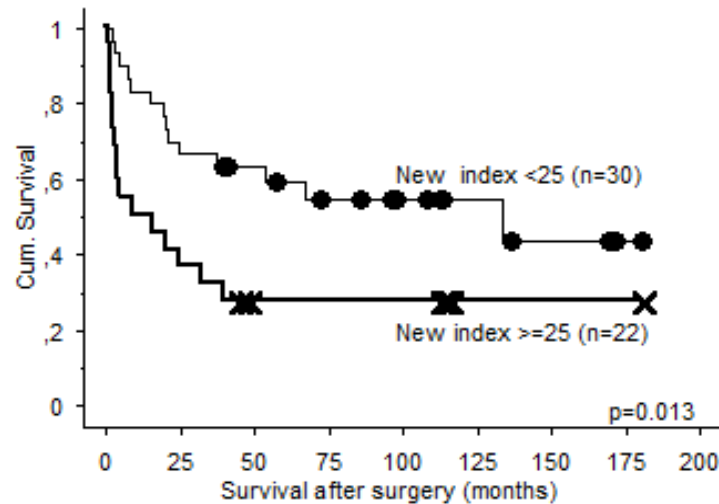


Figure 5. Survival of patients after second emergency laparotomy with low values of the postoperative index ($p < 0.013$)

The analysis of the interaction of the new index and survival rates in patients with second emergency laparotomy showed an association mainly for patients in initial stage of the disease and severe peritonitis ($p = 0.065$, Fig. 6). On the

contrary, the survival in the groups of patients with advanced disease was not influenced by the parameters included in the new index ($p = 0.546$, Figure 7).

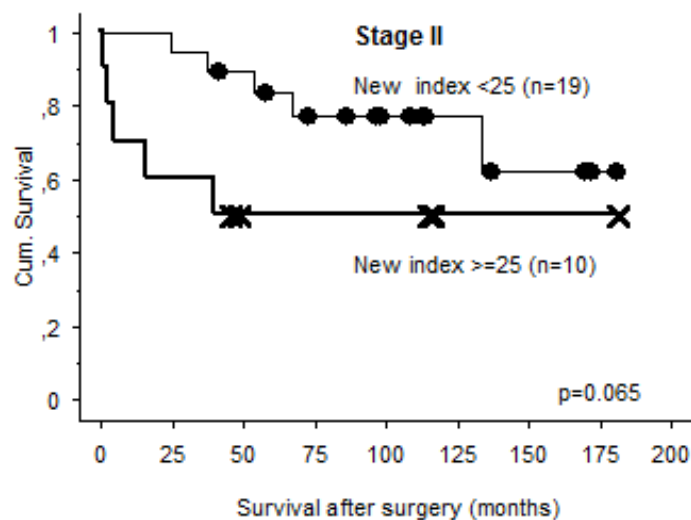


Figure 6. Survival of patients in clinical stage II on the basis of the newly proposed postoperative index for evaluation of the clinical severity of the disease ($p = 0.065$)

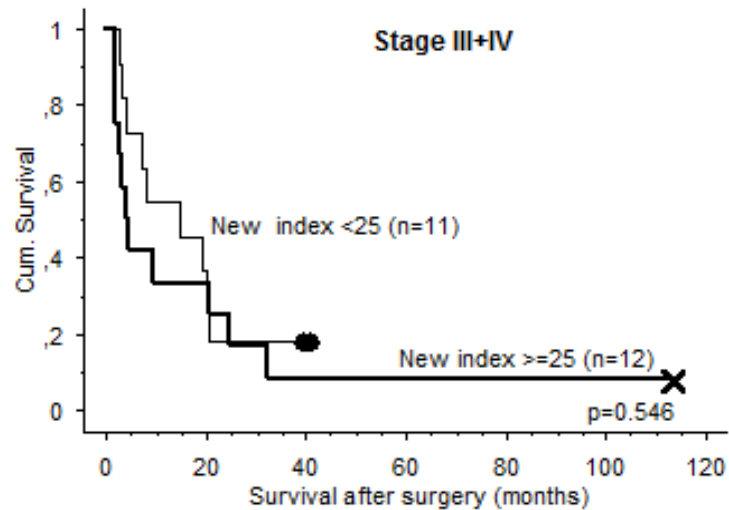


Figure 7. Survival of patients in clinical stages III and IV on the basis of the newly proposed postoperative index for evaluation of the clinical severity of the disease ($p=0.546$).

DISCUSSION

In this survey including 58 patients with severe peritonitis as a complication from colorectal carcinoma, 17 were submitted to emergency second operation due to anastomotic leakage. The average time for active observation in patients was 4.5 days. This period is similar to data reported by Sutton et al. for duration of 4 days (14). Having studied the risk for occurrence of insufficiency, Alves et al. (17) have established that the presence of 3 or more parameters was accompanied by insufficiency in 67% of patients. In the postoperative period, a part of patients with severe peritonitis are still producing toxins and toxic exudates containing bacteria and detritus masses that maintain the infection (18 - 25).

The observed deviations in studied parameters resulted in clinical signs and symptoms requiring a re-evaluation of the clinical status. This motivated us to analyze the importance of these parameters and to elaborate an evaluation scoring system. Thus, at the very beginning, we were able to determine criteria that were directly related to and important in decision making for relaparotomy. Furthermore, data about statistically significant parameters for evaluation of the need for second operation, available in the medical literature, are rather contradictory (17). We have introduced a numerical score, that, added to the standard preoperative score, has generated a new index for postoperative

evaluation of the severity of the clinical status in patients with indications for second laparotomy. In this survey, a thorough review of clinical and laboratory indices prior to and after the second operation was performed, looking for a relationship between them, the second operation and the clinical outcome. Such a relationship was not established, suggesting that the investigation of these clinical parameters was not necessary in future retrospective studies, performed by others as well.

In a number of reports, the use of radiography for diagnostic imaging of anastomotic leakage was questioned (25). Contrast radiography was performed in 6 patients and although it provided additional information to the tentative diagnosis, it caused also a delay of relaparotomy with more than 24 hours. This fact also put forward the question about the need for radiography and its importance in decision-making for relaparotomy. The retrospective clinical survey performed by Nicksa et al. (22) has discussed the informativity of diagnostic imaging in detecting anastomotic leakage in 36 clinical cases and concluded that radiology assisted for identification of the problem in only 3/18 (17%) patients. In the other 18 cases, anastomotic leaks were identified only by computed tomography. Further, false negative data were obtained in 52% of cases when radiology was used. Another study in 16 patients showed that even when radiological evidence for anastomotic insufficiency were present, the interpretation of images was not properly done

(23). Similar sensitivity was recorded by Akyol et al.(24) in 233 patients with left colostomy. After the contrast enema, false negative results was observed in 22% of patients (11 out of 51 with leaks). Despite the radiography performed, it did not result in performance of emergency relaparotomy but on the contrary, the second surgery was delayed for several days (24). Here arises the question about parameters, influencing the decision making for relaparotomy in patients with anastomotic insufficiency (28 - 34). In a large part of our patients, the causes were the presence of intestinal content in drain fluids, accompanied with increased peritoneal irritation and/or progressing paresis of gastrointestinal organs. These clinical signs were leading with regard to the decision for relaparotomy. On the basis of these facts, we have developed a numerical scoring system to evaluate the postoperative parameters described above and that later turned out to be essential in our evaluation for the need of relaparotomy. Thus, our decisions were better motivated and there were no flaws in our evaluation of the need for emergency second operation.

It was interesting to find out whether this parameter was important in decision making or it was a precise, but relatively late sign, that together with earlier positive signs has made second emergency laparotomy inevitable. The clinical evaluation was further challenged by the multiple prognostic signs and the decision implied assessment of these parameters and of the probability of the event (for instance, the presence of intestinal content). In addition, we had to calculate the optimal moment when the benefit of the operation would be higher than the probability for occurrence of complications. The decision for reoperation should always appear correct if it was not associated with significant mortality and what is worse, with mortality following emergency operation. The issue was to identify when the risk of death due to disease was higher than the risk related to the surgery. The acknowledged risk factors and systems for evaluation of severity of disease as APACHE II, the use of corticosteroids or the need for massive blood transfusion are preliminary parameters that reduce the probability for a strong anastomosis (3, 5, 7, 10, 11).

Unlike these reports, our survey has shown that the index for evaluation of clinical severity of patients' postoperative status, developed by us, was highly statistically significant and relevant with regard to subsequent second laparotomy. It

was also shown that this index was not influenced considerably by prognostic factors mentioned above and at the same time, was directly related only to data about the function of gastrointestinal organs. Thus, the newly proposed index for evaluation of the clinical severity in the early postoperative period became most important in the decision making for relaparotomy in patients with occurred complication.

When investigating the relationship of the new index to survival rates, we have found out that despite the existing literature data about the ontological disease stage and survival, this parameter was important for the outcome of the disease only in association with the severity of the inflammation in the postoperative period. Thus, the survival in patients with advanced ontological diseases (stage III and IV) was not influenced by main index categories ($p < 0.001$). The appearance of ileus or non treatable gastrointestinal paresis in the early postoperative period, peritoneal irritation with increasing high leukocytes, additionally aggravated and increased this risk, and also, were preoperative parameters that influenced the decision for second operation in these patients.

These clinical signs could be however falsely positive and thus, could be reasons for unneeded and high-risk second surgery. In this study, their complete diagnostic evaluation including sensitivity, specificity and positive/negative predictive values was not possible. Nevertheless, these clinical signs have been analyzed in 655 patients in the study of Alves et al. (16), and have raised a number of contradictory views as to the insufficiency of anastomosis after colorectal surgery and the need for emergency second operation. Although the data are obtained in planned operations, two days before the anastomotic leak was established, a major part of patients were with increased body temperature, and with no evidence for recovery of intestinal peristalsis for 4 days. In support of this, our survey did not establish a statistically significance of high leukocytes as a prognostic factor influencing the decision for relaparotomy. Therefore these parameters become high-risk factors in the evaluation of the need for second operation.

The statistical analysis performed by us aimed to determine, among described clinical signs, those risk factors that could lead to a proper decision for each individual patient. As far as we know,

there are no other publications dealing with these parameters and this made possible to determine the incidence of a possible risk for anastomosis leakage and the clinical risk for the patient.

In the postoperative period, some of the patients were still producing toxins and toxic exudates containing bacteria and detritus, maintaining the infection (18, 35, 36), and the antibiotic treatment aimed at the eradication of microbial agents involved.

The necessity for antibiotic therapy in patients with severe peritonitis and the decision on whether to apply one, two or more antibiotics is still important. Clinical experience has shown that surgeons choose antibiotics on the basis of anticipated presence of bacteria. In this survey we were able to determine the outcome of antibiotic therapy that included two antibiotics (cephalosporin and Metronidazole). Some investigations on that subject showed a similar or better outcome for patients treated with a single drug against multiple drugs. The studies of Huiziga WK *et al.* in patients with peritonitis and sepsis (25), demonstrated a satisfactory response in 82% of patients treated with Cefotetan, vs 65% in those treated with Ampicillin, Gentamicin and Metronidazole. There are other reports stating that the double antibiotherapy was not better or was equal to the application of a single broad-spectrum antibiotic (27, 28, 29).

The present study confirmed the efficacy of the empirical double antibiotic therapy in patients with severe peritonitis and oncological disease of the colon and rectum, although antibiotics were changed in 3 patients postoperatively. According to our data, the outcome was influenced by the choice and the appropriateness of the antibiotic used. This fact makes empirical treatment a method of choice between treatment initiated during or after the operation. On the other side, if not adequate, the empirical treatment appeared to be related to a poorer outcome. In this study, the period between sending the materials for examination and obtaining the microbiological results was the factor that influenced the outcome. It was found out that if this time interval was > 4 days, all further manipulation or change in antibiotic therapy were useless. It was also established that antibiotics that were initially chosen by the surgeon were unlikely to be replaced after receiving the information from the microbiology lab. The causes could be the lack of trust in the ability of the microbiological analysis to identify all pathogens in the exudates, the lack of trust in data about the sensitivity of

anaerobes and the contemporary recommendations for antibiotic coverage advanced by “authorities” on peritonitis treatment. According to Solomkin JS *et al.*, the routine coverage of Enterococci in patients with community-acquired intra abdominal infection is not needed as many prospective studies have not shown any advantage of this therapy with regard to survival. Such a therapy should be however used in patients with hospital-borne infections (30). This is in support of the present surgical practice for treatment of bacteria that are anticipated and usually present, instead of controlling bacteria that could be isolated in the lab. This approach of ours would be as good as or better as the treatment of patients according to the results of culturing in this study.

We could not however affirm whether the duration of the preoperative administration of antibiotics has influenced the lethal outcome or not. The retrospective clinical investigation of Kumar A *et al.* has shown that each hour of delay in antibiotic therapy increased hospital mortality with 7.6%, but the control of the infection agent was found to be the limiting factor for the outcome (33).

The issue of the effect of hospital stay duration upon the outcome of the treatment has been discussed in a number of publications, whose results, unlike ours, have established an effect of the antibiotics chosen upon the duration of hospitalization on one part, and on the occurrence of postoperative complications on the other (31,32,33). The death of 3 of our patients, including one after the second emergency laparotomy, did not influence the duration of the hospital stay.

The operation itself and even the drainage could also explain the achieved excellent results. There are data evidencing that the mortality rate in patients with prolonged preoperative preparation prior to the second operation was higher as compared to patients treated surgically during the first 24 hours after detecting anastomotic leaks. The present study could not confirm the importance of this time interval for the outcome of the disease because of the few patients that died. Yet, the urgent second laparotomy in patients with detected anastomotic leaks has reduced considerably the spread of the inflammation in the peritoneal cavity and in the organism and the related lethality.

From the very beginning, patients with severe peritonitis exhibited clinical signs related to

insufficiency of colonic anastomosis, although the time to the emergency second operation remained relatively long (median 48 hours). The double antibiotic therapy is advantageous to the triple one, if it covers both aerobic and anaerobic infection. In the early postoperative period, the surgical team should actively observe the patients with a number of deviations in their status or such in whom technical difficulties in anastomosis were met. A thorough interpretation of radiology data is necessary and comparison with clinical parameters introduced by us with regard to a more accurate evaluation of anastomosed intestinal segments. The adequate evaluation of the clinical status by means of the newly introduced postoperative index has assisted a lot the decision making for a timely and synchronized emergency second laparotomy.

CONCLUSION

We have introduced in the clinical practice new clinical indices and have developed a protocol taking into consideration the occurring intra abdominal complications. The newly proposed index turned out to be with higher statistically significance as compared to the parameters used so far for evaluation of the postoperative clinical risk. We assume that its introduction by other teams working on treatment of severe peritonitis would assist for its adequate use in the clinical practice. Apart the criteria discovered by us, the vigilance and the careful appraisal of clinical signs after surgery depend mostly on the qualification of the surgical team, especially in patients with a performed anastomosis in conditions of severe peritonitis.

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