

## Application of the Program of Enhanced Recovery in Surgical Treatment of Patients with Colorectal Cancer Complicated by Acute Obstruction (Our Experience)

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### Abstract

Over the last years, the number of publications devoted to the concept of enhanced recovery after surgery (ERAS) in emergency abdominal surgery application increases. The purpose of this study was a comparative analysis of the results of the ERAS-program application in surgical treatment of the patients with colorectal cancer complicated by large bowel obstruction (LBO).

The study included 89 patients with obstructive colorectal carcinoma (OCRC), divided in the ERAS and control group (n=45 and n=44, respectively).

During the treatment of the patients of the ERAS group in preoperative period, the following measures were taken: patient information, his psychological preparation, prevention of postoperative pain, nausea and vomiting, thromboembolic and infectious complications. Intraoperative measures included local anaesthesia of the skin in the line of laparotomy access, colon and small (under indications) intestines decompression, small intestine lavage, embryology oriented surgery and D3 lymphadenectomy, temporary installation of polyurethane catheter distal to the ligament of Treitz for early enteral nutrition, rectus sheath catheterization to carry out rectus sheath block of the anterior branches of the spinal nerves, control drainage installation into the small pelvis. In postoperative period, the early mobilization, urinary catheter and drainage removal after the patient transfer from intensive care unit were carried out.

The following criteria were used as the criteria for comparative evaluation: pain syndrome intensity, need for analgesics, time of enteric deficiency arresting, postoperative complications and mortality, postoperative period duration, and patients' life quality after discharge from the hospital.

It has been established that the proposed original ERAS program for this category of the patients is safe and effective due to improving the immediate results of surgical treatment.

**Keywords:** Colorectal cancer; Large bowel obstruction; Enhanced recovery after surgery; Fast track

### Introduction

Colorectal cancer is the steadily occupying the leading positions in the structure of cancer morbidity in the world according to World Health Organization data [1-13]. A specificity of this pathology is a high incidence of life-threatening complications, the most frequent (up to 70%) of which is LBO. This complication develops in 20%-40% of the patients with CRC, the majority of which belongs to elderly and senile age group (50%-80%) and, as a rule, has an unfavorable premorbid status. In addition, an important clinical feature in case of colon obstruction is the lack of distant metastases in patients, which significantly increases the requirements for the surgical care organization and scope. A high incidence of postoperative complications (35%-50%), as well as a significant postoperative mortality, which can reach 50%, continues to persist [10,12-19].

In our opinion, it is necessary to distinguish three main components of the problem. First, the objective severity of the patients' condition (age, premorbid status) and the life-threatening complication that has developed as a result of oncological process, which inevitably causes the significant failures of basic metabolism and immune deficiency, which to a large extent determine the unsatisfactory short-term results. Secondly, the need for simultaneous solution during the emergency surgery of two, at first sight, incompatible tasks: severe complication elimination and oncological radicalism provision, which, as is known, is a significant and independent predictor of survival rate. Thirdly, low number, according to the world literature data, of effective and purposeful attempts to integrate modern achievements of elective colorectal surgery into operative measures system for the patients with LBO of tumor genesis.

One of the potential directions for improving the immediate results of surgical treatment of the patients of this category is concept of fast track surgery or enhanced recovery after surgery-ERAS, proposed more than 20 years ago by Henrik Kehlet [4-7]. Strongly demonstrating its absolute clinical and economic effectiveness in

elective surgery, this program, for different reasons, has not found general application in the surgery of complicated CRC at present. In some publications the preliminary results of clinical approbation of the ERAS within the surgical treatment of patients with LBO of tumor genesis are stated [8-15].

At the same time, the enhanced recovery program (ERP) application, with obvious advantages, can open broad horizons for operative interventions short-term results significant improvement in these patients.

The purpose of this study was a comparative analysis of ERP application results in the surgical treatment of patients with colorectal cancer complicated by LBO.

## Materials and Methods

A randomized clinical trial, previously approved by the Independent Ethics Committee, included 89 patients with LBO of tumor genesis, who were admitted by acute indications to the clinic of Navy Surgery Department of S.M. Kirov Military Medical Academy and St. Petersburg I.I. Dzhanelidze Research Institute of Emergency Medicine (St. Petersburg, Russia). Randomization was carried out using the tables of random numbers. The study included only the patients with decompensated colonic obstruction. Exclusion criteria were: widespread peritonitis, multiple organ dysfunction and associated complications of cancer (bleeding, perforation, abscess). In addition, with intraoperative detection of non-tumor causes of obstruction or tumor localization in the rectum, patients were also excluded from the study conducted.

All the patients (n=89) were divided into two groups: the ERAS group, in which the ERP was applied (n=45), and the control group, where the patients received traditional surgical treatment (n=44). Patients of both groups were comparable by sex, age, degree of operative and anesthetic risk (ASA), physiology and operative severity score, morbidity and mortality predictable (CR-POSSUM), comorbidity index (Charlson), tumor location and type of surgery (Table 1). All the patients included in the study performed partial resections of colon various parts with the total mesocolonectomy: right hemicolectomy or left obstructive resections (of Hartmann's procedure type).

Indicator	ERAS group (n=45)	Control group (n=44)	p
Age (Me)	70 (63.75; 80.25)	70.5 (61; 78.75)	0.515
Sex, n (%)			
Male	19 (42.2)	20 (45.5)	0.94
Female	26 (57.8)	24 (54.5)	0.973
Location of cancer, n (%)			
Cecum	7 (15.5)	6 (13.6)	0.923
Ascending	4 (8.9)	3 (6.8)	0.84
Hepatic flexure	1 (2.2)	2 (4.6)	0.55
Transverse	4 (8.9)	3 (6.8)	0.84
Splenic flexure	5 (11.1)	4 (9.1)	0.887

Descending	4 (8.9)	5 (11.4)	0.832
Sigmoid	12 (26.7)	10 (22.7)	0.91
Recto-sigmoid	8 (17.8)	11 (25)	0.778
Types of surgery, n (%)			
Right hemicolectomy	12 (26.7)	13 (29.5)	0.927
Left obstructive resection (of Hartmann's procedure type)	33 (73.3)	31 (70.5)	0.987
Duration of obstruction, day (SD)	3.8 ± 1.2	3.6 ± 1.5	0.45
Operative duration, min (Me)	175 (140; 222.5)	200 (151.25; 240)	0.822
Anesthesia duration, min (Me)	222.5 (183.75; 280)	260 (205; 290)	0.71
ASA, n (%)			
≤ 3	27 (60)	24 (54.5)	0.95
>3	18 (40)	20 (45.5)	0.91
CR-POSSUM			
Morbidity, % (Me)	52.5 (29.5; 71.75)	45 (37; 64.5)	0.229
Mortality, % (Me)	19.5 (10; 33.75)	21.5 (14.5; 34.5)	0.62
Co-morbidity index (Charlson), (SD)	8.13 ± 2.92	7.96 ± 2.15	0.26

**Table 1.** Patient characteristics and operative details

When treating the patients of the ERAS group, the following ERP components were used: in preoperative period-a detailed information about the patient's condition, planned surgery and postoperative period features, his training to do early postoperative follow-up activities, anterior abdominal wall skin marking (presumed and alternative) for possible colostomy, postoperative nausea, vomiting, as well as insulin resistance, thromboembolic and infectious complications prevention. Intraoperative activities included local skin anaesthesia in the line of laparotomy access, large and small (according to indications) intestines decompression, small intestines lavage with polyelectrolyte mixtures with antihypoxant, embryology oriented surgery and D3 lymphadenectomy, rejection of prolonged nasogastrintestinal intubation and temporary installation of polyurethane catheter distal to the ligament of Treitz for early enteral nutrition, one control drainage installation into the small pelvis and sheath of rectus muscle of abdomen catheterization with the aim of prolonged postoperative pain relief. In postoperative period, the early follow-up care measures were performed within the bed immediately after extubation in the intensive care unit, early vertical orientation, urinary catheter and drainage from the pelvis removal after the patient transfer to the surgical department. In addition, the use of opioid analgesics was excluded and the volume of targeted fluid therapy, which was terminated after the onset of early enteral nutrition, was minimized. The detailed ERP of the patients' in the ERAS group is presented in Table 2.

Preoperative period	Intraoperative period	Postoperative period
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<ul style="list-style-type: none"> <li>- detailed information to the patient (immediate family member), psychological training</li> <li>- front belly wall skin marking (presumed and alternative) for possible colostomy</li> <li>- mechanical preparation of the colon sub stenotic part (within the framework of conservative treatment)</li> <li>- postoperative insulin resistance prevention</li> <li>- postoperative nausea and vomiting prevention</li> <li>- thromboembolic complications prevention (compression stockings)</li> <li>- infectious complications prevention</li> <li>- pain syndrome prevention</li> </ul>	<ul style="list-style-type: none"> <li>- local infiltration anesthesia along the skin incision line</li> <li>- colon decompression</li> <li>- single-step decompression and lavage of the small intestine (under indications)</li> <li>- enteral therapy (polyelectrolytic mixtures, antihypoxants)</li> <li>- embryology oriented surgery and D3 lymphadenectomy</li> <li>- long-term nasogastrintestinal intubation rejection</li> <li>- temporary installation of polyurethane catheter distal to the ligament of Treitz for early enteral nutrition</li> <li>- small pelvis draining</li> <li>- sheath of rectus muscle of abdomen catheterization for postoperative pain relief</li> </ul>	<ul style="list-style-type: none"> <li>- early activation (a complex of rehabilitation actions within the bed immediately after extubation into the intensive care unit)</li> <li>- early vertical orientation (the first day of postoperative period)</li> <li>- urinary catheter removal after transfer to the clinic</li> <li>- drain tube removal from the pelvis in the first day after the surgery</li> <li>- early enteric nutritional support</li> <li>- volume and duration of infusion therapy reduction with enteral support increase</li> <li>- prokinetics usage</li> <li>- early oral nutrition</li> <li>- preventive antibiotics within 48-72 hours of postoperative period</li> <li>- postoperative multimodal analgesia (segmental anesthesia, NSAIDs, opioid analgesics rejection)</li> <li>- anticoagulants from the first day of postoperative period</li> </ul>
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**Table 2.** ERP components in the surgical treatment of patients with LBO of tumor genesis

The following indicators were analysed as the criteria for comparative evaluation of ERP approval results:

- pain syndrome intensity (numerical rating scale-NRS);
- time of enteral deficiency elimination (the noises of intestinal peristalsis occurrence, passage of flatus and stool, myoelectrical activity of the gastrointestinal tract);
- patient's readiness timing to be discharged after surgery (questionnaire QoR-40) [16];
- postoperative period duration;
- postoperative morbidity (frequency and severity of postoperative complications by Clavien-Dindo classification) [1];
- postoperative mortality;
- patients' quality of life after surgery (MOS SF-36 questionnaires, Barthel scale).

Myoelectric activity of the gastrointestinal tract was recorded by means of a computer gastroenterologist Gastroscan-GEM (Russia).

In addition, the percentage of activities was included in the guidelines for perioperative care in elective colonic surgery [3].

All the data were prepared and compiled using the Excel Microsoft Office 2010 computer program. A statistical analysis was performed in

Statistical 10.0 program. Data are analysed using the descriptive and analytical statistics. To test the nature of data distribution, the Kolmogorov-Smirnov test was used. A paired t-test was used to compare data between these two groups when they showed a normal distribution. The Mann-Whitney U test was used when the data did not have normal distribution. Pearson's  $\chi^2$  or Fisher's exact test were used for categorical data. A p-value less than 0.05 was considered as statistically significant. Most of the results are presented in the form of indicator median indicating 25<sup>th</sup> and 75<sup>th</sup> percentiles.

## Results

### ERAS group

The pain syndrome after surgery did not exceed 5-6 points on the first day with a gradual regression to 0.5-1 points to day 4-5. There was no need to use the opioid analgesics. A shorter period of the gastrointestinal tract functions recovery was observed in patients: nausea and vomiting absence, enteral feeding was started, on average, 36-48 h after the surgery, with intestinal peristalsis noise occurrence during the first day, and the passage of flatus-within 24-36 h, defecation-2-3 d after the surgery. The gastrointestinal tract (GIT) motor and evacuation functions early recovery, enteral deficiency timely elimination, as well as reliable pain management were clearly reflected in the results of 34 patients (75.6%) of this group readiness to discharge from hospital for follow-up care (outpatient therapy, day hospital) to day 5 of postoperative period objective assessment (under early postoperative complications absence). On average, the duration of postoperative period was  $8.67 \pm 1.7$  d. Eight cases of postoperative complications were noted: 6 are of I-IIIa grade and 2 are of IIIb-IV grade according to Clavien-Dindo classification. Mortality was 14% (n=6). The recovery to initial level of quality of life indicators, as well as physical and psychological components of health on day 30 after discharge from the hospital were observed in 29 patients (64.4%).

### Control group

The pain syndrome in the early postoperative period which reached 7-8 points was observed in 26 patients (59.1%), thus requiring use of opioid analgesics in 11 patients (25%). It should be noted that the majority of patients (n=36, 81.8%) have the pain syndrome at the level of 4-5 points for 4 days of postoperative period. The attention was given to GIT motor activity slow recovery, which was manifested by nausea and vomiting in 23 patients (52.3%) during 36-72 h after the surgery. In addition, the intestinal peristalsis noise occurrence was noted, on average, only to the end of day 2, the onset of flatus passage-2-3 d and defecation-3-4 d, respectively. Objective readiness for discharge from hospital, based on the questionnaire, was registered on day 9 of postoperative period, the average duration of which was  $14 \pm 2.3$  d. 13 cases of early postoperative complications were registered: 8 are of I-IIIa grade and 5 are of IIIb-IV grade according to Clavien-Dindo classification. It should be noted that to correct postoperative complications, 4 patients (9%) required relaparotomy. Postoperative mortality was 25% (n=11). Quality of life indicators were reduced, mainly due to self-care ability, pain, emotional and social functioning slow recovery incidence

The incidence of increasing multi drug-resistant tuberculosis and emergence of extensively drug resistant tuberculosis presents a tremendous challenge for global effort to battle with tuberculosis [13]. It is not feasible to measure incidence by counting cases arising in cohorts under continuous observation because such studies would

require cohorts of hundreds of thousands of people. According to the previous studies of infection using tuberculin skin testing (TST) was used in the past to derive the estimates of incidence of tuberculosis, the interpretation of such surveys is often burdensome and their performance unpredictable [14].

XDR-TB is a rare type of the tuberculosis. However, almost 117 countries globally were reported at least one case of extensively drug-resistant tuberculosis every year. This information provided from the different countries with trustworthy data suggests that around 9.5% of multi-drug resistant tuberculosis (XDR-TB) instances of global have extensively drug-resistant tuberculosis. In 2015, there were estimated 485,000 incidence cases of multi-drug resistant tuberculosis in global among an estimated 590,000 incidence rifampicin-resistant tuberculosis instance [14]. Exclusively a small proportion of the extensively drug-resistant tuberculosis cases among all are detected, and numerous small and lower middle-income countries still lack adequate diagnostic capability to test for resistance to the second line drugs (SLDs) and thus observe extensively drug resistant tuberculosis [15].

## Discussion

The satisfactory results obtained to date in the study, in our opinion, represent ERP use high effectiveness and safety in the surgical treatment of patients with LBO of tumor genesis. It should be noted that the ERP developed and used in emergency surgery is, in fact, the result of the adaptation of the recommendations of the ERAS society for perioperative care in elective colonic surgery [3]. It is evident that a number of provisions that cannot be applied in emergency situation have been excluded from the proposed multimodal program. At the same time, a significant positive role in fundamental improvement of short-term results of the surgical treatment of patients with complicated CRC was played such components as the rejection of prolonged nasogastrintestinal intubation, large and small (according to indications) intestines intraoperative decompression, early enteral therapy and nutritional support, number of drain tubes minimization, early removal of probes and catheters, and widespread use of regional analgesia.

In our opinion, the intraoperative stage, namely, embryology-oriented surgery and D3 lymphadenectomy is of particular importance for ERP successful implementation in emergency surgery. This all-important component plays, in fact, a core role for the entire postoperative component of the proposed multimodal ERP. Preliminary central ligation of the main vessels, along with the principal rejection of transmesocolar partial resections in favour of removed organ complex mobilization within the conjugation fascia boundaries, allows not only to minimize a blood loss and ensure a high safety of intervention, but also to obtain a high-quality drug that fully meets the modern requirements of oncological radicalism within the so-called specimen-oriented surgery. The injury rate of a widespread open surgical intervention reduction in certain, and in our opinion, significant level lows down its unconditional disadvantages in comparison with laparoscopic technic, which, as is known, is a key element in the principle of operative access minimization implementation within the fast track concept in colorectal surgery. Despite the seeming contradictory nature of above-mentioned condition, exactly this one creates the prerequisites for sufficiently ambitious tactical decisions making in terms of common tendencies in urgent surgery (early removal of drain tubes, catheters, probes, etc.). It should be noted that the ideology of modern principles of oncological

radicalism application in emergency surgery of complicated CRC is currently being discussed in the world scientific literature and is considered as the most upcoming trend for the modern operative surgery development [17].

In general, 63%-68% of ERP components recommended by the ERAS society for use in elective colonic surgery were used in the adapted multimodal program of enhanced recovery after urgent surgery in patients with OCRC.

The principles that underlie the modern tactics of surgical treatment of this category of patients must be separately discussed. The fundamental circumstance that determined the success of adopted ERAS concept application in emergency surgery of complicated CRC is, in our opinion, the identity of its pathogenetic content and principles of LBO of tumor genesis surgical treatment modern tactics.

What determines the prospects of ERP successful implementation in emergency surgery and improvement of its results? Refusing the concept analysis based on the principles of ERAS individual components' effects description, we can state that the perioperative multimodal techniques complex application in emergency surgery creates the necessary conditions for the key task of emergency surgery effective solution-the life-threatening complication elimination. In this regard, one of the basic conditions is the timely weakening of hypercatabolic metabolic response to emergency surgery, which lies within the metabolic optimized fast track concept (MOFA), the purpose of which is, first of all, to provide the necessary conditions for multiple organ dysfunction effective multicomponent intensive therapy, inevitably, to some extent, causing the postoperative complications and mortality [9]. A multiple organ dysfunction in patients with LBO, as a rule, develops against the background of expressed co-morbidity decompensation. In this case, the trigger mechanism, in our opinion, based on ERAS concept pathophysiological analysis, is an enteral deficiency with its regular manifestations in the form of dismetabolic, including trophological, protein-energetic, water-electrolytic, acid-base and, as a rule, immune alterations. The persistence and intensity of these pathological consequences of decompensated colon obstruction determine the vector and dynamics of multiple organ dysfunction development in this category of the patients. Exactly these pathological syndromes are the purpose of direct or indirect, but, as preliminary results of the randomized trial showed, high-efficiency effect of various ERP components in patients with complicated colorectal cancer.

Timely elimination and prevention of key pathogenetic factors as a natural result affected the short-term results of patients' surgical treatment. First of all, the use of the multimodal enhanced recovery system significantly reduced the incidence of postoperative complications, mainly of IIIb-IV grade according to Clavien-Dindo classification. A natural consequence of severe complications incidence reduction was, on the one hand, a reduction in postoperative mortality, and on the other hand-a reduction in duration of postoperative period. Moreover, the obvious, but still important, in our opinion, dependence of postoperative period duration on the complications and their severity availability should be noted. In case of uncomplicated subsequent period of his life in the ERAS group was 8 d; under complications of I-IIIa grade-17 d, and under complications of IIIb-IV degree-up to 40 d, respectively. Thus, an analysis of preliminary results of the study allows making a number of conclusions.

Firstly, the ERAS ideology application in emergency surgery of complicated colorectal cancer is a possible, safe and effective



technology that provides a significant improvement of its immediate results.

Secondly, the main clinical effect of ERP principles implementation is a reduction in postoperative, primarily severe complications (of IIIb-IV grade according to Clavien-Dindo) and, as a consequence, mortality.

Thirdly, ERP allows reducing the duration of postoperative period to 8 days in case of its uncomplicated course.

Fourthly, it should be noted that, in general, the short-term results of surgical treatment of the patients with LBO of tumor genesis in cases of the developed enhanced recovery program application are comparable with the same ones of elective surgical treatment of the patients with colon cancer. The latter circumstance, considering the nature of the main disease, the severity of complications and the extremely unfavorable premorbid background in patients with LBO, merits special attention.

In our opinion, it can be stated with certainty that ERS introduction into the practice of emergency surgery is a modern and the most promising strategy of the patients with OCRC treatment results improvement.

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