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том 22, № 2, 2023

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ЦЕЛИ И ЗАДАЧИ

Целью журнала «Колопроктология» является освещение современных тенденций и научно-практических достижений в колоректальной хирургии.

Заболевания толстой кишки, заднего прохода, тазового дна и промежности являются одними из наиболее распространённых, а колопроктология — наиболее динамично развивающейся хирургической специальностью.

Колоректальный рак занимает одну из ведущих позиций в структуре онкологических заболеваний, наблюдается неуклонный рост воспалительных заболеваний кишечника, дивертикулярной болезни. Постоянно изменяются диагностические и лечебные подходы при лечении геморроидальной болезни, свищей заднего прохода, анальной трещины, анальной инконтиненции.

Колопроктологи в России, как и во всем остальном мире, интенсивно взаимодействуют с онкологами, гастроэнтерологами, общими хирургами, эндоскопистами, патофизиологами и специалистами других научно-практических направлений врачебной деятельности.

Целевой аудиторией журнала являются колопроктологи, а также врачи других специальностей, интерес которых сконцентрирован на заболеваниях толстой кишки, заднего прохода, тазового дна и промежности.

Журнал «Колопроктологии» объединяет колопроктологов России в тесном сотрудничестве с профессиональными объединениями мира и ведущими международными экспертами в области колоректальной хирургии.

В журнале публикуются оригинальные статьи, результаты фундаментальных исследований, направленные на изучение общепатологических процессов с целью улучшения лечения больных, описание клинических наблюдений, мета-анализы и обзоры литературы по широкому спектру вопросов колопроктологии, а также результаты клинических и экспериментальных исследований.

AIM AND SCOPE

The purpose of the journal *Koloproktologia* (Russian Journal of Coloproctology) is to highlight current trends and scientific achievements in colorectal surgery.

Diseases of the colon, anus, pelvic floor, and perineum are among the most common; and coloproctology is the most dynamically developing surgical specialty.

Colorectal cancer occupies one of the leading positions in the structure of oncological diseases. There is a steady increase in inflammatory bowel diseases, diverticular disease, stoma patients.

Diagnostic and treatment options for hemorrhoid disease, anal fistula, anal fissure, and anal incontinence are constantly changing.

Coloproctologists in Russia, as in the rest of the world, intensively interact with oncologists, gastroenterologists, general surgeons, endoscopists, pathophysiologists, and specialists in other scientific and practical areas of medical activity.

The target audience of the journal is coloproctologists, as well as doctors of other specialties, whose interest is focused on diseases of the colon, rectum, anus, pelvic floor and perineum.

The journal *Koloproktologia* (Russian Journal of Coloproctology) unites coloproctologists of Russia in close cooperation with professional associations of the world and leading international experts in the field of colorectal surgery.

The journal publishes original articles, the results of basic research aimed at studying general pathological processes in order to improve the treatment of patients, clinical cases, meta-analyses, and literature reviews on a wide range of coloproctology issues, as well as the results of clinical and experimental studies.

Журнал включен в перечень рецензируемых научный изданий, рекомендуемых ВАК, для публикации основных научных результатов диссертаций на соискание ученой степени кандидата наук, на соискание ученой степени доктора наук по научным специальностям (по состоянию на 07.12.2022)

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CLINICAL GUIDELINES
Acute malignant colorectal obstruction (K56.6; C18, C19, C20), adults

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Coding according to the International Statistical Classification of Diseases and Health-Related Problems:
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DEVELOPER OF CLINICAL RECOMMENDATIONS
- Russian Association of Coloproctology
- Association of Oncologists of Russia
- Russian Society of Surgeons

LIST OF ABBREVIATIONS
AP — arterial pressure

RF — respiratory failure
GIT — gastrointestinal tract
CT — computed tomography
ABS — acid-base state
GBT — general blood test
ALIO- acute large intestine obstruction
US — ultrasound
CKD– chronic kidney disease
CHF — chronic heart failure
RMR — respiratory movements rate
HR — heart rate
Rg — radiography
ScvO2 — saturation of venous blood of central vessels with oxygen
SpO2 — saturation of arterial blood with oxygen

TERMS AND DEFINITIONS

Endotoxicosis, or **endogenous intoxication syndrome**, is a complication of various diseases associated with a violation of homeostasis due to the accumulation of endogenous toxic substances in the body, including bacterial endotoxins with pronounced biological activity.

Peritoneal carcinomatosis is one of the forms of metastasis of cancer of the abdominal cavity and pelvis, characterized by tumor foci on the visceral and parietal peritoneum.

1. BRIEF INFORMATION ON THE DISEASE OR CONDITION (GROUP OF DISEASES OR CONDITIONS

1.1 Definition of a disease or condition (group of diseases or conditions)

Intestinal obstruction of tumor genesis is a syndrome characterized by a violation of the movement of contents through the digestive tract caused by a mechanical obstacle, which is a malignant or benign neoplasm of the intestine.

1.2 Etiology and pathogenesis of a disease or condition (groups of diseases or conditions)

Acute large intestine obstruction of tumor etiology refers to mechanical obstruction and predominantly is located in the large intestine. Much less often, ALIO is caused by malignant neoplasms of the small intestine and benign intestinal tumors. Obturation can occur due to the overlap of the intestinal lumen, both by the primary tumor of the intestine, and by compression from the outside by a tumor originating from neighboring organs and tissues.

The most characteristic is an erased, slowly progressing onset in the form of a transit disturbances due to incomplete overlap of the intestinal lumen. The acute onset may be due to complete obturation of the narrowed area by a tumor or dense fecal masses.

In the early stage of obstruction, peristalsis increases, while the intestine, with its contractions, seems to strive to pass through the tumor. At this stage, the bowel movements in the proximal loop shortened, but more frequent. Later, because of hypertonicity of the sympathetic nervous system, overstretching of the intestine, severe inhibition of tissue perfusion, a phase of significant inhibition of the motor function of the intestine occurs, and in the later stages of obstruction, its complete paralysis develops. The disorder of metabolism of intestinal wall tissues is aggravated by increasing endogenous intoxication, which, in turn, increases tissue hypoxia.

Water-electrolyte disorders are associated with the loss of a large amount of fluid, electrolytes and proteins. The fluid is lost with vomit, deposited in the proximal to the tumor part of the intestine, accumulates in the edematous intestinal wall, its mesentery, as well as in the free peritoneal cavity. Fluid loss per day can reach 4 liters or more. There is a shift of the electrolyte balance, first, the loss of potassium. Along with liquid and electrolytes, a significant amount of proteins (up to 300 g/day) is lost due to starvation, vomiting, sequestration into the intestinal lumen and abdominal cavity. Violation of the barrier function of the intestinal wall leads to the translocation of bacteria into the portal bloodstream, lymph and peritoneal exudate. These processes underlie the systemic inflammatory response and abdominal surgical sepsis.

A significant pathogenetic role assigned to intra-abdominal hypertension — compartment syndrome, which leads to a poor blood supply in abdominal organs, a decrease in the viability of tissues, multiple organs failure. The main principles of treatment of compartment syndrome are early surgical decompression and rational infusion therapy.

1.3 Epidemiology of a disease or condition (groups of diseases or conditions)

Colorectal cancer is one of the most common malignant neoplasms both in Russia and around the world [1,2]. Acute intestinal obstruction is a complication of colorectal cancer, which occurs in 15–20% of patients of all age groups, but more often in patients older than 50 years. In Russia, an increase in the number of patients with tumor acute intestinal obstruction is registered annually. According to data for 2019, 22,221 cases of ALIO detected in Russia. Hospital and postoperative mortality was 15.39% and 17.05%, respectively [3].

1.4 Features of coding a disease or condition (group of diseases or conditions) according to the International Statistical Classification of Diseases and Health-Related Problems

Class — Diseases of the digestive system (XI):

K56.6 — other and unspecified intestinal obstruction

Class — Neoplasms (II):

C18.0 — Malignant neoplasm of the cecum, ileocecal valve

18.1 — Malignant neoplasm of the appendix

C18.2 — Malignant neoplasm of the ascending colon

C18.3 — Malignant neoplasm of the hepatic (right) flexure of the colon

C18.4 — Malignant neoplasm of the transverse colon

C18.5 — Malignant neoplasm of the splenic (left) flexure of the colon

C18.6 — Malignant neoplasm of the descending colon

From 18.7 — Malignant neoplasm of the sigmoid colon

C18.8 — Colon lesion extending beyond one or more of the abovementioned sites

C 18.9 — Malignant neoplasms of the colon of unspecified location

C19 — Malignant neoplasm of the rectosigmoid

C 20 — Malignant neoplasm of the rectum

Note: *the cipher "C" is used for histological confirmation of the malignant nature of the neoplasm that caused the ALIO.*

1.5 Classification of a disease or condition (groups of diseases or conditions)

To date, there is no generally accepted classification of tumor colorectal obstruction.

The working group for Clinical Guidelines for the treatment of patients with ALIO of tumor etiology proposed to divide it depending on the degree of compensation [4]:

- Compensated ALIO: intermittent retention of stool and difficulty in gas discharge; pneumatization of the large intestine with single fluid levels in it may be detected on an overview radiograph of the abdominal cavity;
- Subcompensated ALIO: retention of stool and gases for less than 3 days, pneumatosis and Kloiber cups detected on abdominal X-ray — horizontal fluid levels with domed gas above them; there are no signs of multiple organ dysfunction; conservative treatment is effective;
- Decompensated ALIO: retention of stool and gases for more than 3 days; radiological signs of both large and small bowel obstruction with small bowel levels and arches in all parts of the abdominal cavity; vomiting with stagnant contents; the presence of organ dysfunction.

However, scientific evidence of the validity of the use of this classification to determine surgical approach in patients with intestinal obstruction is insufficient.

The classification of Colo Rectal Obstruction Scoring System (CROSS) proposed by The Japanese Research group on the Safety of colonic stents (The Japan Colonic Stent Safety Procedure Research Group — JCSSPRG) does not provide for its use as a tool for determining the time and type of treatment of intestinal obstruction [5].

- To determine the need for surgical treatment, stratification of patients by stability is necessary in accordance with the criteria of sepsis (septic shock). **— C (Level of evidence — 5)**

Comments: *the criteria for sepsis are organ dysfunction, the cause of which may be intestinal obstruction or perforation. Patients with sepsis due to intestinal perforation on the background of intestinal obstruction need emergency surgical treatment. It reported that the delay of surgery over 6 hours in patients with septic shock due to gastro-intestinal perforation leads to zero 60-day survival [6]. Criteria of instability of septic patients proposed in determining the approach of treatment in guidelines of The World Society of Emergency Surgery (WSES)*

[7]. To assess organ dysfunction, it is recommended to use the Sequential Organ Failure Assessment (SOFA) and quick (fast) SOFA scales.

Examples of diagnosis formulation:

1. "Cancer of the sigmoid colon complicated by acute intestinal obstruction."
2. "Cancer of the ascending colon complicated by acute intestinal obstruction."

A more accurate formulation of the diagnosis using the international classification TNM is possible when obtaining data on the morphological structure and the tumor stage.

1.6 Clinical picture of the disease or condition (group of diseases or conditions)

The clinical manifestations of tumor ALIO are diverse and depend on many factors. The most common of them are abdominal pain, bloating, lack of stool and gases.

2. DIAGNOSIS OF A DISEASE OR CONDITION (GROUP OF DISEASES OR CONDITIONS), MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF DIAGNOSTIC METHODS

Many different diseases and their clinical forms can lead to acute intestinal obstruction syndrome. At the same time, diagnostic tests are universal, regardless of the disease: exclusion of conditions requiring immediate surgical intervention (strangulation, perforation, peritonitis, etc.); differential diagnosis of mechanical and paralytic obstruction; determination of the level and cause of obstruction.

Detection of perforation, strangulation and septic shock is a priority task of the diagnostic stage in patients with colorectal obstruction.

It was found that delay of surgery for more than 6 hours with intestinal perforation and septic shock is associated with 100% 60-day mortality [6].

Therefore, an important goal of primary diagnosis and follow-up during nonoperative treatment is early detection of perforation or threat of perforation of the colon. At the same time, the role of time before surgery in stable patients without peritonitis should not be overestimated. A direct correlation between the time delay of the operation in ALIO with a 30-, 90-day, as well as one-year mortality has not been established [8].

2.1 Complaints and anamnesis

Acute intestinal obstruction often occurs suddenly, manifests itself by the absence of gas discharge and bloating. Bloating and the absence of gas discharge are pathognomonic symptoms of ALIO.

Abdominal pain is a non-permanent symptom in ALIO, it can be cramping, with periods of intensification during the wave of peristalsis. With the progression of the disease, the peristaltic activity of the intestine decreases, which is why the pain, as a rule, changes from cramping to constant for 2–3 days, which serves as a bad prognostic sign.

Vomiting in the early stages of ALIO may be absent, later it becomes repeated, not bringing relief. In the late period, the vomit masses acquire the appearance and smell of intestinal contents.

2.2 Physical checkup

Upon admission to the hospital in case of suspected ALIO, first of all, a clinical checkup should be carried out, in which the condition of the skin is assessed, the body mass index is calculated, thermometry is carried out, pulse measurement, respiratory rate and blood pressure indicators are measured. Auscultation, percussion and palpation of the abdomen are performed. Digital rectal examination is performed in all patients, and vaginal examination is additionally performed in women.

2.3 Laboratory diagnostic tests

There is no specific laboratory diagnosis of ALIO of tumor etiology.

The basis of laboratory diagnostics in ALIO is the identification of systemic disorders that require correction and additional therapy. In a clinical blood test, it is necessary to pay attention to the presence or absence of anemia, which may be one of the markers of the development of postoperative complications, a sign of chronic blood loss, the presence or absence of leukocytosis, changes in the leukocyte formula, as markers of systemic inflammatory response and translocation of intestinal microflora through its stretched wall. Biochemical analysis of blood, determination of electrolytes in blood serum allows to identify water-electrolyte disorders occurring during the development of intestinal insufficiency syndrome as a result of obstruction of the intestinal lumen, changes in the level of liver enzymes and nitrogenous bases,

which may indicate the development of hepatic-renal insufficiency as a consequence of vomiting and dehydration, endotoxicosis against the background of intestinal insufficiency [9].

2.4 Instrumental diagnostic tests

• Patients with suspected acute obstructive colonic obstruction in the absence of contraindications should undergo computed tomography of the thorax, abdominal cavity and pelvis as a method of choice [10].

Grade of recommendations — C (Level of evidence — 5)

Comments: *abdominal CT in patients with suspected acute obstructive colonic obstruction allows us to visualize the tumor; to stage it; to find distant metastases; to assess the extent of the pathological process in the large intestine [10]; to exclude free gas in the abdominal cavity and identify the presence of gas bubbles in pericolic tissue as an early radiological symptom of tumor perforation and other complications of ALIO. Limitations for the method are the presence of contraindications to the use of X-ray contrast agents containing iodine (drug intolerance, increased levels of urea and createnine in the blood), the inability to transport the patient to the radiology unit. In this case, preference in diagnostics should be given to ultrasound [11–13].*

• For all patients with suspected ALIO, if computed tomography is not possible, abdominal ultrasound and abdominal X-ray are **recommended** [14].

Grade of recommendations — C (Level of evidence — 4)

Comments: *in the absence of the possibility of performing computed tomography, the diagnostic algorithm includes transabdominal ultrasound and abdominal X-ray. Abdominal ultrasound is an operator-dependent method of investigation, but in the presence of an experienced doctor, it is more effective than abdominal X-ray and can also be performed in a hospital unit, which does not require patient transportation [13,15].*

• For all patients with suspected ALIO, determined by ultrasound and radiology, if it is impossible to perform computed tomography, it is **recommended** to perform irrigoscopy using water-soluble nephrotropic high-osmolar radiopaque agents (V08AA01 Sodium amidotrizoate) [16,17].

Grade of recommendations — C (Level of evidence — 2)

Comments: *if ALIO suspected according to abdominal ultrasound and abdominal X-ray, if it is not possible to perform computed tomography, it is advisable to perform irrigoscopy (A06.18.001) with a water-soluble contrast agent in order to determine the level of the obstruction. Contrast enema with barium sulfate** is not recommended, as it makes it difficult to further visualize the intestinal mucosa during colonoscopy [17,18].*

• It is **recommended** that hemodynamically stable patients with suspected ALIO, in the absence of a high risk of intestinal perforation, undergo colonoscopy to verify the diagnosis and biopsy of the tumor [5,19].

Grade of recommendations — C (Level of evidence — 5)

Comments: *during colonoscopy, the diameter of the tumor stenosis and the possibility of intestinal stenting evaluated, tumor tissue is taken for morphology. In order to prepare the intestine for examination, it is preferable to use cleansing enemas, the performance of which in some cases allows for the resolution of intestinal obstruction, at the same time, may cause diastatic perforation of the proximal colon. Colonoscopy before surgery is not recommended in unstable patients, as well as when the caecum dome is expanded more than 10 cm due to the high risk of intestinal perforation during the procedure [20]. In this case, colonoscopy should be performed in the postoperative period to exclude neoplasms in the remaining parts of the large intestine [7]. In order to reduce the risk of intestinal perforation, insufflation using CO_2 is preferable [21].*

2.5 No other diagnostic tests

No.

3. TREATMENT, INCLUDING DRUG AND NON-DRUG THERAPY, DIET THERAPY, ANESTHESIA, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF TREATMENT METHODS

The main purpose of medical care for patients with tumor ALIO is the elimination of intestinal obstruction, which allows creating favorable conditions for the early start of oncological treatment.

Surgery is the main method of treatment of tumor ALIO. The volume, urgency and stage of surgical treatment depend on the technical support of the medical institution, the level of surgical and anesthesiological teams, the functional status and degree of surgical and anesthesiological risk of the patient, the extent and presence of complications of cancer, including perforation with peritonitis, abscess, sepsis and septic shock.

3.1 Conservative treatment

Non-operative treatment is a stage of preparation for surgery and, unlike small bowel obstruction, is not considered as an independent final method of treatment of tumor ALIO.

• Initial non-operative treatment may be **recommended** for patients with ALIO without signs of intestinal perforation, the purpose of which is to prepare for surgery in the most favorable conditions [20].

Grade of recommendations — C (Level of evidence — 5)

Comments: *to achieve the best conditions, correction of water-electrolyte disorders, anemia, nutritional status, provision of a qualified anesthesiological and surgical team is necessary.*

As an indication for immediate surgical intervention, persistent acidosis and dilation of the dome of the cecum greater than 10 cm (a threat of perforation). In the absence of signs of compromise of the intestinal wall, treatment can be continued to optimal conditions with monitoring of laboratory and instrumental parameters every 6–12 hours [20].

• All patients with ALIO should be corrected for hypovolemia and water-electrolyte disorders [22,23].

Grade of recommendations — C (Level of evidence — 4)

Comments: *hypovolemia can have catastrophic consequences for surgical patients and is a major factor in preventable mortality. Hypovolemia in patients before surgery should be eliminated whenever possible.*

At the initial stage of correction of hypovolemia, preference should be given to balanced crystalloid solutions (solutions affecting the water-electrolyte balance, ATX B05BB) [22].

• It is **recommended** to provide decompression of the proximal gastrointestinal tract by aspiration of the contents through a nasogastric or nasointestinal probe in patients with ALIO showing symptoms of gastrostasis [20,24].

Grade of recommendations — C (Level of evidence — 5)

Comments: *although in international guidelines [7] for ALIO, in contrast to small bowel obstruction, the procedure for decompression of the gastrointestinal tract at the preoperative stage not described, its use in small-large bowel obstruction allows us to decrease intra-abdominal pressure, to decrease the concentration of microbial flora, the toxic effect of stagnant contents of the stomach and small intestine. Recommendations for decompression of the gastrointestinal tract at the preoperative stage may be relevant, first, for right colon cancer, manifested by small intestinal obstruction with dilatation of the proximal gastrointestinal tract. With left-sided ALIO, dilatation of the proximal part of the small intestine and stomach is less common, and therefore, in the absence of stagnant contents in the stomach, there is no need to install a probe for decompression of the upper gastrointestinal tract. A Russian study of the effect of gastric decompression on the survival of patients with small bowel obstruction has not been estimated [25]. However, preliminary decompression of the gastrointestinal tract makes it easier to manipulate in the abdominal cavity. In this regard, decompression of the gastrointestinal tract using a naso-gastric (intestinal) probe may be recommended.*

• All patients with ALIO are **recommended** to stop enteral nutrition [26].

Grade of recommendations — C (Level of evidence — 5)

Comments: *enteral nutrition has a trophic effect on the intestinal epithelium, prevents mucosal atrophy, prevents bacterial translocation. However, enteral nutrition is not possible in case of gastrointestinal tract obstruction, perforation or ischemia of the intestinal wall [26].*

• All patients with ALIO are **recommended** to evaluate the effectiveness of the treatment, clinical — every 6 hours, instrumental (abdominal X-ray or ultrasound) — every 12 hours [6,19,20].

Grade of recommendations — C (Level of evidence — 5)

Comments: *the most important clinical signs of improvement — conservative resolution of ALIO should*

include the restoration of gas discharge and natural bowel emptying. Clinical and radiological data indicating intra-abdominal complications (perforation), high lactate levels (serum lactate above 2 mmol/L) and leukocytosis (more than 18x10⁹), a temperature of more than 38.5 °C, an increase in creatinine (more than 2 times compared with admission) should be taken as criteria for stopping non-surgical treatment [20]. In addition, the expansion of the dome of the cecum of more than 10 cm, non-correctable acidosis should be considered as indications for urgent surgery [20]. The decision on the possibility of further conservative therapy should be made every 6 hours. It has been shown that postponement at the beginning of surgery for more than 6 hours with intestinal perforation and septic shock is associated with 100% 60-day mortality [6].

- For unstable patients with ALIO, peritonitis and septic shock, surgery is recommended after intensive therapy and stabilization [27].

Grade of recommendations — C (Level of evidence — 3)

Comments: *patients with ALIO, peritonitis and septic shock need intensive preoperative therapy. Risk factors for death include hypothermia (less than 35°C), metabolic acidosis, the presence of clinical or laboratory signs of coagulopathy [27]. In addition, comorbid patients and persons over 70 years of age need intensive care [28]. The target indicators of stabilization of the condition are the restoration of central venous pressure to 8–12 mmHg, average blood pressure > 65 mmHg, central venous saturation to (Scv02) > 70% [29,30]. Treatment of unstable patients with ALIO is advisable to be carried out in the conditions of the intensive care unit.*

- Patients with established intestinal perforation and peritonitis need antibacterial therapy as early as possible [31–33].

Grade of recommendations — A (Level of evidence — 1)

Comments: *intraabdominal infections caused by perforation of the large intestine are often caused by a mixture of aerobic and anaerobic bacteria. Antimicrobial therapy recommended for intraabdominal infections [31] includes monotherapy with a drug from the carbapenem group and combination therapy with metronidazole** with third-generation cephalosporins or fluoroquinolones. Although metronidazole has been used as standard therapy for trichomoniasis, anaerobic and amoebic infections worldwide since the 1970s, resistance to metronidazole** remains low [33]. It has been shown that combination therapy with metronidazole** can be an effective and safe treatment option for intraabdominal infections, similar to carbapenem monotherapy [32].*

- In order to prevent thromboembolic complications in patients with ALIO, the administration of heparin group drugs and the use of compression knitwear are **recommended** [34].

Grade of recommendations — B (Level of evidence — 1)

Comments: *patients undergoing surgery for colorectal cancer are at high risk of thromboembolic complications. In the presence of intestinal obstruction, the risk of such complications is regarded as extremely high. The use of low molecular weight heparins (ATC — heparin group) can significantly reduce the likelihood of deep vein thrombosis of the lower extremities and pulmonary embolism. The use of other drugs of the heparin group does not differ in effectiveness, however, it is associated with a large number of hemorrhagic complications and the development of heparin-induced thrombocytopenia. Additionally, compression stockings are used, as well as a therapeutic pneumatic compression system. At the same time, early termination of bed rest is one of the conditions for successful prevention of venous thrombosis and is practiced in all cases where possible. In patients who have undergone extensive surgery for oncological surgeries, it is advisable to carry out preventive measures combined with the introduction of low-molecular-weight heparins for at least 4 weeks [35,36].*

3.2 Non-invasive methods of treatment

No.

3.3 Surgical treatment

The main objective of surgical treatment of ALIO is to save the patient's life from the complications of large intestine cancer, as well as to create favorable conditions for the early start of oncological treatment. Surgery to remove a colorectal tumor in ALIO should be resorted to only in cases where it is necessary to save the patient's life, as well as in situations where the potential risk of an unfavorable outcome of a

staged treatment exceeds the benefits of a one-stage approach.

There are two options for surgical treatment of ALIO, namely: 1) Initial decompression of the large intestine followed by elective colorectal resection; 2) primary colorectal resection. In order to decompress the large intestine, a proximal intestinal stoma can be done; a stent or a decompression colonoscopic catheter (colorectal probe, in the English literature "Dennis Colorectal Tube") is installed. Primary resection surgery include obstructive segmental resection of the large intestine without anastomosis (Hartmann's procedure, right hemicolectomy with end ileostomy / ileoascendostomy), subtotal resection of the colon and segmental resection of the colon with primary anastomosis. The problem of choosing the optimal surgical approach not solved yet, the search for optimal approaches continues.

3.3.1 Endoscopic decompression minimally invasive surgeries

Minimally invasive methods of surgical treatment of patients with ALIO of tumor etiology include the installation of a self-expanding stent, as well as a colonoscopic decompression catheter proximal to the large intestine tumor. The resolution of intestinal obstruction makes it possible to avoid performing emergency or urgent surgery, which makes it possible to use additional therapeutic and diagnostic measures to prepare the patient for elective surgical treatment, including laparoscopic access. Elimination of ALIO at the first stage of treatment of complicated large intestine cancer reduces the likelihood of severe complications and death, creates conditions for performing surgery with primary anastomosis, and in some cases without preventive intestinal stoma [37].

3.3.1.1 Endoscopic stenting for tumor stenosis

The most common non-invasive method of treatment that allows to stop ALIO is intestinal stenting with a self-expanding system (a metal uncovered large intestine stent) inserted into the intestinal lumen at the tumor level using an endoscope.

- In the absence of signs of perforation, peritonitis, bleeding, complete occlusion of the intestinal lumen by a tumor of the left colon, the installation of a self-expanding metal stent (uncovered metal stent for the large intestine) is **recommended** [38].

Grade of recommendations — B (Level of evidence — 2)

Comments: *the technical efficiency of the method is 80–100%, while clinical improvement is observed in 73–89% of patients. The most dangerous complication of stenting is perforation, which is observed in 12.8% of cases, while "hidden" perforation, detected only by instrumental examination, occurs in 26.7% of cases [39]. Tumor perforation during stenting is a factor of unfavorable prognosis [40], after stenting, lymph node damage and perineural tumor invasion are more often detected [41]. At the same time, with sufficient experience of stenting (at least 40 procedures) and performing radical surgery to remove a colorectal tumor within 14 days, the overall and disease-free survival in the group of stenting and primary resection does not differ [38,42], the rate of anastomosis failure and stoma formation during stenting is lower [43]. Earlier guidelines did not allow the routine use of this method of treatment due to concerns about the deterioration of late results [44].*

- In order to avoid recurrence of obstruction, radical surgery is **recommended** to be performed within 14–30 days from the moment of elimination of ALIO in patients who do not require additional treatment, including neoadjuvant drug and/or radiation therapy [45].

Grade of recommendations — B (Level of evidence — 3)

Comments: *after stenting, there were no significant differences in post-resection complications, duration of hospital stay or laparoscopic resections during surgery after 11–17 days compared to 5–10 days. Of the complications associated with the stent, 48% occurred in patients operated on more than 17 days after decompression. Compared with the procedures within 14 days after stoma, the operations within 14–28 days after decompression followed by a significantly higher rate of laparoscopic resections, a higher rate of primary anastomoses and a shorter hospital stay. There was no demonstrated effect of the timing of radical surgery on mortality, disease-free or overall survival [45].*

- Stenting of the tumor in ALIO against the background of antitumor therapy with monoclonal antibodies inhibiting the biological activity of vascular endothelial growth factor (bevacizumab**) is **not recommended** [46].

Grade of recommendations — B (Level of evidence — 2)

Comments: *the presence of a stent in the tumor channel in patients receiving bevacizumab** for a long time is associated with a high risk of tumor perforation [46].*

• Stenting is **not recommended** in patients with ALIO caused by tumors of the lower and middle rectum [47].

Grade of recommendations — C (Level of evidence — 4)

Comments: *with a low rectal cancer, a dentate line can get into the stenting zone, which causes severe pain, bleeding, tenesmus and anal incontinence [47].*

3.3.1.2 Retrograde decompression colonoscopic catheter

The method consists in transanal decompression of a colonoscopic catheter through the tumor canal, followed by washing of the proximal colon. It is performed during colonoscopy under the control of abdominal X-ray.

• In the absence of signs of perforation, peritonitis, bleeding and complete occlusion of the intestinal lumen by a tumor of the left colon, the installation of a decompression colonoscopic catheter is **recommended** as an alternative to stenting [48].

Grade of recommendations — C (Level of evidence — 4)

Comments: *carrying out a contrast tube is possible with a diameter of the tumor channel of at least 3 mm. The technical efficiency of the method is 80%, clinical — 72.5%; the rate of intestinal perforation can reach 10%.*

A potential advantage of the method is the ability to perform lavage of the proximal large intestine, and, presumably, less trauma of the intestine in the tumor zone due to the absence of stretching of the tumor canal that occurs during stenting. A significant limitation of the method for use is the lack of data on its oncological safety [43].

3.3.2 Surgical treatment

The primary task of surgical treatment is the elimination of intestinal obstruction and the preservation of the patient's life. In the presence of a colorectal oncologist or coloproctologist in a medical institution, the decision on the scope of surgical treatment made based on the individual features of the patient — in the absence of peritonitis, both resection and decompression procedures (intestinal stoma) are permissible. A rational method of surgical treatment for ALIO in non-specialized hospitals is the proximal stoma followed by radical surgery to remove a large intestine tumor, which is preferably performed in specialized medical institutions of oncological and proctological profile.

• The presence of persistent acidosis and/or expansion of the cecum dome more than 10 cm should be considered an indication to discontinue further therapy and perform urgent surgery [20].

Grade of recommendations — C (Level of evidence — 5)

• In all patients planning for intestinal stoma are **recommended** to mark the area of the presumed stoma before surgery [49].

Grade of recommendations — C (Level of evidence — 5)

Comments: *if the patient supposed for a stoma, then the course of the procedure itself and its consequences should be carefully explained to him. The most optimal before performing the operation is to consult a specialist in the rehabilitation of stoma patients. In emergency situations, it is not always possible to comply with the above recommendations, in such cases, the marking of the area of the intended removal of the stoma should be carried out by the operating surgeon. Marking is performed in the patient's standing, lying and sitting position, taking into account his/her individual and constitutional characteristics, in accordance with clinical recommendations for the treatment of patients with intestinal stoma [50].*

• Patients without signs of intestinal perforation, peritonitis, abscess formation, operated on for ALIO of tumor etiology, are recommended to undergo antibiotic prophylaxis with systemic antibacterial drugs (ATC J01) [51].

Grade of recommendations — A (Level of evidence — 1)

Comments: *a single administration of a broad-spectrum antibacterial drug (ATC: J01CA, J01DC, J01DD, J01DE, J01DH, J01M) is considered effective immediately before surgery, and if the duration of surgery is more than 3 hours, its repeated administration. The administration of systemic antibacterial drugs can reduce the incidence of infectious complications, shorten the patient's hospital stay, and reduce the cost of treating complications after surgeries [51].*

• Intraoperative decompression of the small intestine is **recommended** for all patients with ALIO [49].

Grade of recommendations — C (Level of evidence — 5)

Comments: *decompression of the small intestine is necessary to eliminate abdominal compartment syndrome, provide conditions for suturing the abdominal wall wound without tension, reduce the concentration of microbial flora, eliminate the toxic effect of stagnant stomach and small intestine contents, normalize respiratory function, reduce the risk of aspiration pneumonia, improve perfusion of the intestinal wall, restore motor and suction functions of the intestine.*

According to a systematic review, there are no statistically significant differences in the results of treatment of patients with ALIO when using a nasogastric probe with manual decompression of the small intestine or "open" decompression of the intestine [52]. According to the results of the meta-analysis, the use of a nasointestinal probe has no advantages over a nasogastric one in the treatment of a thin-bowel obstruction [53].

The choice of the method of decompression of the digestive tract should be decided individually for each patient, based on the characteristics of his/her disease, the experience of the medical institution and the operating surgeon.

3.3.2.1 Loop stoma

The loop ileostomy/colostomy is an alternative to stenting in the "bridge to surgery" strategy, when treatment aimed only at eliminating acute intestinal obstruction in order to create optimal conditions for performing the main stage of surgery–removal of a large intestine tumor [37,54].

• In case of in effective treatment, absence of signs of peritonitis, as well as an alternative to stenting, proximal loop intestinal stoma is **recommended** [55–57].

Grade of recommendations — B (Level of evidence — 2)

Comments: *the advantage of a loop stoma is the relative simplicity of the surgery, reliable decompression of the large intestine, the possibility of performing a total colonoscopy (during the formation of a double-barrelled colostomy), which allows detecting synchronous neoplasm in 2.3–12.4% of cases [55]. The question of choosing an ileo- or colostomy is decided individually, depending on the specific clinical situation. The rate of complications in both variants of surgery is comparable. However, patients with ileostoma have a higher risk of dehydration [56]. It was shown that patients who underwent the formation of a loop stoma at the first stage were statistically significantly less likely to have an intestinal stoma after surgery to remove a large intestine tumor — 29% versus 67% in the stenting group ($p < 0.001$) [57].*

At the same time, it should be pointed out that there was a higher incidence of severe complications in the stented patients — 15.3% versus 5.8% in the stenting group, but this did not affect the overall and disease-free survival, which was comparable in the groups [57]. In comparison with primary large intestine resection, the rate of cumulative mortality and complications are comparable. However, in the group of patients with stoma, it is more often possible to form an inter-intestinal anastomosis — in 89.3%, as opposed to 49.2% when removing a large intestine tumor at the first stage of treatment. In 9.4% of cases, patients remain with a permanent stoma, while in the group of primary resections this indicator is 21.6% [54]. In the case of intestinal obstruction caused by a rectal tumor, it is advisable to refuse from performing primary resection of the rectum by Hartmann, since this significantly complicates the subsequent rehabilitation of the patient. In addition, when the tumor located in the middle or low rectum, especially in the case of locally advanced tumors, resection deprives the possibility of neoadjuvant chemoradiotherapy, thereby discrediting the principles of oncological radicalism [58,59].

• In unstable patients with tumor ALIO or with technical difficulties in removing a loop colostomy, a wall colostomy can be used as a decompression surgery [60].

Grade of recommendations — C (Level of evidence — 3)

Comments: *for patients with tumor ALIO, it is not recommended to form a parietal colostomy, including a cecostomy, because it does not provide a complete shutdown of the passage of intestinal contents and full-fledged relief of complications of the tumor process. This surgery can be justified only in limited casesin critical condition, when stenting or the formation of a loop intestinal stoma cannot be performed [60].*

3.3.2.2 Colorectal resection

The most frequently performed radical surgery for cancer of the left half of the colon complicated by ALIO is colon resection with the formation of a terminal colostomy (Hartmann's procedure) [12]. When neoplasms are located in the right parts of the colon, operations performed with anastomosis, and if necessary, resection of the colon performed without creating an anastomosis, a single-stem ileostomy is formed.

The advantage of this type of surgery is the exclusion of the likelihood of anastomosis leakage, as well as the removal of the tumor at the initial stage of treatment. However, it should be noted that resections are associated with a high level of postoperative mortality — 9% and postoperative complications, including those associated with intestinal stoma. The risk factors for death are the elderly age of patients — over 70 years old, high anesthetic risk — ASA3, cardiovascular insufficiency and neurological disorders. The low rate of stoma reversal is also important — only 35% of patients subsequently manage to restore natural defecation [12]. It was shown that the average number of lymph nodes in the removed specimen after emergency surgeries is lower than in elective surgery (8.7 vs. 21.0) [61]. It should be noted that dozens of randomized studies and meta-analyses have been done on choosing the optimal strategy for surgical treatment for patients with ALIO. In the analysis of Pubmed over the past 5 years, 10 meta-analyses were found on the request of "large bowel obstruction", dedicated to choosing the optimal primary surgery: stoma, stent, resection. Of these, the only study showed that primary decompression surgery, in particular a stent, had advantages over primary resection in terms of hospital — 90-day mortality: 6.5% vs. 8.1% (HR 0.65, P = 0.01) [62]. The same results of the overall 3- and 5-year survival were obtained when comparing the stoma and stent with primary resection, with the exception of the only meta-analysis where the stoma and stent had advantages. In the same study, a higher 5-year disease-free survival rate was established with the use of a stoma and a stent. According to 3-year disease-free survival in two meta-analyses, the advantages of primary resection were established [63,64]. The stoma and stent groups had clear advantages in terms of the rate of complications and the primary anastomosis, with some advantage of primary resection in terms of the total duration of inpatient treatment. The number of removed lymph nodes was either equal [63], or the stoma and stent group had an advantage[65].

In general, compared with emergency surgery, self-expanding metal stents and stomas improve short-term surgical treatment results with comparable overall and disease-free survival. At the same time, stable patients can benefit from emergency resection surgery, including primary anastomosis, unstable patients — from decompression with a stoma, stent or colorectal probe [66]. Analysis of the results of surgical treatment of ALIO, according to the prospective national registry of the Netherlands, showed mortality after emergency resection from 2.9% in patients < 70 years old to 32.2% in elderly patients with high risk. For frail elderly patients, postoperative mortality of over 30% requires the search for alternative treatment strategies [67].

- In stable patients with ALIO without perforation and peritonitis caused by a colon tumor, in the presence of a qualified team of oncological surgeons or coloproctologists, after further examination in accordance with clinical guidelines for the treatment of colon cancer and rectosigmoid junction, it is possible to perform surgery to remove a colon tumor [63,64].

Grade of recommendations — C (Level of evidence — 1)

Comments: *taking into account the data available today, resection should be resorted to only in cases when they are performed by a qualified team of surgeons, oncologists or coloproctologists, there are conditions for conducting a qualitative morphological examination of the removed tumor, as well as when other treatment options cannot be applied. The availability of a qualified team is of particular importance in the case of resection that require compliance with oncological principles of surgery. The surgery volume for emergency resection in the absence of perforation and peritonitis should not differ from the elective surgery, with the exception of the issue of the formation of an inter-intestinal anastomosis. If it is impossible to perform surgery according to the established principles of colorectal cancer treatment in patients without perforation,*

resection should not be performed. The surgery volume must be limited by decompression stoma.

• If perforation, peritonitis, abscess formation, diastatic ruptures and ischemic changes of the colon are detected, colon resection is **recommended** without anastomosis [12,27].

Grade of recommendations — C (Level of evidence — 4)

Comments: *Two main mechanisms lead to intestinal perforation and peritonitis against the background of ALIO of tumor etiology. Firstly, it is the formation of a defect in the intestinal wall at the tumor level due to necrosis and decay of tumor tissue; secondly, a diastatic rupture of the wall of the distended intestine located proximal to the site of obstruction. The second variant often more severe and is associated with high mortality due to diffuse contamination of the abdominal cavity and the rapid development of severe septic shock [68]. In general, in this situation, it is necessary to make every effort to remove the affected area of the intestine together with the tumor. However, the treatment approach should be balanced and take into account the severity of the patient's condition. Unstable patients can undergo only those procedures that they can tolerate, and this usually corresponds to technically simple and quickly performed operations (Hartmann's procedure, right hemicolectomy without anastomosis, subtotal colon resection is without anastomosis) [12,27].*

• Operations to remove tumor of the large intestine with anastomosis are **recommended** to be performed only after the resolution of the symptoms ALIO in stable patients without severe comorbidities, in the presence of a qualified team of surgeons-oncologists or coloproctologists, in accordance with clinical guidelines for the treatment of patients with colorectal cancer [7,89,90].

Grade of recommendations — C (Level of evidence — 4)

Comments: *with ALIO, the risk of potentially fatal complication is higher — the anastomosis leakage. The rate of anastomosis leakage in ALIO is 11.2% — 14.3%, while the mortality rate reaches 17.1% [69,70]. The most common anastomosis leakage occurs after subtotal colectomy — 14%, left hemicolectomy — 13%, resection of the transverse colon — 10.3% [12]. Risk factors for an unfavorable prognosis during surgery with anastomosis include the patient's age over 70 years, high anesthetic risk (ASA > 3), anemia (Hb < 75 g / l), chronic kidney disease (glomerular filtration rate (GFR) < 45 ml/min /1.73 m^2), chronic heart failure, respiratory failure, neurological deficit.*

In the presence of any listed risk factors, the formation of an anastomosis should avoided in favor of stoma [12,71]. The complicated postoperative period may be the reason for the late start of chemotherapy, or even refusal to carry it out.

3.4 Palliative treatment of patients with ALIO

The main goal of treating patients with stage IV large intestine cancer and acute intestinal obstruction is to increase the patient's life expectancy and improve its quality. Available treatment options include the use of systemic corticosteroids and gastrointestinal motility stimulants, symptomatic treatment — nasogastric intubation and parenteral nutrition, intestinal stenting and surgeries — proximal stoma formation and intestinal resection. However, overall survival is low, regardless of the type of treatment. Universally poor outcomes suggest that acute intestinal obstruction against the background of incurable large intestine cancer should be considered as a preterminal event [72]. In such situations, an individualized multidisciplinary approach with increased patient participation in choosing the scope of treatment is preferable [73]. If signs of perforation, strangulation and peritonitis detected in patients with stage IV large intestine cancer, emergency surgical treatment is necessary. It is necessary to strive for the implementation of the minimum possible surgery volume, giving preference to the formation of a proximal stoma. If intestinal perforation, ischemia and abscess detected, resection should performed.

In patients with a disseminated form of large intestine cancer complicated by compensated large intestine obstruction, it is possible to perform surgery in the volume of palliative large intestine resection. The basis for performing such a surgery is the decision of a multidisciplinary oncological council. Currently, there is no convincing data on the benefits or disadvantages of performing palliative bowel resection in patients with disseminated cancer. The results of existing studies contradict each other; most of the studies

are retrospective, which is why many significant variables, such as the number of metastases, their size, and characteristics of target organs may not be taken into account, which does not allow using accurate methods of statistical information processing [74]. The reasons for performing palliative resection are the expected improvement in the patient's quality of life and ensuring optimal conditions for chemotherapy.

The issues of pain syndrome control and nutritional status support in palliative patients are not considered in these recommendations.

- In case of tumor ALIO in patients with stage IV colorectal cancer with a short life expectancy, the use of the intestinal stenting method is **recommended** [75].

Grade of recommendations — B (Level of evidence — 2)

Comments: *bowel stenting as part of palliative treatment of patients with obstructive pulmonary embolism can eliminate the need for the formation of an intestinal stoma, which potentially allows for an acceptable quality of life for patients [53]. However, despite the high rate of technically successful stenting (in the presence of only one tumor obstacle) — from 90% to 100% of cases, a shorter duration of hospitalization compared to the formation of a stoma [76], early postoperative complications more often occurred during stenting [44]. The recurrence rate of acute intestinal obstruction is higher in the group of patients undergoing stenting — 20.7% versus 9% in the surgical treatment group [75].*

- In patients with stage IV cancer, if it is impossible to stent the intestine, there are several areas of intestinal obstruction, as well as, if drug antitumor treatment is carried out, surgery is **recommended** in the volume of proximal colostomy / ileostomy [77].

Grade of recommendations — C (Level of evidence — 4)

Comments: *the basis for treatment of patients with disseminated colorectal cancer is chemotherapy. Because the presence of a stent in the tumor canal in patients receiving bevacizumab** for a long time is associated with a high risk of tumor perforation, other methods of large intestine decompression should be used [46]. Stoma is a relatively simple procedure that allows rapid and reliable decompression of the large intestine [77].*

4. MEDICAL REHABILITATION AND SPA TREATMENT, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF REHABILITATION METHODS, INCLUDING THOSE BASED ON THE USE OF NATURAL THERAPEUTIC FACTORS

- In patients with laparotomy access, it is recommended to use epidural anesthesia based on local anesthetics and opioids in order to control pain syndrome [78].

Grade of recommendations — B (Level of evidence — 3)

Comments: *the optimal analgesia regimen after extensive surgeries should provide a sufficient level of anesthesia, promote early mobilization, more active restoration of intestinal function and nutrition, and not cause complications [78]. It is preferable to use multimodal analgesia, combining regional methods of anesthesia, as well as, if possible, and the rejection of opioids in order to avoid the development of side effects.*

Opioids followed by drowsiness and adynamic patients, ileus, episodes of nausea and vomiting.

*In open laparotomy, epidural analgesia is the optimal method of analgesia in the first 72 hours after surgery, contributing to an earlier restoration of intestinal function and a reduction in the number of complications [79,80]. The use of 0.2% ropivacaine** in combination with fentanyl** provides optimal anesthesia and minimizes the risk of motor block and hypotension due to sympathetic blockade [78,81]. To eliminate hypotension caused by sympathetic blockade, vasopressin and its analogues should be prescribed in the absence of hypovolemia. Preferably, the epidural catheter should be removed 48–72 hours after surgery.*

- After surgery and recovery from post-acute depression, it is **recommended** to prescribe nutritional support in the form of oral, including probe supplemental nutrition, with the restoration of normal intestinal peristalsis, the usual meal can be resumed [82,83].

Grade of recommendations — C (Level of evidence — 2)

Comments: *the use of enteral infusions of salt, monomer-salt and nutrient mixtures, adsorbing intestinal preparations in the postoperative period contributes to a faster restoration of gastrointestinal*

function [84]. Additional oral nutrition (for convenience, special mixtures used, including the sipping method) can increase the total food intake, which allows achieving the target alimentary indicators [85,86].

• Removal of the urethral catheter is **recommended** after activation of the patient, preferably on the 2nd day after surgery [87].

Grade of recommendations — C
(Level of evidence — 2)

Comments: *bladder catheterization used for precise control of diuresis, with urinary retention and the patient's inability to control pelvic functions. Prolonged presence of a urinary catheter increases the risk of urinary infection, prevents early mobilization. If the patient is able to control pelvic functions, then removal of the urinary catheter is possible as early as on the 1–2 days after surgery [87]. A longer stay of the urinary catheter may be required for patients with epidural analgesia.*

• Early mobilization in the postoperative period is **recommended** for patients operated for ALIO [81,88].

Grade of recommendations — B (Level of evidence — 3)

Comments: *Prolonged stay in bed increases the frequency of thromboembolic complications, respiratory disorders, reduces muscle strength and increases the risk of hemodynamic disorders. The patient's activity determined by both objective and subjective factors. Adequate anesthesia, timely removal of drains and catheters is important. In addition, the patient needs to explain the safety of motor activity after surgery, reassure him about the risk of "suture divergence" in the early postoperative period. The patient's rise from bed, starting from the 1st day after surgery, and regular activity followed by a decrease in the frequency of postoperative complications and the duration of hospital stay [88].*

5. PREVENTION AND DISPENSARY SUPERVISION, MEDICAL INDICATIONS AND CONTRAINDICATIONS TO THE USE OF PREVENTION METHODS

5.1 Prevention

Prevention of ALIO is early diagnosis of colorectal cancer and should be carried out in accordance with the guidelines for the treatment of rectal and colon cancer [89,90].

5.2 Dispensary management

• All patients who have undergone surgery for ALIO are subject to dispensary observation by an oncologist or a coloproctologist [91–93].

Grade of recommendations — C (Level of evidence — 4)

Comments: *after radical colorectal resection and adjuvant chemotherapy (if indicated), dispensary observation of patients is carried out, the purpose of which is to identify possible complications, diagnosis of cancer recurrence, detection of synchronous or metachronous neoplasms. Analysis of data from 18 large randomized trials, which included a total of 20,898 patients, showed that in the first 3 years after resection, up to 80% of all cases of recurrence of colorectal cancer develop [91], and within 5 years after surgery — up to 95% of all recurrences [92].*

For stage II-III patients who have undergone successful removal of a malignant large intestine tumor (in the absence of a "residual" tumor), an examination may be recommended every 3–6 months after surgery for 2 years, then every 6 months — up to 5 years. Colonoscopy should be prescribed in 1 year after the surgery (or in 1–3 months if a total colonoscopy was not performed at the preoperative stage of the examination). Colonoscopy should repeated annually for up to 3 years, and then every 5 years [93]. However, if an adenomatous/villous polyp or severe epithelial dysplasia detected, colonoscopy should be repeated annually. More frequent colonoscopy may be recommended for young patients (up to 50 years old). Colonoscopy as part of dispensary follow-up is necessary, first, for the diagnosis of metachronous polyps and their subsequent removal, since patients with a history of large intestine cancer have a risk of developing a second cancer, especially in the first 2 years after surgery [94].

Computed tomography is recommended to detect potentially resectable metastases, mainly in the lungs and liver. It follows from this that CT scanning may not be used routinely in patients with asymptomatic generalized form of cancer who are not candidates for potentially radical surgical treatment. Computed tomography of the thorax, abdominal cavity and pelvic organs should be performed every 6–12 months up to 5 years at stage III, and in patients with stage

II who have a high risk of developing the disease recurrence [95].

6. ORGANIZATION OF MEDICAL CARE

6.1 Indications for admission in a medical organization

All patients with suspected intestinal obstruction should be urgently admitted in a surgical hospital. In case of acute intestinal obstruction caused by a large intestine tumor, help is **urgent**. The timing of admission of such patients may determine the outcome of the disease. Postponement of the start of treatment or violation of the timing of the stages of treatment leads to a decrease in the overall and disease-free survival rates in these patients and makes the prognosis of a particular patient heavier.

Diagnostic measures at the stage of diagnosis should be carried out in a surgical hospital. The working group recommends that planned surgical treatment, drug antitumor treatment, and radiation therapy be carried out in the conditions of specialized hospital units (oncological, coloproctological).

All patients who are scheduled to undergo surgical procedure for large intestine cancer must give informed consent. It implies that the patient provided with information about the possible benefits and hypothetical risks of treatment, as well as the availability of any alternative methods of treatment. If possible, informed consent should obtained directly by the operating surgeon. In accordance with the Law of the Russian Federation of November 21, 2011, No. 323-FL "On the Basics of Protecting the Health of Citizens in the Russian Federation", obtaining voluntary informed consent is a mandatory and necessary procedure that reflects compliance with legal and ethical human rights to make an independent decision concerning his health. The conditions for the possibility of obtaining informed consent are the ability of the patient to make informed decisions regarding therapeutic measures, the accessible provision of all information necessary for decision-making. The main issues are: the benefits and risks of the proposed treatment, the planned amount of therapeutic measures, the consequences of refusing treatment.

- It is **recommended** to perform surgeries to remove colon tumors in ALIOin surgical, coloproctological or oncological unit, by a specialist with experience in performing oncological surgeries on the large intestine [69].

Grade of recommendations — C (Level of evidence — 4)

Comments: *the lack of specialization of the doctor in the field of colorectal surgery is a factor of unfavorable prognosis [69]. It has been shown that the overall rate of postoperative complications and postoperative mortality is higher if the surgery was performed by a surgeon who does not have special training. The failure of the interstitial joint in general surgical hospitals is twice as high as in specialized medical institutions (21.3% vs. 10.3%) [96]. In patients operated on in general surgical units, the number of examined lymph nodes in the specimen in 98.3% of cases does not correspond to the required number — 12 or more [96]. Overall and disease-free survival is statistically significantly lower in the group of patients operated on in non-specialized hospitals. In stage III patients operated on after the resolution of ALIO in oncological units, the 5-year overall survival is 50%, while among those operated on against the background of ALIO in non-specialized hospitals — 28% (p = 0.02) [97].*

6.2 Indications for the patient's discharge from the medical organization

In case of hospitalization for acute intestinal obstruction, the timing of the patient's discharge from the medical organization depends on the amount of medical care provided, the nature of the surgery, and the course of the postoperative period. Discharge during the uncomplicated course of the postoperative period is performed with the improvement of the patient's condition, restoration of gastrointestinal function, relief of endotoxicosis and normalization of red blood indicators. An extract from a non-specialized surgical unit with mandatory referral of the patient to an oncological or coloproctological hospital is performed when the symptoms of acute intestinal obstruction are relieved by means of intestinal stenting, or the formation of a proximal loop stoma.

In a situation when the AIO was resolved against the background of conservative treatment, in

order to avoid recurrence of obstruction, the patient is transferred to a specialized hospital (unit) of oncological or coloproctological profile.

7. ADDITIONAL INFORMATION (INCLUDING FACTORS AFFECTING THE OUTCOME OF THE DISEASE OR CONDITION)

Negatively affect the outcome of treatment:
- *Intestinal perforation*
- *Non-radical removal of the tumor*
- *Incomplete pathomorphological description of the specimen of the removed tumor*
- *Refusal to perform adjuvant chemotherapy if there are indications for its implementation.*

CRITERIA FOR ASSESSING THE QUALITY OF MEDICAL CARE

№	Quality assessment criteria	Performance Assessment (yes/no)
1	A digital rectal examination was performed	Yes/No
2	The effectiveness of conservative therapy was evaluated every 6 hours	Yes/No
3	Marking of the intestinal stoma removal area before surgery for ALIO was performed	Yes/No
4	The elimination of intestinal obstruction was performed	Yes/No

When performing resection surgeries for colorectal cancer complicated by ALIO, the quality of medical care provided should be evaluated in accordance with clinical recommendations for the treatment of colon and rectal cancer [89,90].

Table 1. *Scale of assessment of CEL (levels of evidence credibility) for diagnostic methods (diagnostic surgeries)*

CEL	Decoding
1	Systematic reviews of trials with reference method control or systematic review of randomized clinical trials using meta-analysis
2	Separate studies with reference method control or separate randomized clinical trials and systematic reviews of studies of any design, with the exception of randomized clinical trials, using meta-analysis
3	Studies without sequential control by a reference method or studies with a reference method that is not independent of the method under study or non-randomized comparative studies, including cohort studies
4	Non- comparative studies, description of a clinical case
5	There is only a justification of the mechanism of action or the opinion of experts

Table 2. *CEL assessment scale for methods of prevention, treatment and rehabilitation (preventive, curative, rehabilitation interventions)*

CEL	Decoding
1	Systematic review of RCTs (randomized clinical trials) using meta-analysis
2	Separate RCTs and systematic reviews of studies of any design, with the exception of RCTs, using meta-analysis
3	Non-randomized comparative studies, including cohort studies
4	Non-comparative studies, description of a clinical case or series of cases, case-control studies
5	There is only a justification of the mechanism of action of the intervention (preclinical studies) or the opinion of experts

Table 3. *The scale of assessment of RC (Grade of recommendations) for methods of prevention, diagnosis, treatment and rehabilitation (preventive, diagnostic, therapeutic, rehabilitation interventions)*

RC	Decoding
A	Strong recommendation (all considered performance criteria (outcomes) are important, all studies have high or satisfactory methodological quality, their conclusions on the outcomes of interest are consistent)
B	Conditional recommendation (not all considered performance criteria (outcomes) are important, not all studies have high or satisfactory methodological quality and/or their conclusions on the outcomes of interest are not consistent)
C	Weak recommendation (lack of evidence of proper quality (all considered performance criteria (outcomes) are unimportant, all studies have low methodological quality and their conclusions on the outcomes of interest are not consistent)

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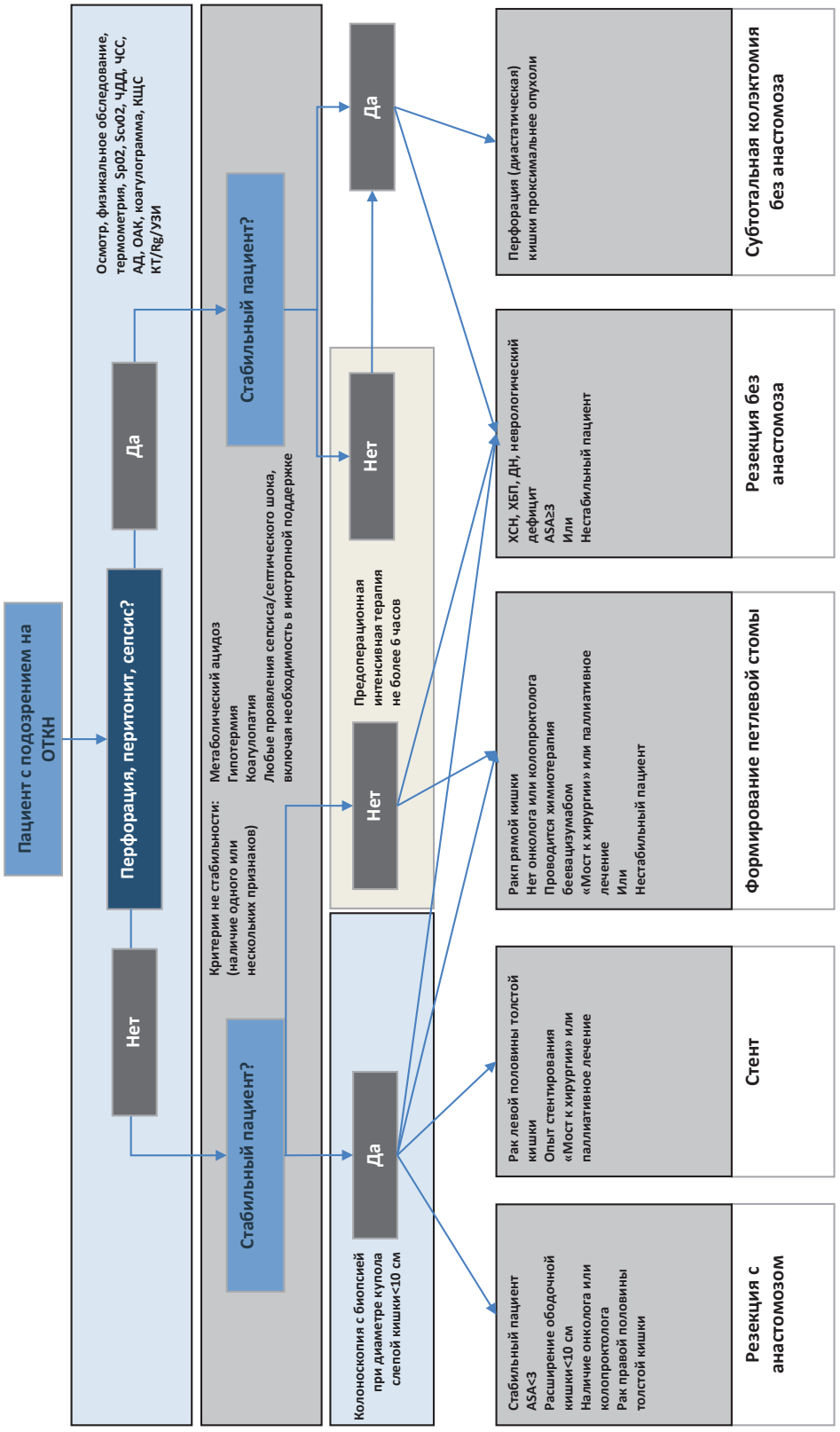
APPLICATION. Diagnostic algorithm



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Neurogenic bladder dysfunction after total mesorectumectomy

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ABSTRACT *AIM: to estimate the rate, causes and features of neurogenic bladder dysfunction in patients with rectal cancer after total mesorectumectomy.*

PATIENTS AND METHODS: the results of surgical treatment of 103 patients with rectal cancer were analyzed in the light of immediate and long-term outcomes, who underwent total mesorectumectomy using traditional (56-54.4%) and laparoscopic (47-45.6%) technologies. In 20 (19.4%) of 103 patients, the course of the immediate postoperative period was complicated by the development of neurogenic bladder dysfunction. In order to study the frequency of neurogenic bladder dysfunction depending on the technique of mesorectumectomy, the patients were divided into 2 groups. Group 1 included 9 patients who underwent laparoscopic total mesorectumectomy. Group 2 included 11patients who underwent traditional (open) mesorectumectomy.

RESULTS: the study of the functional state of the bladder according to the flowmetric indicators revealed that the frequency of development of postoperative bladder dysfunction has a gender dependence. The frequency of neurogenic bladder dysfunction was 25% in men and 10,7% in women. It is shown that during 1 week and 6 months after surgery, the average urination rate tends to increase in women and decrease in men, regardless of the technique of total mesorectumectomy. In both groups, there was not a statistically significant decrease in the maximum volumetric velocity in both men and women within 6 months after surgery. At the same time, during this period, there was a decrease in the average rate of urination only in men, regardless of the technique of total mesorectumectomy. And in women, this indicator remained unchanged or slightly increased.

CONCLUSION: it is shown that a complex system of therapeutic measures, including drug stimulation of the detrusor and urethral sphincter, repeated catheterization of the bladder, as well as epicystostomy performed according to indications, allows adequate correction of bladder dysfunction after total mesorectumectomy in patients with rectal cancer.

KEYWORDS: *rectal cancer, total mesorectumectomy, open total mesorectumectomy, laparoscopic total mesorectumectomy, neurogenic bladder dysfunction*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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INTRODUCTION

Global trends in the epidemiology of colorectal cancer (CRC) clearly demonstrate the high incidence of rectal cancer (RC), which consistently occupies the 4–5th place in the overall structure of malignant tumors [1–4]. According to our data, after total mesorectumectomy (TME) performed using traditional (open) TME (OTME), the actual survival rate was 81.8%, the disease-free 3-year survival rate was 60.6%. In patients who underwent TME using laparoscopic technology (LTME), these indicators were 80% and 56.7%, respectively. After OTME, the 5-year actual survival rate was 54.5%, the disease-free 5–year survival rate was 31.8%. In patients who underwent LTME, these data were 57.8% and 31.6%, respectively [5].

The presented data demonstrating the level of morbidity and mortality convincingly indicate

the global medical and social significance of the problem of CRC in general, and RC in particular. Since the 80th year of the twentieth century, the transition from the standard, so-called "orthodox" surgery for RC to the TME technique, developed by Heald, R.J. et al. [7], and providing for the removal of the rectum in a single block together with anatomical structures located within its fascial "case" with the preservation of elements of the autonomic nervous system of the pelvis (ANSP), marked the beginning of a new era in oncoproctology and opened a new direction in the surgical treatment of RC. However, many authors [1,6] regret to note that, despite the obvious advantages, it has not yet been possible to achieve the widespread introduction of the TME technique as a standard surgery for RC.

Meanwhile, being a functionally sparing and sphincter-preserving surgery, TME meets all the principles of oncological radicality and makes it possible to improve not only long-term outcomes, but also the early functional results of surgical treatment of RC. As a nerve-sparing surgery, TME allows to ensure the safety of the visceral fascia of the rectum and the integrity of the autonomous (autonomic) nervous system of the pelvis (ANSP) and thus does not lead to a significant violation of the function of the lower urinary system and a decrease in the quality of life in operated patients [8]. According to Sidorov, D.V. et al. [6], the use of the nerve-sparing technique during TME makes it possible to significantly reduce the incidence of urological complications and restore bladder function in 90.3% of patients in the early postoperative period. However, despite the undeniable advantages, TME is not without drawbacks, which include urological complications, sexual disorders, anal incontinence. This is due to the fact that rectal surgeries in general, TME — in particular, belong to the category of technically complex, traumatic procedures with a high risk of complications and mortality.

To denote the disorder of the function of the lower urinary system in patients with RC after TME, many similar terms are used in the literature: "urodynamic disorders", "urological complications", "detrusor dysfunction", "neurogenic bladder dysfunction", etc. It seems to us that using different terms reflecting different linguistic interpretations, the authors put a single semantic meaning into them.

Regarding the causes of neurogenic bladder dysfunction (NBD) after TME, there are different opinions among surgeons. Many authors [9–12] believe that the development of this complication is directly caused by intraoperative damage to the elements of the ANSP associated with insufficient visualization of the surgical field during surgery. According to other authors [13,14], an important role in the development of NBD is played by the local spread of the tumor with involvement in the malignant process of ANSP, requiring the removal of affected adjacent tissue structures. The frequency of locally advanced RC with involvement of the visceral fascia of the rectum and invasion of the tumor into adjacent organs and anatomical structures of the pelvis, is 26–35% [15,16]. At the same time, in 50.3–60.2% of cases, the lesion falls on the urinary system involvement [17,18]. After TME, bladder dysfunction occurred in 9–40%, according to some authors [27,30] from 9% to 40%. Other authors revealed it in 48–80% [20,21].

The high percentage of NBD is due to the close anatomical and topographic relationship of the pelvic organs on the one hand and the involvement of neighboring organs and anatomical structures of the pelvis in the tumor process on the other hand. And finally, an important role in the structure of the causes of the development of this complication is played by the traumatic nature of surgeries performed in patients with locally advanced RC, as well as neoadjuvant chemoradiotherapy performed in the preoperative period. According to the literature [22–24], 5.2–17.6% of patients develop persistent bladder a tony after neoadjuvant chemoradiotherapy. The development of NBD significantly aggravates the course of the postoperative period and worsens the quality of life of patients. Chronic bladder dysfunction contributes to a violation of the passage of urine with the possible development of hydronephrosis and, as a consequence, chronic renal failure [6].

In recent years, publications have appeared in the literature demonstrating the effectiveness

Table 1. *Neurogenic bladder dysfunction in patients with rectal cancer, depending on gender and TME technique*

TME Technique	Total	Males	Females	Total
LTME	27	6 (22.2%)	3 (11.1%)	9 (33.3%)
OTME	29	8 (27.6%)	3 (10.3%)	11 (38%)
Total	56	14 (25%)	6 (10.7%)	20 (35.7%)

Note: The table does not include 36 patients (18 patients from each group), in whom independent urination was restored after the first catheter removal.

of the intraoperative neuromonitoring method in order to identify and preserve the integrity of the elements of the ANSP [25–27]. However, the authors declare that as an intraoperative method for determining the ANSP, this method currently can hardly be qualified as the main one, but it has prospects from the point of view of studying the physiology of the pelvis. According to the cited authors, further accumulation of experience in the use of the intraoperative neuromonitoring method will allow determining its significance in RC surgery.

Thus, the presented literature data allow us to state that the study of the causes, frequency and features of NBD in patients with RC after TME has important scientific and practical significance, and the search for rational surgical methods that ensure compliance with the principles of anatomical zonality and oncological radicalism seems very relevant.

AIM

To assess causes and features of the clinical picture of NBD in patients with RC after TME.

PATIENTS AND METHODS

The retrospective study is based on the results of checkup and surgical treatment of 103 patients aged 20 to 70 years with cancer of the middle and lower ampullary segments of the rectum. The diagnostic algorithm included general clinical, laboratory, biochemical and instrumental methods of diagnostics (thorax X-ray, transabdominal, endorectal and transvaginal ultrasound, colonoscopy, CT of the thorax and abdominal cavity, MRI of the pelvic organs, electrocardiography, echocardiography). The diagnosis was verified also by cancer markers (CEA and CA-19-9) and pathomorphologyof biopsy and removed specimen. To assess the functional state of the urinary system, uroflowmetry was performed.

All patients under endotracheal anesthesia underwent total mesorectumectomy, using traditional (open) technology in 56 (54.4%), laparoscopic — in 47 (45.6%) cases. Particular attention was paid to the macroscopic examination of the removed specimen in order to visually assess the preservation of the visceral fascia, the degree of severity and integrity of mesorectum, the presence or absence of intraoperative perforation of the intestinal wall. In all patients, the histological structure of the tumor was represented by adenocarcinoma of various degrees of differentiation. In the early postoperative period, bladder dysfunction occurred in 56 (54.4%) of 103 patients. There were 31 men (55.4%) and 25 women (44.6%). All patients had locally advanced RC ($T_{3-4}N_{1-2}Mo$).

All patients underwent neoadjuvant chemoradiotherapy in the preoperative period. Analysis of the causes of NBD shows that these complications were caused either by tumor lesions (in 29 cases) or intraoperative lesions (in 27 cases) of the visceral nerves during surgery. In 27 (48.2%) of 56 patients, TME was performed using laparoscopic technology (Group 1), in 29 (51.8%) — traditional (Group 2) (Table 1).

All patients underwent procedures without nerve-sparing technique. Assessment of the degree of preservation of the visceral nerves was

carried out visually. In the group of patients who underwent LTME, urodynamic disorders developed as a result of iatrogenic damage to the visceral nerves in 15, tumor lesion — in 12 cases. Of the 29 patients who underwent OTME, the occurrence of urodynamic disorders was due to intraoperative damage to the ANSP in 12, tumor lesions in 17 cases. It should be noted that intraoperative damage to the visceral nerves was due to technical difficulties in performing certain stages of TME associated with anatomical and topographic features of the location of organs and the complexity of intraoperative identification of the nerve trunks of the pelvis.
The manifestation of the "NBD" syndrome was characterized by acute urinary retention, an increase in the volume of residual urine, and a weakening of the feeling of filling the bladder. This symptom complex was evaluated taking into account the complaints of patients, characteristic clinical manifestations, the results of physical examination and ultrasound examination of the pelvic organs. In order to objectively assess the contractility of detrusor, all patients underwent daily registration of the state of urination by uroflowmetric monitoring. Uroflowmetry was performed using a portable device — uroflowmeter, model "AGAT" (Russia). The uroflowgram based on the registration of urination parameters was evaluated according to the following indicators: — urination time (normally < 10 sec); — maximum volume urination rate (normally > 15–20 ml per second); — average urination rate (normally > 10 ml per second); — time to reach maximum speed; — total volume of urination (more than 50 ml); — waiting time for the start of urination (normally < 10 seconds).
Of these parameters, the maximum volumetric velocity and average urination rate were considered practically significant.
Statistical processing of the results of the study was carried out on a personal computer using software tools and the SPSS for Windows 13.0 package. The significance of the differences was assessed using the nonparametric Wilcoxon-Mann-Whitney method for independent samples. The differences were considered statistically significant at $p < 0.05$.

RESULTS

After the first catheter removal, self-urination was restored in 9 (60.0%) men and 9 (75.0%) women who underwent LTME. Self-urination after the first catheter removal was restored in 10 (77.0%) women and 8 (50.0%) men who underwent OTME. As can be seen from the presented data, after the first catheter removal, the restoration of self-urination was equally often observed both in patients who underwent LTME and in patients who underwent OTME. For the first 3 days of the postoperative period, it was not possible to restore independent urination in 9 patients who underwent LTME (6 men, 3 women). A similar pattern was observed in 11 patients (8 men, 3 women) after OTME. In 18 patients (in 8 — after LTME, in 10 — after OTME), urine removal was carried out by repeated catheterization of the bladder and the installation of a permanent catheter. The age of the patients in the study group ranged from 53 to 70 years. In the middle age group (44–66 years) there were 7 (35.0%) patients, in the elderly (60–70 years) — 13 (65.0%). There were 14 men (70.0%), 6 women (30.0%).
For the purpose of drug correction of NBD, all the patients were prescribed a cholinomimetic drug — 0.05% solution of neostigmine (proserin). The drug was administered intramuscularly 1 ml 3 times a day for a week.
To stimulate the contractile function of detrusor in men, omnik (tamsulosin, a drug from the group of α_1-blockers) was prescribed 1 capsule per day for 2 weeks. Independent urination by the time of discharge from the hospital was restored in all these patients. Urine derivation was performed by trocar epicystostomy in two patients aged over 60 years who underwent LTME (1) and OTME (1) and suffered from benign prostatic hyperplasia. Restoration of self-urination in these patients occurred within 6 months after TME. No cases of "catheter-associated" urinary tract infection were detected. A comparative assessment of the degree of postoperative NBD according to the parameters of uroflowmetry, taking into account the patients' gender, revealed that within 1 week and 6 months after surgery, the average urination rate (AUR) tends

Table 2. *Dynamics of the maximum volume and average urination rate according to uroflowmetry data at different times after TME in patients with rectal cancer*

	LTME				OTME			
Gender	**MVRU**		**AUR**		**MVRU**		**AUR**	
	1 week	**6 months**	**1 week**	**6 months**	**1 week**	**6 months**	**1 week**	**6 months**
Males	20.8 ± 2.1	20.6 ± 4.2	16.2 ± 2.5	16.2 ± 3.2	20.1 ± 1.9	20.5 ± 4.1	16.3 ± 2.4	16.3 ± 3.4
Females	20.1 ± 1.0	18.1 ± 3.9	17.4 ± 1.6	17.8 ± 3.5	20.2 ± 1.1	17.9 ± 3.7	17.5 ± 1.7	17.9 ± 3.6

Note: The table does not include 36 patients (18 patients from each group), in whom independent urination was restored after the first catheter removal.

to decrease in men, regardless of the TME technique. In both groups, there was a significant decrease in the maximum volumetric rate of urination (MVRU) in both men and women within 6 months after surgery. At the same time, for this period, there was a decrease in AUR only in men, regardless of the TME technique. And in women, this indicator remained unchanged or slightly increased. The changes of MVRU and AUR according to uroflowmetry data at various times after TME is presented in Table 2.

Thus, the analysis of our clinical cases shows that NBD after TME in patients with RC is almost equally common in patients who have undergone both LTME (in 33.3%) and OTME (in 38%). The occurrence and clinical picture of NBD have a gender feature, regardless of the TME technique. Thus, the incidence of NBD in men was 25%, which is over 2 times more than the same indicator in women — 10.7% (Table 1).

DISCUSSION

The relevance of the RC problem is due not only to the complexity of solving oncological problems associated with ensuring long-term actual and disease-free cancer survival, but also to the difficulty of improving the immediate functional results of surgical treatment. One of the unresolved problems of RC surgery is NBD, which develops in the early postoperative period [9–14]. The complexity of topographic anatomical relationships of the pelvic organs create prerequisites and potential threats to damage the visceral nerves, innervating organs of the genitourinary system. In addition to intraoperative damage to the visceral nerves, with RC, the spread of the malignant process through the perineural spaces is possible, which is also an unfavorable prognostic sign in relation to both immediate functional and long-term oncological results of surgical treatment [6,17–20]. On the other hand, reliable methods for determining the degree of tumor invasion into the visceral nerves and intraoperative identification of the nerve structures of the pelvis have not yet been developed [6]. Meanwhile, the report of individual authors [25–27] on the effectiveness of the intraoperative neuromonitoring method in order to identify and preserve the integrity of the visceral nerves, inspires some optimism about improving the functional results of surgical treatment of patients with RC.

The introduction of functional-sparing surgeries into the arsenal of surgical treatment of patients with RC allows to preserve the integrity of the ANSP elements as much as possible and reduce the frequency of bladder dysfunction. The frequency of NBD after TME in patients with RC varies widely, varying from 40% to 80% [16,19–21]. According to our data, the total proportion of NBD in patients with RC was 35.7%, which developed both after OTME (in 38%) and after LTME (in 33.3%).

Treatment and rehabilitation of patients with NBD after TME is a difficult and complex task. Unfavorable is the fact that to date there is no generally accepted concept of treatment of NBD in patients with RC after TME in the literature.

The principles of correction of postoperative disorders of bladder function include a multicomponent system of therapeutic measures taking into account the clinical manifestation of NBD in accordance with uroflowmetric parameters. One of the important criteria for objectively assessing the functional state of the bladder is the restoration of self-urination after the first catheter removal. Sidorov, D.V. et al. [6] revealed recovery of spontaneous urination after the first catheter removal in 90.3% of the operated patients. According to the authors, in 9.7% of cases in the early postoperative period (for no more than 3 days), it was not possible to restore independent urination, which required repeated catheterization of the bladder. In our study, in the absence of restoration of self-urination, 18 (90.0%) of 20 patients underwent repeated catheterization of the bladder with the installation of a permanent catheter. Two (10.0%) patients aged over 60 years, suffering from benign prostatic hyperplasia had urine excretion performed by trocar epicystostomy. Independent urination in all these patients was restored within 6 months after surgery. The effectiveness of prolonged catheterization with persistent bladder atony in patients after TME is confirmed by the works of other authors [19,28]. Along with routine methods (permanent catheterization of the bladder, drug stimulation of detrusor, etc.), some authors [29] consider advisable the use of α_1(alpha$_1$)-adrenoblockers (tamsulosin, terozosin, alfuzosin, silodosin), among which tamsulosin and silodosin have the greatest uroselectivity, for the purpose of pharmacological correction of NBD in men. It is also recommended to use α_{1-}adrenoblockers combined with phosphodiesterase inhibitors of type 5 (PDE-5) (sildenafil, vardenafil, tadalafil, etc.) in men whose NBD is accompanied by sexual dysfunction.

AUTHORS CONTRIBUTION

Research concept and design: *Saday A. Aliyev*
Collection and processing of material: *Saday A. Aliyev*
Statistical processing: *Saday A. Aliyev, Elman G. Azimov*
Writing a text: *Saday A. Aliyev*
Editing: *Saday A. Aliyev*
Approval of the final version of the article: *Saday A. Aliyev*
Responsibility for the integrity of all parts of the article: *Saday A. Aliyev*

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Clinical features and quality of life of patients with idiopathic megacolon

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ABSTRACT *AIM: to assess the quality of life (QoL) of patients with idiopathic megacolon and its relationship with clinical and diagnostic features.*

PATIENTS AND METHODS: the retrospective study of clinical features and diagnostic tests results included 81 patients with idiopathic megacolon/megarectum (2004–2022). The diagnosis of megacolon/megarectum was confirmed with a barium enema, Hirschsprung's disease was excluded based on anorectal manometry and (if needed) rectal Swenson biopsy. The QoL was assessed by IBSQOL questionnaire; clinical symptoms were assessed with a point scale.

RESULTS: the quality of life in patients with idiopathic megacolon has most affected energy (emotional and physical) and physical role (work/main activity). In univariate analysis the significant correlation was revealed between QoL and age, sex, rate of defecation without assistance, rate of integral parameters "abdominal discomfort" and "defecation difficulties", duration of anamnesis, Wexner constipation scale rate and gut transit time ($p < 0,05$). In the same time, the presence or absence of constipation or anal incontinence (leakage), colon and rectum sizes (based on barium enema), parameters of defecografy and rectal compliance test have not correlated with a QoL. No significant difference of QoL in patients added to conservative treatment and operated. Due to multivariate analysis (multiple linear regression) the age and rate of "abdominal discomfort" and "defecation difficulties" were only independent factors affected quality of life.

CONCLUSION: in terms of quality of life, idiopathic megacolon has the greatest impact on general tone and ability to perform basic professional activities. Independent factors that statistically significantly affect the assessment of quality of life are the age of patients and the severity of symptoms of abdominal discomfort and defecation disorders.

KEYWORDS: *Idiopathic megacolon, idiopathic megarectum, quality of life*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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INTRODUCTION

Idiopathic megacolon is a chronic enlargement of the large intestine for which it is not possible to identify a clear etiological factor. The prevalence of idiopathic megacolon is unknown, but it is generally considered to be a fairly rare condition. So, according to Knowles, C.H. et al. (2003), 1,600 patients suffering from chronic constipation were treated at the Royal London Hospital for 10 years. Only 20 of them had megacolon/megarectum detected during the examination [1]. At the same time, since, on the one hand, constipation and symptoms of abdominal discomfort are the main manifestation of megacolon, and, on the other, special tests are needed for its diagnosis, it can remain unrecognized in a significant part of cases, passing under the mask of irritable bowel syndrome or slow-transit constipation, and, according to a number of authors, makes up to 10–20% of patients with refractory constipation [2]. However, this is a separate group of patients with an excellent algorithm for diagnosis and treatment, a significantly higher risk of complicated course and, accordingly, significantly wider indications for surgery [3].

Table 1. *The width of the lumen of various parts of the colon is normal*

Part of the large intestine (*n* = 160)	**Lumen width (min-max, cm)**	
	Achkasov, S.I., 2003 (*n* = 160)	Preston DM, Lennard-Jones JE, et al., 1985 (*n* = 50)
Caecum	4.0 — 9.0	–
Ascending colon	2.5 — 9.0	5.0 — 9.3
Transverse colon	2.5 — 8.5	4.5 — 8.3
Descending colon	1.5 — 6.0	3.7 — 7.1
Sigmoid colon	1.5 — 6.0	3.3 — 6.3
Rectum	4.5 — 8.5	2.2 — 6.5

Currently, according to the systematic review by Cuda, T. et al. 2018 [4] and our analysis of the PubMed database for the subsequent period (2018–2022), there is no data in the literature on the quality of life of patients with idiopathic megacolon. Therefore, the purpose of the study was to assess the quality of life of patients with idiopathic megacolon and its relationship with the clinical picture and the results of diagnostic tests.

PATIENTS AND METHODS

A retrospective analysis of the quality of life, clinical picture and check-up results of 81 patients with idiopathic megacolon/megarectum, observed in the Ryzhikh National Medical Research Center of Coloproctology from 2004 to 2022, was carried out.

Currently, there are no generally accepted criteria for the diagnosis of idiopathic megacolon/megarectum. This study included patients whose diagnosis was established on the basis of barium exam (irrigoscopy) if the width of one or another part of the large intestine exceeded the normal parameters determined earlier in our clinic during barium exam morphometric study [5]. These parameters are very close to the results of the second of the two currently available studies of the normal size of the large intestine, performed at the Royal London Hospital (Table 1) [6].

The idiopathic nature of megacolon/megarectum was confirmed by excluding Hirschsprung's disease according to irrigoscopy, anorectal manometry (*n* = 76) and, if necessary, a full-thickness biopsy of the rectal wall by Swenson (*n* = 7). Extra-intestinal causes of megacolon were also excluded.

The study did not include patients with stomas who had previously undergone colorectal resections in other clinics for megacolons and had applied to our Center for stoma takedown.

The IBSQOL questionnaire was used to assess the quality of life (QoL). It was developed in 1997 by a group of German researchers led by Dr. Hahn, B.A. with the support of the pharmaceutical company Glaxo Welcome and recommended for use at the World Congress of Gastroenterologists in Rome in 1999 [7]. The IBSQOL questionnaire includes 30 questions with gradation of answers on a point scale (from 1 to 5 or from 1 to 6 points). These questions are grouped into 9 sections reflecting the impact of intestinal symptoms on various aspects of human life: 1) emotional sphere; 2) mental health; 3) sleep; 4) tone; 5) physical activity; 6) nutrition; 7) social activity; 8) main activity; 9) sexual relations.

A point assessment is made for each section and in total. Domain indicators are calculated as a percentage of the best possible total score for this section and thus range from 0 to 100:

The total score is calculated as the average of the indicators by section:

Table 2. *Scale of assessment of symptoms of abdominal discomfort and defecation disorder*

Symptoms of abdominal discomfort	None	Very rarely	Sometimes	Often	Most of the time	Always
Symptoms of difficult defecation	None	Very rarely (0–25% of defecations)	Sometimes (25–50% of defecations)	Often (50–75% of defecations)	Most of the time (75–100% of defecations)	Always
Duration of defecation	Less than 5 min.	5–15 min.	16–30 min.	Over 30 min.		
Points	0	1	2	3	4	5

Table 3. *Scale of assessment of the safety of an independent stool and the urge to defecate*

Is there an independent stool (without using laxatives, enemas, candles, manual aids):	No	Very rarely	Sometimes	Often	Most of the time	Always
Urge to defecate	No	Very rarely	Sometimes	Often	Most of the time	Always
Points	0	1	2	3	4	5

The lower the score, the worse the quality of life.

When analyzing the relationship of QoL with the clinical picture, signs such as gender, age, anamnesis data (duration of disease, the history of volvulus, surgical procedures) and the following symptoms: the presence or absence of constipation, independent stool, urge to defecate, anal incontinence (leakage), defecation rate, symptoms of abdominal discomfort and difficulties with defecation, were taken into account.

In addition, clinical manifestations were assessed using a special questionnaire with a gradation of frequency-severity of symptoms, which allowed to do a quantitative analysis on a point scale. Previously, we used this questionnaire to assess the severity of clinical symptoms in patients with chronic constipation [8]. For the convenience of the analysis, some of the symptoms were conditionally grouped into two integral indicators: "abdominal discomfort" and "defecation disorder". "Abdominal discomfort" included symptoms such as belching, nausea, vomiting, bloating, rumbling in the abdomen, heaviness in the abdomen, abdominal pain. The indicator "defecation disorder" was determined by the duration of defecation and complaints about "difficulties with defecation", "the need for intensive straining during defecation", "feeling of incomplete emptying". The value of both indicators was calculated as a simple sum of points for each of the symptoms (Table 2).

In addition to the symptoms of abdominal discomfort and defecation disorder, the duration of symptoms and the preservation of the urge to defecate, the preservation of an independent stool and the defecation rate without enemas and laxatives were evaluated on a point scale (Tables 3–5).

In addition, the questionnaire made it possible to assess the intensity of constipation on a modified Wexner scale. Its differences from the original version were minimal and consisted in the gradation of the severity of difficulties with defecation and the feeling of incomplete emptying not in 5 (0–4 points), but in 6 (0–5 points) step scale.

The analysis of the relationship of the quality of life assessment was carried out with the following signs of diagnostic tests:

- irrigoscopy (n = 81)
  - the width of the large intestine
  - the length of the sigmoid and transverse colon
  - the multiplying of the maximal width by the length of the sigmoid colon is a conditional indicator with which we tried to more accurately

Table 4. *The scale of assessment of the defecation rate*

Defecation rate (if you do not use laxatives, enemas, candles)	3 times a week or more	Twice a week	Once a week	Less than 1 time a week	Less than 1 time a month
Points	5	4	3	2	1

Table 5. *Anamnesis duration assessment scale*

Duration of symptoms (years)	Up to 1 year	1-5	6-10	11-20	Over 20
Points	1	2	3	4	5

Table 6. *Estimation of transit time for the gastrointestinal tract in points*

Transit time (hours)	Up to 24	24-48	49-72	73-96	Over 96
Points	1	2	3	4	5

take into account the correlation of symptoms with the size of the intestine.

It should be noted that not in all patients it was possible to measure the length of the sigmoid and transverse colon and the multiplying of width by length due to the imposition of intestinal loops on irrigograms.

- Defecography (n = 52)
  - o residual volume (V_{RES})
  - o defecation Time (T_{DEF})

For technical reasons, the defecation time during defecography was recorded in 47 out of 52 patients who underwent this study.

- Transit time of barium suspension through entire GI tract for 5 days (n = 52). In the statistical analysis, the severity of transit disorders was estimated in points (Table 6). In addition, the presence or absence of distal delay, that is, predominant contrast delay in the sigmoid colon and rectum, was taken into account.
- Reservoir function of the rectum test (n = 40)
  - o maximum tolerated volume (MTV, ml)
  - o index of the maximum tolerated volume (IMTV) — the ratio of the maximum tolerated volume to the amount of residual rectal pressure created by it
  - o adaptation coefficient ($\Delta V/\Delta P$) is the ratio of volume increase to residual pressure increase from the sensitivity threshold to the maximum tolerated volume.

In 8 patients, when examining the reservoir function of the rectum, only the volumes of air injected into the rectal balloon corresponding to the sensitivity thresholds were recorded, without taking into account the residual rectal pressure created by them. Therefore, the calculation of the index of the maximum tolerated volume and the coefficient of adaptation was impossible. In another 12 cases, it was not possible to calculate the adaptation coefficient due to the fact that patients were unable to differentiate the first threshold of rectal sensitivity to filling.

STATISTICAL ANALYSIS

Statistical analysis was performed using the Statistics program, version 13.3. Given the abnormal distribution, Spearman's criterion was used for correlation analysis, and differences in binary data were evaluated using the Mann-Whitney criterion. Multivariate analysis was carried out using multiple linear regression equations. The differences were recognized as statistically significant at $p < 0.05$.

RESULTS

An analysis of the assessment of the QoL by patients with idiopathic megacolon according to the domains of the IBSQOL questionnaire showed that the lowest indicators were characteristic of general tone and ability for the main professional activity (Fig. 1).

This indicates that the disease had the greatest impact on these areas of life. In the relevant sections of the questionnaire, patients often noted a

feeling of emotional and physical fatigue, agreed with the statement that the disease interferes with their ability to work successfully, forces them to avoid certain types of work, "does not allow them to do the work as they would like".

The relationship of the total quality of life assessment ($\sum_{IBSQOL}$) with clinical symptoms and the results of diagnostic tests was evaluated using Spearman's correlation analysis for rank values (Table7) and the Mann-Whitney test for qualitative (binary) features (Table 8).

As can be seen from Table 7, the final QoL score ($\sum_{IBSQOL}$) decreased statistically significantly with the age of patients, as well as with an increase in the integral indicators "abdominal discomfort" and "defecation disorder". The value of $\sum_{IBSQOL}$ also depended on the gender of patients — in men it was significantly higher than in women (Table 8). The safety of an independent stool, assessed both in points and as a binary sign (yes/no), a high defecation rate without using laxatives and enemas correlated with a significantly higher final IBSQOL rating. In addition, a significant inverse correlation of the QoL level with the duration of anamnesis, the intensity of constipation on the Wexner scale and the degree of transit disorders was revealed according to the study of the transit of barium suspension in the gastrointestinal tract (Table 8).

At the same time, neither the presence or absence of constipation or anal incontinence (leakage), nor the size of the large intestine according to irrigoscopy, as well as the results of other objective diagnostic methods, with the exception of transit time test, correlated with the overall assessment of quality of life. The quality of life also did not significantly differ in patients who got conservative treatment and those who were later operated on. At the same time, the volvulus in the history, although it was one of the main indications for surgical treatment, nevertheless, turned out to be associated with a significantly higher $\sum_{IBSQOL}$ index (Table 8).

Factors that demonstrated a significant correlation with the assessment of QoL were included in a multivariate analysis performed using multiple linear regression. As can be seen from Table 9, only the age and severity of the indicators "abdominal discomfort" and "defecation disorder" turned out to be independent factors significantly influencing the assessment of QoL by patients. Neither gender, nor the defecation rate without laxatives and enemas, nor the intensity of constipation on the Wexner scale, as well as the degree of transit disorders, have demonstrated an independent effect on the quality of life.

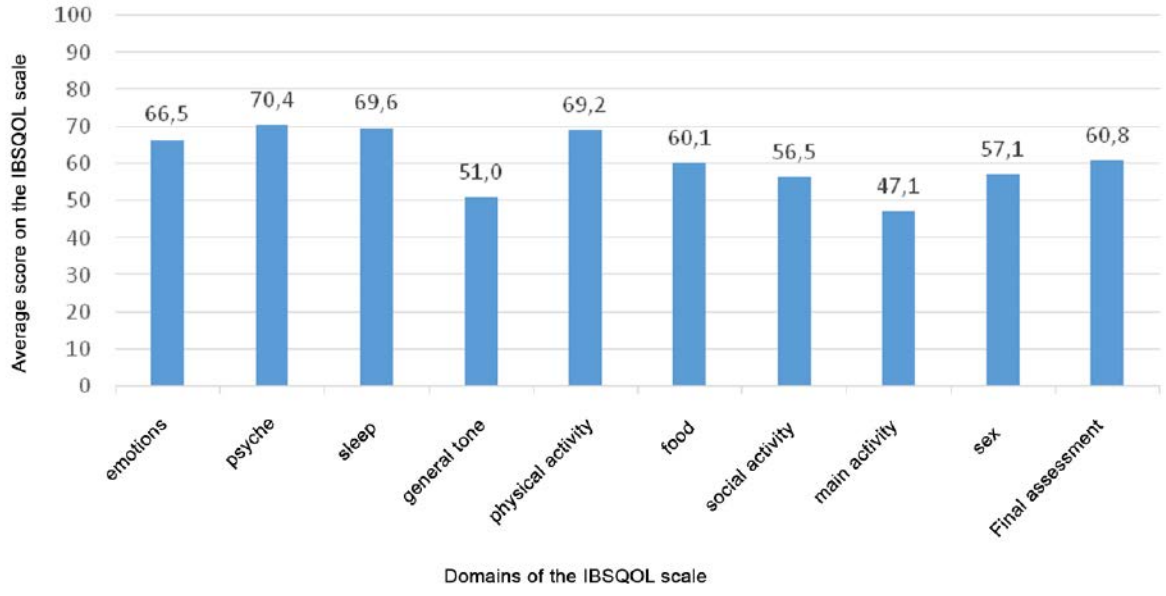

Figure 1. *Health related quality of life measured with IBSQOL scales and summary index (mean rate)*

Table 7. *Relationship of the final QoL assessment ($\sum_{IBSQOL}$) with clinical signs and examination results (rank signs — Spearman correlation)*

Sign		*n*	R	*p*
Age		**81**	**–0.22**	**0.04**
Independent stool (points)		**80**	**0.46**	**0.000**
Defecation rate		**77**	**0.24**	**0.04**
Urge to defecate		79	0.19	0.09
"Abdominal discomfort"		**78**	**–0.55**	**0.000**
"Defecation disorder"		**78**	**–0.44**	**0.000**
Duration of anamnesis		**80**	**–0.26**	**0.02**
Constipation intensity (Wexner scale)		**79**	**–0.50**	**0.000**
Ирригоскопия Irrigoscopy	Sigmoid colon length	44	0.09	0.56
	Transverse colon length	10	–0.24	0.51
	Width of the rectum	65	–0.18	0.16
	Width of the sigmoid colon	56	0.07	0.59
	Width × length of the sigmoid colon	36	0.06	0.71
	Width of the transverse olon	23	–0.30	0.16
Transit time through the gastrointestinal tract		**52**	**–0.33**	**0.02**
Defecography	T_{DEF}	47	0.07	0.64
	V_{RES}	52	0.04	0.79
Reservoir function of the rectum	MTV	40	–0.01	0.96
	I_{MTV}	32	0.08	0.66
	$\Delta V/\Delta P$	20	0.21	0.37

Note: R is Spearman's rank correlation coefficient

Table 8. *The relationship of the final assessment of QoL ($\sum_{IBSQOL}$) with clinical and diagnostic signs (binary signs — Mann-Whitney test)*

Sign	*n*	Z	*p*
Gender	**81**	**2.01**	**0.04**
Complaints of constipation (yes/no)	81	–1.0	0.31
Independent stool (yes/no)	**81**	**2.17**	**0.03**
Anal incontinence (leakage) (yes/no)	71	–0.28	0.78
History of volvulus in the anamnesis (yes/no)	**81**	**1.97**	**0.049**
Surgical treatment in the future (yes/no)	81	1.20	0.23
Distal delay (passage through the gastrointestinal tract)	44	0.36	0.72

Note: Z –confidence criterion

Table 9. *Independent factors affecting $\sum_{IBSQOL}$ (multiple linear regression)*

Sign	β	*p*
Age	**–0.25**	**0.009**
Gender	1.89	0.56
Independent stool (points)	1.45	0.74
Defecation rate	–1.79	0.22
“Abdominal discomfort”	**–1.21**	**0.000**
“Defecation disorder”	**–0.99**	**0.008**
Duration of anamnesis	0.68	0.59
History of volvulus in the anamnesis (yes/no)	3.86	0.25
Constipation intensity (Wexner scale)	0.44	0.41
Transit time through the gastrointestinal tract	–1.12	0.59

Note: $R^2_{\text{regression rate}}$ = 0,377–0,399, p < 0,000; β — regression coefficients; $R^2_{\text{regression rate}}$ – coefficient of determination

DISCUSSION

The influence of a particular disease on the quality of life of patients is becoming an increasingly urgent problem of modern medicine. Moreover, this applies to such a basically benign condition as idiopathic megacolon. In the case of uncomplicated clinical picture, megacolon does not pose a significant threat to the health of patients and assumes, first of all, conservative treatment. At the same time, even the most successful therapy is not able to normalize the size of the intestine. Accordingly, the treatment is mainly aimed at making the life of patients with megacolon as convenient as possible. In such conditions, it is the assessment of the quality of life that is one of the determining criteria for the effectiveness of therapy. And the inability to achieve an acceptable quality of life is a reason to consider the feasibility of surgical treatment. But on the other hand, in order to predict the effectiveness of surgery, it is necessary to understand which factors have the most significant impact on the assessment of quality of life and to what extent our diagnostic methods allow us to evaluate these factors.

Currently, there are no questionnaires designed specifically to assess the quality of life of patients with idiopathic megacolon. In this paper, we used the IBSQOL questionnaire. This disease is a specific questionnaire, in the sense that it was developed to assess the impact of irritable bowel syndrome on the quality of life. In our opinion, its use in patients with megacolon is quite justified, since the symptoms of these two conditions are very close. And since the diagnosis of irritable bowel syndrome is established based on the analysis of symptoms and is not so much a final diagnosis as a stage in understanding the patient and a guide to prescribing a certain type of treatment, patients with idiopathic megacolon often begin their journey to doctors just under the “mask” of IBS. In addition, the use of the IBSQOL questionnaire allowed us to compare the quality of life of patients with idiopathic megacolon and patients with chronic constipation not associated with large intestine enlargement. The results of this analysis will be the subject of subsequent publications. The disadvantage of using a disease-specific questionnaire, in contrast to a general questionnaire, such as, for example, SF-36, is the inability to compare the quality of life of patients with population data or with the effect on QoL of other diseases. At the same time, IBSQOL allows to assess the impact of megacolons on various areas of life and identify the most affected areas. The analysis showed that the idiopathic megacolon has the greatest impact on the overall tone and ability to perform the main professional activity. This is the difference from irritable bowel syndrome, which is characterized by a predominant influence on the emotional sphere, that is, the degree of life satisfaction due to the disease [7].

As for the relationship between quality of life and clinical symptoms, as well as the results of diagnostic tests, a statistically significant correlation of the final assessment of IBSQOL was found with the age and gender of patients, the safety of an independent stool, the magnitude of the indicators "abdominal discomfort" and "defecation disorder", the independent defecation rate, the duration of anamnesis, the intensity of constipation according to the Wexner scale and the severity of transit violations. At the same time, neither the presence or absence of constipation or anal incontinence (leakage), nor the size of the large intestine according to irrigoscopy, as well as the results of other objective examination methods, with the exception of transit studies, correlated with the overall assessment of quality of life. The quality of life also did not significantly differ in patients who were prescribed conservative treatment and those who were later operated on. On the one hand, this is not surprising, given that the main indication for surgery in the presence of idiopathic megacolon/megarectum was a complicated course of the disease (volvulus, formation of fecal stones). On the other hand, the absence of differences indicates a minor impact of complications on the quality of life. Moreover, the quality of life of patients with a history of volvulus turned out to be even significantly better than in patients who did not face such a problem.

In multivariate analysis, only the age and severity of the indicators "abdominal discomfort" and "defecation disorder" turned out to be independent factors significantly influencing the assessment of QoL by patients.

Neither gender, nor the defecation rate without laxatives and enemas, nor the intensity of constipation on the Wexner scale, as well as the degree of transit disorders, have demonstrated an independent effect on the quality of life.

We hope to present an analysis of the relationship between the clinical manifestations of idiopathic megacolon and the results of objective methods for assessing the anatomical and functional state of the large intestine in the future. The unavoidable limitations associated with the observational and retrospective nature of this study require caution in interpreting its results. Nevertheless, there is a discouraging lack of a significant relationship between QoL and the results of diagnostic tests. It should also be noted that, despite the statistical significance of the dependencies found in the multivariate analysis, the coefficient of determination of the obtained multiple linear regression did not exceed 0.4 (Table 9). In our opinion, this indicates the presence of factors that have a significant impact on the quality of life of patients with idiopathic megacolon, but which we were unable to identify either in the analysis of clinical symptoms or in the check-up of patients. Thus, the methods available to us for assessing the condition of patients, both clinical and instrumental, do not allow us to predict with any confidence the effect, in particular, of surgery on the quality of life. Accordingly, in the case of uncomplicated megacolon, the intention to improve the quality of life is a dubious reason for active surgical approach.

CONCLUSION

From the point of view of the quality of life, the idiopathic megacolon has the greatest impact on the overall tone and ability to perform the main professional activity. Independent factors that statistically significantly affect the assessment of quality of life are the age of patients and the severity of symptoms of abdominal discomfort and defecation disorders.

AUTHORS CONTRUBUTION

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Effectiveness of minimally invasive and surgical methods of treatment of chronic hemorrhoids using phlebotonics

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ABSTRACT *PURPOSE: to evaluate the effect of phlebotropic therapy on the results of surgical treatment of hemorrhoids.*
PATIENTS AND METHODS: a comparative analysis of the results of treatment of 406 patients with chronic hemorrhoids of stages III and IV was performed. With surgical treatment of hemorrhoids, standard conservative therapy was performed in 205 patients (group I) and 201 patients (group II) in the perioperative period, as well as at the rehabilitation stage, the standard program of drug treatment was supplemented with phlebotropic therapy using Detralex (1000 mg).
RESULTS: in group II patients, compared with group I patients, pain syndrome was stopped faster, quality of life and working capacity were restored, and the period of epithelization of the anal canal wound was shortened (21.4 ± 1.7 days versus 26.8 ± 2.1 days). This made it possible to increase the number of good and satisfactory results of surgical treatment of hemorrhoids from 82.4% to 91.5%.
CONCLUSION: outpatient surgical treatment of hemorrhoids of stages III-IV in combination with phlebotropic therapy can reduce the number of postoperative complications from 17.6% to 8.5% and increase the overall number of good and satisfactory treatment results from 82.4% to 91.5% ($p < 0.005$).

KEYWORDS: *hemorrhoids, surgical treatment, prolonged phlebotropic therapy, outpatient treatment*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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INTRODUCTION

The modern concept of surgical treatment of chronic hemorrhoids provides for the use of both minimally invasive methods and hemorrhoidectomy [1,2]. In recent years, such minimally invasive methods of surgical treatment of hemorrhoids as desarterization of hemorrhoids with mucopexia and laser submucous destruction of hemorrhoids are becoming more widespread and are used, including in outpatient settings. Minimally invasive surgical methods are used mainly in the I–II stages of hemorrhoids, as well as in the treatment of chronic internal hemorrhoids of stages III-IV without a pronounced external component [2–4]. Most coloproctologists perform Milligan-Morgan hemorrhoidectomy in patients with hemorrhoids of stages III-IV, especially when this disease is combined with another pathology of the anal canal (polyp, anal fissure) [3–6].

In recent years, such high-tech surgeries as closed seamless hemorrhoidectomy based on such technologies as LigaSure and Harmonica have been actively introduced into clinical practice in the treatment of patients with late stages [1,2,6].

The most significant disadvantages of Milligan-Morgan hemorrhoidectomy and its various modifications include a severe pain syndrome in the early stages after surgery, postoperative bleeding, inflammatory wound complications, which significantly increases the rehabilitation time of patients. In addition, in the long-term period after hemorrhoidectomy, 6–9% of patients develop cicatricial stricture of the anal canal, and 1.8–4% of patients develop sphincter insufficiency [1,2,6].

When choosing a method for the treatment of late-stage chronic hemorrhoids, a combination

of various minimally invasive techniques is used as an alternative to Milligan-Morgan hemorrhoidectomy (for example, a combination of transanal Doppler-controlled ligation of hemorrhoidal arteries with submucous laser destruction). They are often combined with the removal of single hemorrhoidal piles, which does not significantly affect the surgical radicalism, and at the same time it reduces its duration and trauma [3,6–8].

Currently, the pathogenetic validity of the use of phlebotropic therapy in the conservative treatment of acute hemorrhoids has been proven, and data on the positive effect of phlebotonics on the effectiveness of minimally invasive surgeries in patients with chronic hemorrhoids have been presented [9,10,11].

The long clinical practice of using Detralex (micronized purified flavonoid fraction) has clearly shown the high efficacy and safety of using this phlebotonic in the treatment of patients with various forms of hemorrhoidal disease [10–12]. At the same time, there are no studies justifying and clearly regulating the regimen of phlebotropic therapy during the entire perioperative period, as well as at the stage of rehabilitation in patients with stages III-IV of the disease after surgical treatment. This prompted us to develop a rational strategy for phlebotropic therapy before and after surgical treatment of patients with chronic hemorrhoids of stages III-IV and to evaluate its clinical effectiveness.

AIM

To evaluate the effectiveness of surgical treatment of hemorrhoids of stages III-IV in outpatient settings with the use of phlebotropic therapy in the perioperative period.

PATIENTS AND METHODS

The present study included 406 patients with chronic hemorrhoids of stages III and IV who were on outpatient treatment at the MMC “URO-PRO” in Krasnodar in the period of 2018–2022. There were 179 men (44.1%) and 227 women (55.9%). The age of the patients ranged from 18 to 73 years. Most of the patients were of working age. The average age of the patients was 45.5 ± 3.7 years. All patients underwent checkup on an outpatient clinic with conventional clinical, laboratory and instrumental tests. Colonoscopy was performed in patients aged over 40 years. All patients underwent surgical treatment of hemorrhoids, including the use of traditional and minimally invasive technologies.

Depending on the variant of drug treatment in the perioperative period and at the stage of rehabilitation, two groups were created. In 205 (50.4%) patients of the I (control) group, generally accepted drug therapy was performed in the perioperative period, including the use of topical combined agents. In 201 (50.6%) patients of group II (main) in the perioperative period, as well as at the rehabilitation stage, the standard program of drug treatment was supplemented with prolonged phlebotropic therapy using Detralex (1000 mg).

When choosing a phlebotropic drug prescribing scheme, the severity of the inflammatory process in the area of hemorrhoids was taken into account. In patients with chronic hemorrhoids with mild symptoms of exacerbation of the disease, Detralex 1000 mg was prescribed 1 tablet 2 times a day for 7 days before surgery. In the presence of clear signs of exacerbation of chronic hemorrhoids (edema, node soreness), in addition to topical remedies, in order to stop the inflammatory component before surgery, patients received Detralex 1000 mg 1 tablet 3 times a day for 4 days, then 1 tablet 2 times a day for 3 days. After surgery, the drug was prescribed to patients of group II according to the same scheme as in case of exacerbation of the disease (1 tablet 3 times a day for 4 days, then 1 tablet 2 times a day for 3 days). Subsequently, patients received the drug 1 tablet 1 time a day for 2 months. After that, they took a break from taking the drug for 60 days, and then a second course of phlebotropic therapy (1 tablet per day) was carried out for 2 months.

At the start of the treatment, the groups of patients were comparable in clinical manifestations of chronic hemorrhoids in accordance with the stage of the disease (Table 1).

Sixty-one (15.0%) patients were diagnosed with posthemorrhagic anemia, which required hemotrans fusions and the administration of

Table 1. *Distribution of patients by clinical signs and stages of chronic hemorrhoids*

Clinical signs/stages of chronic hemorrhoids	Number of patients			
	I Group (*n* = 205)		II Group (*n* = 201)	
	Abs.	%	Abs.	%
Piles prolapse from the anal canal (stage III)	33	16.1	38	18.9
Piles prolapse (stage III) + bleeding	73	35.6	71	35.3
Piles prolapse (stage IV)	3	1.5	3	1.5
Piles prolapse (stage IV) + bleeding	96	46.8	89	44.3

Table 2. *Surgeries performed in patients with chronic hemorrhoids of stages III-IV in groups I and II*

Surgeries	Number of patients			
	I Group (*n* = 205)		II Group (*n* = 201)	
	Abs.	%	Abs.	%
Hemorrhoidectomy by Milligan-Morgan + HAL-RAR	9	4.4	13	6.5
Hemorrhoidectomy by Milligan-Morgan + LHP	26	12.7	21	10.4
Hemorrhoidectomy by Milligan-Morgan + HAL-RAR + LHP	14	6.8	16	8.0
Hemorrhoidectomy with LigaSure + HAL-RAR	22	10.7	18	8.9
Hemorrhoidectomy with LigaSure + LHP	21	10.2	24	11.9
Hemorrhoidectomy with LigaSure + HAL-RAR + LHP	33	16.1	29	14.4
Hemorrhoidectomy with harmonic + HAL-RAR	26	12.7	19	9.4
Hemorrhoidectomy with harmonic + LHP	30	14.6	29	14.4
Hemorrhoidectomy with harmonic + HAL-RAR + LHP	24	11.7	32	15.9

iron-containing drugs at the stage of preoperative preparation.

When choosing the method of surgical treatment of chronic hemorrhoids, individual clinical and anatomical features of the pathological process were taken into account (the size and "stage of development" of each individual node, its location in relation to other hemorrhoids, as well as the relationship between the external and internal components). Guided by this principle, two or more hemorrhoidal node removal techniques were used in a personalized manner for each patient, including a combination of traditional surgeries and minimally invasive methods. The types of surgeries performed in both groups of patients are presented in Table 2.

Traditional hemorrhoidectomy according to Milligan-Morgan in various combinations with minimally invasive methods was performed in 49 (23.9%) patients of group I and 50 (24.9%) of group II. At the same time, as minimally invasive methods of treatment, dearterisation of hemorrhoids

with mucopexia (HAL-RAR technology) using the A.M.I. "HAL-Doppler II" device (Austria) and laser submucous destruction of hemorrhoids (Laser Hemorrhoid Plasty, LHP) with the LAKHTA-MILON device ("Touch screen" model, Russia) were used. Closed seamless hemorrhoidectomy by LigaSure apparatus (ValleylabFT10, USA) in various combinations with HAL-RAR and LHP techniques was performed in 76 (37.1%) patients of group I and 71 (35.3%) patients of group II. Closed seamless hemorrhoidectomy with Covidien ultrasound scalpel (USA) in combination with minimally invasive methods was performed in 80 (39.0%) patients of group I and 80 (39.8%) patients of group II. A rational combination of traditional operations and minimally invasive techniques in the surgical treatment of patients with chronic hemorrhoids of stages III-IV, without generally affecting the radicality of the surgery, significantly reduced the level of its traumatism, as it allowed avoiding excessive excision of the anoderm when removing internal hemorrhoids with uneven degree of their loss.

In both groups of patients, we compared the degree of pain syndrome after surgery (according to the numerological evaluation scale, NRS: from 0 to 10 points), as well as the severity of postoperative inflammatory changes in the anal area (pain in the anus and discomfort during exercise and defecation, perianal edema, blood spotting during defecation). The comparison parameters in the study groups took into account the healing time of wounds in the anal area, the number of postoperative complications and recurrences of the disease. We considered the complete elimination of the main manifestations of the disease to be good results; satisfactory results — preservation of perianal edema, a feeling of discomfort in the anal area during defecation; unsatisfactory results — the presence of postoperative complications and/or recurrence of the disease. The quality of life of patients after surgery was assessed using the SF-36questionnaire.

Statistical analysis was performed using Statistica 7.0 for Windows. To check the normality of the distribution of values in the samples, the Kolmogorov-Smirnov and Shapiro-Wilk criteria were used. The statistical significance of the differences between the groups was assessed using the Mann-Whitney criterion (U). When assessing changes in parameters within one group of patients in the dynamics of observation, the Wilcoxon rank criterion of paired comparisons was used. The differences were considered statistically significant at $p < 0.05$.

RESULTS

In patients of group II, in whom surgical treatment of hemorrhoids of stages III-IV in the perioperative period and at the stage of rehabilitation was accompanied by phlebotropic therapy, the degree of pain syndrome after surgery was significantly lower compared to patients of group I. At the same time, in patients of group II, the pain syndrome was largely stopped by 5.6 ± 1.2 days after surgery, while in group I patients — only by 8.3 ± 1.3 days (Fig. 1).

Along with a decrease in pain syndrome in patients of the main group, there was a more distinct regression of clinical signs due to postoperative inflammatory changes (Table 3).

In patients of the main group, reduction of perianal edema and cessation of bloody discharge during the act of defecation were noted earlier after surgery, and at the same time, a decrease in pain and discomfort in the anus during defecation and during physical exertion. In the majority of cases in patients of group II, the elimination of acute inflammatory changes in the surgery site was noted on the 6.1 ± 1.2 days after surgery, and in a large number of patients of group I, these manifestations regressed only on the 10.2 ± 1.7 postoperative days. In patients of the main group, the healing time of postoperative wounds of the anal area decreased (respectively, 21.4 ± 1.7 days versus 26.8 ± 2.1 days in patients of the control group). In patients of the main group, the ability to work was restored at an earlier time after surgery (respectively 4.2 ± 1.1 days versus 6.9 ± 1.4 days in patients in the control group). Group II patients with prolonged phlebotropic therapy showed a decrease in the total number of postoperative complications by more than 2 times compared with group I patients (8.5% vs. 17.6%) (Table 4). First of all, it concerned a significant reduction in the number of wound inflammatory complications (early eruption of the anoderm

Table 3. *Postoperative inflammatory changes in the perineum in groups I and II (P ± m) %*

Clinical signs	Group of patients	Day after surgery (*n* = 406)				
		1st	3rd	5th	7th	10th
Pain in the anal canal during the act of defecation, %	I Group	98.6 ± 1.3	84.8 ± 3.1	62.6 ± 3.7	44.8 ± 2.2	11.2 ± 1.6
	II Group	98.1 ± 1.4*	75.6 ± 2.8	37.3 ± 4.4	15.9 ± 3.3	4.6 ± 1.4
Pain and discomfort in the anus during exercise, %	I Group	97.5 ± 2.7	60.1 ± 3.3	43.4 ± 3.8	22.4 ± 4.1	8.7 ± 2.3
	II Group	93.2 ± 2.1*	54.3 ± 2.7*	18.5 ± 3.1	9.1 ± 2.2	3.4 ± 1.2
Perianal edema, %	I Group	89.5 ± 2.1	78.4 ± 2.7	57.8 ± 3.3	34.1 ± 4.2	12.3 ± 3.2
	II Group	85.3 ± 2.6*	45.4 ± 4.2	24.3 ± 2.1	13.5 ± 1.3	3.1 ± 1.9
Blood spotting during the act of defecation, %	I Group	97.5 ± 1.2	85.6 ± 2.8	72.1 ± 2.7	56.1 ± 3.9	40.9 ± 4.3
	II Group	97.1 ± 1.4*	78.1 ± 3.5	49.2 ± 3.8	35.3 ± 3.0	21.3 ± 3.4
Note: * — *Statistically unreliable differences between groups (p > 0.05)*						

sutures and suppuration of wounds). In the main group of patients, postoperative thrombosis of residual cavernous tissue developed significantly less frequently in the projection of cutaneous-anodermal bridges (2.5% versus 5.8% in the control group), which required additional therapeutic measures, including excision of this tissue together with excess perianal skin and segment of the anoderm.

In addition, in 2 (0.5%) cases, postoperative bleeding from anal canal wounds was noted in patients requiring emergency surgical hemostasis. Stricture formation of the anal canal was observed in 6 (2.9%) patients of group I and 5 (2.5%) patients of group II due to cicatricial retraction of the mucous layer and anoderma later after surgery. Of these, 7 patients had stricture eliminated conservatively (multiple finger augmentation) and 4 patients required reconstructive surgery (stricturoplasty). There were no recurrences of the disease during the entire follow-up period in patients in both groups.

Good and satisfactory outcomes of surgical treatment were obtained in 184 (91.5%) patients in

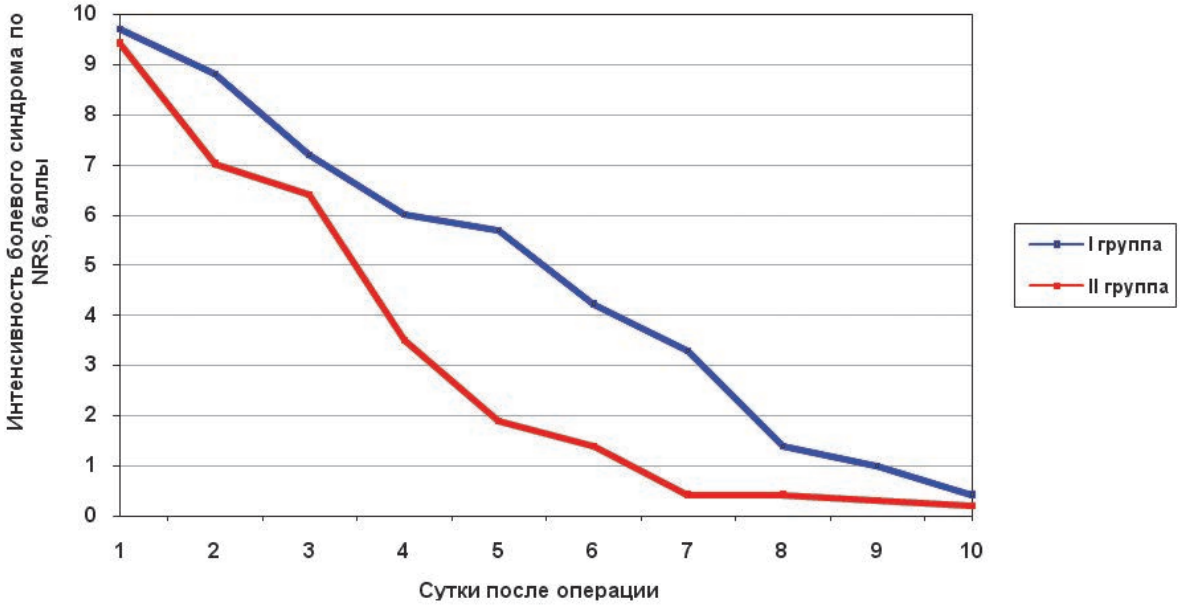

Figure 1. *The intensity of pain syndrome according to a 10-point numerological evaluation scale in patients with chronic hemorrhoids of stages III–IV in groups I and II after surgery*

Table 4. *Structure of postoperative complications in patients of groups I and II*

The nature of complications	Number of patients			
	I Group (*n* = 205)		II Group (*n* = 201)	
	Abs.	%	Abs.	%
Bleeding from anal canal wounds	1	0.5	1	0.5
Thrombosis of residual cavernous tissue	12	5.8	5	2.5
Eruption of the anoderm sutures	6	2.9	2	1.0
Purulent-inflammatory wound complications	11	5.4	4	2.0
Stricture of the anal canal	6	2.9	5	2.5
Total patients with complications	36	17.6	17	8.5

Table 5. *Comparative characteristics of the quality of life of patients of groups I and II after surgery*

Follow-up periods after surgery	I Group		II Group	
	PH (M ± m)	MH (M ± m)	PH (M ± m)	MH (M ± m)
Day 5	64.2 ± 2.7	68.2 ± 2.2	76.2 ± 3.1	74.2 ± 2.8
Day 10	67.2 ± 3.2	72.2 ± 2.9	78.2 ± 3.3	80.2 ± 3.4
Day 20	74.2 ± 2.6	78.2 ± 3.0	81.2 ± 2.9	86.2 ± 2.7
Day 30	81.2 ± 3.1	84.2 ± 2.1	87.9 ± 2.4	89.. ± 3.1
3 months	85.1 ± 2.7	87.1 ± 2.8	91.5 ± 3.1	93.8 ± 3.0
6 months	92.1 ± 2.5	89.3 ± 2.4	96.5 ± 3.2*	95.8 ± 2.7
*Note: * — Statistically unreliable differences between groups (p > 0.05)*				

the main group and in 169 (82.4%) patients in the control group.

The results of the survey of patients based on the SF-36 questionnaire showed that after surgery, patients of the main group assessed their physical health (PH) and mental status (MH) higher than patients of the control group (Table 5).

DISCUSSION

The results of the study showed that when the clinic is equipped with modern high-tech equipment, it is quite possible to provide high-quality surgical treatment of patients with chronic hemorrhoids of stages III-IV in the "one-day hospital" mode. In this category of patients, it is most rational to use high-tech hemorrhoidectomy (LigaSure, Harmonica) in combination with modern minimally invasive methods of treatment (desarterization of hemorrhoids, LHP). This combination does not significantly affect the surgery radicality, but significantly reduces the degree of its traumatism. At the same time, a personalized approach should be applied taking into account the individual clinical and anatomical features of the pathological process, including the size and "stage of development" of each individual node, the presence of boundaries between internal nodes, as well as external and internal nodes.

The inclusion of phlebotropic therapy (Detralex 1000 mg) in the program of comprehensive drug support in this category of patients throughout the entire perioperative period and the rehabilitation stage is pathogenetically justified. In this case, prolonged phlebotropic correction using micronized purified flavonoid fraction is primarily aimed at reducing vein distension and limiting the inflammatory reaction in the venous wall, eliminating increased microvascular permeability, improving venous outflow and lymphatic drainage in the area of altered tissues. At the same time, the scheme of prescribing the drug assumes an individualized approach to choosing the mode of prolonged phlebotropic correction, depending on the severity of the initial inflammatory changes in the area of hemorrhoids.

The best results of surgical treatment obtained by us in patients of the main group who additionally underwent phlebotropic therapy were achieved mainly due to a decrease in the severity of postoperative perianal edema, which, in turn, contributed to a decrease in the number of inflammatory wound complications. It is noteworthy that the early eruption of the anoderm sutures against the background of inflammatory perianal edema, as a rule, was accompanied by

the development of persistent sphincterospasm and severe pain syndrome. The effectiveness of surgeries using phlebotropic drugs is confirmed by a large number of good and satisfactory treatment results in patients of the main group, as well as a higher assessment of the quality of life after surgery (compared with patients of the control group).

CONCLUSION

Thus, conducting targeted phlebotropic drug therapy in the perioperative period during surgical treatment of chronic hemorrhoids and at the stage of postoperative rehabilitation of patients is pathogenetically justified and is primarily aimed at reducing the severity of perianal edema and pain syndrome, as well as preventing inflammatory wound complications. In this case, surgical treatment of hemorrhoids of stages III-IV on an outpatient basis in combination with phlebotropic therapy contributes to the relief of pain syndrome earlier after surgery, regression of inflammatory changes in the surgery area, acceleration of the healing rate of postoperative wounds, improvement of the quality of life of patients and improvement of their social rehabilitation. This makes it possible to reduce the number of postoperative complications from 17.6% to 8.5% and increase, in general, the number of good and satisfactory results of surgical treatment of hemorrhoids from 82.4% to 91.5%.

AUTHORS CONTRIBUTION

Concept and design of the study: *Boris M. Belik, Aleksey N. Kovalev*

Collection and processing of the material: *Boris M. Belik, Aleksey N. Kovalev*

Statistical processing: *Boris M. Belik, Aleksey N. Kovalev*

Writing of the text: *Boris M. Belik, Aleksey N. Kovalev*

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Роль режима питания при подготовке толстой кишки к колоноскопии. Проспективное обсервационное исследование

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РЕЗЮМЕ *ЦЕЛЬ ИССЛЕДОВАНИЯ: оценка влияния соблюдения режима питания при подготовке к колоноскопии на качество эндоскопического исследования.*
ПАЦИЕНТЫ И МЕТОДЫ: в проспективное обсервационное исследование включено 1000 пациентов, которым было запланировано проведение диагностической колоноскопии. Качество подготовки кишечника оценивалось с помощью Бостонской шкалы. Проводилось изучение состояния толстой кишки, в случае обнаружения новообразований проводилась их эндоскопическая оценка. На основании оптической верификации опухолей рассчитывались индексы выявленных аденом и полипов (ADR и PDR).
РЕЗУЛЬТАТЫ: медиана качества подготовки толстой кишки, оцениваемая по Бостонской шкале, составила 6 (6;8) баллов. Не соблюдали рекомендованную диету 198 (19,8%) обследуемых. Плохая подготовка, не позволившая провести полноценный осмотр толстой кишки, была констатирована у 91 пациента, что составило 9,1% всех диагностических процедур. Показатель ADR составил 37,4%, PDR — 43,4%. При проведении логистического регрессионного анализа предикторов неадекватной подготовки кишечника обнаружено, что единственным фактором, значимо негативно влияющим на ее качество, явилось несоблюдение диеты.
ЗАКЛЮЧЕНИЕ: неудовлетворительная подготовка кишечника констатирована у 9,1% пациентов. Основным фактором, ухудшающим ее качество, оказалось несоблюдение перед эндоскопической процедурой назначенной диеты.

КЛЮЧЕВЫЕ СЛОВА: *подготовка к колоноскопии, подготовка толстой кишки, режим питания, колопроктология, PDR*

КОНФЛИКТ ИНТЕРЕСОВ: *Авторы заявляют об отсутствии конфликта интересов*

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The role of diet in bowel cleansing for colonoscopy (results of prospective observation study)

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ABSTRACT *AIM: to evaluate the impact of dietary compliance in bowel cleansing for colonoscopy on the quality of the procedure.*
PATIENTS AND METHODS: one thousand patients who scheduled for diagnostic colonoscopy were included in the prospective observation study. The quality of bowel preparation was assessed using the Boston scale. Neoplasms were detected and endoscopically evaluated. The optical verification of tumors was used to calculate the indicators of identified adenomas and polyps (ADR and PDR).

RESULTS: the quality of bowel cleansing by the Boston Scale was 6 (6; 8) points. One hundred eight (19.8%) patients did not follow the recommended diet. Poor preparation, which did not allow a total colonoscopy was found in 91 (9,1%) cases. The ADR was 37.4%, PDR — 43.4%. Logistic regression analysis showed that the non-compliance for diet recommendation was the only one significantly negative factor associated whit inadequate bowel cleansing.
CONCLUSION: the leading factor worsening the quality of bowel cleansing was non-compliance with the prescribed diet before the colonoscopy.

KEYWORDS: *colonoscopy preparation, colon preparation, diet, coloproctology*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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АКТУАЛЬНОСТЬ

Колоноскопия в настоящее время является одним из основных методов обследования толстой кишки и скрининга колоректального рака. Доказано, что её своевременное выполнение ассоциировано со снижением летальности от злокачественных опухолей указанной локализации на 75% [1]. Проведение эндоскопического исследования возможно лишь при хорошей подготовке кишечника, однако в 35% случаев она бывает недостаточной, что значимо ухудшает качество исследования, проявляясь более низкой частотой интубации слепой и подвздошной кишки, а также уменьшением показателей выявления аденом и полипов (ADR и PDR), характеризующих качество выполнения колоноскопии [2].

Требования к подготовке кишечника для эндоскопического исследования сформулированы в консенсусе американского общества колоректальных хирургов (American Society of Colon and Rectal Surgeons, ASCRS), американского общества гастроинтестинальной эндоскопии (the American Society for Gastrointestinal Endoscopy, ASGE) и американского общества гастроинтестиальных и эндоскопических хирургов (the Society of American Gastrointestinal and Endoscopic Surgeons, SAGES) [3]. В соответствии с ними подготовка толстой кишки должна соответствовать следующим характеристикам:

1. Полное и быстрое очищение всего кишечника от каловых масс;
2. Отсутствие повреждений слизистой оболочки пищеварительного тракта используемыми препаратами;
3. Отсутствие дискомфорта у пациента во время приема препарата;
4. Невысокая стоимость;
5. Несложная схема приема препарата;
6. Отсутствие влияния на водно-солевой баланс организма пациента.

Большинство публикаций, относящихся к вопросу подготовки к эндоскопическому исследованию, было посвящено оценке эффективности и безопасности различных препаратов для лаважа кишечника, схеме и сроках их применения [4,5]. Были также разработаны рекомендации по диете, которую пациенты должны использовать во время подготовки к обследованию. Так, российское эндоскопическое общество в клинических рекомендациях по подготовке к колоноскопии предложило стандартный способ с применением бесшлаковой диеты в течение 1–4 дней в сочетании с различными слабительными средствами на основе полиэтиленгликоля, пикосульфата натрия или фосфата натрия [6].

Следует отметить, что публикаций, посвященных изучению влияния данного способа подготовки кишечника к эндоскопическому исследованию на его качество крайне мало, а также неизвестно, как несоблюдение протокола может отразиться на качестве колоноскопии, что послужило поводом для проведения настоящего исследования.

ПАЦИЕНТЫ И МЕТОДЫ

С целью оценки приверженности больных рекомендованной стандартной схеме подготовки кишечника к колоноскопии было проведено проспективное обсервационное исследование.

Таблица 1. *Бостонская шкала оценки качества подготовки толстой кишки*
Table 1. *Boston Colon Preparation Quality Assessment Scale*

Баллы	Описание
3	Слизистая оцениваемого отдела толстой кишки хорошо видна на всем протяжении, отсутствуют даже незначительные остатки кишечного содержимого и непрозрачной/ окрашенной жидкости
2	Небольшое количество окрашенного содержимого и остатков кишечного содержимого и/или непрозрачной жидкости, но слизистая оцениваемого отдела толстой кишки хорошо видна
1	Видна только часть слизистой оболочки оцениваемого отдела толстой кишки, но другие участки слизистой оболочки этого отдела кишки видны плохо из-за наличия окрашенного содержимого, остаточного кишечного содержимого и/или непрозрачной жидкости
0	Оцениваемый отдел кишки не подготовлен к исследованию. Осмотреть слизистую оболочку невозможно, так как ее невозможно отмыть от плотного кишечного содержимого

В него были включены 1000 совершеннолетних пациентов, обратившиеся в консультативную поликлинику Центра с июля по октябрь 2021 года, которым было запланировано проведение диагностической колоноскопии и подписавшие добровольное информированное согласие на участие в исследовании.

Всем пациентам проводилась подготовка по стандартной методике, рекомендованной Российским эндоскопическим обществом. Назначалась бесшлаковая диета, включающая в себя прием легко усваиваемой, рафинированной пищи с минимальным содержанием неперевариваемых веществ, в течение 1–4 дней перед исследованием.

Для лаважа кишечника применялись препараты полиэтиленгликоля (ПЭГ), средства, содержащие пикосульфат натрия и цитрат магния.

Изучалась частота несоблюдения предписанного режима, проводилась оценка субъективной переносимости подготовки кишечника по 10-балльной визуально-аналоговой шкале (ВАШ), где 1 балл соответствовал отсутствию каких-либо жалоб, а 10 — максимальной негативной оценке. Также проводилась оценка частоты развития неблагоприятных симптомов, таких как тошнота, рвота, общий дискомфорт, боль и вздутие живота.

Качество подготовки кишечника оценивалось врачом-эндоскопистом с помощью Бостонской шкалы (Табл. 1) в правых отделах ободочной кишки, поперечной ободочной кишке и левых отделах ободочной кишки [7]. Во время колоноскопии проводилась оценка слизистой оболочки, при обнаружении новообразований осуществлялась их эндоскопическая оценка. Ямочный и сосудистый рисунок выявленных новообразований описывался в соответствии с классификациями Sano Y. и Kudo S., что позволяло дифференцировать данные находки как гиперпластические полипы, зубчатые новообразования, аденомы либо аденокарциномы [5,8]. На основании оптической верификации опухолей рассчитывался индекс выявленных полипов PDR (polyp detection rate), как отношение числа колоноскопий, при которых визуализирован один или несколько полипов к общему числу выполненных колоноскопий [7,9].

В исследование было включено 1000 пациентов — 439 мужчин и 561 женщина. Медиана возраста участников составила 52 (38;64) года. Колоноскопия была назначена 334 больным, у которых в поликлинике Центра были диагностированы доброкачественные заболевания толстой кишки (хронический геморрой, свищ прямой кишки, анальная трещина и др.). Направлено на эндоскопическое исследование с диагнозом «воспалительные заболевания кишечника» 110 больных. По поводу дивертикулярной болезни и синдрома раздраженного кишечника колоноскопия выполнена у 242 пациентов. Направительный диагноз «новообразование ободочной и прямой кишки» был у 312 больных, и 2 человека обратились для скринингового исследования (Табл. 2).

Для подготовки кишечника 372 пациента применяли средства, содержащие пикосульфат натрия, 628 — препараты ПЭГ.

Статистическая обработка полученных данных была произведена при помощи программного обеспечения

Таблица 2. *Характеристика пациентов*
Table 2. *Characteristics of patients*

Параметр	*n* = 1000
Пол (муж/жен)	439/561
Возраст, лет (Me, квартили)	52 (38;64)
Направительный диагноз	
Доброкачественные заболевания прямой кишки и заднего прохода	334
Новообразования толстой кишки	312
ВЗК*	110
Дивертикулярная болезнь ободочной кишки и СРК**	242
Скрининг	2

*Примечание: *ВЗК — воспалительные заболевания кишечника; **СРК — синдром раздраженного кишечника*

Таблица 3. *Анализ предикторов неадекватной подготовки кишечника. Однофакторная логистическая регрессия.*
Table 3. *Analysis of predictors of inadequate bowel preparation. One-factor logistic regression.*

Предиктор	Коэффициент регрессии, B	Среднеквадратичная ошибка	*p*	Отношение шансов, ОШ	95% доверительный интервал ОШ	
					Нижняя граница	Верхняя граница
Пол (мужской/женский)	0,343	0,22	0,12	1,4	0,915	2,17
Возраст, лет	–0,041	0,101	0,688	0,960	0,787	1,171
Соблюдение диеты (да/нет)	2,497	0,243	< 0,001	12,152	7,541	19,581
Препарат, используемый для подготовки (ПЭГ/пикосульфат натрия)	–0,293	0,444	0,509	0,746	0,313	1,78
Оценка субъективной переносимости подготовки кишечника по ВАШ, баллы	0,37	0,29	0,9	1,038	0,578	1,863
Тошнота (да/нет)	–0,44	0,31	0,156	0,644	0,351	1,183
Рвота (да/нет)	2,197	1,2	0,068	9	0,854	94,9
Общий дискомфорт (да/нет)	–0,385	0,309	0,214	0,681	0,371	1,248
Боль в животе (да/нет)	0,413	0,607	0,496	1,511	0,46	4,968
Вздутие живота (да/нет)	–0,724	0,241	0,003	0,485	0,302	0,777

GraphPadPrism 9 и IBMSPSS Statistics. Для описания параметрических и непараметрических данных использовалась медиана с верхним и нижним квартилями. Для выявления возможных предикторов неадекватной подготовки кишечника применялась простая логистическая регрессия. Оценку уровня логистической регрессии проводили по значению χ^2 и стандартизированному коэффициенту.

РЕЗУЛЬТАТЫ

Медиана качества подготовки толстой кишки, оцениваемая по Бостонской шкале, составила 6 (6;8) баллов. Плохая подготовка, не позволившая провести полноценное обследование, была констатирована у 91 пациента, что составило 9,1% всех диагностических процедур. Этим больным была рекомендована повторная колоноскопия [18]. Проведенный опрос больных показал, что при подготовке к колоноскопии не соблюдали рекомендованную диету 198 (19,8%) обследуемых. Следует отметить, что из числа пациентов с неудовлетворительной подготовкой кишечника не следовали рекомендациям по питанию 57 (62%) человек, а в группе с удовлетворительной подготовкой — 141 (15,5%).

Медиана субъективной оценки переносимости подготовки кишечника по ВАШ составила 2 (1;3) балла, что соответствовало минимальной степени дискомфорта. Во время подготовки к эндоскопическому исследованию 686 (68,6%) пациентов не отмечали никаких неприятных явлений и жалоб. В то же время, при выполнении лаважа кишечника у 109 (10,9%) человек отмечалась тошнота, у 48 (4,8%) — рвота; 197 (19,7%) пациентов предъявляли жалобы на вздутие живота; 47 (4,7%) обследуемых жаловались на боль в животе, а 114 (11,4%) отмечали общий дискомфорт.

В ходе исследования изолированные доброкачественные заболевания заднего прохода были диагностированы в 12 случаях, у 361 пациента были обнаружены полипы толстой кишки, изменения, характерные для ВЗК, выявлены у 97 больных, дивертикулы ободочной кишки — у 77. Злокачественные опухоли были обнаружены у 53 больных. В 91 наблюдении не было обнаружено патологии в ходе проведения колоноскопии. Показатель PDR составил 36,1%.

Для определения предикторов неадекватной подготовки кишечника был проведен логистический регрессионный анализ. При этом обнаружено, что единственным фактором, значимо негативно влияющим на качество подготовки к эндоскопическому исследованию, явилось несоблюдение диеты. Не вполне объясним факт того, что пациенты, которые отмечали вздутие живота в ходе очистки кишечника, были лучше подготовлены к исследованию, что подтверждено статистическими данными (Табл. 3).

ОБСУЖДЕНИЕ

Подготовка кишечника к эндоскопическому исследованию является одним из основных условий проведения качественной колоноскопии. В связи с этим в мировой литературе можно найти достаточно много исследований, посвященных данной проблематике.

Научные работы были систематизированы в метаанализе Mahmood et al., в который вошли данные о лечении 49868 больных. При этом среди факторов, влияющих на качество подготовки кишечника, были выделены: возраст (ОШ = –1,20; 95% ДИ: –2,20;– 0.19; p = 0,02), мужской пол (ОШ = 0,85; 95% ДИ: 0,77–0,93; p < 0,0003), раса (ОШ = 1,44; 95% ДИ: 1,12–1,86; p < 0,0003), нахождение в стационаре (ОШ = 0,57; 95% ДИ: 0,43–0,75; p < 0,00001), сахарный диабет (ОШ = 0,58; 95% ДИ: 0,43–0,79; p = 0,00001), гипертоническая болезнь (ОШ = 0,58; 95% ДИ: 0,36–0,95; p = 0,03), цирроз печени (ОШ = 0,49; 95% ДИ: 0,32–0,72; p = 0,001), употребление наркотиков (ОШ = 0,59; 95% ДИ: 0,47–0,74; p = 0,00001), запоры (ОШ = 0,61; 95% ДИ: 0,49–0,76; p = 0,0001), последствия острого нарушения мозгового кровообращения (ОШ = 0,51; 95% ДИ: 0,35–0,74; p = 0,0004), и использование трициклических антидепрессантов (ОШ = 0,51; 95% ДИ: 0,34–0,75; p = 0,0008). Другие аспекты, такие как индекс массы тела, профилактический характер исследования, использование блокаторов кальциевых каналов, хирургические вмешательства в анамнезе и наличие ВЗК — не имели существенного значения [10].

Следует отметить, что в большинстве исследований, посвященных изучению качества подготовки кишечника, диетический фактор часто опускается или рассматривается как компонент соблюдения общих инструкций по подготовке кишечника, что затрудняет оценку точного влияния диеты в клинической практике [10,11].

В связи с вышесказанным можно сделать вывод о том, что соблюдение определенного режима питания в период подготовки к эндоскопическому исследованию является мало изученным вопросом [17]. С одной стороны, обсуждается роль компонентов, которые рекомендуется исключить из рациона, длительность этих ограничений. С другой стороны, следует отметить, что доказательная база этих рекомендаций является недостаточной [12]. Большинство исследований последних лет, признавая важность аспекта соблюдения диетических рекомендаций перед колоноскопией, чаще концентрируются на сравнении диеты, включающей только употребление жидкости и специализированных питьевых смесей (Clear Liquid Diet, CLD) с бесшлаковой диетой (Low-Residue Diet, LRD) [13–15]. Их результаты объединены в метаанализе Ahumada et al. [16], опубликованном в 2021 г. В него вошли данные о лечении 2587 пациентов. Было продемонстрировано, что как при использовании CLD, так и при применении просто бесшлакового питания, качество подготовки кишечника является сопоставимым (ОР = 1,02; 95% ДИ: 0,99–1,05), однако последнее ассоциировано с лучшей переносимостью (ОР = 1,17; 95% ДИ: 1,12–1,23) и меньшим риском развития нежелательных явлений (ОР = 0,89; 95% ДИ: 0,84–0,94).

ЗАКЛЮЧЕНИЕ

В проведенном нами исследовании было продемонстрировано, что в настоящее время в условиях специализированного центра неудовлетворительная подготовка кишечника констатирована у 9,1% пациентов. При этом основным фактором, ухудшающим ее качество, оказалось несоблюдение назначенной диеты перед эндоскопической процедурой. Таким образом, следует констатировать важность аспекта режима и рациона питания перед колоноскопией, её большой вклад в итоговый результат эндоскопического исследования и необходимость дальнейшей работы по данному направлению.

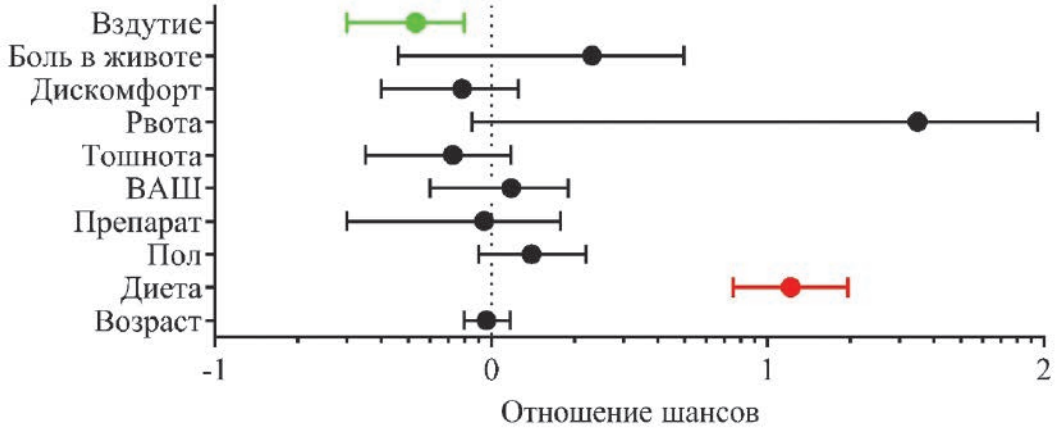

Рисунок 1. *Однофакторный анализ предикторов неадекватной подготовки кишечника*
Figure 1. *One-factor analysis of predictors of inadequate bowel preparation*

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Скрининг колоректального рака у работников предприятий РОСТЕХ Свердловской области. Пилотный проект.

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РЕЗЮМЕ *ЦЕЛЬ ИССЛЕДОВАНИЯ: оценка пилотной программы скрининга рака толстой кишки, выполненного в период с 01 апреля по 10 октября 2021 г., включающего на первом и втором этапе иммунохимический фекальный тест и анкетирование, а на третьем этапе — колоноскопию.*
МАТЕРИАЛЫ И МЕТОДЫ: реализована пилотная программа трёхэтапного скрининга рака толстой кишки. На первом этапе сотрудникам в возрастном интервале от 45 до 65 лет выполнен иммунохимический фекальный тест. На втором этапе — анкетирование. Сотрудники предприятий с положительным фекальным тестом и потенциальным риском канцерогенеза толстой кишки по результатам анкетирования направлены на третий этап для выполнения колоноскопии.
РЕЗУЛЬТАТЫ: на первом и втором этапах выполнено 969 фекальных иммунохимических тестов и анкетирований. В 149 случаях выявлен положительный фекальный тест. В 22 случаях сотрудники с отрицательным фекальным тестом направлены для выполнения колоноскопии по результатам анкетирования. На третьем этапе выполнено 168 скрининговых колоноскопий. У 87 (51,5%) пациентов выявлены эпителиальные образования прямой и ободочной кишки, верифицированы из них в 57 (33,7%) случаях аденома, в 4 (2,4%) случаях аденокарцинома, в том числе T_0 — 3 пациента, T_2 — 1 пациент. В 182 случаях локализации верифицированная патология локализовалась в 17,6% в прямой кишке и 82,4% — в ободочной кишке.
ЗАКЛЮЧЕНИЕ: программа скрининга колоректального рака показала свою высокую эффективность.

КЛЮЧЕВЫЕ СЛОВА: *рак толстой кишки, фекальный иммунохимический тест, анкетирование, скрининговая колоноскопия, аденома*

КОНФЛИКТ ИНТЕРЕСОВ: *авторы заявляют об отсутствии конфликта интересов*

ДЛЯ ЦИТИРОВАНИЯ: Десятов Е.Н., Алиев Ф.Ш., Цветков М.С., Верховодова И.С., Яковлева И.Л. Скрининг колоректального рака у работников предприятий РОСТЕХ Свердловской области. Пилотный проект. *Колопроктология*. 2023; т. 22, № 2, с. 64–69. https://doi.org/10.33878/2073-7556-2023-22-2-64-69

Screening for colorectal cancer in employees of ROSTECH enterprises in the Sverdlovsk region. Pilot project.

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ABSTRACT *AIM: to evaluate the pilot program results for colorectal cancer (CRC) screening of the Sverdlovsk region (April — October 2021)*
PATIENTS AND METHODS: a pilot program of three-stage CRC screening included at the first stage, the fecal immunochemical test was performed (patients aged 45–65 years). The second stage included questionnaire. According to the results of the questioning, patients with a positive fecal test and a potential risk of CRC underwent colonoscopy at the third stage.
RESULTS: at the first and second stages, 969 fecal immunochemical tests and questionnaires were performed. In 149 (15.4%) cases, a positive fecal test was detected. In 22 cases, employees with a negative fecal test were referred for colonoscopy according to the results of the questionnaire. At the third stage, 168 screening colonoscopies were performed. In 87 (51.5%) patients, epithelial colorectal neoplasia was detected, adenoma — in 57

(33.7%) cases, adenocarcinoma in 4 (2.4%), including T_0 — in 3 patients, T_2 — in 1 patient. In 182 cases, neoplasia occurred in 17.6% in the rectum and in 82.4% in the colon.
CONCLUSION: colorectal cancer (CRC) screening showed high efficacy.

KEYWORDS: *colon cancer, fecal immunochemical test, questionnaire, screening colonoscopy, adenoma*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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ВВЕДЕНИЕ

В структуре первичной заболеваемости в 2020 году в Свердловской области колоректальный рак (КРР) находился на первом месте (14,1%), опережая ЗНО лёгких (11,0%). По причине смертности колоректальный рак находится на втором месте (15,3%) после ЗНО лёгких (17,3%). С учетом высоких показателей заболеваемости и смертности разработка и внедрение региональной скрининговой программы диагностики колоректального рака является приоритетным направлением для сохранения жизни и здоровья населения области. Суммарные показатели заболеваемости раком прямой и ободочной кишки в Свердловской области в 2020 году составили 59 случаев на 100 тыс. населения, при этом 27,9% из них — пациенты с запущенными формами рака. К сожалению, в Свердловской области рак первой стадии диагностируется в 9,3% случаев — при локализации в ободочной кишке и в 10,3% — при локализации в прямой кишке [1,2].

Канцерогенез в толстой кишке представлен последовательностью аденома-карцинома, при этом риск малигнизации аденом возрастает при наличии дисплазии тяжёлой степени [3]. Колоректальный рак приблизительно в 70% случаев развивается из аденоматозных полипов и в 25–30% случаев из зубчатых аденом [4]. Эндоскопическое удаление полипов снижает заболеваемость и смертность от рака толстой кишки [5,6]. Таким образом, основным инструментом профилактики колоректального рака на современном этапе является скрининг, направленный на верификацию с последующим удалением аденом и карцином толстой кишки. «Идеальный» скрининговый тест должен быть неинвазивным, обладать высокой чувствительностью и специфичностью, безопасным, легкодоступным, удобным и недорогим. Для скрининга колоректального рака существует несколько утвержденных тестов и стратегий. Один из подходов к скрининговым тестам КРР заключается в разделении их на 1-этапные тесты (Колоноскопия, которая является диагностической и терапевтической) или 2-этапные тесты, которые требуют колоноскопии, если они положительные, для завершения процесса скрининга. По ряду организационных причин в России выполнение 1-этапного теста — выполнение колоноскопии населению старше 50 лет в настоящее время невозможно ввиду недостаточной обеспеченностью подготовленными кадрами, недостаточным количеством кабинетов для выполнения скрининговой колоноскопии с седацией, отсутствием необходимого количества эндоскопов, а также низких тарифов ТФОМС. В этой связи в РФ для ранней диагностики колоректального рака доминирует идея выявления «группы риска» в популяции. Считается, что методами анкетирования и тестирования кала на скрытую кровь возможно формирование «группы риска», что позволит ограничиться обследованием около 20% населения и при этом выявить до 80% КРР. Однако до настоящего времени неизвестны все факторы риска развития рака толстой кишки, увеличивающие вероятность его возникновения более чем в 100 раз. Следовательно, скринингу для ранней диагностики рака толстой кишки должно подвергаться все население [7]. Согласно международным клиническим рекомендациям, риск развития рака толстой кишки возрастает при наличии семейного анамнеза и с увеличением возраста пациента [8]. После 50 лет вероятность развития рака толстой кишки удваивается с каждым последующим десятилетием [9]. В этой связи показаниями для выполнения скрининговой колоноскопии являются возраст пациента 50 лет и старше, отягощенный семейный анамнез и положительный фекальный иммунохимический тест. К первой группе

методов скрининга КРР относится анкета для выявления отягощенного семейного анамнеза и наличие клинических проявлений — слизь, кровь в стуле, запоры. Ко второй группе методов относят лабораторные тесты. Фекальный иммунохимический тест выявляет в стуле наличие человеческого гемоглобина. Результат теста специфичен и позволяет исключить диетические ограничения в период выполнения исследования. К третей группе методов скрининга КРР относится колоноскопия, позволяющая диагностировать и верифицировать неоплазии толстой кишки.

ЦЕЛЬ ИССЛЕДОВАНИЯ

Оценка эффективности пилотной программы скрининга злокачественных образований толстой кишки, состоящей из трёх этапов: фекальный иммунохимический тест, анкетирование, колоноскопия.

МАТЕРИАЛЫ И МЕТОДЫ

На первом этапе скрининга рака толстой кишки работникам ряда промышленных предприятий Свердловской области в возрастном интервале от 45 до 65 лет выполнялся фекальный иммунохимический тест иммунохроматографическим количественным методом на экспресс-анализаторе Vedalab (Франция). На втором этапе — заполнение анкеты-опросника. На третий этап направлялись работники с положительным фекальным тестом либо по результатам анкеты-опросника. Колоноскопию с седацией выполняли амбулаторно на базе отделения внутрипросветной диагностики. В период с 01 апреля 2021 г. по 10 октября 2021 г. выполнено 969 фекальных тестов и анкетирование. У 149 работников выявлен положительный фекальный тест кала на скрытую кровь. 22 человека с отрицательным фекальным тестом направлены на колоноскопию по результатам анкетирования. Из них 2 человека от выполнения колоноскопии отказались. Таким образом, выполнено 168 колоноскопий пациентам в возрастном интервале от 45 до 65 лет с положительным фекальным иммунохимическим тестом на скрытую кровь и пациентам группы высокого риска развития КРР по результатам анкетирования. Скрининговые колоноскопии выполнены с фотофиксацией устья червеобразного отростка и выявленной патологии. У обследованных работников предприятий в анамнезе отсутствовали данные о полипах или раке толстой кишки. Подготовка к исследованию начиналась за 3 суток до колоноскопии и заключалась в соблюдении диеты (исключение овощей и фруктов, снижение объема принимаемой пищи и т.д.). Накануне и в день проведения исследования пациентам назначались препараты Эзиклен® по двухэтапной схеме — прием 2 доз препарата накануне и в день исследования — 82,7% пациентов или Мовипреп® — 17,3% пациентов. Качество подготовки к колоноскопии оценивали по BBPS — Бостонская шкала оценки уровня подготовки толстой кишки к исследованию. Видеоколоноскопия выполнялась в амбулаторных условиях с 13 до 15 ч. в отделении внутрипросветной эндоскопической диагностики под внутривенной анестезией. Скрининговую колоноскопию выполняли 3 врача первой и высшей квалификационной категории на видеоэндоскопической системе ELUXEO™ 7000, (Fujifilm, Япония). Осмотр выполнялся в белом свете эндоскопами высокого разрешения, с широким углом обзора 170° (EC-760R-VL) и применением оптического увеличения ×135 (EC-760ZP-VL). Высокоинтенсивный диодный источник света с технологией MultiLight® обеспечивал режимы осмотра в узком спектре изображения (режим BLI) и с усилением связанных цветов (режим LCI).

РЕЗУЛЬТАТЫ

Интубация слепой кишки была достигнута в 99,7% случаев. Время выведения видеоколоноскопа из толстой кишки без учёта времени на выполнение биопсии или полипэктомию составило более 6 минут. У 89 (52,9%) человек выявлены эпителиальные неоплазии, из них аденомы и аденокарциномы прямой и ободочной кишки составили 80 (47,3%) и 4 (2,4%) случаев, соответственно (Табл. 1). Всего обнаружено 182 патологических образования, из которых в 17,6% они располагались в прямой кишке и в 82,4% — в ободочной кишке (Табл. 1).

Эпителиальные образования удалены 87 пациентам. 61 (79,1%) пациенту — во время скрининговой колоноскопии. Пациенты с верифицированным раком толстой кишки (Табл. 1) направлены для внутрипросветного эндоскопического или хирургического удаления в стационар ГАУЗ СО «Свердловский областной онкологический диспансер». Кроме того, 10 пациентам с выявленной патологией выполнено эндоскопическое внутрипросветное удаление в условиях дневного стационара отделения клинической эндоскопии ГАУЗ СО «Свердловский областной онкологический диспансер».

ОБСУЖДЕНИЕ

Нейросетевое моделирование различных стратегий скрининга показало сопоставимую

Таблица 1. *Локализация верифицированной патологии толстой кишки*
Table 1. *Localization of verified pathology of the colon*

Локализация	Число случаев локализации, абс.			Случаев локализации, всего
	Гиперпластический полип	Аденома	Карцинома	
Прямая кишка				
Прямая кишка	5	25	2	32
Ободочная кишка				
Сигмовидная ободочная кишка	7	45	2	54
Нисходящая ободочная кишка	2	16	0	18
Поперечная ободочная кишка	5	30	0	35
Восходящая ободочная кишка	2	28	0	30
Слепая кишка	2	11	0	13
Итого	23	155	4	182

продолжительность жизни, полученную при следующих комбинациях: ежегодный фекальный иммунохимический тест, колоноскопия каждые 10 лет, гибкая сигмоидоскопия каждые 10 лет с ежегодным фекальным иммунохимическим тестом, компьютерная колонография каждые 5 лет, фекальный mtsДНК-тест каждые 3 года [10]. В другом моделирующем исследовании повторный скрининг через 10 лет после отрицательного результата колоноскопии в возрасте 50 лет снизил частоту возникновения КРР по сравнению с отсутствием дальнейшего скрининга рака толстой кишки [11]. Метод скрининговой видеоколоноскопии позволяет диагностировать аденомы, выполнять биопсию и эндоскопическую полипэктомию в большинстве случаев. Качество подготовки к скрининговой колоноскопии зависит от мотивации пациента и выбора препарата для подготовки к исследованию. Во время исследования отмывание слизистой оболочки толстой кишки выполняли с помощью водяной помпы с последующей оценкой подготовки по Бостонской шкале. Подготовка считалась достаточной при оценке 6–9 баллов. В связи с тем, что скрининговые колоноскопии выполнялись во 2-й половине дня, препараты назначались по двухэтапной схеме приёма. Обязательным условием скрининговой колоноскопии является интубация слепой кишки — введение колоноскопа в купол слепой кишки проксимальнее илеоцекального клапана с возможностью прикоснуться к устью червеобразного отростка кончиком эндоскопа с фотографированием устья червеобразного отростка, илеоцекального клапана и терминального отдела подвздошной кишки [12]. Этот индикатор качества предложен ввиду хорошо известных выводов о том, что большое число колоректальных новообразований расположены в проксимальной части толстой кишки, включая слепую кишку [12]. Частота интубации слепой кишки должна составлять не менее 90% — при выполнении рутинных колоноскопий и не менее 95% — при выполнении скрининговых колоноскопий [13]. В нашем исследовании частота интубации слепой кишки составила 99,7%, что позволило верифицировать аденомы ободочной кишке в 49% случаев. Исключение составил случай со стенозирующим раком сигмовидной кишки. Считаем, что этот показатель является демонстрацией диагностического преимущества колоноскопии перед сигмоскопией. В нашем исследовании время выведения эндоскопа составляло более 6 минут, что является важным индикатором качества выполненной колоноскопии и коррелирует с показателями ADR (Adenoma Detection Rate — частота выявления аденом) и частоты выявления КРР [14]. Минимальное значение ADR у пациентов в возрастной группе старше 50 лет должно составлять не менее 25% [15]. В нашем исследовании значение ADR составило 47,3%, что может отражать имеющийся контакт работников с вредным производством, применение видеоэндоскопов экспертного уровня, а так же квалификацию врачей отделения эндоскопии. Считаем, что своевременное удаление неоплазий у данной группы пациентов в значительной степени снизит вероятность развития рака толстой кишки.

В 79,1% случаев выявленные эпителиальные образования удалены во время скрининговой колоноскопии. Это является признаком эффективности выполненного колоректального скрининга, а также важным экономическим показателем, так как исключаются траты на этап последующей госпитализации пациентов для удаления выявленных образований. Так же считаем, что определяющими условиями скрининговой колоноскопии являются соблюдение рекомендованной диеты перед приемом препаратов Эзиклен® или Мовипреп®, выбор широкоугольного видеоколоноскопа, наличие помпы для отмывания слизистой

оболочки толстой кишки и применение внутривенной анестезии во время исследования.

ЗАКЛЮЧЕНИЕ

Программа скрининга колоректального рака представляется весьма эффективным инструментом в диагностике и лечении колоректальных новообразований.

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Краткосрочная преабилитация у больных колоректальным раком — протокол рандомизированного клинического исследования

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РЕЗЮМЕ *ЦЕЛЬ: определить влияние унимодальной краткосрочной преабилитации на функциональные резервы пациентов, сроки госпитализации, послеоперационные осложнения и качество жизни.*

ПАЦИЕНТЫ И МЕТОДЫ: в одноцентровое проспективное рандомизированное исследование будет включено 128 пациентов, перенесших резекцию толстой кишки по поводу колоректального рака. Пациентов разделят на группу вмешательства, которой будет проведена 14-дневная унимодальная преабилитации (группа 1) и контрольную группу, которой не будет проводиться преабилитация (группа 2). Периоперационное ведение пациентов обеих групп будет проходить в соответствии с рекомендациями по ускоренному восстановлению после операции (ERAS). Первичной конечной точкой исследования будет: результат теста шестиминутной ходьбы (6MWT). Вторичными конечными точками будут: количество послеоперационных осложнений (по Clavien-Dindo), продолжительность послеоперационного периода, послеоперационная летальность, качество жизни больных и приверженность больных к прохождению программы преабилитации.

ОБСУЖДЕНИЕ И ВЫВОДЫ: ожидается, что краткосрочная унимодальная преабилитация улучшит функциональные резервы пациентов, сократит продолжительность стационарного лечения и уменьшит количество и тяжесть послеоперационных осложнений, что может привести к снижению послеоперационной летальности и улучшению качества жизни больных. Будет проанализирована приверженность отечественной когорты пациентов к преабилитации.

КЛЮЧЕВЫЕ СЛОВА: *преабилитация, колоректальная хирургия, функциональные резервы, ускоренное восстановление после операции, послеоперационные осложнения, колоректальный рак*

КОНФЛИКТ ИНТЕРЕСОВ: *авторы заявляют об отсутствии конфликта интересов*

ДЛЯ ЦИТИРОВАНИЯ: Захаренко А.А., Завгородняя М.В., Афанасьев А.А., Потапчук А.А. Краткосрочная преабилитация у больных колоректальным раком — протокол рандомизированного клинического исследования. *Колопроктология*. 2023; т. 22, № 2, с. 70–78. https://doi.org/10.33878/2073-7556-2023-22-2-70-78

Short-term prehabilitation of patients with colorectal cancer — protocol of a randomized trial

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ABSTRACT *AIM: to estimate effect of unimodal short preabilitation on functional reserves of patients, hospital stay, complication rate and quality of life.*

PATIENTS AND METHODS: a single-centre, prospective, randomized study will include 128 patients undergoing colon resection for colorectal cancer. Patients will be divided into an intervention group that will receive 14 days of unimodal prehab (Group 1) and a control group that will not receive prehab (Group 2). Perioperative management of patients in both groups will be carried out in accordance with the guidelines for accelerated recovery after surgery (ERAS). The primary endpoint of the study will be the six-minute walk test (6MWT). Secondary endpoints will be: number of postoperative complications (by Clavien-Dindo), duration of the postoperative period, postoperative mortality, quality of life of patients and adherence of patients to the passage of the prehabilitation program.

DISCUSSION AND CONCLUSION: it is expected that short-term unimodal prehabilitation will improve the functional reserves of patients, reduce the duration of inpatient treatment and reduce the number and severity of postoperative complications, which can lead to a decrease in postoperative mortality and an improvement in the quality of life of patients. The adherence of the domestic cohort of patients to prehabilitation will be analyzed.

KEYWORDS: *prehabilitation, colorectal surgery, functional reserves, accelerated recovery after surgery, postoperative complications, colorectal cancer*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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ВВЕДЕНИЕ

Колоректальный рак является вторым по распространённости онкологическим заболеванием в мире с ежегодной заболеваемостью и смертностью 1.4 млн и 693.900 случаев, соответственно [1].

Хирургический этап является основным компонентом лечения. Однако почти у половины пациентов возникают послеоперационные осложнения, которые определяют послеоперационную летальность и ухудшение качества жизни пациентов, высокие затраты на лечение, продлевают стационарный этап [2].

Большой объём хирургического вмешательства неизбежно приводит к снижению функциональных резервов организма больного на 20–40% [3]. Сниженные резервы определяют длительную послеоперационную слабость и утомляемость [4]. Только 40% больных возвращаются к исходному функциональному статусу, но адъювантная химиотерапия усугубляет состояние большинства пациентов [5].

Имеются данные о снижении негативных последствий агрессивных хирургических вмешательств за счёт ослабления хирургического стресса. Это, преимущественно, интраоперационные (малоинвазивная хирургия, блокада афферентных нервов) [6] и послеоперационные (концепция "fasttrack" — ранняя мобилизация и энтеральное питание) методы [7]. Протоколы ускоренной реабилитации "fasttrack" были разработаны для облегчения восстановления функциональной активности и ускорения выздоровления, однако послеоперационный период может быть не лучшим временем для существенных изменений пищевого поведения пациентов и выполнения ими физических упражнений. Больные отмечают усталость и обеспокоенность тем, что могут нарушить процесс заживления ран. Предоперационный период может оказаться оптимальным для воздействия на факторы, способствующие послеоперационному восстановлению, как физическому, так и психическому, а также для облегчения некоторых эмоциональных переживаний, связанных с ожиданием операции [8–10]. Процесс повышения функциональных возможностей человека, с целью стимулирования ответной реакции стрессовым факторам хирургической агрессии, был назван преабилитацией [2,11]. Проблему стали изучать с оценки роли физических упражнений (унимодальная преабилитация) на восстановление функциональной способности после хирургии рака толстой кишки. Было проведено несколько пилотных исследований, показавших положительные результаты [9,12–15]. Подгрупповой анализ исследований Carli и соавт. показал, что пациенты, чья функциональная толерантность к физической нагрузке улучшилась до операции, хорошо восстанавливались в послеоперационном периоде, независимо от техники упражнений [16]. В исследованиях на сегодняшний день, преимущественно, используется одномодальная циклическая высокоинтенсивная интервальная тренировка [17]. С другой стороны, состояние каждого третьего пациента ухудшалось до операции, независимо от режима упражнений, с повышением риска более длительного восстановления после операции. Плохое предоперационное физическое состояние (усталость, недоедание и сниженная работоспособность), наличие тревоги и депрессии также были предикторами длительного восстановления [18–20]. Отмечена положительная роль детального информирования пациентов о предстоящей операции [21]. Эти результаты показывают, что для снижения реакции на стресс одних только физических упражнений недостаточно и важно обращать внимание на такие факторы, как питание и психологический статус. Gillis и др. провели рандомизированное клиническое исследование, которое показало значимое превосходство преабилитации над реабилитацией в контексте повышения функциональных резервов и времени восстановления после операции [22]. Однако авторы не определили взаимосвязь между дооперационными функциональными резервами и уровнем послеоперационных осложнений, который предположительно должен снижаться. В других исследованиях доказана

связь между количеством и тяжестью послеоперационных осложнений с предоперационными функциональными резервами, нутритивным статусом, курением и психологическим благополучием. Это повысило интерес исследователей к мультимодальным программам преабилитации [14]. Успех преабилитации возможен при комбинировании физических упражнений, включающих непрерывные аэробные упражнения умеренной интенсивности с более традиционными упражнениями на основные группы мышц с отягощениями, правильного питания, отказа от курения и психологической поддержке [23].

Реализация мультимодальных подходов зависит от физической способности человека выполнять такие упражнения (при этом исключается большая группа физически слабых пациентов), а также от наличия времени перед операцией, достаточного для того, чтобы достичь эффективности. Показано, что достичь клинически значимых эффектов можно в течение 4–5 недель между постановкой диагноза и операцией [9,17,24]. Сроки предоперационного периода сильно различаются у больных раком ободочной и прямой кишки, где при проведении неоадъювантного лечения нет временных ограничений для проведения преабилитации.

Сроки оказания различных этапов медицинской помощи онкологическим пациентам определены в законе «О Территориальной программе государственных гарантий бесплатного оказания гражданам медицинской помощи в Санкт-Петербурге на 2021 год и на плановый период 2022 и 2023 гг.» (от 16 декабря 2020 года). Так для проведения консультаций врачей-специалистов в случае подозрения на онкологические заболевание выделяется 3 рабочих дня. Сроки проведения диагностических инструментальных и лабораторных исследований в случае подозрения на онкологические заболевания не должны превышать 7 рабочих дней со дня назначения исследований. Сроки ожидания оказания специализированной (за исключением высокотехнологичной) медицинской помощи для пациентов с онкологическими заболеваниями — 7 рабочих дней с момента гистологической верификации опухоли или с момента установления предварительного диагноза заболевания (состояния). В большинстве случаев через 2 недели после консультации онколога, пациент с диагностированным раком толстой кишки, должен попасть на специализированный этап медицинской помощи. В связи со сжатыми сроками предоперационного периода, проведение преабилитации в общепринятых сроках (4–6) недель представляется проблематичным, и встаёт вопрос о сокращении этих сроков и, соответственно, оценки эффективности краткосрочных программ.

Влияние нутритивной и психологической поддержки, а так же менеджмента крови имеют высокий уровень доказательности и входят в протокол предоперационной поддержки ERAS [25], которую получат все пациенты. Различия между группами будут заключены именно в исследуемом компоненте преабилитации — физических нагрузках, а значит, преабилитация исследуемой группы будет являться унимодальной.

ЦЕЛИ ИССЛЕДОВАНИЯ

Главной целью исследования является определение роли физических упражнений, в составе краткосрочной (14 дней) преабилитации на повышение функциональных резервов организма больного и, соответственно, снижение послеоперационных осложнений, летальности, продолжительности сроков стационарного лечения. Первичной конечной точкой исследования будет: результат теста шестиминутной ходьбы (6MWT). Вторичными конечными точками будут: продолжительность послеоперационного периода, количество послеоперационных осложнений (по Clavien-Dindo), послеоперационная летальность, качество жизни больных, статус питания, приверженность больных к прохождению программы преабилитации.

МЕТОДЫ

Дизайн исследования

Это одноцентровое проспективное рандомизированное исследование с двумя исследуемыми группами. От каждого пациента будет получено письменное информированное согласие. Исследование будет проводиться в соответствии с правилами надлежащей клинической практики с осуществлением мониторинга нежелательных явлений и осложнений. Исследование одобрено локальным этическим комитетом ФГБОУ ВО ПСПбГМУ им. И.П. Павлова Минздрава России от 28.11.2022.

МАТЕРИАЛ ИССЛЕДОВАНИЯ

В исследование будут включены взрослые пациенты (старше 18 лет), которым будет проведена резекция толстой кишки по поводу рака. Планируется включить 216 больных, по 108 в каждой группе. Ожидаемое улучшение результатов функционального теста в основной группе — 19 метров или 30% от исходного показателя. Предполагаемый период набора пациентов 3 года. Из исследования будут исключаться пациенты с отдалёнными метастазами,

показаниями к неоадъювантной химиолучевой или химиотерапии, любыми нарушениями опорно-двигательного аппарата, препятствующими выполнению физических упражнений, когнитивными расстройствами, хронической болезнью почек (диализная стадия или креатинин более 250 ммоль/л), высоким анестезиологическим риском по ASA 4 и более.

Рандомизация

Пациенты будут рандомизированы с распределением 1:1 с помощью программного обеспечения для рандомизации, стратифицированы по возрасту, ИМТ, риску ASA. Пациенты будут разделены на группу вмешательства для проведения 14-дневной унимодальной преабилитации (группа 1) и контрольную группу, которой не будет проводиться преабилитация (группа 2). Периоперационное ведение пациентов обеих групп будет проходить в соответствии с рекомендациями по ускоренному восстановлению после операции (ERAS).

При первичной консультации и подозрении на злокачественное новообразование толстой кишки после оценки соматического статуса и выставления показаний к хирургическому вмешательству принимается предварительное решение о включении больного в исследование. Пациенту предоставляется письменная и устная информация об исследовании и времени для ознакомления и принятия решения о желании участвовать в нём. Пациент должен будет подписать форму информированного согласия в присутствии врача-исследователя. Блок-схема проведения исследования показана на рисунке 1. После рандомизации при попадании в группу исследования пациенту будет предоставлен выбор одного из 3 режимов ЛФК (очно с инструктором, онлайн с инструктором, оффлайн на дому без инструктора). После того, как получено согласие на участие, пациентам будет проведён консилиум участников исследовательской группы (хирург, диетолог и психолог для группы контроля; хирург, диетолог, психолог и врач ЛФК для группы исследования) и назначена 14-дневная программа преабилитации.

План исследования

До и после преабилитации проводится тест 6-минутной ходьбы (6MWT), определение качества жизни по EORTC Quality of Life Questionnaire — C30, индекса массы тела, индекса саркопении, взятие анализа крови (гемоглобин, эритроциты, гематокрит, железо сыворотки, трансферрин, ферритин, общий белок, альбумин), сбор информации о активности пациента за 2 недели (на основании ведения дневника, результатов браслета-шагомера). Подробный план исследования со всеми этапами регистрации контрольных точек представлен в таблице 1.

Физические упражнения представляют собой специально разработанный на кафедре физического воспитания и здоровья ПСПбГМУ им. акад. И.П. Павлова универсальный комплекс упражнений на все группы мышц (резонансная тренировка) (6 занятий по 28–32 минуты). Планируется 3 занятия в неделю.

Общепринято считать, что тренировочные блоки продолжительностью 3–5 минут и тренировки высокой интенсивности особенно эффективны с точки зрения повышения функциональных резервов.

Продолжительность интервальной тренировки составляет 28–32 минуты, и она выполняется с 4 минутами разминки средней интенсивности, 4 интервалами высокой интенсивности (2–3 мин.) и 4 интервала умеренной интенсивности (4 мин.). Кроме того, пациентам основной группы будет рекомендована аэробная нагрузка в виде прогулки, скандинавской ходьбы или лёгкой пробежки в течение часа, ежедневно.

ЛФК будет проводиться в 3 вариантах: при очных визитах с инструктором, онлайн занятия с инструктором, в групповом или индивидуальном формате, и дома самостоятельно без инструктора.

Пациенты, как в экспериментальной, так и в контрольной группе будут носить акселерометр (спортивные часы) в течение двух недель, чтобы подсчитывать количество пройденных шагов и регистрировать общую активность (количество потраченных ежедневно ккал).

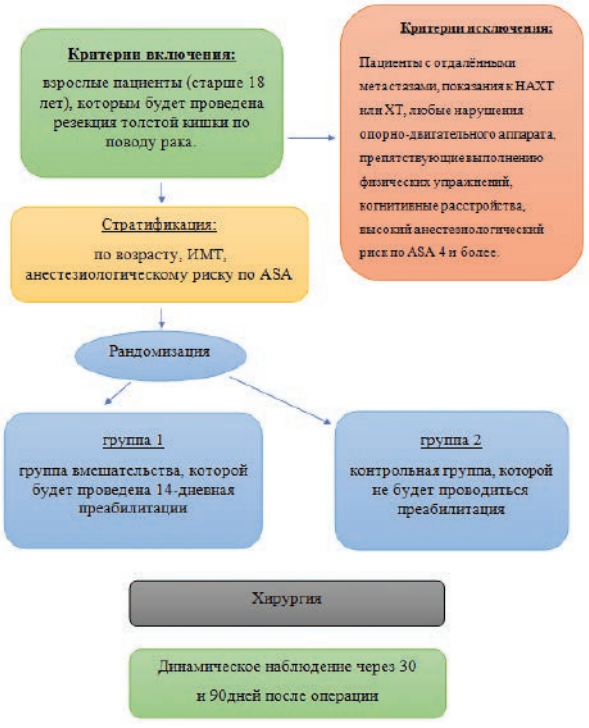

Рисунок 1. *Блок-схема проведения исследования*
Figure 1. *Flowchart of the study*

Таблица 1. *Этапы регистрации контрольных точек*
Table 1. *Checkpoint registration steps*

	До преабилитации	После преабилитации	30 суток после операции	90 суток после операции
Тест шестиминутной ходьбы (6MWT)	+	+	+	+
Клинический анализ крови (гемоглобин, эритроциты, лимфоциты)	+	+	+	+
Биохимический анализ крови (общий белок, альбумин, железо, ферритин)	+	+	+	+
ИМТ	+	+	+	+
Индекс саркопении	+	+	+	+
Необходимость нутритивной поддержки по результату NRS-2002	+	+	+	+
Индекс нарушения питания по Buzby G.P.	+	+	+	+
Дефицит массы тела от идеальной	+	+	+	+
Качество жизни (EORTCQLQ-C30)	+	+	+	+
Доля посещённых занятий ЛФК		+		
Доля выполненных упражнений на занятии ЛФК		+		
Длительность стационарного лечения после операции			+	
Осложнения после операции по Clavien-Dindo			+	
30-дневная летальность			+	
90-дневная летальность				+

Каждым пациентом основной группы ведётся индивидуальный дневник тренировок с описанием повседневной активности. Специалистом ЛФК проводится оценка каждой тренировки на предмет выполнения всех упражнений, интенсивности упражнений, динамики ЧСС.

В результате определяется индивидуальная приверженность к тренировкам: фиксируются количество и причины пропусков, количество и полноценность проведённых тренировок, общее время преабилитации.

Мы ожидаем увеличение результатов 6MWT после преабилитации у больных основной группы более чем на 19 метров или на 30% по отношению к исходным данным. Так же высока вероятность, что после операции участники основной группы более быстро вернутся к исходным показателям 6MWT.

Для оценки влияния исключительно физической нагрузки — периоперационное ведение пациентов обеих групп уравновешено рекомендациями по ускоренному восстановлению после операции (ERAS), в рамках которой в нашей клинике внедрён менеджмент крови и коррекция нарушений питания (по показаниям).

Физические упражнения в предоперационном периоде — главное отличие между пациентами исследуемых групп.

Менеджмент крови является обязательной составляющей в подготовке к операции. При диагностировании анемии проводится её коррекция внутривенным введением Железа карбоксимальтозата 1000 мг 1 раз в неделю.

Конечные точки исследования

Первичной конечной точкой исследования будет значение 6MWT, измеренное исходно и непосредственно перед операцией. Дополнительно 6MWT будет измеряться через 30 и через 90 суток после операции.

Тест оценивает способность человека ходить с умеренной интенсивностью, и связан с возможностью выполнять повседневную деятельность, валидирован на хирургических пациентах [26] и линейно коррелирует с пиковым потреблением кислорода [14] и анаэробным порогом [27]. Он характеризует силу и выносливость человека и легко воспроизводим. В помещении определяется интервал длиною 50 метров, ограничивается специальными метками каждые 5 метров. Подсчитывается количество меток, которые пациент прошёл за 6 минут. Во время ходьбы разрешается делать остановки на отдых, время теста при этом не останавливается. Участники оповещаются об истечении каждой минуты.

Индивидуальный прогнозируемый результат 6MWD (i) («норма»), учитывающий возраст, пол и ИМТ рассчитывался по формулам. Значение для мужчин: 6MWD (i) = 1140 — 5,61 × ИМТ — 6,94 × возраст. Значение для женщин: 6MWD (i) = 1017 — 6,24 × ИМТ — 5,83 × возраст [28].

Вторичными конечными точками будут: послеоперационные осложнения (по классификации

Clavien-Dindo), фиксируемые в течение 30 дней после операции; послеоперационная летальность через 30 и 90 суток после операции; динамика ИМТ; динамика значения гемоглобина, ферритина, железа; динамика показателей качества жизни по данным опросника EORTCQLQ-C30; срок стационарного лечения после операции и соблюдение режима ЛФК (доля посещённых занятий и доля выполненной нагрузки).

Статистический анализ

Для однородности исследуемых групп будет использована блоковая рандомизация со стратификацией по возрасту, ИМТ, риску ASA. Будет проведён intention-to-treat анализ.

Первичная конечная точка 6MWT является непрерывной переменной. Эти данные будут указаны как среднее значение (mean) плюс стандартное отклонение (SD) в каждый момент фиксации результата.

Все вторичные конечные точки будут описаны как среднее плюс стандартное отклонение или медиана плюс интерквартильный размах IQR при непрерывных переменных и нормальном и ненормальном распределении данных. Категориальные параметры будут описаны как число плюс процент на момент времени. Статистические методы будут включать t-критерий и U-критерий Манна-Уитни (Mann-Whitney). Категориальные результаты проанализируются с помощью тестирования χ^2 или регрессионного анализа (логистического, порядкового или номинального, в зависимости от определения параметра) для отдельных моментов времени. В исследовании заложена ошибка 1 рода альфа 0,05 и мощность 0,80 (двусторонний тест). На основании данных предыдущих исследований [29], клинически значимой межгрупповой разницей для теста 6-минутной ходьбы считается 19 метров, а максимальные стандартные отклонения SD = 47. Мы ожидаем выбывание 10% участников в процессе исследования и с учётом этого, размер выборки составит 216 человек, по 108 в каждой группе. В нашей клинике ежегодно подвергаются хирургическому вмешательству около 70 подходящих пациентов с колоректальным раком. Это означает, что мы завершим включение больных в исследование в течение трех лет, и потребуется ещё 3 месяца для завершения динамического наблюдения за последним включённым пациентом. Из-за минимального количества клинических данных относительно приверженности к преабилитации отечественной популяции пациентов и её эффективности будет проведен промежуточный анализ. Промежуточный анализ планируется, если половина предполагаемого числа пациентов завершила обследование через 12 недель после операции (т.е. сроки оценки первичной конечной точки). Целью промежуточного анализа является оценка полученных различий между группами и прекращение исследования при наличии статистически значимой разницы между исследуемыми группами или перерасчет выборки для получения статистических различий.

ОБСУЖДЕНИЕ

Данное исследование побуждено рядом вопросов, которые не освещены в отечественной литературе.

Крайне дискутабельны допустимые сроки проведения преабилитации. С одной стороны, стоит необходимость в выполнении операции «как можно быстрее», с другой — существует повышенный риск послеоперационных осложнений при плохой предоперационной подготовке. Доказано, что послеоперационные осложнения значимо ухудшают онкологические результаты. Систематический обзор и метаанализ 23 клинических исследований показал значимое влияние сроков преабилитации (более 3 недель) на частоту послеоперационных осложнений, особенно у коморбидной группы пациентов. В 14 исследованиях на 1648 пациентах продемонстрировано статистически значимое увеличение 6MWD на 31 метр (95% ДИ: 13–45 м) после одно- и мультимодальной преабилитации с упражнениями. Авторы оценили, что такие вмешательства улучшили функциональную способность к физическим нагрузкам, а так же выявили тенденцию к меньшему количеству послеоперационных осложнений, при проведении занятий не менее 3 недель, а предпочтительно дольше [30].

Отсутствуют доказательства об ухудшении отдалённых результатов лечения рака толстой кишки при задержке операции до 60 суток с момента диагностики. Систематический обзор и метаанализ, включивший 13514 пациентов показал отсутствие влияние сроков предоперационного периода на показатели отдалённой выживаемости. Так, Южнокорейское исследование не выявило разницы в 5-летней выживаемости у пациентов, которым лечение было проведено в срок до 30 дней и свыше 30 дней. В Датском исследовании не было различий в общей и опухоль-специфичной выживаемости у пациентов, получавших лечение в срок до 59 дней после установки диагноза и более 60 дней (ОР: 1,01 95% ДИ: 0,74). В одном из Канадских исследований не было выявлено различий в общей выживаемости между сроками до 42 и до 56 дней, а в другом — была обнаружена клинически незначимая сниженная общая выживаемость в группе лечения через 43 дня по сравнению с лечением в 1–14 сутки после установки диагноза [31].

Тем не менее, сроки оптимального обследования и начала специализированного этапа лечения в нашей стране определены законодательно, и на этом строится

финансирование лечебного процесса. Соответственно, в течение 2 недель пациент, которому показана операция — должен быть госпитализирован в хирургическую клинику и в ближайшее время прооперирован. Оценка эффективности краткосрочной преабилитации — одна из задач представленного исследования. Данная научная гипотеза подкреплена рядом научных исследований в кардиохирургии, где краткосрочные режимы показали свою эффективность [32].

Очень вариабельный вопрос приверженности и комплаентности пациентов к физическим нагрузкам. Одна часть исследователей приводит значительную вовлечённость (90–98%), особенно когда занятия проводит инструктор. С другой стороны, много данных о плохой посещаемости занятий, особенно трудоспособного населения, причём даже при применении финансовой мотивации. Подобных отечественных данных в настоящее время нет, и это является одной из вторичной точек исследования.

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Отдаленные результаты хирургического лечения пациентов с параколостомической грыжей

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РЕЗЮМЕ *ЦЕЛЬ: улучшение отдаленных результатов хирургического лечения больных с параколостомической грыжей (ПГ).*

ПАЦИЕНТЫ И МЕТОДЫ: в проспективное сравнительное исследование были включены 60 пациентов с ПГ, оперированные в 2013–2019 гг. Больные разделены на две группы по 30 человек в каждой. Группы были сопоставимы по размерам и типу грыж, возрасту, полу, характеру основного заболевания, перенесенной операции и качеству жизни. Пациентам контрольной группы выполнена пластика по Шугабейкеру, основной группы — пластика по Шугабейкеру с ушиванием грыжевых ворот. Критериями эффективности метода были частота рецидивов ПГ и качество жизни (EQ-5D-5L) в послеоперационном периоде. Сравнение результатов производили через 1 и 2 года после операции.

РЕЗУЛЬТАТЫ: частота рецидивов ПГ в основной группе была достоверно ниже через 1 и 2 года после операции (3 против 13; p = 0,01). Качество жизни пациентов в основной группе было достоверно выше уже через 1 год после операции (в основной группе медиана взвешенного коэффициента составила 0,92, в контрольной — 0,89; p = 0,04). Достигнутые различия сохранялись и через 2 года после операции.

ЗАКЛЮЧЕНИЕ: ушивание грыжевых ворот при пластике по Шугабейкеру при парастомальной грыже существенно снижает частоту рецидивов, что улучшает качество жизни в отдаленном послеоперационном периоде.

КЛЮЧЕВЫЕ СЛОВА: *параколостомическая грыжа, аллопластика, качество жизни*

КОНФЛИКТ ИНТЕРЕСОВ: *авторы заявляют об отсутствии конфликта интересов*

ДЛЯ ЦИТИРОВАНИЯ: Мальгина Н.В., Родоман Г.В., Долгина Т.Ю. Отдаленные результаты хирургического лечения пациентов с параколостомической грыжей. *Колопроктология*. 2023; т. 22, № 2, с. 79–85. https://doi.org/10.33878/2073-7556-2023-22-2-79-85

Late outcomes of parastomal hernia repair

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ABSTRACT *AIM: to assess late results of parastomal hernia repair using Sugarbaker's technique modifications.*

PATIENTS AND METHODS: prospective non-randomised study included 60 patients with parastomal hernia, which underwent surgery in 2013-2019. Patients were divided in two groups. The control group included 30 patients with "classic" Sugabacker method, the main group included 30 patients with Sugarbaker's procedure added by suture of abdominal wall defect. Both groups were homogenous by age, gender, hernia size, type of primal disease and preoperative quality of life (EQ-5D-5L). The efficacy of the treatment was estimated by recurrence rate and quality of life 1 and 2 years after surgery.

RESULTS: the recurrence rate in the main group was significantly lower after 1 and 2 years (3 vs 13; p = 0.01). Quality of life in the main group was significantly higher after the first year of follow-up (the median of the weighted coefficient 0.92 vs 0.89; p = 0.04) and this trend has preserved 2 years after surgery.

CONCLUSION: suture of abdominal wall defect in Sugarbaker's procedure for parastomal hernia reduces recurrence rate significantly and provides better quality of life.

KEYWORDS: *parastomal hernia, alloplastics, quality of life*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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ВВЕДЕНИЕ

Проблема хирургического лечения пациентов с парастомальными грыжами является актуальной и до конца нерешенной [1,2]. Наиболее часто используемые виды операций: пластика местными тканями, перенос стомы и интраперитонеальная аллопластика. Распространенная ранее пластика местными тканями в настоящий момент не рекомендована к применению, т.к. частота рецидива параколостомических грыж после этой операции составляет от 46 до 100% [3,4]. Не менее часто используемая методика — транспозиция колостомы, имеет частоту рецидива до 76,2%, в связи с чем представляет лишь исторический интерес [5]. В настоящий момент операция Шугабейкер, описанная в 1985 году [6], считается «золотым стандартом» хирургического лечения параколостомических грыж. Эта методика основана на использовании сетчатых аллотрансплантатов, которые размещают интраперитонеально. Частота рецидива после этой операции составляет, в среднем, 15% [7,8]. Настоящее исследование посвящено разработке и внедрению в клиническую практику комбинированного хирургического метода лечения параколостомических грыж с использованием операции гибридной интраперитонеальной аллопластики.

ПАЦИЕНТЫ И МЕТОДЫ

В исследование было включено 60 пациентов с параколостомическими грыжами, оперированных в период с 2013 по 2019 гг. в Городской клинической больнице №24 г. Москвы. Проведено проспективное одноцентровое клиническое исследование эффективности гибридной интраперитонеальной аллопластики при параколостомических грыжах. Объем выборки предварительно не рассчитывали. Отбор пациентов для данного исследования проводили на основании приведенных в таблице 1 критериев включения и исключения.

Группа исследования и контрольная группа были сопоставимы по полу, возрасту, степеням параколостомической грыжи по классификации EHS, учитывающей размер дефекта в апоневрозе и наличие параколостомической грыжи [9,10], в зависимости от заболевания, по поводу которого больному была выведена постоянная кишечная стома. В таблице 2 представлено распределение больных группы исследования и группы сравнения по инициальным характеристикам [11].

Пациенты, включенные в исследование, были распределены на две группы. Контрольную группу составили 30 пациентов с параколостомической грыжей, которым выполнена классическая операция Шугабейкера: ненатяжная герниопластика с установкой сетчатого аллотрансплантата интраперитонеально вокруг стомированной кишки, без ушивания грыжевого дефекта [6].

В основную группу вошли 30 больных, которым была выполнена операция Шугабейкера с ушиванием грыжевых ворот («гибридная интраперитонеальная аллопластика»). При этом производят первоначальное ушивание грыжевого дефекта брюшной стенки отдельными узловыми швами под диаметр стомированной кишки. Затем линию шва и переднюю брюшную стенку укрепляют композитным аллотрасплантатом вокруг стомированной кишки, из которого

Таблица 1. *Критерии включения и исключения пациентов*
Table 1. *Criteria of inclusion ana exclusion of patients*

Критерии включения:	Критерии исключения:
Наличие параколостомической грыжи, обуславливающей снижение качества жизни	Невозможность выполнить КТ с внутривенным контрастированием
Наличие параколостомической грыжи, осложненной периодическими эпизодами ущемления и кишечной непроходимости	риск IV–V по шкале MHOAP [9], степень риска IV по индексу Ли [10], ХОБЛ с ОФВ1/ФЖЕЛ < 0,70
Подписанное информированное согласие	Неспособность ознакомиться и подписать согласие для участия в исследовании
Комплаентность пациента	Прогрессирование и генерализация опухолевого процесса
Активное желание пациента следовать рекомендациям, полученным от врача	Возможность выполнения операции восстановления непрерывности кишечника

Таблица 2. *Инициальные характеристики пациентов, включенных в исследование*
Table 2. *Initial charecteristics of patients, included in the study*

Параметр	Общее число пациентов (*n* = 60)	Основная группа (*n* = 30)	Группа сравнения (*n* = 30)	*p*	Критерий
Пол					
– Мужской	21 (35%)	10 (33%)	11 (37%)	0,787	χ^2
– Женский	39 (65%)	20 (67%)	19 (63%)		
Медиана возраста, лет	65,5 (61,75; 72.0)	66,5 (62,25; 72,0)	65,0 (61,25; 71,75)	0,246	Манна–Уитни
Степень грыжи					
– III	35 (58%)	20 (67%)	15 (50%)	0,191	χ^2
– IV	25 (42%)	10 (33%)	15 (50%)		
Заболевание					
– Рак нижнеампулярного отдела прямой кишки	15 (25%)	7 (23%)	8 (27%)	0,763	χ^2
– Рак анального канала	42 (70%)	22 (73%)	20 (67%)		
– Осложненное течение дивертикулярной болезни	1 (2%)	0 (0%)	1 (3%)		
– Травма заднего прохода	2 (3%)	1 (3%)	1 (3%)		
Хирургический анамнез					
– Брюшно-анальная резекция прямой кишки	18 (30%)	7 (23%)	11 (37%)	0,394	χ^2
– Колостомия	3 (5%)	1 (3%)	2 (7%)		
– Брюшно-промежностная экстирпация прямой кишки	39 (65%)	22 (73%)	17 (57%)		

формируют «чехол». Протез фиксируют при помощи герниостеплера к париетальной брюшине с наложением фиксирующих швов [11,12]. Этапы операции продемонстрированы на рисунках 1,2,3.

По своему характеру операция по поводу параколостомической грыжи является условно контаминированной из-за близости к операционному полю кишечной стомы. Для снижения степени бактериальной контаминации использовалась специальная система, изначально разработанная для лечения парапроктитов и для ведения пациентов с псевдомембранозным колитом — Stool-management-system компании DigniShield®. Она представляет собой полую трубку с раздуваемой манжетой на конце. В случае применения у пациентов со стомой конец системы с манжетой вводили в кишечную стому и при помощи специального проводника манжету раздували воздухом, чтобы герметично фиксировать её в просвете кишки. Таким образом, это позволяет добиться отсутствия сообщения просвета кишки с операционным полем, а также создает оптимальное контурирование стомированной кишки со стороны брюшной полости, что на этапе фиксации при помощи герниостеплера сетчатого аллотрансплантата к передней брюшной стенки обеспечивает безопасность и снижает риск интраоперационной травмы стомированной кишки скрепкой

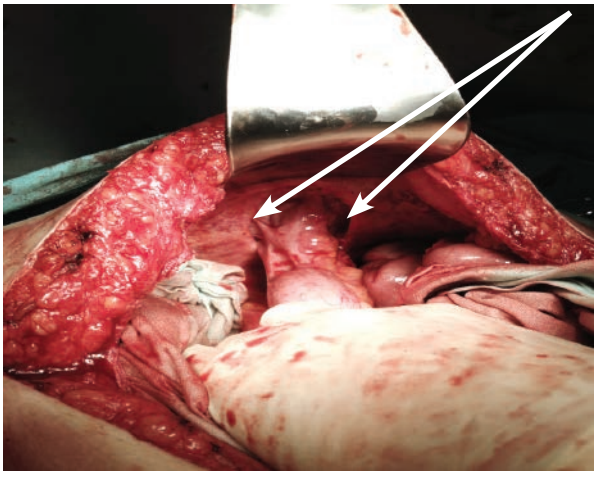

Рисунок 1. *Стомированная кишка с грыжевыми воротами. Дефект апоневроза проиллюстрирован стрелками*
Figure 1. *Stomied colon with hernia gate. Defect in aponeurosis is illustrated by arrows*

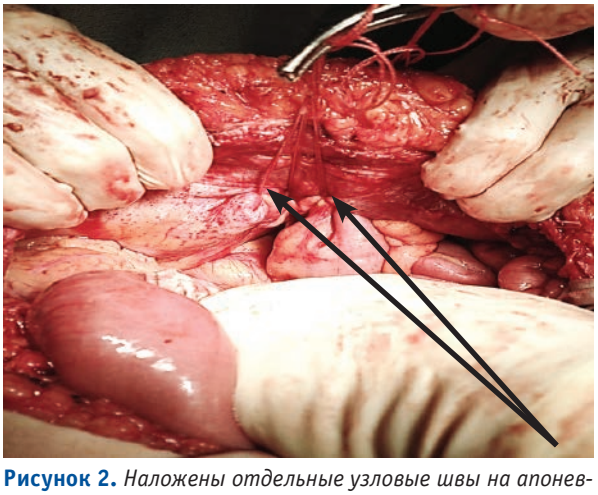

Рисунок 2. *Наложены отдельные узловые швы на апоневроз*
Figure 2. *Separate nodal sutures are laid on aponeurosis*

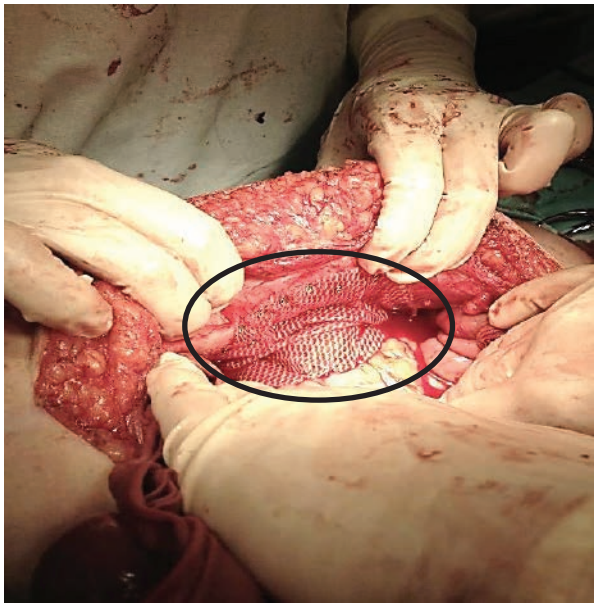

Рисунок 3. *Фиксация композитного аллотрансплантата при помощи герниостеплера*
Figure 3. *Fixation of composite allotransplant by means of herniostepler*

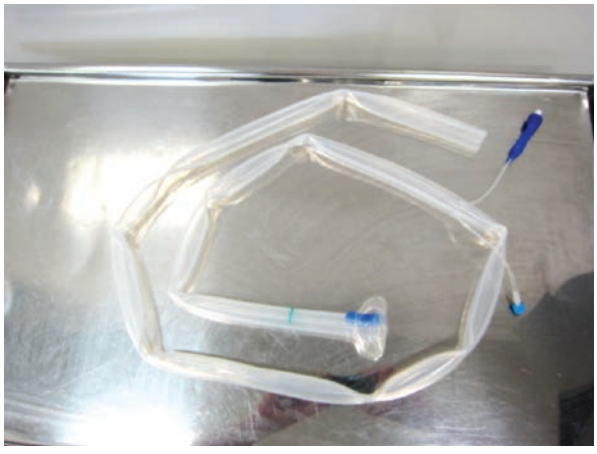

Рисунок 4. *Система Stool-management*
Figure 4. *Stool-management-system*

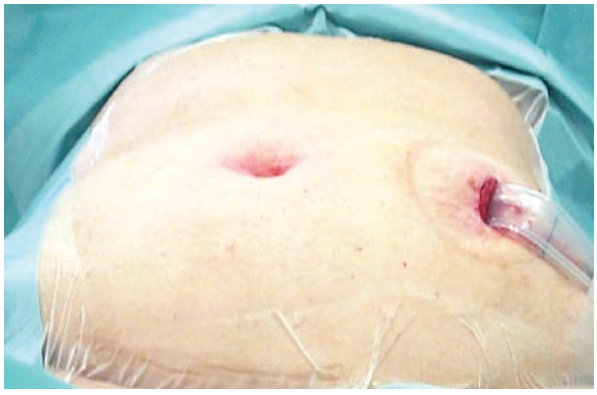

Рисунок 5. *Система Stool-management, установленная в стомированную кишку*
Figure 5. *Stool-management-system, inserted in colostomy*

герниостеплера. Использование Stool-management-system продемонстрировано на рисунках 4 и 5.

Для профилактики спаечного процесса с образованием кишечных свищей для интраперитонеальной аллопластики параколостомических грыж необходимо использовать аллотрансплантаты с различными свойствами поверхностей. При этом наружная поверхность должна обладать хорошими адгезивными свойствами для надежной фиксации, а внутренняя — обладать антиадгезивными свойствами [13]. Нами использовалась двухслойная композитная сетка фирмы Covidien тип parietex compositepco (представлена на рисунке 3), состоящая из противоспаечной мембраны (состав: коллаген, жирные спирты) и объемной сетки из монофиламентного полипропилена. Сплошная гидрофильная коллагеновая пленка защищает органы от контакта с сеткой. Края пленки выступают на 5 мм, закрывая край сетки. Коллагеновая пленка не теряет противоспаечных свойств от контакта с кровью. Пленка рассасывается за 20 дней. К моменту рассасывания брюшина покрывает сетку. Противоспаечная мембрана предупреждает развитие спаек между органами и сеткой. Полипропиленовая объемная сетка, с другой стороны, обеспечивает быстрое и качественное прорастание и максимальную устойчивость к инфицированию. С целью более надежной фиксации сетчатого аллотранплантата и технической простоты и быстроты исполнения оптимально использовать для фиксации аллотрансплантата герниостеплер Covidien Absorba-Tack с рассасывающимися скрепками. Срок рассасывания скрепок составляет 15 месяцев, что обеспечивает надежную фиксацию сетчатого аллотрансплантата на время его биоинтеграции в ткани. В дальнейшем отсутствие инородного материала способствует профилактике хронического воспалительного процесса и хронического болевого синдрома, который наблюдается при использовании для аллопластики герниостеплера с нерассасывающимися скрепками. Герниостеплер Covidien Absorba-Tack представлен на рисунке 6.

Для оценки качества жизни пациентов перед операцией, а также через год и через 2 года после операции в работе был использован опросник EuroQoL (EQ-5D-5L) [14]. В первой части опросника пациенту необходимо оценить своё состояние по пяти пунктам: подвижность, самообслуживание, активность в повседневной жизни, боль и дискомфорт, тревога и депрессия [14–16]. Вторая часть опросника представляет собой визуально-аналоговую шкалу (ВАШ), позволяющая пациенту наглядно оценить общее состояние здоровья в процентах от 0 до 100. EQ-5D-5L был модифицирован нами по отношению к пациентам с ПГ таким образом, чтобы анкетируемый четко понимал смысловую нагрузку вопросов, относящихся

к повседневной жизни и эмоциональной оценке происходящего только на основании влияния на вышеперечисленные аспекты именно осложненной кишечной стомы. Данный опросник оказался эффективным и удобным в использовании для пациентов, которые в своем большинстве являются людьми старшей возрастной группы, часто испытывающие затруднения при заполнении более объемных анкет [17]. Всем пациентам проводилось клиническое обследование, включающее оценку размеров грыжевого выпячивания в положении стоя и лёжа, определение «симптома кашлевого толчка», а также возможности самостоятельного вправления грыжи в брюшную полость и при ручном пособии. Осмотр пациента в обязательном порядке включал бимануальное обследование стомы. При этом определяли ширину просвета стомы на уровне кожи и апоневроза, что позволяло исключить стеноз и определить размеры дефекта в апоневрозе. В качестве метода инструментальной диагностики ПГ была выбрана методика КТ органов брюшной полости с внутривенным контрастированием, при этом подтверждали диагноз ПГ; оценивали характер грыжевого содержимого и размеры грыжевых ворот; проводили дифференциальную диагностику ПГ с подкожным пролапсом колостомы (ложная ПГ); исключали прогрессирование и генерализацию опухолевого процесса; оценивали состояние тканей передней брюшной стенки; подбирали размеры аллотрансплантата, необходимого для укрытия дефекта [18], а также применяли КТ для исключения рецидива ПГ после операции [12].

РЕЗУЛЬТАТЫ

Был выполнен сравнительный анализ результатов лечения больных обеих групп путем оценки частоты рецидивов параколостомических грыж на основании КТ органов брюшной полости с внутривенным контрастированием и оценки изменения качества жизни пациентов при помощи модифицированного опросника EUROQOL 5D-5L в исследуемых группах.

По данным КТ органов брюшной полости с внутривенным контрастированием, через 2 года после операции в основной группе выявлено 3 (10%) случая рецидива грыжи. В контрольной группе у 13 (43%) пациентов был выявлен рецидив (p = 0,01; χ^2 с поправкой Йейтса) [14].

При оценке качества жизни, медиана взвешенного коэффициента (ВК) перед операцией статистически значимо не различалась в исследуемых группах и составила в основной группе 0,56 (0,42; 0,69), а в контрольной группе — 0,46 (0,29; 0;68) (p = 0,113). Медианы значения по ВАШ до операции также статистически значимо не различалась: в основной группе — 52,5 (41,25; 67,5), в контрольной группе — 47,5 (40,0; 60,0) (p = 0,156).

Через год после операции, как в основной группе, так и в контрольной произошли статистически значимые изменения и по ВК (p < 0,001*), и по ВАШ (p < 0,001*). Однако изменения в группах различались между собой: медианные значения ВК и ВАШ стали статистически значимо выше в основной группе, чем в контрольной (ВК: в группе исследования — 0,92 (0,81; 1,0), в контрольной группе — 0,89 (0,5; 1,0), p = 0,046*; ВАШ: в группе исследования — 95,0 (86,25; 100,0), в контрольной группе — 85,0 (62,5; 100,0), p = 0,021*). Через два года после операции медианное значение взвешенного коэффициента (ВК) сохранило статистически значимое превосходство в группе исследования (в группе исследования — 1,0 (0,93; 1,0), в контрольной группе — 0,8 (0,46; 1,0), p = 0,048*). Однако стоит отметить, что в исследуемой группе с первого по второй год после операции значение ВК достоверно выросло с 0,92 (0,81; 1,0) до 1,0 (0,93; 1,0) (p = 0,033*), а в контрольной группе достоверно снизилось с 0,89 (0,5; 1,0) до 0,8 (0,46; 1,0) (p = 0,028*). На второй год после операции в группе исследования значения очень консолидированы около 1 ((0.93, 1.0)), а в контрольной группе значения были значительно разбросаны от 0,46 до 1,0, что говорит о неустойчивом эффекте по школе ВК спустя два года после операции. Значения ВАШ через два года после операции в группе исследования также было выше, чем в контрольной группе, однако без статистически достоверных различий (в группе исследования — 95,0 (85,0; 100,0), в контрольной группе — 85,0 (50,0; 95,0), p = 0,054). При этом в группе исследования значение ВАШ стабилизировалось ко второму году после операции на значении 95 и не показало статистически

Рисунок 6. *Герниостеплер Absorba-Tack*
Figure 6. *Herniostepler Absorba-Tack*

значимых изменений. В контрольной группе медианное значение осталось на прежнем уровне — 85, но межквартильный отрезок расширился и сместился в сторону более низких значений, что отразилось на появлении достоверных различия в значении ВАШ от первого ко второму году после операции с 85,0 (62,5; 100,0) до 95,0 (50,0; 95,0) ($p = 0,004$*). Анализ разности взвешенных коэффициентов через год после операции и до операции (эффект 1), и через 2 года после и через 1 год после операции (эффект 2) продемонстрировал статистически значимую эффективность проведенного лечения (Рис. 4,5). В исследуемой и контрольной группе по результатам как через 1 год после операции (эффект 1; $p = 0,004$*), так и через 2 года после операции (эффект 1; $p = 0,028$*).

ОБСУЖДЕНИЕ

На основании анализа результатов хирургического лечения 60 пациентов с параколостомическими грыжами доказана высокая эффективность гибридной интраперитонеальной аллопластики ПГ по сравнению с классической операцией Sugabecker. Установлены статистически значимые различия в количестве рецидивов заболевания, подтвержденных данными мультиспиральной КТ органов брюшной полости с внутривенным контрастированием, а также статистически значимое улучшение качества жизни пациентов группы исследования. Основным фактором достоверно более высокого уровня жизни при этом было отсутствие рецидива

ЗАКЛЮЧЕНИЕ

Ушивание грыжевых ворот при пластике по Шугабейкеру при парастомальной грыже существенно снижает частоту рецидивов, что улучшает качество жизни в отдаленном послеоперационном периоде.

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Лечение комбинированного геморроя 2–3 стадии методом трансмукозной лазерной абляции

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РЕЗЮМЕ *АКТУАЛЬНОСТЬ: лазерное лечение комбинированного геморроя является предметом дискуссии, поскольку удаление наружного компонента заболевания может привести к усилению болевого синдрома и невыполнимости его устранения в амбулаторных условиях.*
ЦЕЛЬ ИССЛЕДОВАНИЯ: изучить результаты лечения больных с хроническим комбинированным геморроем II–III стадии методом вапоризации внутренних узлов с одновременным устранением наружных узлов и геморроидальных бахромок.
ПАЦИЕНТЫ И МЕТОДЫ: амбулаторно, одним хирургом выполнено 136 трансмукозных лазерных вапоризаций внутренних узлов с иссечением после деструкции наружных геморроидальных узлов — группа исследования и 90 изолированных лазерных деструкций внутренних узлов, группа контроля. Процедура выполнялась под местной анестезией на аппарате Лахта-Милон с длиной волны 1,47 мкм мощностью 8,0 ватт. У пациентов определялись продолжительность операции, интенсивность болевого синдрома. В послеоперационном периоде — его продолжительность, наличие осложнений и в отдаленном периоде в течение 18 месяцев — возникновение рецидивов болезни.
РЕЗУЛЬТАТЫ: в группе исследования продолжительность вмешательства была 15,0 мин., интенсивность боли во время операции пациенты определили в 2,5 балла, продолжительность ее в послеоперационном периоде была 6 суток. Послеоперационные кровотечения возникли у 4 (2,9%), рецидив заболевания в течение года диагностирован у 3 (4,8%) больных. У пациентов контрольной группы медиана продолжительности вмешательства составила 10 (10;15) мин. Интенсивность болевых ощущений во время операции оценена пациентами в 2,5 (2,0; 3,0) балла. Продолжительность болевых ощущений после операции была 5 дней. У 8 (8,9%) больных послеоперационный период осложнился кровотечением, рецидив болезни возник у 1 (1,1%) больной.
ЗАКЛЮЧЕНИЕ: интенсивность болевого синдрома при изолированных и комбинированных вмешательствах была расценена пациентами одинаково по 2,5 балла, что можно объяснить малоинвазивностью обоих этапов операции, адекватностью местной анестезии. Получены доказательства хорошей переносимости лазерной вапоризации, что является мотивацией более широкого ее применения в лечения больных с хроническим комбинированным геморроем в амбулаторных условиях.

КЛЮЧЕВЫЕ СЛОВА: *Комбинированный геморрой, трансмукозная лазерная термоабляция, болевой синдром, амбулаторное лечение*

КОНФЛИКТ ИНТЕРЕСОВ: *Авторы заявляют об отсутствии конфликта интересов*

ДЛЯ ЦИТИРОВАНИЯ: Матвеев И.А., Гиберт Б.К., Матвеев А.И., Бородин Н.А., Морозова Л.А., Поварнин Н.Н. Лечение комбинированного геморроя 2–3 стадии методом трансмукозной лазерной абляции. *Колопроктология.* 2023; т. 22, № 2, с. 86–91. https://doi.org/10.33878/2073-7556-2023-22-2-86-91

Transmucosal laser ablation for combined hemorrhoids of 2–3 stages

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ABSTRACT *AIM: to assess of the results of transmucosal laser ablation (TMLA) for internal piles and simultaneous elimination of external piles in patients with combined hemorrhoids of 2–3 stages.*
PATIENTS AND METHODS: the retrospective study included 226 patients. TMLA of internal nodes with excision or destruction of external piles was performed in 136 patients (the main group) and 90 laser destructions of internal nodes only consisted the control group. The procedure was performed under local anesthesia on a Lakhta-Milon device with a wavelength of 1.47 μm with a power of 8.0 W. The operation time, the pain syndrome, its duration after surgery, the complication rate and the recurrence rate up to 18 months were estimated.
RESULTS: the operation time in the main group was 15.0 minutes (10 min in control group; p = 0.001), the pain intensity during procedure was determined by patients at 2.5 points of VAS (2.5 — in controls; p = 0.81). Postoperative pain was detected up to 6 days (5 days in controls; p = 0.44). Postoperative bleeding occurred in 4 (2.9%) (8 — in controls; p = 0.051), recurrence occurred in 3 (4.8%) patients after 12 months (1 patient in controls; p = 0.5).
CONCLUSION: TMLA has a good tolerability and good late results, which is the motivation for wide implementation for patients with hemorrhoids in outpatient basis.

KEYWORDS: *Combined hemorrhoids, submucous laser thermal ablation, pain syndrome, outpatient treatment*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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АКТУАЛЬНОСТЬ

Трансмукозная лазерная термоабляция (ТЛТ) получила широкое распространение в лечении хронического геморроя. Она чаще применяется изолированно при внутреннем геморрое и реже — при комбинированных формах с иссечением наружных узлов и перианальных бахромок или их лазерной деструкцией [1–5]. Это связано с тем, что при лазерном лечении комбинированного геморроя после деструкции внутренних узлов устраняются основные причины, приведшие пациента в операционную. В тоже время остаются наружные геморроидальные узлы, которые могут в последующем представлять для больного определенные проблемы, связанные с возможностью их тромбоза, а перианальные бахромки приносят не только эстетические неудобства, они могут травмироваться, воспаляться, а у пациента остается чувство незавершенности лечения [2,5].

Наружные геморроидальные узлы и перианальные кожные складки у больных с хроническим геморроем встречаются часто. Так, по данным Ломоносова А.Л. и соавт., среди пациентов с хроническим внутренним геморроем 1–2 степени наружные геморроидальные узлы были средней величины у 46,8% и большими — у 15,9%, перианальные бахромки, соответственно, у 57,3% и 15,9% больных [6]. Геморроидальные бахромки могут образовываться и после лазерной деструкции наружных геморроидальных узлов, причиной их появления является формирующийся избыток перианальной кожи, остающийся после лазерной деструкции наружных геморроидальных узлов [2,5]. У 9–12% перенесших такие вмешательства в последующем проводят иссечение перианальных бахромок [5]. На этот же недостаток лазерной деструкции указывает Черепенин М.Ю. и соавт.: после лазерной коагуляции у 18 (14,5%) больных имелись остаточные анальные бахромки, не доставляющие какого-либо дискомфорта, у 5 (4,0%) пациентов потребовалось проведение иссечения гипертрофированных бахромок перианальной области [2].

Необходимость устранения наружных улов и перианальных бахромок при лазерном лечении комбинированного геморроя 2–3 степени является предметом дискуссий, поскольку они расположены ниже зубчатой линии, в зоне болевой чувствительности, а это может вызвать интенсивные боли и поставить под сомнение возможность выполнения операции в амбулаторных условиях под местной анестезией [3,4].

ЦЕЛЬ

Изучить результаты лечения больных с хроническим комбинированным геморроем II–III стадии методом вапоризации внутренних узлов с одновременным устранением наружных узлов и геморроидальных бахромок.

ПАЦИЕНТЫ И МЕТОДЫ

В 2018–2021 гг. в амбулаторной клинике одним хирургом выполнено 378 лазерных вапоризаций геморроидальных узлов 2–3 стадии. Из всей когорты больных отобрана группа исследования — 136 пациентов с комбинированным геморроем, которым выполнены вапоризация внутренних узлов и устранение наружных узлов или перианальных бахромок. Геморрой 2 стадии был у 109 (80,1%) и у 27 (19,9%) — 3 стадии. Медиана возраста пациентов в этой группе была 44,0 года, мужчин — 88 (64,7%), женщин — 48 (35,3%).

Контрольная группа сформирована из 90 пациентов, пролеченных только лазерной вапоризацией внутренних узлов. Вторая стадия заболевания была у 86 (95,6%), 3 стадия — у 4 (4,4%) пациентов. Возраст больных варьировал от 20 до 84 лет Me = 36,0 (31,75; 50,0); (40,56 ± 12,98), мужчин было 51 (56,7%), женщин — 39 (43,3%).

Сравнение пациентов в изучаемых группах показало, что возрастные и гендерные различия были не значимыми. В группе пациентов с комбинированным геморроем преобладали пациенты с 3 стадией заболевания.

Показаниями к оперативному лечению пациентов обеих групп являлись: боль, рецидивные кровотечения, выпадение узлов. Процедура выполнялась на аппарате Лахта-Милон с длиной волны 1,47 мкм мощностью 8,0 ватт. После трансмукозной лазерной термоабляции внутренних узлов проводилось устранение наружных узлов и бахромок лазерной деструкцией или иссечением их скальпелем. Вне зависимости от способа иссечения, с целью гемостаза дно раны обрабатывалось лазером. В результате ткани в равной степени были подвержены воздействию лазера, и особенностей в их заживлении не наблюдалось.

Операция выполнялась под местной анестезией. 2% раствор лидокаина в объеме 4 мл разводился в 20 мл физиологического раствора и вводился перианально на 3, 7 и 9 часах условного циферблата, кроме того анестетик вводился под наружные геморроидальные узлы перед вапоризацией и последующим их иссечением. Общее количество введенного раствора варьировалось от 20,0 до 40,0 мл в зависимости от выраженности болевой чувствительности пациента и размеров узлов. Вапоризация внутренних узлов выполнялась трансмукозно: после введения аноскопа визуализировался геморроидальный узел, лазерный проводник с проколом слизистой над геморроидальным узлом вводился в проксимальную часть узла, и выполнялась термоабляция в проекции сосудистой ножки в 2–4 точках со временем воздействия от 1 до 4 секунд. Ножка узла не перевязывалась. По мере выведения аноскопа обрабатывалась основная часть геморроидального узла, критерием эффективности являлось изменение цвета и редукция тканей. Воздействие прекращалось в 0,5 см проксимальнее зубчатой линии. Обращали внимание на кратковременность импульса излучения, для предотвращения некроза слизистой, который может привести к усилению болевых ощущений и возможности эрозивных кровотечений в послеоперационном периоде. Для лучшего манипулирования световодом, сконструирована ручка-держатель оптоволокна (Патент на полезную модель 213083 U1, 23.08.2022. Заявка № 2022115318 от 07.06.2022). Она позволяет хирургу прецизионно управлять лазерным проводником, оперативно изменять расположение световода и выполнять более эффективно вапоризацию геморроидальной ткани.

После выполнения ТЛТ внутренних узлов устранение наружных геморроидальных узлов проводилось следующим способом: выполнялась частичная вапоризация узла, после чего уменьшенный в размерах узел иссекался лазерным торцевым проводником диаметром 0,500 мкм, следя за тем, чтобы рана не переходила в анальный канал, и полностью располагалась перианально, в противном случае провоцировался болевой синдром и длительное заживление раны. Методика иссечения узла после его вапоризации позволяет экономно иссечь патологически измененные ткани, при этом остается узкая, быстро заживающая рана.

У пациентов определялись продолжительность операции, по визуально-аналоговой шкале (ВАШ) интенсивность болевого синдрома после операции, его длительность, наличие послеоперационных осложнений. Отдаленные результаты изучались через полтора года. Послеоперационные осложнения и рецидив заболевания расценивались как неудовлетворительный результат лечения. Для оценки тяжести осложнений использовалась классификации Clavien-Dindo [7].

Дизайн исследования: ретроспективное, одноцентровое (все вмешательства выполнялись одним хирургом).

Статистический анализ

Все полученные данные были собраны в одну базу в программе Microsoft® Excel® 2019 MSO. Статистический и графический анализ был выполнен программах Excel и IBM SPSS Statistics 26.

Полученные количественные результаты были проверены на нормальность распределения, для этого использовали критерий Шапиро-Уилка. При уровне значимости критерия $p < 0,05$ считали выборку не подчиняющейся закону нормального распределения,

Таблица 1. *Характеристика изолированных и комбинированных операций при трансмукозной лазерной термоабляции хронического геморроя 2–3 стадии*
Table 1. *Characteristics of isolated and combined operations for transmucous laser thermal ablation of chronic hemorrhoids of the 2nd-3rd stage*

Критерии	изолированные вапоризации (*n* = 90)	комбинированные операции (*n* = 136)	*p*
продолжительность операции (мин.)	10 (10;15)	15 (15:20)	0,001
интенсивность болевого синдрома во время операции (баллы по ВАШ)	2,5 (2,0; 3,0)	2,5 (2,0;3,0)	0,81
продолжительность боли в послеоперационном периоде (сутки)	5 (4;7)	6 (4;7)	0,44
послеоперационные кровотечения N (%)	8 (8,9%)	4 (2,9%)	0,051

и данные представляли в виде медианы 25% и 75% квартилей Me [Q1;Q3]. Для сравнения независимых групп применен непараметрический анализ критерий Манна-Уитни (Mann-Whitney U-test). Для проверки гипотез о наличии либо отсутствии различий между двумя независимыми группами использовали критерий χ^2 Пирсона. При этом разница между группами считалась достоверной при $p \leqslant 0,05$, где p — уровень статистической значимости.

РЕЗУЛЬТАТЫ

В группе исследования (n = 136) продолжительность вмешательства была 15,0 (15:20) мин., минимальная — 10 мин., максимальная — 25 мин. Интенсивность боли во время операции пациенты определили в 2,5 (2;3) балла, от 1 балла до 4. Длительность его в послеоперационном периоде была 6 (4;7) суток, минимальное значение 2 суток, максимальное — 12. Послеоперационные кровотечения возникли у 4 (2,9%), рецидив заболевания в течение 1,5 лет диагностирован у 3 (4,8%) больных.

У пациентов контрольной группы (n = 90) медиана продолжительности вмешательства составила 10 (10;15) мин. Минимальная длительность была 5 мин., максимальная — 25 мин. Интенсивность болевых ощущений во время операции оценена пациентами в 2,5 (2,0; 3,0) балла. Минимальное значение составило 1 балл, максимальное — 4 балла. Продолжительность болевых ощущений после операции была 5 суток, минимальное значение — 2, максимальное — 12 суток. У 8 (8,9%) больных послеоперационный период осложнился кровотечением, 2 (2,2%) из них с 3В стадией тяжести потребовалась госпитализация и операция (Табл. 1).

Как видно из таблицы статистически значимые различия между изучаемыми группами больных при лазерном лечении внутреннего и комбинированного геморроя 2–3 стадии были по времени его выполнения — комбинированные операции были в 1,5 раза продолжительнее изолированных вапоризаций.

После операции пациентам обеих групп назначали флеботропные препараты, рекомендовали диету с увеличенным содержанием клетчатки, прием осмотических слабительных. Отличия местного лечения пациентов с иссеченными наружными узлами от больных с изолированной вапоризацией внутренних узлов заключались в перевязках ран с мазью Левомеколь до их заживления с обязательными гигиеническими процедурами со слабым раствором антисептика после дефекации и перед перевязкой. Эпителизация ран в первые 4 недели произошла у 123 (90,4%), в сроки свыше 4-х, но меньше 8 недель — у 12 (8,8%) пациентов и больше 8 недель лечение раны проводилось у 1 (0,7%) пациентки.

Отдаленные результаты изучены у 63 человек в течение 18 месяцев после оперативного лечения комбинированного геморроя. Рецидив наружного геморроидального узла был у 3 (4,8%), в контрольной группе — у 1 (0,01%, p = 0,5). Полиповидных образований кожи на месте наружных узлов после их вапоризации и иссечения не наблюдалось.

ОБСУЖДЕНИЕ

Бесспорным преимуществом лазерной деструкции внутренних геморроидальных узлов перед другими способами лечения является низкий уровень болевого синдрома во время операции и в послеоперационном периоде, что является одной из главных причин широкой распространенности этого метода лечения в проктологии [1,2,4,5,8]. Устранение наружного геморроидального узла выполняется в зоне повышенной чувствительности и может вызвать, по мнению ряда хирургов, не только увеличение продолжительности операции, но и усиление болевого синдрома, как во время выполнения операции, так и в послеоперационном периоде, увеличение частоты послеоперационных осложнений, что, в определенной степени, и является тормозом распространения лазерного лечения хронического комбинированного геморроя [3,4].

Операции при комбинированном заболевании, в сравнении с изолированным внутренним геморроем, продолжительнее по времени их исполнения, медиана, соответственно, была 15 и 10 мин., $p = 0,001$, что связано с дополнительным этапом устранения наружного компонента комбинированного геморроя. Сопоставление времени выполнения операций показало, что для устранения наружного узла необходимо было 5 мин., в структуре времени выполнения вмешательства этот этап составил 33,3% от всей продолжительности хирургического лечения комбинированного геморроя.

Интенсивность болевого синдрома по шкале ВАШ при изолированных и комбинированных вмешательствах была расценена пациентами одинаково по 2,5 балла, что можно объяснить малоинвазивностью основного и симультанного этапов операции, адекватностью местной анестезии. Повышенное число пациентов с 3 стадией болезни в группе исследования не повлияло на восприятие боли при хирургическом лечении комбинированного геморроя.

Интенсивность болевого синдрома во время операции при комбинированном и внутреннем геморрое в 2,5 балла по ВАШ соответствует результатам, полученным другими хирургами, и свидетельствует о хорошей переносимости лазерных методик в лечении обеих форм заболевания [1,2,4].

Послеоперационные кровотечения возникли у 8 (8,9%) больных при изолированной лазерной вапоризации, что более чем двукратно превышает этот показатель при комбинированном лечении геморроя — 4 (2,9%), $p = 0,051$.

Полученные различия можно объяснить тем, что хирург начал осваивать лазерное лечение хронического геморроя с деструкции только внутренних узлов, как более легкого и менее продолжительного вмешательства, и только по мере приобретения опыта стал выполнять операции при комбинированном геморрое с устранением наружных узлов. Проведенные ранее в клинике исследования показали, что при внедрении в практику лазерной коагуляции, в том числе с устранением наружного компонента геморроя и сопутствующей патологии анального канала, частота негативных результатов (послеоперационные осложнения и рецидивы заболевания) у оперированных в период накопления опыта, была достоверно выше. Это позволяет сделать вывод о связи возникновения кровотечений с периодом обучения, который сопровождается наиболее высоким уровнем осложнений, а не с особенностями лазерного лечения внутреннего и комбинированного геморроя [8].

Заживление ран перианальной области у 123 (97,6%) человек в первые 4 недели послеоперационного периода связаны со следующими факторами: рассечение тканей лазером благоприятно влияет на заживление ран за счет уменьшения воспалительных и ускорения репаративных процессов; раны располагались в хорошо кровоснабжаемой зоне в отсутствии воспалительных процессов; были неглубокими и имели щелевидную форму (длина преобладала над шириной) [1,2].

Таким образом, получены доказательства хорошей переносимости лазерной деструкции внутренних, а также вапоризации наружных геморроидальных узлов с их иссечением, что является мотивацией более широкого применения этого способа лечения больных с хроническим комбинированным геморроем 2–3 стадии в амбулаторных условиях под местной анестезией.

ЗАКЛЮЧЕНИЕ

Лазерная деструкция внутренних и иссечение наружных узлов после их вапоризации, несмотря на достоверно большую продолжительность вмешательства, по интенсивности и продолжительности болевого синдрома аналогична вапоризации изолированных внутренних геморроидальных узлов, что позволяет рекомендовать эту тактику при лечении хронического комбинированного геморроя 2–3 стадии в амбулаторных условиях.

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AI-based algorithm for clinical decision support system in colonoscopy

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ABSTRACT *AIM: to estimate the implementation of the original method that uses artificial intelligence (AI) to detect colorectal neoplasms.*
MATERIALS AND METHODS: we selected 1070 colonoscopy videos from our archive with 5 types of lesions: hyperplastic polyp, serrated adenoma, adenoma with low-grade dysplasia, adenoma with high-grade dysplasia and invasive cancer. Then 9838 informative frames were selected, including 6543 with neoplasms. Lesions were annotated to obtain data set that was finally used for training a convolution al neural network (YOLOv5).
RESULTS: the trained algorithm is able to detect neoplasms with an accuracy of 83.2% and a sensitivity of 77.2% on a test sample of the dataset. The most common algorithm errors were revealed and analyzed.
CONCLUSION: the obtained data set provided an AI-based algorithm that can detect colorectal neoplasms in the video stream of a colonoscopy recording. Further development of the technology probably will provide creation of a clinical decision support system in colonoscopy.

KEYWORDS: *colonoscopy, endoscopy, artificial intelligence, computer vision, machine learning, adenoma, cancer, neoplasm*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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INTRODUCTION

Colorectal cancer (CRC) is a socially significant oncological disease, occupying leading positions in the rate of detection and causes of death from neoplasms in different countries of the world. In the Russian Federation, more than 38 thousand deaths from this pathology are registered annually, and the number of newly detected cases of CRC exceeds 71 thousand [1]. CRC in the majority of cases passes the stage of benign neoplasm — adenoma. Large epidemiological studies have shown that timely endoscopic removal of adenomas reduces the risk of colorectal cancer by 90% [2]. In this regard, great importance is attached to screening colonoscopy, during which the rate of detection of adenomas (in English-language literature –adenoma detection rate, ADR) ranges from 30% to 64% [3–6]. At the same time,

various studies demonstrate a relatively high percentage of lost neoplasms. Thus, the rate of adenomas missed during colonoscopy, according to Hassan, C.'s meta-analysis, is 37.5% [4]. The omission of adenomas during colonoscopy depends on the size of the neoplasm — in the study by van Rijn, J.C., the rate of missed polyps was 2.1%, 13% and 26% for adenomas over 10 mm, 5–10 mm and less than 5 mm, respectively [5]. In addition, poor bowel cleansing, as well as the human factor, are considered possible reasons for skipping [6,7].

Thus, an increase in the information content of colonoscopy is expected to reduce morbidity and mortality from CRC due to the timely performance of endoscopic polypectomy.

One of the tools for solving this problem is artificial intelligence (AI) technology for processing and preliminary analysis of video colonoscopy data [8–11]. According to the papers, the use of automation of video processing of colonoscopy during screening colonoscopy will help to level the subjectivity of the endoscopist and increase diagnostic accuracy and sensitivity regarding the detection of adenomas and adenocarcinomas of the large intestine, as well as reduce the time of the study description [10]. This technology is not an independent diagnostic option, but is considered as a clinical decision support system (CDSS).

In the world literature, every year more and more attention is paid to the use of AI in colonoscopy. The data obtained inspire some optimism.

In the study by Luo, Y., et al. [11], based on a survey of 150 patients, it was shown that the AI system increases the rate of detection of polyps in real clinical conditions (38.7% vs. 34.0%, $p < 0.001$). At the same time, colonoscopy using an AI system significantly increases the detect ability of polyps smaller than 6 mm (91% vs. 69%, $p < 0.001$), but does not detect differences in relation to larger neoplasms.

Wallace, M.B., et al. [12] conducted a study with two consecutive colonoscopies — standard and using AI. The rate of missed adenomas was 32.4% and 15.5%, respectively. The average number of adenomas during repeated colonoscopy was determined less in the group in which AI was used in the first study, compared with the group in which AI was not used in the first study (0.33 ± 0.63 vs. 0.70 ± 0.97, $P < 0.001$). The rate of false false-negative results was 6.8% and 29.6% at the first colonoscopies with and without the use of AI, respectively (OR 0.17; 95% CI 0.05–0.67). Thus, AI provided approximately a twofold reduction in the rate of colorectal neoplasia skipping, reducing the perception errors of small and inconspicuous neoplasms.

In the study by Xu, H., et al. [13], in addition to ADR, the average number of adenomas per colonoscopy was estimated, the correlation of ADR with the experience of the endoscopist and the time of removal of the device during colonoscopy.3,059 patients were randomly assigned to a group for colonoscopy using the AI system (n = 1,519) and without it (n = 1,540).In the process of colonoscopy using AI, the Eagle-Eye polyp detection system was used, with real-time notification on the same monitor of the endoscopic system. The level of total ADR (39.9% vs. 32.4%; $p < 0.001$), ADR in experts (42.3% vs. 32.8%, $p < 0.001$) and non-specialist endoscopists (37.5% vs. 32.1%; $P = 0.023$) were significantly higher during colonoscopy using the AI system. The average withdrawal time of the device (8.3 minutes vs. 7.8 minutes; $P = 0.004$) was slightly longer in the AI group. It was concluded that in asymptomatic patients, colonoscopy using AI increased the overall ADR level, as well as the rate of detection of adenomas by both experts and less experienced specialists [13].

An increase in the detection of adenomas during colonoscopy has a significant economic effect. For example, Areia, M., et al. [14], based on modeling the use of machine vision technology in colonoscopy, concluded that this tool would reduce the number of colorectal cancer cases in the United States by 7,194 cases annually, and the number of deaths from this disease by 2,089 people. At the same time, the economic benefit from the implementation of AI in colonoscopy is estimated to be US$ 290 million annually due to the reduction of costs for the diagnosis and treatment of colorectal cancer and

other costs associated with the development of colorectal tumors.

The available Russian literature provides a single experience of using artificial intelligence technology in colonoscopy, while there is no data on the widespread use of the described approach in clinical practice [15,16].

Thus, the development and implementation of the domestic CDSS in colonoscopy based on AI is relevant from a scientific and practical point of view. Such study was started in the RNMRC of Coloproctology of the Health Ministry of Russia in 2022.

MATERIALS AND METHODS

The material of the study was an electronic archive of video recordings of colonoscopies performed at the RNMRC of Coloproctology of the Health Ministry of Russia. The studies included in the work were performed on the Pentax 7010 (Japan) and Olympus Exera-III (Japan) with high definition (HD) in the period from January 2021 to October 2022.

The design of the study is shown in Figure 1.

Video recordings of the studies, during which were detected colorectal tumors subsequently removed and pathomorphologically examined in accordance with the protocol in force at the Center, were selected for the work. Neoplasms belonging to one of the five types listed below were subjected to marking:

1) Hyperplastic polyp
2) Serrated neoplasm
3) Adenoma with low-grade dysplasia
4) Adenoma with high-grade dysplasia
5) Invasive cancer

The allocation of these classes is due to the rate of occurrence and their clinical significance, which is determined by different approaches to the treatment of such neoplasms. At the same time, cases were excluded from further analysis when the colorectal neoplasm did not correspond to the above classes by histological structure or was not confirmed. Video recordings of colonoscopy of patients

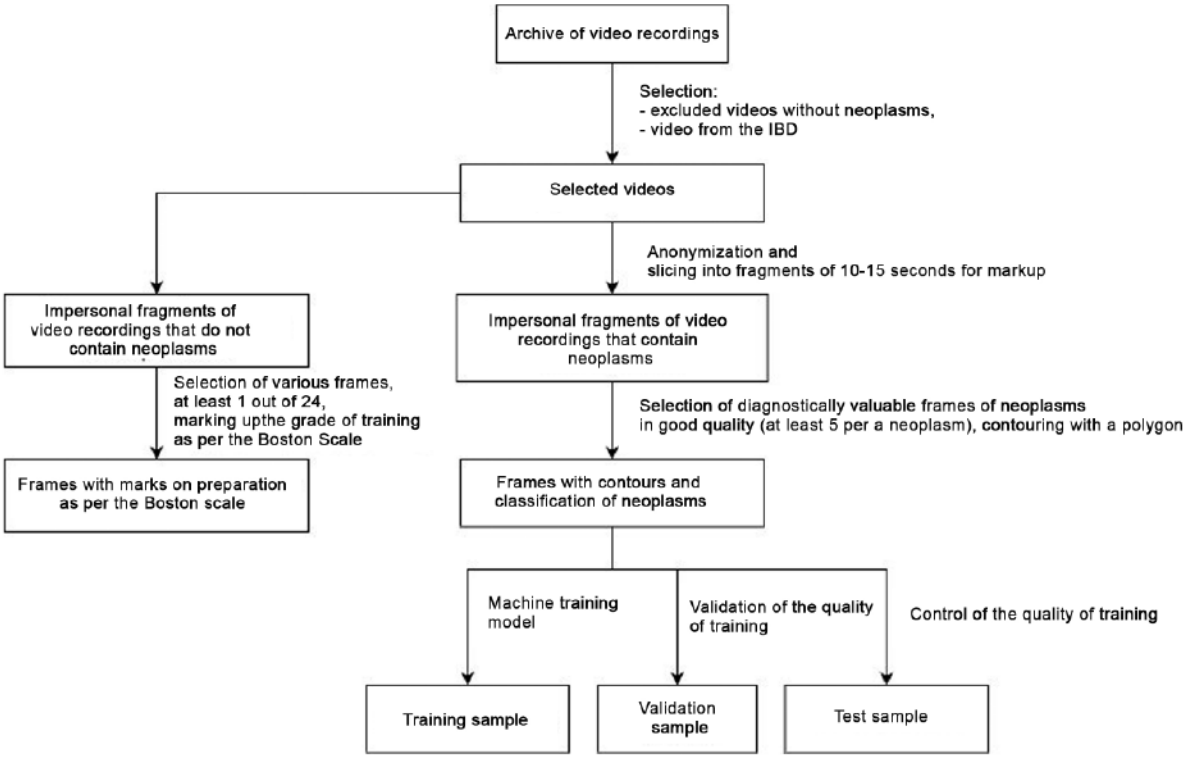

Figure 1. *Flow-chart of preliminary work for the creation of CDSS in colonoscopy*

Table 1. *Marking main characteristics*

№	Class	Label Name	Markup Color
Main classes (slices on the frame)			
1	Hyperplastic polyp	Hyperplastic polyp	
2	Serrated neoplasm	Serrated neoplasm	
3	Adenoma with low-grade_dysplasia	Adenoma with low-grade_dysplasia	
4	Adenoma with high-grade_dysplasia/ early_cancer	Adenoma with high-grade_dysplasia/ early_cancer	
5	Carcinoma_cancer	Carcinoma_cancer	
Additional classes			
6	Clean_frame	Clean_frame	

suffering from inflammatory bowel diseases were also excluded.

Thus, for further study, 1070 videos of colonoscopy were selected, corresponding to the selected criteria, with a total volume of 46 gigabytes.

Video colonoscopy recordings were characterized by a rate of 29, 30 or 50 Hz. The frame height was at least 1,080 pixels — the source videos are overwhelmingly presented in a definition of 1300x1080 (66.4%) or 1920x1080 (27.3%).

The frames that meet the quality criteria were selected from these video fragments:

- clear;
- without dimming;
- without seriousblurring of neoplasm;
- out of the moment of switching between modes (white light/NBI);
- out of the moment of irrigation.

For the subsequent marking of the identified neoplasm, at least 5 frames of good quality were selected from different angles for each study mode (white light / NBI), while the time interval between frames was at least 1 second. Also, frames that did not contain neoplasms were randomly selected in a ratio of 1:2 as a norm control. These frames were marked with video quality and a score of bowel cleansing according to the Boston scale.

In total, 9838 frames were selected in accordance with the above approach, which served as the material for the final data set.

All the data have been anonymized (depersonalized) in order to ensure the protection of personal data by deleting the frame area containing information about the patient.

The marking of the selected and depersonalized data was performed by 12 endoscopists at the Center with 5–24 years of independent practical work experience. The 3 most experienced specialists with over-15-year experience validated the markup and were involved for a “second opinion” in difficult cases.

Each study was marked up by one endoscopist. Markup validation was carried out selectively by a specialist of higher qualification, and in 20% of cases cross-validation was performed by a second expert.

The markup was carried out in accordance with the following strategy. For each neoplasm, the endoscopist selected at least 5 diagnostically most informative frames on the video fragment. Then, with the help of a graphic editor, he outlined the neoplasm with a polygonal line on each of the selected frames and assigned a class label in accordance with the table below (Table 1). In all the cases, the conclusion of the pathomorphology removed specimen was used as a method of verification and final

Table 2. *Interpretation of the algorithm results on the test sample*

Algorithm output	Opinion of 2 experts	The result of the work
The neoplasm isolated	The neoplasm is present in the frame	True positive
There is no isolation	There is no neoplasm	True negative
The neoplasm isolated	There is no neoplasm	False positive
There is no isolation	The neoplasm is present in the frame	False negative

attribution of the neoplasm to a particular class.

The marking of neoplasms was performed by polygons with a large number of points corresponding to the contours of neoplasms. Since rectangles adjacent to the boundaries of neoplasms were needed for training and testing the machine training algorithm, polygons were converted into rectangles.

The marked-up data set was divided into training, test and validation samples in the proportions of 70%, 15% and 15%, respectively. The distribution of frames by samples was carried out in proportion to the distribution by class.

To evaluate the possibility of machine training in order to automate the detection of neoplasms during colonoscopy in real time, the YOLOv5 neural network algorithm was used, which is one of the most common algorithms for detecting objects, due to its speed and accuracy [17].

Machine training of a neural network was carried out by downloading a training sample of a data set (4668 marked-up frames). An independent validation sample (957 marked-up frames) was used to optimize the algorithm, increase its accuracy by fine-tuning the neural network.

$$\text{Sensitivity} = \frac{TP}{TP + FN} \times 100\%$$

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FN + TN} \times 100\%$$

Figure 2. *Formulas for the sensitivity and accuracy of a diagnostic test. TP — true positive; TN — true negative; FP — false positive; FN — false negative*

The most significant parameters characterizing the effectiveness of the algorithm in detecting colorectal neoplasms are sensitivity and accuracy. To calculate these parameters, we used the generally accepted formulas for diagnostic tests (Fig. 2) and the following interpretations of the results of the algorithm (Table 2).

RESULTS

We have studied the distribution of frames with neoplasms by class (Fig. 3). It is necessary to note a pronounced imbalance of classes due to the natural difference in the rate of occurrence of neoplasms of these types. The structure of 4140 (58.3%) marked neoplasms corresponded to adenoma without high-grade dysplasia.

The recognition of neoplasms by the algorithm was influenced by the number of objects in the frame. In 414 (6.4%) cases, 2 or more neoplasms were present on the marked frames (Fig. 4).

In order to assess the quality of the obtained data set, as well as to predict the possibility of developing a CDSS based on it, the action of the trained algorithm was tested on 828 marked frames that made up the test sample.

The sensitivity of the algorithm was 77.2%, the accuracy of detecting neoplasms was 83.2%.

We analyzed the errors of the model and identified the most common causes of missing neoplasms on the frame or false positive triggering.

Thus, the model tends to skip the neoplasm that is in the foreground of the frame: this may be due to an insufficient number of marked

neoplasms close to the borders of the frame (Fig. 5).

A similar problem occurred with multiple neoplasms in one frame, when the model recognized only one of several objects (Fig. 6).

Another situation when polyp omissions were recorded was neoplasms of a small size (Fig. 7).

During testing, we recorded false positive triggering when the model identified areas on the frame that did not contain neoplasms — these are folds, glare, dirt. At the same time, during the testing of the model, we noted 5 cases when the model detected neoplasms that were not taken into account during the initial marking by a specialist (Fig. 8). The presence of objects of interest in such cases was confirmed when considering the frame by two experts, as well as by reviewing the original video fragment of the colonoscopy recording.

Thus, errors in the operation of the algorithm are registered in the following cases:

1. Neoplasm in the foreground
2. Small size of the neoplasm
3. "Blurred" neoplasm
4. Neoplasm on gaustra
5. Multiple neoplasms

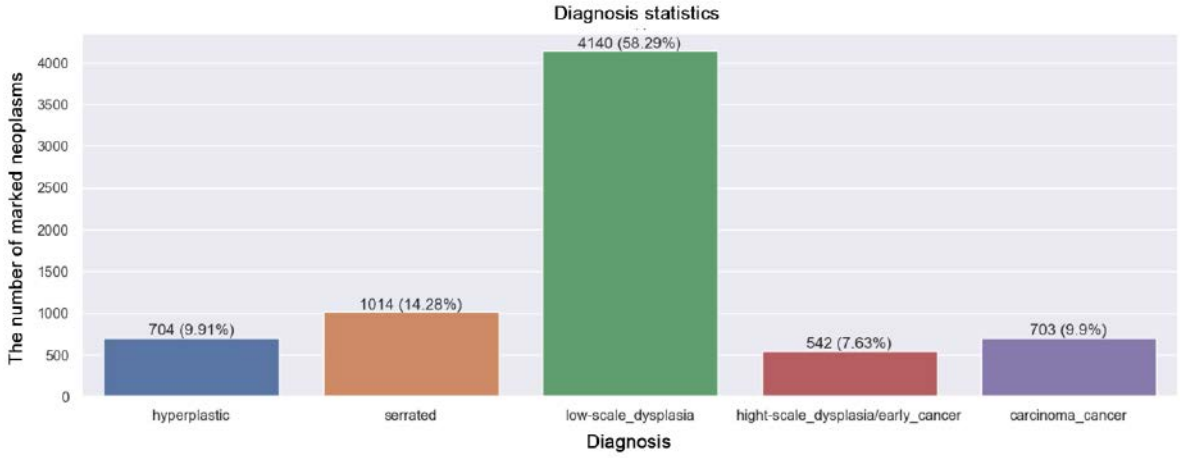

Figure 3. *Distribution of annotated lesions by classes*

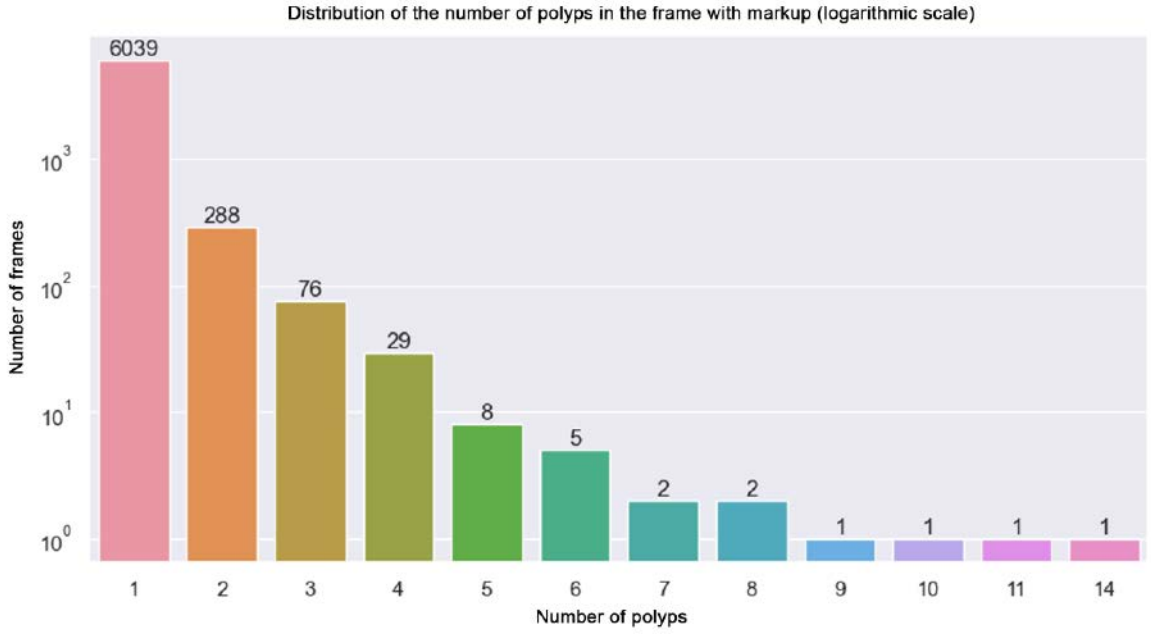

Figure 4. *Distribution of frames by amount of annotated lesions*

6. Colonoscopy in NBI mode;
7. The presence of foreign objects (biopsy cap, clip) in the frame.

DISCUSSION

Artificial intelligence technology is one of the most actively developing fields of science, the widespread use of which is expected to have a significant impact on various aspects of life. In healthcare, this technology has also been actively used in recent years, with the greatest success achieved in medical imaging. The first reports about the use of artificial intelligence to help a doctor perform a colonoscopy are encouraging. At the same time, the technology requires further development, technical issues of unification of the corresponding software have not been resolved, the effectiveness of the clinical decision support system based on artificial intelligence has not been sufficiently studied. In addition, the regulatory framework for the application of this technique in everyday medical practice has not been developed.
Our study is aimed at creating an original universal algorithm based on machine training, which will allow providing support to an endoscopist during colonoscopy in real time, highlighting neoplasms in the video stream. It is assumed that the algorithm will classify the detected neoplasms, and in the future also

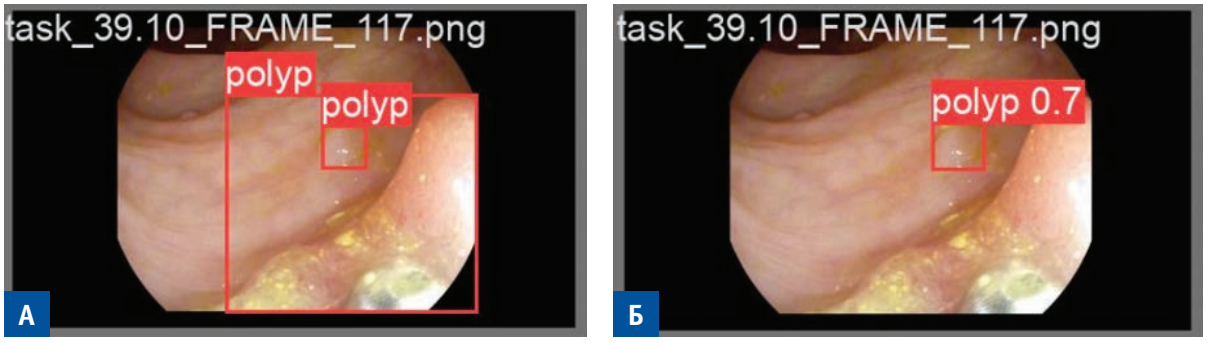

Figure 5. *An example of an algorithm error. Missing of the lesion in the foreground. А. Annotation by specialist. Б. Algorithm output*

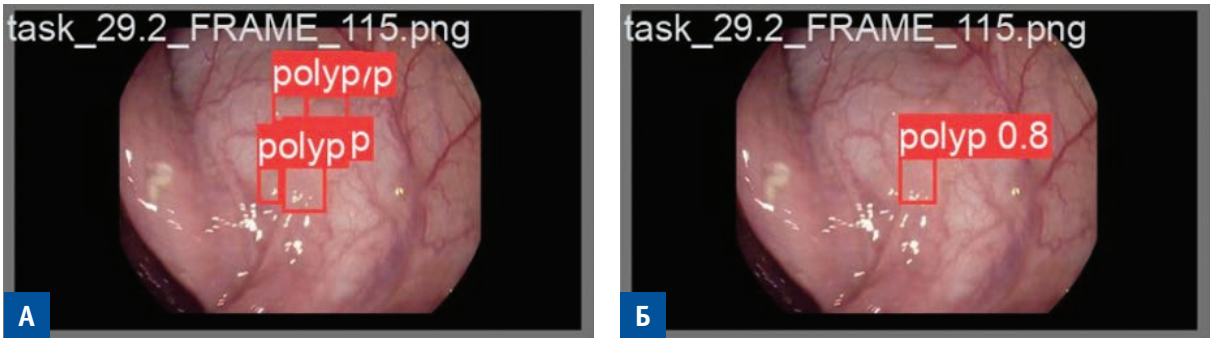

Figure 6. *An example of an algorithm error. Missing of the multiple lesions. А. Annotation by specialist. Б. Algorithm output*

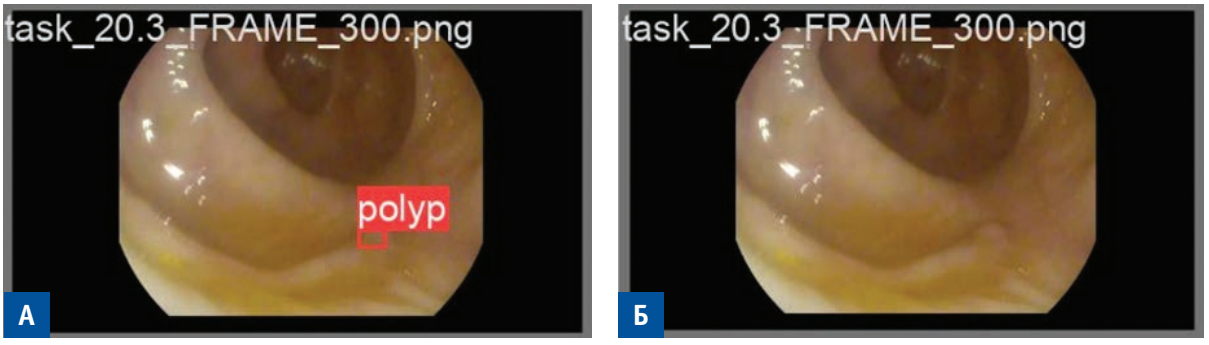

Figure 7. *An example of an algorithm error. Missing of the small lesion. А. Annotation by specialist. Б. Algorithm output*

Table 3. *Comparative characteristics of different data sets*

Data-set	Description	Format	Image Definition	Object of Detection
Kvasir-SEG / Hyper Kvasir	1,000 images	Image	Different	Masks, BBox
PICCOLO	3,433 images (2,131 WL and 1,302 NBI) of 76 neoplasms from 48 patients	Image	854 × 480, 1920 × 1080	Masks. Classification: Paris and NICE, Adenocarcinoma, Adenoma, Hyperplastic
KUMC	Collected from several datasets; more than 30,000 images	Image	Different	BBox. Classification: Adenoma, Hyperplastic
SUN	49,136 images; 100 neoplasms; 109,554 images without neoplasms	Image	N/A	BBox polyp, non-polyp annotations
Colorectal Polyp Image Cohort (PIBAdb)	~31,400 images (~22,600 WL and ~8,800 NBI); 1,176 neoplasms; ~17,300 images without neoplasms	Video and Image	768 × 576	BBox BBox Classification: Adenoma, Hyperplastic, Sessile Serrated Adenoma, Traditional Serrated Adenoma, Non Epithelial Neoplastic, Invasive
Data-set by RNMRC of Coloproctology	1,070 videos, 6,453 images with neoplasms	Video and Image	Different, at least 1,080 in height	Masks. Classification: Hyperplastic, serrated, low-grade_dysplasia, high-grade_dysplasia/ early_cancer, carcinoma_cancer

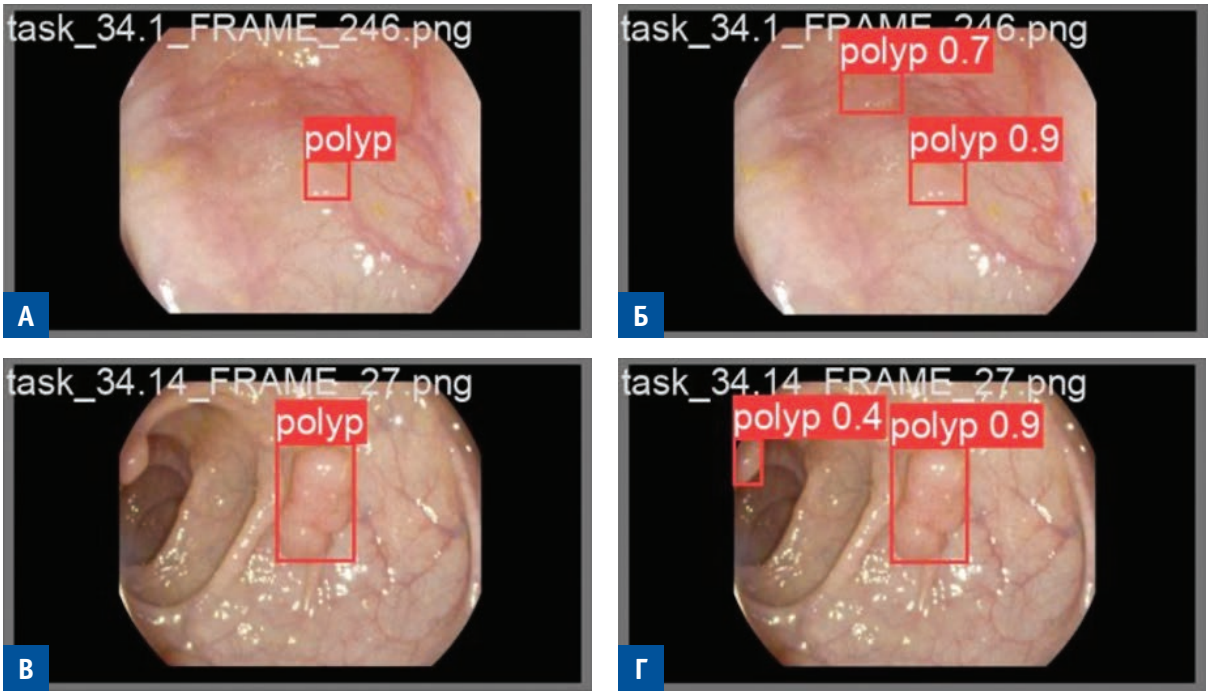

Figure 8. *An example of revealing by the algorithm not annotated lesions. A,B. Primary annotation by specialist. Б,Г. Algorithm output*

Table 4. *Comparative characteristics of artificial intelligence algorithms in the detection of neoplasms during colonoscopy*

Authors	Year	Data-Set	Sensitivity	Accuracy
Pacal et al.	2022	Training and test: piccolo	79.9%	92.6%
Nogueira-Rodríguez et al.	2022	Training: private Test: piccolo	60.0%	76.0%
Li K. et al.	2021	Training and test: kumc	86.2%	91.2%
RNMRC of Coloproctology	2022	Collected data-set	77.2%	83.2%

form a preliminary examination protocol, noting the level of examination of the intestine and the quality of its preparation, the number, size and class of detected changes.

At this stage of our study, the algorithm of a promising CDSS demonstrated an acceptable level of sensitivity and accuracy on a test sample — 77.2% and 83.2%, respectively. At the same time, an interesting observation is the cases of the allocation of neoplasms by the algorithm that were not mistakenly annotated by an endoscopist. We also analyzed various situations that are difficult to interpret with machine vision, which makes it expedient to retrain the program by expanding the data set by including additional marked frames.

When comparing with the data sets published in the public domain, it can be stated that our data set is assembled from higher-definition frames, contains a large number of images of neoplasms, while 5classes of objects are differentiated (Table 3).

The potential operability of a promising CDSS based on the obtained algorithm trained on this data set is illustrated by the relatively high specificity and accuracy of the test. At the same time, according to these characteristics, the developed algorithm in the current version is inferior to a number of the most developed analogues (Table 4).

The presented data should be interpreted with caution, since the sensitivity and accuracy of the algorithm were determined on test samples, while the declared parameters can be significantly improved by further training the model. The real effectiveness of the algorithm and the CDSS created on its basis should be studied through comparative clinical trials. Developing the design of this kind of research is a non-trivial task, since colonoscopy does not have a verification method for the detection of adenomas, and performing two consecutive endoscopic examinations in one patient is not entirely ethical. In this regard, it seems appropriate to abandon direct comparison in favor of large studies on homogeneous groups of patients.

CONCLUSION

The marked-up data set made it possible to develop an algorithm based on artificial intelligence technology that determines colorectal neoplasms in the colonoscopy recording video stream with an accuracy of 83.2%. The technology seems promising. However, it requires further development, improvement to the CDSS and study of effectiveness from the standpoint of evidence-based medicine.

AUTHORS CONTRIBUTION

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Chemotherapy efficacy in metastatic neuroendocrine colorectal cancer

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ABSTRACT *AIM: to evaluate the effectiveness of first-line chemotherapy in patients with colorectal neuroendocrine cancer (NEC).*
PATIENTS AND METHODS: a retrospective study included patients with metastatic colorectal NEC (2000-2020). The main analyzed parameter was the response rate to treatment according to the RECIST criteria, depending on the regimen used in the first line. The overall survival was additional parameter.
RESULTS: the study included 27 patients (13 with initial stage IV disease and 14 with progression after primary radical treatment). Ten patients in the 1st line underwent chemotherapy according to the EP scheme, 4 — XELOX, 2 — FOLFIRI, 2 — Irinotecan and Cisplatin, 1 — Samarium, 1 — Nivolumab, 1 — 5-FU-LV. Most often, the treatment effect (partial response or stabilization) was observed against the background of chemotherapy according to the EP scheme — in 60% of patients. The median OS was 7 months.
CONCLUSION: the use of chemotherapy according to the EP regimen is the preferred options for the treatment of metastatic colorectal NEC. The median OS in this group of patients remains extremely low, and new clinical trials are needed.

KEYWORDS: *neuroendocrine cancer, first-line chemotherapy, metastatic cancer*

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INTRODUCTION

Colorectal neuroendocrine cancer (NEC) is a rare malignant neoplasm. Only a small number of clinical cases series are available in the scientific literature [1–7].

An important issue in the treatment of colorectal NEC is the choice of the optimal first-line CT regimen. There are a small number of articles that consider the effectiveness of first-line chemotherapy (CT) for colorectal neuroendocrine cancer, mainly in the framework of publications that combine various types of NEC of the gastrointestinal tract. The main treatment regimen is a combination of etoposide and cisplatin [8,13]. At the same time, the effectiveness of CT and the prognosis of the disease may vary significantly depending on the tumor site, and the data on colorectal NEC are limited to small retrospective studies [9, 10].

AIM

The aim of our study was to evaluate the response rate of metastatic colorectal NEC to the first line of chemotherapy, as well as to study the clinical

characteristics of a group of patients with metastatic colorectal NEC.

PATIENTS AND METHODS

The study is based on a retrospective study of the medical histories of patients treated at the N.N. Blokhin Oncology Research Center and the Tyumen Medical City State Medical Institution in the period from 2000 to 2020.

According to the ICD codes-0 1.4.1 8249/3, 82401, 8240/1, 8240/3.1, 8240/3, 82403, 82443, 8045/3.2, 8013/3, 80123, 85103, 8510/3, 8041/3.3, 80413, 8041/3, 8246/3, 8240/3.2 and ICD-X C20, C21.1 a request was sent to archive for the selection of patient case histories for the period 2000–2020. The criteria for inclusion in the study group were: histologically verified colorectal neuroendocrine cancer (Ki-67 > 20%, moderate or low degree of tumor differentiation). Staging was carried out on the basis of pelvic MRI, chest and abdominal CT with intravenous contrast. Histology was carried out due to WHO pathomorphological classification 2019 [11]. Staging was carried out due to the UICC TNM system (8th edition). Also, an IHC study was conducted in all patients, which finally confirmed the diagnosis of neuroendocrine cancer.

The following chemotherapy regimens were used: EP (Etoposide 100 mg/m^2 i/v on days 1–3 + cisplatin 75 mg/m^{2}i/v on day 1 once every 3 weeks, 6 cycles), XELOX (Oxaliplatin 130 mg/m^2 i/v on day 1 + capecitabine 2000 mg/m^2 inside on days 1–14, 1 time in 3 weeks, 6 cycles), FOLFIRI (Irinotecan 180 mg/m^2 i/v on day 1 + calcium folinate 400 mg/m^2 i/v on day 1 + 5-fluorouracil 400 mg/m^2 i/v on day 1-day 5 + fluorouracil 2400 mg/m^2 i/v 46-hour infusion once every 2 weeks, 9 cycles), *cisplatin and irinotecan* (Cisplatin 60 mg/m^2 i/v on day 1 + irinotecan 65 mg/m^2 i/v on days 1 and 8, every 3 weeks), 5-FU-LV (5–fluorouracil 370–400 mg /m^2 1–5 days, in combination with a high dose of leucovorin (200 mg/m^2 1–5 days) 6 cycles with an interval of 4 weeks), *Nivolumab* (240 mg i/v 30-minute infusion every 14 days), *Samarium* (1.5 mCi/kg weight of the patient's body).

The main analyzed parameter was the frequency of response to treatment according to the RECIST 1.1 criteria [12], additional parameters were the overall survival. The effect of treatment according to

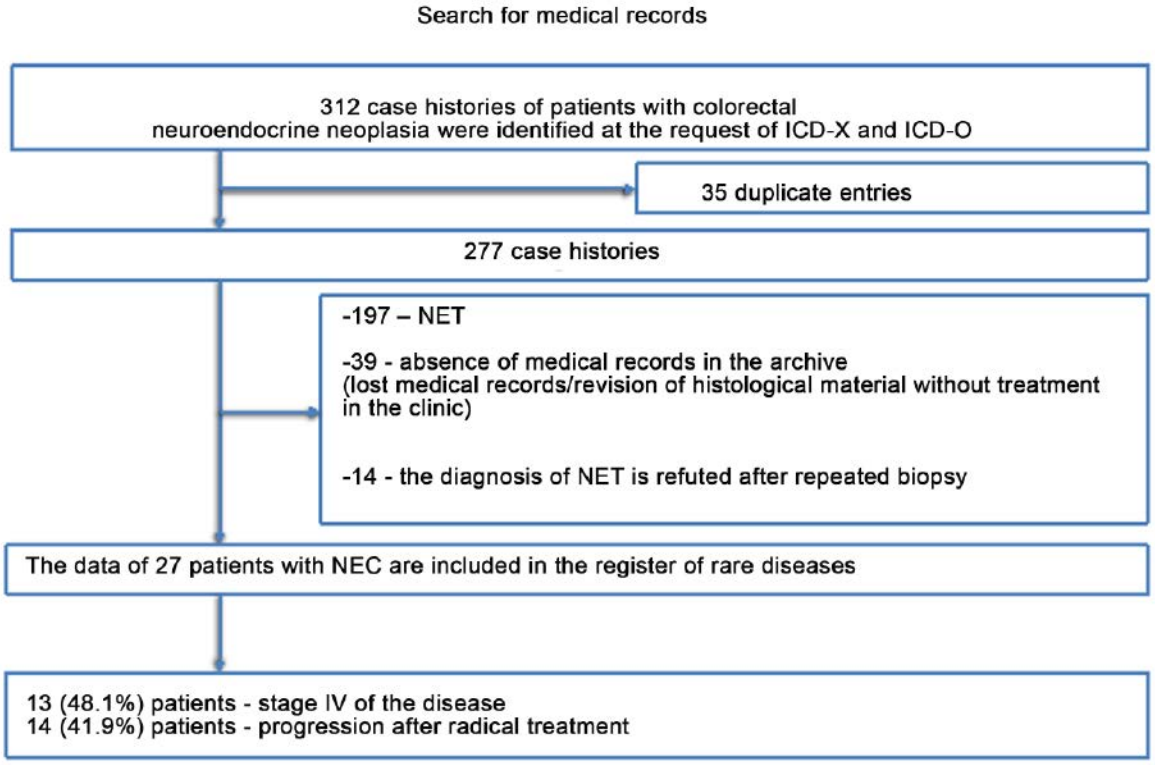

Figure 1. *Recruitment of patients to the study group*

Table 1. *Characteristics of the group of patients with colorectal NEC*

Characteristic	N = 27 (100%)
Gender	
Male	12 (44.6%)
Female	15 (55.6%)
Age	
30-50 years	9 (33.3%)
50–70 years	16 (59.3%)
> 70 years	2 (7.4%)
ECOG	
0-1	23 (85.2%)
2-3	4 (14.8%)
Initial Stage	
IA-IIB	4 (14.81%)
IIIA-IIIB	10 (37.04%)
IV	13 (48.15%)
Localization	
rectum and anal canal	16 (59.3%)
left colon	6 (22.2%)
right colon	5 (18.5%)
Dimensions	
2-5 cm	12 (44.4%)
> 5 cm	15 (55.6%)
cT	
1-2	8 (29.6%)
3-4	19 (70.4%)
cN	
0	6 (22.2%)
1	21 (77.8%)
Histological structure	
Microcellular cancer	8 (29.6%)
Macrocellular cancer	8 (29.6%)
No data	11 (40.8%)

the RECIST criteria was evaluated in the presence of at least 1 control examination within 4 months after the start of chemotherapy. Statistical analysis was performed using the IBM SPSS software package (version 25). Qualitative criteria were compared using a chi-squared test, using a two-sided R. Overall survival was calculated from the date of detection of metastatic disease to the date of death of the patient. Progression-free survival was calculated from the date of detection of metastatic disease to the date of disease progression or the date of death from other causes. Survival was analyzed using the Kaplan-Meier method.

RESULTS

The study included 27 patients (Fig. 1), 14 of whom had progression after primary radical surgery, 13 had initially metastatic NEC. Most of the patients were aged in the range of 50–70 years (59%). Primary multiple malignant neoplasms occurred in 4 (14.8%) patients, among whom in 1 (25%) patient NEC was synchronous and in 3 (75%) — metachronous. The most frequent site were the rectum and anal canal (59%). Lymph node lesion occurred in 21 (78%) patients (Table 1).

The nature of distant metastasis was diverse (Table 2). However, isolated liver lesion was most often occurred, in 10 (76.9%) patients.

Other, the rarest location of distant metastasis in patients in the study were isolated metastases in the left lateral pelvic lymph node, left internal iliaclymph nodes, on the peritoneum along the right-common iliac vessels, peritoneal carcinomatosis, metastases to the anterior abdominal wall, metastatic lesion of cervical and supraclavicular lymph nodes, ovarian metastases, bone metastases.

Table 2. *Pattern of metastasis in patients with metastatic colorectal NEC*

Metastasis zones	N(%), (*n* = 27)
Liver	11 (40.7%)
Retroperitoneal lymph nodes	7 (26.0%)
Brain	2 (7.4%)
Lungs	1 (3.7%)
Other	6 (22.2%)

Table 3. *Types of treatment performed in patients with NEC*

Type of Treatment	N (*n* = 27)	%
Removal of the primary tumor		
Was not carried out	13	48.15
Local excision	1	3.7
Colorectal resection	13	48.15
Radiation therapy for the pelvic area		
RT to I Line CT	3	10.3
RT in parallel with the I line CT	2	6.9
RT after the I line CT	1	3.4
First-lined rug treatment		
EP	10	37.1
XELOX	4	14.8
FOLFIRI	2	7.4
IP	2	7.4
Others	3	11.1
The scheme is unknown	1	3.7
Without treatment	5	18.5
Other treatment		
CT 2 line was carried out	5	18.5
Resection of liver metastases	4	14.8

Note: EP — etoposide and cisplatin, XELOX — capecitabine and oxaliplatin, FOLFIRI — 5-fluorouracil, leucovorin and irinotecan, IP — irinotecan and cisplatin.

TREATMENT

Table 3 presents the characteristics of the treatment performed in a group of patients with metastatic NEC. Removal of the primary tumor was performed in 16 (55.2%) patients, 15 (93.8%) of whom underwent colorectal resection, and in 1 (6.3%) patient local excision of the tumor was performed.

Five (18.5%) patients were unable to start 1st line CT due to low functional status. Initially, there were 3 patients with stage IV disease, 2 of whom had primary tumor removal, both urgently (tumor perforation in 1 patient and bleeding in the other) after surgery. So, the patients were unable to start CT due to low functional status. One (20%) of those patients had multiple liver metastases, and the other two (40%) had widespread lung lesion. Two patients with an initially local process also did not start CT. One patient (20%) showed tumor progression in the liver and, as a result, a low functional status.The second (20%) patient refused the treatment.

As for the effect of treatment (Table 4), it was most often observed in the group of patients receiving CT according to the EP scheme (6 patients). Three (50%) of them had microcellular subtype cancer, 1 (17%) had macrocellular cancer, 2 (33%) had no data. Partial response was noted in 4 (40%) patients, of whom 2 (50%) — had microcellular cancer, 1 (25%) — microcellular cancer, 1 (25%) — undifferentiated; stabilization was noted in 2 (20%) patients, of whom 1 (50%) — macrocellular, 1 (50%) — unspecified; progression was noted in 4 (40%) patients, of whom 2 (50%) — macrocellular, 1 (25%) — microcellular, 1 (25%) — unspecified.

Table 5 shows the responses to treatment with the I-line therapy scheme in patients with NEC, depending on the histological type.

In 2 patients, a complete clinical response to CT was noted, but in 1 (microcellular cancer) of them, CT (IP) was prescribed for an unresectable local

Table 4. *Response to treatment depending on the scheme of the first line therapy in patients with NEC*

Treatment regimen	Response to treatment			
	FR	PR	DS	DP
EP	–	4 (40%)	2 (20%)	4 (40%)
XELOX	1 (25%)	–	–	3 (75%)
FOLFIRI	–	–	1 (50%)	1 (50%)
IP	1 (50%)	–	–	1 (50%)
Samarium	–	–	–	1 (100%)
Nivolumab	–	–	–	1 (100%)
5-FU-LV	–	–	–	1 (100%)
The regimen is unknown			1 (100%)	

Note: FR — full response, PR — partial response, DS — disease stabilization, DP — disease progression, EP — etoposide and cisplatin, XELOX — capecitabine and oxaliplatin, FOLFIRI — 5-fluorouracil, leucovorin and irinotecan, IP — irinotecan and cisplatin.

Table 5. *Response to treatment with the first-line therapy regimen in patients with NEC depending on histological type*

Histological structure	Response to treatment			
	FR	PR	DS	DP
Macrocellular	1 (12.5%)	2 (25%)	2 (25%)	3 (37.5%)
Microcellular	1 (14.3%)	1 (14.3%)	–	5 (71.4%)
No data	-	1 (14.3%)	1 (14.3%)	5 (71.4%)

Note: FR — full response, PR — partial response, DS — disease stabilization, DP –disease progression, EP — etoposide and cisplatin

relapse and was performed immediately after the course of RT.

The effect was evaluated only after the completion of RT and CT, which does not allow us to assess the contribution of these components of treatment separately. In another patient (macrocellular subtype), CT (XELOX) was performed for metastatic lesion of pelvic lymph nodes, established according to pelvic MRI data. Metastases were not histologically verified. However, their size and MR signs of metastatic lesion completely regressed after the treatment. One patient received nivolumab therapy in the 1st line, because the progression developed immediately after the completion of adjuvant CT according to the EP scheme. The effect of the treatment was not registered. In two patients in the first line of CT, only fluoropyrimidine or samarium monotherapy was prescribed (it was prescribed in a patient with metastatic bone lesion), in both cases due to low initial functional status. In both cases, no response to the treatment was registered.

The median follow-up was 43.6 months. The 2-year overall survival (OS) of patients with metastatic NEC was 11.3%, the median OS was 6.0 months (95% CI, 2.4–9.7 months) (Fig. 2).

The 2-year PFS was 4.3%. The median survival of patients with metastatic NEC was 2.9 months (95% CI, 0.6–5.3 months) (Fig. 3).

In the study, two patients with high survival rates were also revealed, despite the aggressive nature of the tumor.

In the first patient, the tumor was located in the upper rectum with the initial stage IIIB. The first stage was colorectal resection in 2017. Histologically, microcellular neuroendocrine cancer was verified. After 5.5 months, progression to mesenteric and paraaortic lymph nodes was detected. Histological verification was not carried out. It was decided to do 7 courses of CT according to the XELOX scheme, against which a complete regression of metastases and normalization of the CEA from 60 to 6 were noted. The last checkup was 43 months after the progression. The patient died of unknown causes, the overall survival rate was 50 months. Another female patient had microcellular neuroendocrine cancer of the lower ampullary rectum, stage IIIB in 2009. She underwent preoperative chemoradiotherapy (CRT) with induction and consolidating CT according to the EP scheme (a total of 6 courses), then abdominal-anal resection (AAR) of the rectum was performed. Fourteen months after the initial radical surgery, a recurrence was detected along the posterior semicircle of the upper third of the vagina measuring 55x40 cm with the involvement of the cervix. It was decided to do three CT courses according to the IP scheme

of 1,8,15 days. A complete clinical response was received after 1 course of the therapy. With the third course of CT, RT ROD 2 Gr, SOD 24 Gr was carried out. On MRI, the tumor formation in the vaginal area was not determined. After another 24 months, repeated progression was revealed — solitary metastasis to the brain. In the area of a previously determined relapse — without signs of tumor growth. The removal of metastasis of the right occipital region of the brain was performed, followed by RT of ROD 2.5Gr, SOD 30 Gr on the area of the removed metastasis. In June 2014, a recurrence of the tumor in the area of the sacro-spinous ligament on the left was revealed. Six courses of chemotherapy were carried out according to the scheme: cisplatin 60mg/ m^2i/v in 1 day + irinotecan 60mg/ m^2i/v in 1, 8 days, against which positive dynamics was noted in the form of a decrease in the tumor size in the sacro-spinous ligament.

In June 2015, stereotactic radiation therapy of ROD 9Gr, SOD 27Gr was performed on the area of a recurrent tumor.

In January 2016, a metastasis to the left temporal lobe of the brain revealed and continued growth of a recurrent tumor in the sacroiliac ligament. Chemotherapy was performed according to the scheme: capecitabine 1500 mg/ m^2orally daily for 1–14 days + temozolomide 150 mg/m^2 orally daily for 1–14 days. In March 2016, a gamma knife SOD 44Gr was used to treat metastasis in the temporal lobe of the brain. Avastin was added to the therapy since October 2016. In August 2017, negative shift was noted due to an increase in the focus size in the sacrum. Next, CT Cyclophosphane + Doxorubicin was prescribed. The last checkup was carried out

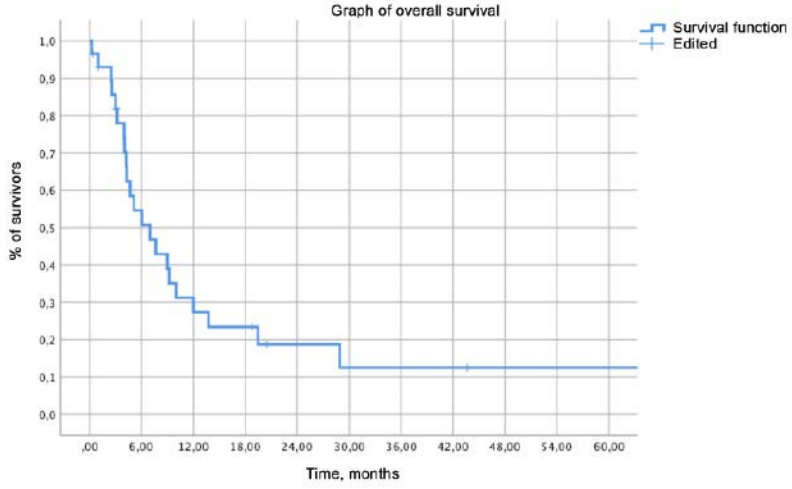

Figure 2. *OS of patients with NEC*

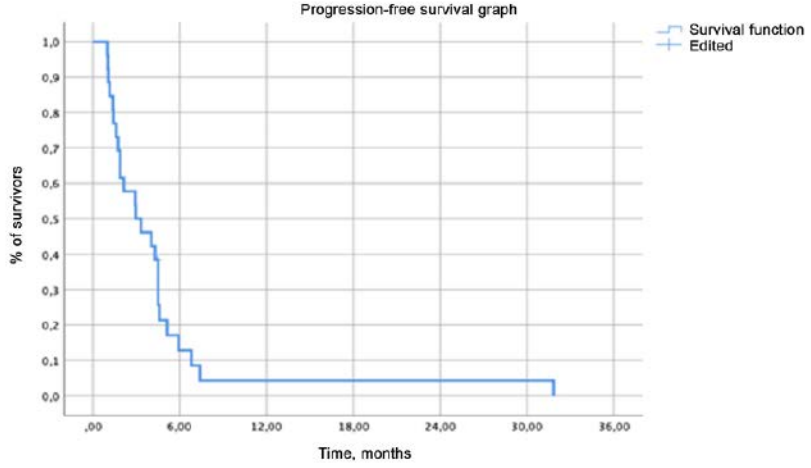

Figure 3. *PFS of patients with NEC*

on 06.12.2018. The patient died from the progression of the disease; the overall survival was 116 months.

DISCUSSION

The use of CT according to the EP scheme is the preferred of the existing treatment options for metastatic NEC. In our study we focused only on data on the effectiveness of this scheme due to the presence of only single cases of the use of alternative treatment regimens. The response rate to the treatment in our study was 60% compared to 56.4–87.5% according to other authors [1–5]. At the same time, the indicators were similar to ours in studies in which the results of treatment of patients with NEC site only in the large intestine were analyzed — 42–62.5% [1,2,4], the indicators in mixed groups with NEC of various gastrointestinal organs were higher — 74.5–87.5% [3,5]. Thus, a lower sensitivity of the colorectal NEC to chemotherapy according to the EP scheme is likely compared to the NEC of other gastrointestinal organs. Another possible explanation for the relatively low response rate to chemotherapy in our study may be the shortcomings of collecting material during retrospective analysis. Responses to treatment for NEC are often unstable [2]. During the retrospective analysis, some of the information about the interim effect assessment could have been lost (we took into account the data of the effect assessments at least once every 4 months, but the interim data during this interval could not be available). It should also be noted that the published data on the response rate to the first line CT in a mixed group of patients with gastrointestinal NEC [3] are usually higher than in studies where patients with colorectal NEC are presented in isolation [4].

In the study, the median OS of patients with metastatic NEC was7.0 months (95% CI, 3.4–10.6 months) and was similar to that obtained in other studies — in patients with colorectal NEC — 4.04–12.5 months. [1,2,4,13], and in mixed groups with NEC of various gastrointestinal organs — 11–14 months [3,5], despite the fact that 27.6% of patients in our study had such rapid progression of the disease that they could not even start the first line CT. The high proportion of patients who were unable to start treatment indicates the need for accelerated clinical decision-making when identifying patients with colorectal NEC. The disadvantages of this trial are directly related to the retrospective nature and the heterogeneity of the study group. There was no single standardized treatment plan. Some patients received CRT in parallel with the 1st line CT, which does not allow an objective assessment of the particular treatment regime. Also, there were no unified approaches to determining indications for surgical treatment, choosing a CT regimen. This led to the formation of small subgroups of patients receiving different types of treatment, comparison between which is difficult. Also, some of the information on the effect of chemotherapy could be lost in the retrospective study, and therefore the incidence of registered responses to treatment could be underestimated.

Despite these limitations, this is one of the few studies in which a group of colorectal NEC is collected, without combining all the NEC of the gastrointestinal tract. This allows us to study in more detail the individual features of the course and forecast of the NEC of this location.

CONCLUSION

Colorectal NEC is a disease with an extremely negative prognosis and a high risk of rapid progression. It is necessary to start treatment quickly, because the progression often prevents the beginning of a special therapy. The accumulated data speak in favor of using the EP scheme as the first line chemotherapy, which was confirmed in our series of cases. It is necessary to further study this disease and accumulate information within large multicenter registries.

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Трансабдоминальное ультразвуковое исследование как метод диагностики дивертикулярной болезни ободочной кишки

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РЕЗЮМЕ *ЦЕЛЬ ИССЛЕДОВАНИЯ: оценка эффективности трансабдоминального УЗИ при дивертикулярной болезни ободочной кишки (ДБОК).*
ПАЦИЕНТЫ И МЕТОДЫ: проведено ретроспективное исследование, включившее в себя 108 больных с осложненной формой дивертикулярной болезни ободочной кишки. У всех больных было левостороннее поражение дивертикулами, при этом у подавляющего большинства пациентов дивертикулы располагались в сигмовидной кишке.
РЕЗУЛЬТАТЫ: трансабдоминальное УЗИ у 91 (84,3%) больного было информативно; в 80 (74,1%) случаях были отчетливо выявлены дивертикулы с определением локализации и размеров, повышение эхогенности параколической клетчатки, жидкости около кишки, при перфорации наличия свищевого хода, включений газа; у 11 (10,2%) пациентов отмечались косвенные признаки, такие как равномерное утолщение стенки кишки, снижение эхогенности, свищевой ход, жидкость около кишки, повышение эхогенности паракишечной клетчатки, наличие параколического абсцесса, отсутствие или замедление перистальтики; у 17 (15,7%) пациентов не выявлено изменений, у одного было ложноположительное заключение.
ЗАКЛЮЧЕНИЕ: трансабдоминальное УЗИ органов брюшной полости является, информативным, малоинвазивным и доступным методом диагностики осложненной дивертикулярной болезни ободочной кишки в экстренной хирургии и колопроктологии.

КЛЮЧЕВЫЕ СЛОВА: *осложненные формы дивертикулярной болезни ободочной кишки, дивертикулит, кровотечение, ультразвуковая диагностика*

КОНФЛИКТ ИНТЕРЕСОВ: *Авторы заявляют об отсутствии конфликта интересов*

ИССЛЕДОВАНИЕ НЕ ИМЕЛО ИСТОЧНИКА ФИНАНСИРОВАНИЯ

ДЛЯ ЦИТИРОВАНИЯ: Семионкин Е.И., Хубезов Д.А., Луканин Р.В., Пучков Д.К., Огорельцев А.Ю., Юдина Е.А., Брагина И.Ю., Гордеева А.С. Трансабдоминальное ультразвуковое исследование как метод диагностики дивертикулярной болезни ободочной кишки. *Колопроктология*. 2023; т. 22, № 2, с. 112–117. https://doi.org/10.33878/2073-7556-2023-22-2-112-117

Transabdominal ultrasound for complicated diverticular disease

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ABSTRACT *AIM: to evaluate the effectiveness of transabdominal ultrasound for complicated diverticular disease (CDD).*
PATIENTS AND METHODS: a retrospective study included 108 patients with CDD. All patients had left-sided diverticula, while in the vast majority of patients, diverticula were located in the sigmoid colon.
RESULTS: transabdominal ultrasound was informative in 84.3% of patients; in 74.1% of cases (80 patients), diverticula were clearly identified with sizing, infiltration of the intestinal wall, fluid around the intestine, the presence of a fistulous tract in perforation, gas collections; 11 (10.2%) patients had indirect signs, such as diffuse hypoechogenic thickening of the intestinal wall, its infiltration, fistulous tract, liquid near the intestine, hyperechogenic structure of fat near the intestine, the presence of a paracolic abscess, absence or slowing down of peristalsis; 17 (15.7%) patients showed no changes, one had a false positive conclusion.
CONCLUSION: transabdominal ultrasound is an informative and non-invasive method for diagnosing complicated diverticular disease in urgent surgery.

KEYWORDS: *complicated forms of diverticular disease of the colon, diverticulitis, bleeding, ultrasound diagnostics*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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ВВЕДЕНИЕ

В настоящее время отмечается рост заболеваемости дивертикулярной болезнью ободочной кишки (ДБОК), в том числе с осложненными формами заболевания [1,2]. Трансабдоминальное ультразвуковое исследование (УЗИ) является современным информативным, безопасным и ценным методом для диагностики дивертикулярной болезни ободочной кишки [3–6]. Трансабдоминальное УЗИ в качестве диагностики первой линии у больных ДБОК с осложненными формами — доступный, низкозатратный метод [7]. Компьютерная томография и УЗИ выходят на первый план визуализации дивертикулярной болезни, особенно в экстренном порядке [8]. Актуальность исследования определяется ростом заболеваемости ДБОК и настоятельной необходимостью оперативной эффективной первичной диагностики, так как ДБОК приходится дифференцировать со многими острыми хирургическими заболеваниями органов брюшной полости, прежде всего с острым аппендицитом, ущемленной грыжей, опухолями толстой кишки, обтурационной кишечной непроходимостью, гинекологическими заболеваниями у женщин и т.п.

ЦЕЛЬ ИССЛЕДОВАНИЯ

Оценить перспективы и эффективность диагностики осложненной формы ДБОК с помощью трансабдоминального УЗИ органов брюшной полости в условиях отделений, оказывающих не только плановую, но и экстренную круглосуточную помощь.

ПАЦИЕНТЫ И МЕТОДЫ

В исследование вошли 108 пациентов с ДБОК с воспалительными осложнениями и кровотечением, находившихся на стационарном лечении в 2021 году в колопроктологическом отделении Рязанской областной клинической больницы. Больные были в возрасте от 35 до 96 лет, средний возраст — 65,2 ± 12,8 лет, в возрасте до 45 лет было 8 (7,4%) пациентов. Мужчин — 41 человек, женщин — 67. Сопутствующие заболевания отмечались у 77 (71,3%) пациентов. 72/108 (66,7%) больных были с воспалительными осложнениями дивертикулярной болезни, 36/108 (33,3%) с кровотечением. У 62 больных с воспалительными осложнениями был дивертикулит, у двух — острый паракишечный инфильтрат, у восьми — перфоративный дивертикулит с гнойным перитонитом. Больные с воспалительными осложнениями поступали экстренно по скорой помощи: в среднем, через 5,8 суток от начала заболевания, с кровотечением через 3,1 суток. У всех пациентов было левостороннее поражение дивертикулами, с преимущественным расположением дивертикулов в сигмовидной кишке. Первичная диагностика включала в себя изучение жалоб, анамнеза заболевания, данных объективного осмотра, лабораторные данные, проводились пальцевое исследование прямой кишки, трансабдоминальное УЗИ органов брюшной полости с осмотром не только паренхиматозных органов, но и осмотром кишечника. УЗИ применено так же в динамике у 14 пациентов для мониторинга течения заболевания и коррекции проводимой терапии. Дополнительная подготовка кишечника не проводилась.

УЗИ проводили на ультразвуковом сканере LOGIQ S7 (фирма GE, США) с использованием мультичастотного конвексного датчика с частотой 3–5 МГц. Использовались — серошкальный В-режим, режим цветного допплеровского картирования (ЦДК). Во время исследования оценивалось: наличие дивертикулов в ободочной кишке, изменения параколической клетчатки, наличие свободной жидкости и газа в брюшной полости и малом тазу, перистальтика кишечника, изменение стенки дивертикула — чаще

всего утолщение, снижение эхогенности, дифференцировка слоев стенки кишки.

РЕЗУЛЬТАТЫ И ОБСУЖДЕНИЕ

Клинически наиболее распространенным признаком дивертикулита являются острые боли внизу живота [9]. Наши наблюдения подтверждают это положение, у больных с воспалительными осложнениями наблюдались боли в нижних отделах живота, больше слева, так же повышенная температура, лейкоцитоз, ускоренное СОЭ. Из 36 больных с кровотечением анемия наблюдалась у 27 пациентов. У 98 (90,7%) пациентов проводилась консервативная терапия с учетом осложнений, которая позволила купировать явления дивертикулита и остановить кровотечение. У 7 (6,5%) больных с тяжелой степенью анемии потребовалось, наряду с гемостатической и противовоспалительной терапией, переливание компонентов крови.

Больные были выписаны в удовлетворительном состоянии. Средняя продолжительность стационарного лечения при дивертикулите составляла 6,9 койко-дней, при кровотечении — 5,2. При выписке давались подробные рекомендации по диете, медикаментозному амбулаторному лечению и проведению эндоскопии, ирригоскопии, КТ брюшной полости.

Малоинвазивная методика — пункция и дренирование ограниченного параколического абсцесса под ультразвуковым контролем выполнена у 5 (4,6%) пациентов. Двое из этих пациентов были оперированы в последующем по срочным показаниям в виду нарастания деструкции стенки кишки. Наши наблюдения подтверждают данные Карпухина О.Ю. с соавт. [7], что даже эффективно проведенное дренирование абсцесса под ультразвуковой навигацией не гарантирует от оперативного вмешательства.

Оперировано 10 (9,3%) больных: экстренно восемь пациентов с перфоративным дивертикулитом, осложненным гнойным перитонитом, двое с острым паракишечным инфильтратом в виду прогрессирования гнойно-некротического процесса, несмотря на дренирование параколического абсцесса под ультразвуковым контролем. Выполнялись лапаротомия, обструктивная резекция типа операции Гартмана, в связи с гнойным и каловым перитонитом. Летальных исходов не было. Наблюдалось одно осложнение, несостоятельность культи прямой кишки, у пациентки 78 лет на 10 сутки после операции. Проведена релапаротомия, ушивание культи, дренирование брюшной полости. Возможной причиной несостоятельности явилось неотмывание культи отключенной кишки на операции.

УЗИ было информативно у 84,3% больных; в 80 (74,1%) случаях были выявлены дивертикулы с указанием локализации и их размеров, инфильтрация стенки кишки, наличие жидкости около кишки, при перфорации определялся свищевой ход, включения газа. У 11 (10,2%) пациентов выявлены косвенные признаки, как равномерное утолщение стенки кишки в зоне воспаления со снижением ее эхогенности, повышение эхогенности параколической клетчатки, жидкость около кишки, свищевой ход, параколический абсцесс, отсутствие или замедление перистальтики (Рис. 1,2,3,4). УЗИ не выявило

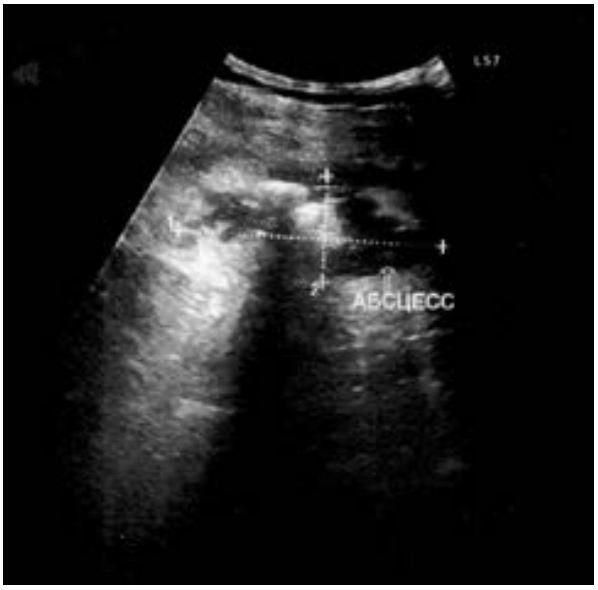

Рисунок 1. *Абсцесс в параколической клетчатке (неоднородное жидкостное образование с анэхогенным содержимым и гиперэхогенным включением, формирующим широкую акустическую тень)*
Figure 1. *Abscess in paracolic tissue (heterogeneous liquid formation with anechoic content and hyperechoic inclusion forming a wide acoustic shadow)*

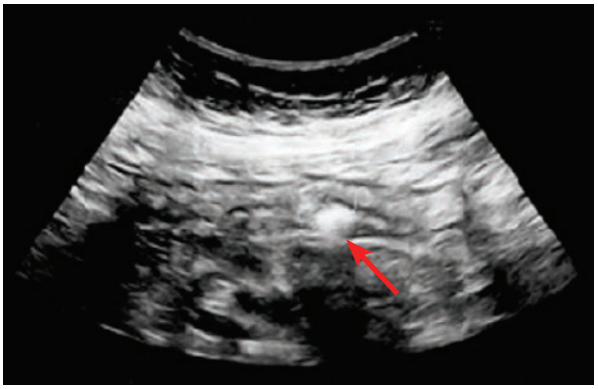

Рисунок 2. *Воспаленный дивертикул (режим Zoom) с гиперэхогенным содержимым (указано стрелкой)*
Figure 2. *Inflamed diverticulum (Zoom mode) with hyperechoic contents (indicated by arrow)*

дивертикулы у 17 (15,7%) пациентов, в одном случае было ложно положительное заключение у больного 57 лет с резко выраженным ожирением, паракишечным абсцессом, перенесенной ковидной инфекцией месяц назад. По УЗИ были выявлены дивертикулы нисходящей кишки до 14 мм, равномерное утолщение стенки кишки до 9 мм, жидкостное образование с неоднородным содержимым около кишки 18 на 25 мм. Проведена обструктивная левосторонняя гемиколэктомия, дренирование забрюшинной флегмоны и брюшной полости. На операции выявлен флегмонозноизмененный левый фланг ободочной кишки, множественные язвы с перфорациями, перитонит, забрюшинная флегмона, в брыжейке множественные абсцессы диаметром до 4 см. Выздоровление, выписан на 12 сутки после операции.

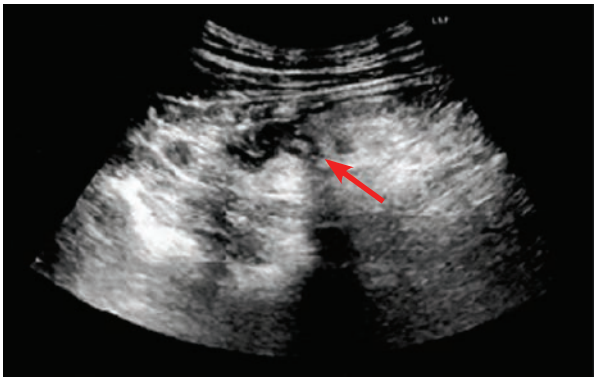

Рисунок 3. *Воспаленный дивертикул с гиперэхогенным содержимым, гипоэхогенной стенкой, рядом повышение эхогенности паракологической клетчатки (указано стрелкой)*
Figure 3. *Inflamed diverticulum with hyperechoic contents, hypoechoic wall, next to an increase in echogenicity of paracolic fiber (indicated by an arrow)*

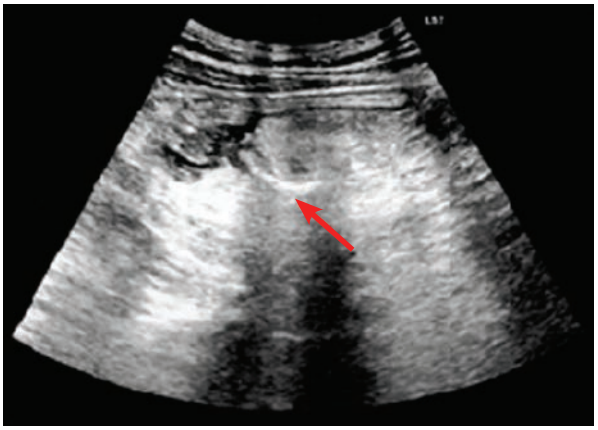

Рисунок 4. *Перфорация дивертикула, четко видна связь газа в паракологической клетчатке с просветом дивертикула (указано стрелкой)*
Figure 4. *Perforation of the diverticulum, the connection of the gas in the paracolic fiber with the lumen of the diverticulum is clearly visible (indicated by the arrow)*

Гистологическое исследование макропрепарата регистрационный №48787/08 от 15.12. 2021 — эрозивно-язвенный энтероколит, очаговые некрозы стенки кишки, перфорация толстой кишки, острые абсцессы брыжейки. Фрагменты большого сальника с очаговыми кровоизлияниями. Края резекции без особенностей.

После купирования обострения заболевания для подтверждения эффективности УЗ диагностики у 58 больных проведена ирригоскопия, у 7 — колоноскопия, у 2 — компьютерная томография, у 2 — магнитно-резонансная томография, которые подтвердили диагноз дивертикулярной болезни. Данные УЗИ подтвердились так же на операции у 10 больных, которые были экстренно оперированы.

Полученные результаты ультразвуковой диагностики представляются важными для ургентной хирургии, так как осложнения ДБОК приходится дифференцировать со многими другими острыми хирургическими заболеваниями органов брюшной полости.

ВЫВОДЫ

Трансабдоминальное УЗИ органов брюшной полости является высокоинформативным, доступным и малоинвазивным методом диагностики дивертикулярной болезни ободочной кишки.

Качество УЗИ в большей степени зависит от квалификации специалиста, поэтому следует регламентировать при обучении врачей УЗ диагностики обязательное обследование кишечника. Необходимо укреплять роль УЗИ как эффективного метода диагностики ДБОК.

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Устранение осложнений лечения болезни Гиршпрунга с использованием заднего сагиттального трансаноректального доступа (ЗСТАР) (клинические наблюдения)

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РЕЗЮМЕ *Представлены возможности использования заднего сагиттального трансаноректального доступа (ЗСТАР) при устранении осложнений оперативных вмешательств по поводу болезни Гиршпрунга со стороны промежности, малого таза и анального канала. На примере клинических случаев показано, что использование описанного доступа (ЗСТАР) позволяет получить достаточный обзор основных анатомических структур малого таза в условиях ситуации «замороженный таз», помогая избежать их повреждения в условиях рубцового изменения тканей.*

КЛЮЧЕВЫЕ СЛОВА: *ЗСТАР, задний трансаноректальный доступ, стеноз неоректум, замороженный таз, приобретенная ректоуретральная фистула, болезнь Гиршпрунга*

КОНФЛИКТ ИНТЕРЕСОВ: *авторы заявляют об отсутствии конфликта интересов*

АВТОРЫ ЗАЯВЛЯЮТ ОБ ОТСУТСТВИИ ФИНАНСОВОЙ ПОДДЕРЖКИ

ДЛЯ ЦИТИРОВАНИЯ: Степанова Н.М., Новожилов В.А., Звонков Д.А., Латынцева И.В. Устранение осложнений лечения болезни Гиршпрунга с использованием заднего сагиттального трансаноректального доступа (ЗСТАР) (клинические наблюдения). *Колопроктология*. 2023; т. 22, № 2, с. 118–124. https://doi.org/10.33878/2073-7556-2023-22-2-118-124

Treatment of complications after surgery for Hirschsprung's disease using posterior sagittal transanal approach (clinical observation)

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ABSTRACT *The experience of complications treatment after surgery for Hirschsprung's disease using posterior sagittal transanal approach is presented. It allows to obtain a sufficient overview of the main anatomical structures of the small pelvis in a "frozen pelvis" situation, helping to avoid their damage at the scar tissue changes.*

KEYWORDS: *PSTRA, posterior transanorectal approach, stenosis neorectum, frozen pelvis, acquired rectourethral fistula, Hirschsprung disease*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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Современный этап развития хирургии болезни Гиршпрунга ознаменован оптимизацией и внедрением минимально инвазивных вмешательств на толстой кишке и промежности. Однако остается довольно высоким процент возникающих послеоперационных осложнений, требующих повторных вмешательств, в том числе со стороны промежности и малого таза. Достижение, в первую очередь, удовлетворительных функциональных результатов при повторных вмешательствах в малом тазу — всегда трудный вызов, требующий поиска оптимальных хирургических приемов.

За последние десятилетия в мировой и отечественной литературе опубликовано незначительное количество работ, посвященных возможностям сагиттальных доступов в лечении различных заболеваний тазовых органов у детей. Преимущественное внимание уделяется переднему сагиттальному трансаноректальному доступу (ПСТАР) для коррекции высокого урогенитального синуса, травматических повреждений уретры и вторичных ректоуретральных свищей [1–7].

Сообщения о применении и результатах использования заднего сагиттального трансаноректального доступа (ЗСТАР) единичны [8]. В конце прошлого столетия Пенья А. с соавторами (1992) описал серию успешных случаев коррекции высокого урогенитального синуса с одномоментным использованием переднего и заднего трансаноректального доступов. Суть способа заключается в продольном срединном рассечении промежности от уровня дистального копчикового/крестцового позвонка до устья урогенитального синуса с рассечением передней и задней стенки прямой кишки. По мнению авторов, данный доступ позволяет увеличить обзор и доступность к основным анатомическим структурам промежности, сохранить аноректальную иннервацию. Использование ЗСТАР при выполнении повторных операций в малом тазу по поводу осложнений хирургической коррекции болезни Гиршпрунга выглядит привлекательным, поскольку реконструкция проводится в условиях выраженных рубцовых изменений тканей.

ЦЕЛЬ РАБОТЫ

Представить возможности использования заднего трансаноректального доступа при повторных вмешательствах по поводу болезни Гиршпрунга в детском возрасте.

ПАЦИЕНТЫ И МЕТОДЫ

С 2020 года на базе Центра аномалий развития аноректальной области и колоректальной хирургии детского возраста ОГАУЗ «Городская Иано-Матренинская детская клиническая больница» г.Иркутска оперировано 3 детей с использованием заднего трансаноректального доступа (ЗСТАР) в условиях формирования ситуации «замороженный таз» после неоднократных оперативных вмешательств по поводу болезни Гиршпрунга. В представленной группе детей с врожденным аганглиозом неоднократные оперативные вмешательства у них закончились формированием приобретенной ректобульбарной фистулы (1), ретракцией и стенозом низведенной кишки (2). Средний возраст больных составил 3,3 года и на момент вмешательства с использованием ЗСТАР пациенты имели в анамнезе до 4 операций. Всем детям изначально выполнено превентивное стомирование (илеостома). Объем повторных реконструктивных вмешательств заключался в комбинированном брюшно-промежностном подходе с использованием лапароскопии (1) и лапаротомии (2), резекции и низведении толстой кишки с формированием эндоректального колоанального анастомоза. Для разобщения ректобульбарной фистулы и иссечения стеноза во всех случаях использовался задний трансаноректальный доступ в описанной авторами модификации.

Клинический пример 1

Мальчик Б., 3 года. В возрасте 1 месяца выполнено лапароскопически ассистированное трансанальное эндоректальное низведение по Соаве-Джорджсену по поводу болезни Гиршпрунга с коротким

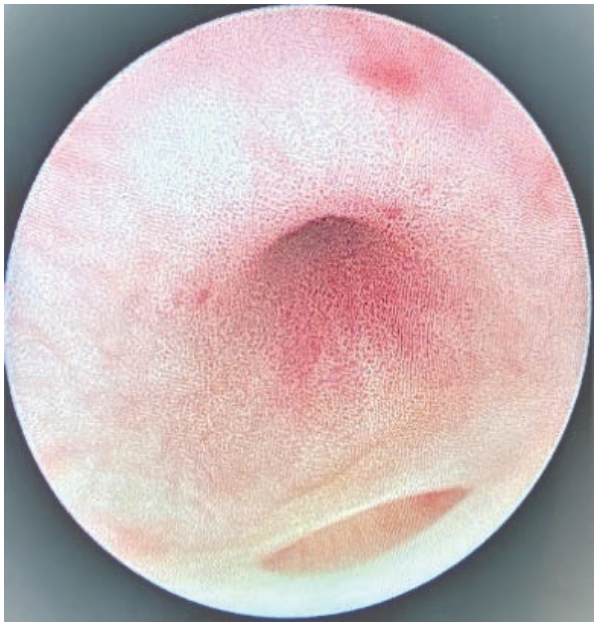


Рисунок 1. *Уретроскопия. Визуализация свищевого отверстия в бульбарной части уретры*
Figure 1. *Urethroscopy. Visualization of the fistulous opening in the bulbar part of the urethra*

аганглионарным сегментом, осложненное в дальнейшем ретракцией и стенозом низведенной кишки. Консервативное лечение бужированием на протяжении более года — без эффекта. Поводом для обращения в Центр явилось появление в моче примеси кала и пузырьков газа при мочеиспускании. При ретроградном заполнении низведенной кишки раствором красителя отмечено появление примеси последнего в моче. Присутствие свища достоверно подтверждено уретроскопией: в бульбарной части уретры — свищевое отверстие диаметром до 2 мм (Рис. 1).

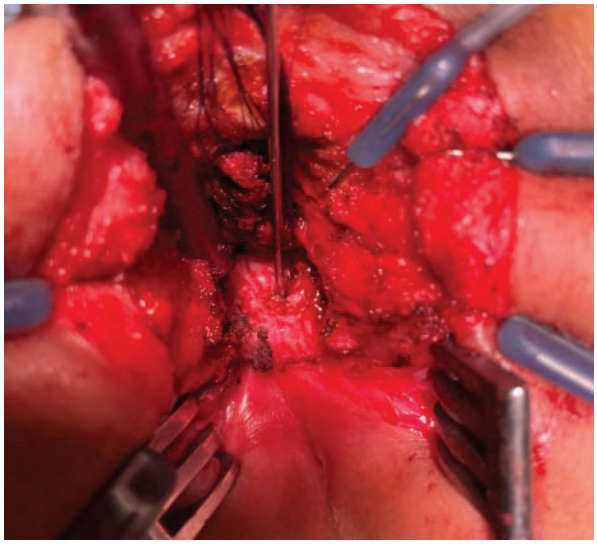
В 3 года выполнено оперативное лечение в объеме лапароскопически ассистированной резекции и низведении толстой кишки с обязательным выполнением интраоперационной биопсии, разобщения ректобульбарной фистулы 3СТАР-доступом.

Основные моменты операции.

I этап — Лапароскопия. Внеслизистая экспресс-биопсия толстой кишки на 8 см от уровня тазовой брюшины, висцероадгезиолизис, мобилизация сигмовидной кишки и ранее низведенной кишки до уровня фистулы.

II этап — 3СТАР доступ, разобщение ректоуретральной бульбарной фистулы. Мобилизация прямой кишки с техническими трудностями, связанными с выраженным рубцовым процессом нижней трети низведенной кишки. В ходе мобилизации обнаружена ректобульбарная фистула с формированием со стороны прямой кишки сосочкообразного выпячивания (Рис. 2, 3). Резекция сегмента прямой и низведенной кишки со свищом на протяжении 15 см до уровня ранее выполненной положительной, относительно присутствия ганглиев, биопсии.

При осмотре под наркозом на 12 сутки установлено расхождение линии швов на уровне анального канала со стороны слизистой на глубину мышечного слоя на протяжении 1,0 см — лечение консервативное. Контрольный осмотр через 3 недели показал полную репарацию линии 3СТАР-доступа без признаков



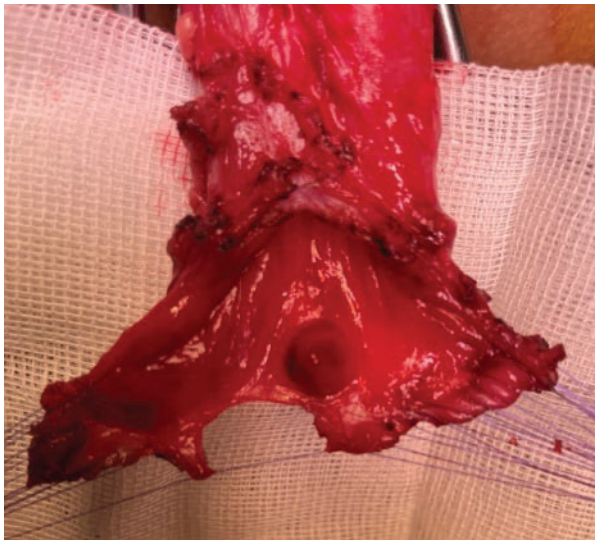


Рисунок 2–3. *В просвет ректоуретральной фистулы установлен пуговчатый зонд. Устье ректоуретральной фистулы после мобилизации прямой кишки и её разобщения*
Figure 2–3. *A bellied probe is placed in the lumen of the rectourethral fistula. The mouth of a rectourethral fistula after mobilization and separation*

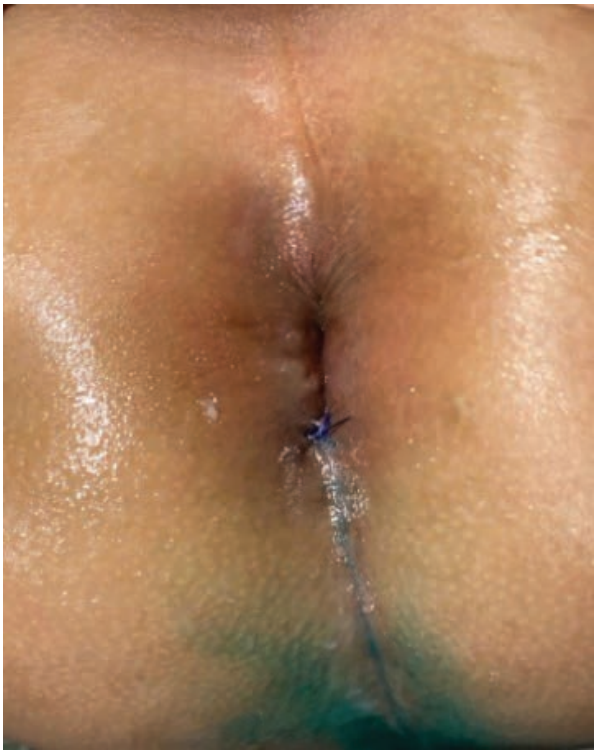


Рисунок 4. *Вид промежности через 3 недели после ЗСТАР*
Figure 4. *Perineal view 3 weeks after PSTRA*

стенозирования и деформации анального канала (Рис. 4).

После подготовительного этапа (лечебно-профилактическое бужирование, тренировочные клизмы) через 3 месяца выполнено закрытие илеостомы. Катамнез прослежен на протяжении 1 года: дефекация осознанная, 1–2 раза/ 24 часа, 4–5 тип кала по бристольской шкале, признаков анальной инконтиненции нет, с программы бужирования ребенок снят.

Клинический пример 2

Мальчик К., 4 года. Диагностирована болезнь Гиршпрунга с протяженным аганглионарным сегментом в возрасте 6 месяцев. После череды неоднократных вмешательств и выполнения брюшно-промежностного трансанального низведения (способ Свенсона) диагностирована протяженная ретракция низведенного сегмента кишки. С целью сохранения сегмента толстой кишки (восходящая ободочная кишка) промежуточным этапом была выполнена резекция на уровне ретракции с формированием концевой асцендостомы сроком на 3 месяца (Рис. 5, 6).

В 4 года выполнено комбинированное оперативное лечение, включающее абдоминальный и промежностный этапы.

Основные моменты операции.

I — абдоминальный этап. Полнослойная экспресс-биопсия стенки толстой кишки с целью определения уровня резекции и низведения, мобилизация восходящей ободочной кишки и илеоцекального угла (деваскуляризация в бассейне a. et v. colica dextra, прием «разворот на 180^0»), висцероадгезиолизис входа в малый таз с техническими трудностями,

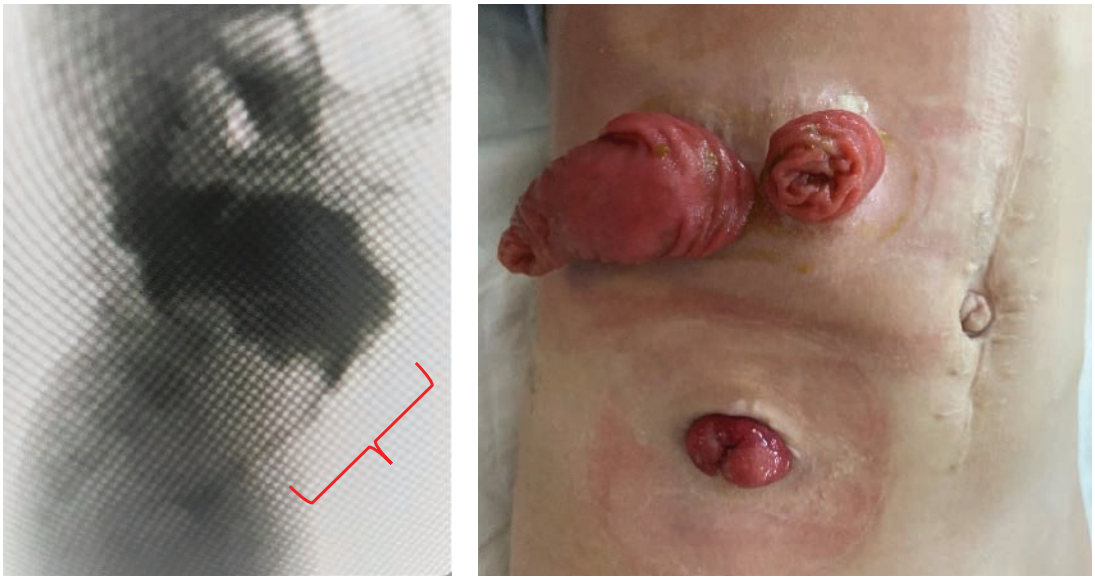


Рисунок 5–6. *Ирригограмма. Протяженная ретракция низведенной толстой кишки (указана стрелкой). Множественные стомы на передней брюшной стенке (двойная раздельная илеостома с эвагинацией приводящего отдела, в правой подвздошной области концевая асцендостома)*
Figure 5–6. *Irrigogram. Extended retraction of the relegated colon (indicated by an arrow). Multiple stomas on the anterior abdominal wall*

связанными с перенесенным воспалением и исходом в облитерацию дистального отдела толстой кишки.

II — 3CTAP-доступ, асцендоректальный анастомоз. При выполнении доступа установлена полная анатомическая сохранность анального канала и стенки прямой кишки на протяжении 2,0 см от зубчатой линии. Проксимальнее от линии ранее сформированного анастомоза — выраженный рубцовый процесс, облитерирующий низведенную кишку и вход в малый таз. С помощью электрокоагуляции выполнен адгезиолизис, после чего произведено низведение кишки и формирование асцендоректального анастомоза (Рис. 7–9).

На 12 сутки осмотр под общим обезболиванием показал состоятельность линии эндоректального анастомоза, отсутствие признаков деформации и стенозирования анального канала. В последующем в план реабилитации были включены лечебно-профилактическое бужирование и тренировочные клизмы. Закрытие двойной раздельной илеостомы выполнено через 3 месяца. Через 1 год 4 мес. при контрольном осмотре проявлений анальной инконтиненции нет, дефекация осознанная, 3–4 раза в сутки, 5 тип кала по Бристольской шкале.

ОБСУЖДЕНИЕ

В доступной отечественной литературе мы не нашли сообщений об использовании заднего трансаноректального доступа в лечении приобретенных ректоорганных фистул и стеноза неоректум при повторных вмешательствах по поводу болезни Гиршпрунга в детском возрасте. В описанных нами наблюдениях представлены пациенты с приобретенной ректобульбарной фистулой, стенозом и ретракцией неоректум. В первом случае повреждение уретры — следствие длительного травматичного бужирования стеноза неоректум, во втором — очевидной причиной стеноза и ретракции явилось нарушение кровообращения низведенного сегмента толстой кишки.

Необходимо отметить, что лечение данных приобретенных состояний сопряжено с рядом трудностей: присоединение местного воспалительного процесса, последующих рубцовых изменений тканей малого таза, промежности, анального канала. Поэтому поиск способов устранения этих осложнений привлекает внимание оперирующих детских хирургов и колопроктологов.

В диагностической программе в случае ректоуретральной бульбарной фистулы наиболее информативным считаем уретроскопию. Состояние малого таза и взаимоотношение структур требует комплекса диагностических мероприятий, зависящих от конкретной клинической ситуации: осмотр под общим обезболиванием, ано/ректоскопия, колоноскопия через стому/ирригоскопия с использованием исключительно водорастворимого контраста, МРТ структур малого таза, УЗИ промежности.

Первый клинический пример демонстрирует использование 3CTAP в случае хирургического лечения приобретенной ректобульбарной фистулы у пациента с болезнью Гиршпрунга после трансанального эндоректального низведения по Соаве-Джорджсену (LAEPT). Вероятной причиной осложнения могло стать повреждение уретры вследствие нарушения технологии бужирования. Использование лапароскопии позволило выполнить интраоперационную экспресс-биопсию с целью определения уровня резекции и ренизведения, адекватно мобилизовать толстую кишку до уровня свища. Выполнение 3CTAP в условиях ограниченного доступа и рубцово-измененных мягких тканей малого таза обеспечило хорошую визуализацию и возможность адекватно разобщить приобретенную ректобульбарную фистулу.

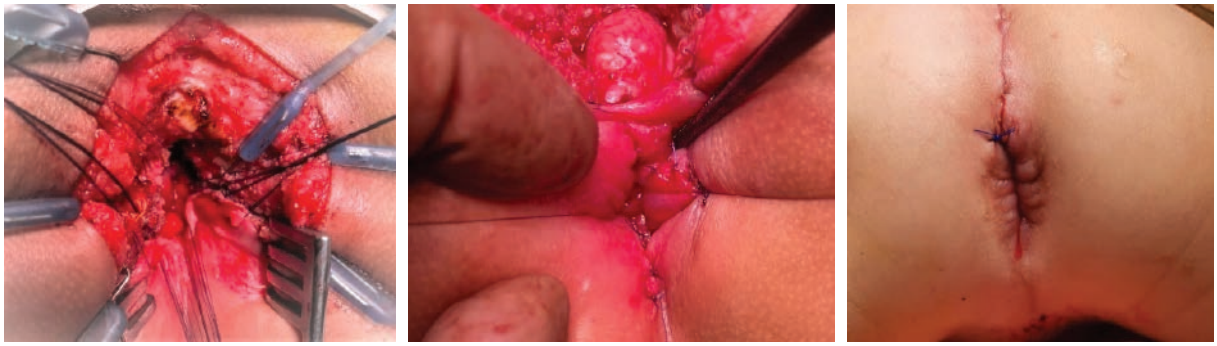


Рисунок 7-9. *Этапы 3CTAP. Мобилизация стенки прямой кишки. Формирование асцендоректального анастомоза. Вид промежности после операции*

Figure 7-9. *Stages of PSTRA. Mobilization of the rectal wall. Formation of the ascendorectal anastomosis. View of the perineum after surgery*

Следует понимать, что каждая повторная операция в малом тазу, сопряженная с развитием осложнений и воспаления, приводит к выраженному спаечно-рубцовому процессу и формированию ситуации «замороженный таз». Протяженная ретракция низведенной кишки, возникшая вследствие регионарного нарушения кровообращения, привела к рубцово-воспалительной облитерации малого таза. Использование заднего трансаноректального доступа позволило под визуальным контролем иссечь рубцовые ткани и низвести сегмент ободочной кишки с последующим формированием эндоректального анастомоза.

Симметричное продольное рассечение тканей сфинктерного аппарата, леваторного комплекса задней стенки неоректум с обязательной интраоперационной маркировкой элементов сфинктера позволяет сохранить в последующем функциональность замыкательного аппарата. У всех детей проявлений анальной инконтиненции не было.

Таким образом, несомненные преимущества данного оперативного приема состоят в том, что в условиях рубцового процесса и ограниченной визуализации возможно резецировать патологически измененную кишку, устранить патологические соустья и выполнить полноценную реконструкцию тазовых структур без утраты удерживающей функции запирательного аппарата неоректум.

ЗАКЛЮЧЕНИЕ

Использование заднего трансаноректального доступа при оперативной коррекции осложнений хирургии болезни Гиршпрунга считаем перспективным, поскольку он позволяет в условиях ограниченного пространства и рубцово-спаечного процесса в полости малого таза выполнить разобщение анатомических структур, локальный адгезиолизис, контроль низведения и формирование эндоректального колоанального анастомоза.

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Комментарии редколлегии к статье

«Устранение осложнений лечения болезни Гиршпрунга с использованием заднего сагиттального трансаноректального доступа (ЗСТАР) (клинические наблюдения)», авторы: Степанова Н.М., Новожилов В.А., Звонков Д.А., Латынцева И.В.

Несомненно, поиск удобного и безопасного оперативного доступа для коррекции осложнений хирургического лечения болезни Гиршпрунга является актуальной проблемой как в педиатрической практике, так и у взрослых пациентов. Авторами использован доступ, который впервые был описан Альберто Пена, сообщившем о применении его с хорошими функциональными результатами у 54 детей, страдавших различными врожденными аноректальными пороками развития. Этот доступ активно применяется детскими хирургами и в настоящее время. В том числе, подобная методика описана как один из вариантов лечения приобретенных стенозов прямой кишки в диссертации Ионова А.Л. Однако имплементация методов, используемых в педиатрической практике, в хирургию взрослых пациентов требует крайней осторожности. Учитывая высокий риск развития анальной инконтиненции после такого радикального рассечения сфинктерного аппарата прямой кишки и мышц тазового дна, необходимы дополнительные исследования, прежде чем рекомендовать применение описанного доступа у взрослых пациентов.

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Palliative primary tumor resection in minimally symptomatic (asymptomatic) patients with colorectal cancer and synchronous unresectable metastases versus chemotherapy alone (a meta-analysis)

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ABSTRACT *AIM: to evaluate outcomes (overall survival, rate of surgical intervention due to complications of first treatment, 30-day mortality rate) of palliative primary tumor resection (PTR) followed by chemotherapy and chemotherapy/radiotherapy (chemo/RT) alone in patients with asymptomatic or minimally symptomatic colorectal cancer (CRC) and synchronous unresectable metastases.*

MATERIALS AND METHODS: a meta-analysis based on Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines was conducted on PubMed and Cochrane database. Odds ratio (OR) and 95% confidence interval (95% CI) were used as the treatment effect measure for comparing results. Combined overall effect measures were calculated for a random effect model. All analyses were performed using the Review Manager 5.3 software.

RESULTS: eighteen non-randomized studies, including a total of 2,999 patients (1,737 PTR and 1,262 chemo/RT) were identified. Gender, age, site of primary tumor and distant metastasis of patients were comparable between groups in all analyzed studies. Two-year (38.2% vs. 21.1%; OR 0.42; 95% CI 0.28–0.64; p < 0.0001) and 5-year (12.7% vs. 5.3%; OR 0.45; 95% CI 0.21–0.97; p = 0.04) overall survival rates were significantly higher in the PTR group than in the chemo/RT group. No significant differences in 30-day mortality rate between the two groups (1.7% vs. 1%; OR 1.92; 95% CI 0.79–4.68; p = 0.15). However, the rate of surgical intervention due to complications of first treatment was significantly lower in the PTR group comparing to the chemo/RT group (2.3% vs. 14.53%; OR 0.18; 95% CI 0.08–0.40; p < 0.0001). At the same time, one hundred and fourteen patients (13.8%; OR 0.19; 95% CI 0.09–0.40; p < 0.0001) in the chemo/RT group required surgery for symptoms associated with a primary tumor.

CONCLUSIONS: PTR in patients with asymptomatic or minimally symptomatic CRC and synchronous unresectable metastases significantly improves overall survival, allows to prevent surgical intervention due to complications related to primary tumor and is not associated with increased postoperative mortality rate comparing to systemic chemotherapy/radiotherapy as a treatment of first line. The current data are based on non-randomized comparative studies and data from early terminated randomized controlled trials (RCTs) and further well-designed RCTs are required.

KEYWORDS: *Colorectal cancer; palliative resection; asymptomatic primary tumor; unresectable metastases; chemotherapy; overall survival; meta-analysis*

CONFLICT OF INTEREST: *The authors declare no conflict of interest.*

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INTRODUCTION

Approximately 20% of patients with colorectal cancer (CRC) are diagnosed with stage IV and substantial number of them have unresectable synchronous metastases [1,2]. Currently, palliative primary tumor resection (PTR) for unresectable metastatic CRC is considered as an option

to control tumor related obstruction, perforation or bleeding.PTR is not recommended for patients with minimally symptomatic primary tumor. The standard treatment for these patients according to NCCN [3,4] and ESMO [5,6] guidelines is a systemic chemotherapy and radiotherapy for rectal carcinomas. Comparative studies investigating the benefit of initial palliative PTR for patients with distant metastatic disease demonstrated conflicting results.

Several randomized clinical trials (RCT) comparing PTR followed by chemotherapy and chemo/RT alone were initiated [7–11], but none of them have been completed to date. Numbers of published non-randomized comparative studies reported that PTR can prolong the survival in asymptomatic or minimally symptomatic patients with CRC and synchronous unresectable metastases [12–16], while others found no benefits of PTR [17–27]. One of the major concerns about PTR is the risks of postoperative morbidity and mortality [28], which potentially can delay the initiation of systemic treatment [29], lead to the progression of disease and decrease survival [30–33]. In addition, some authors reported that liver metastases of colorectal origin increased their growth if primary tumor had been removed [34,35].

Most published meta-analyses included data from patients with both symptomatic and asymptomatic primary tumors, and some included studies with heterogeneous population, which may bias the outcomes [36–39].

Thus, the aim of this analysis was to compare outcomes (overall survival, rate of surgical intervention due to complications of first treatment, 30-day mortality rate) in patients with minimally symptomatic (asymptomatic) CRC and synchronous unresectable metastases after palliative PTR followed by chemotherapy or chemo/RT alone.

MATERIALS AND METHOD

Search Strategy

The meta-analysis was conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (http://www.prisma-statement.org/) [40]. A literature search was performed through PubMed and Cochrane Database of Systematic reviews, using the following search strategy: (colon OR colorectal OR rectal) AND (cancer OR adenocarcinoma OR neoplasms OR carcinoma) AND ("palliative surgery" OR "primary tumor resection"). No restrictions were applied in terms of language, year or status of publication. Reference lists of selected publications, other systematic reviews or meta-analyses were hand-searched for additional relevant studies. The search period was from September, 1954 to March, 2022.

Inclusion and Exclusion Criteria

In accordance with the population, intervention, comparison, outcomes and study design (PICOS) criteria, the following eligibility criteria were selected for inclusion of the publications in the meta-analysis: (a) population: minimally symptomatic/asymptomatic patients with CRC and synchronous unresectable metastases; (b) intervention: surgical treatment, chemotherapy/radiotherapy; (c) comparison: PTR followed by chemotherapy versus chemo/RT alone; (d) outcomes: overall survival(OS), 30-day mortality rate, rate of surgical intervention due to complications of first treatment compared between two groups; and (e) study design: data from early terminated RCT, prospective/retrospective cohort trials or matched case-control (MCC) trials with sample size greater than 15.

The exclusion criteria were as follows: (a) lack of the sufficient data or outcomes of interest; (b) duplicate publication; (c) patients with primary-tumor symptoms and (d) non-comparative studies, reviews, meta-analyses, letters, case reports or conference abstracts. The search strategy is illustrated by Figure 1.

Data Extraction and Quality Assessment

Two authors (I.A. and M.A.) independently reviewed and assessed each study, according to the inclusion and exclusion criteria. In addition, they extracted and summarized the data from the included studies independently. Following information was collected: (a) study characteristics: the first author, country, year of publication, enrollment dates, number of patients, study type; (b) patient baseline characteristics: gender, age, Eastern Cooperative Oncology Group/World

Health Organization Performance Status (ECOG/WHO PS), site of primary tumor, site of distant metastasis, chemotherapeutic regimens; c) study outcomes: overall survival, 30-day mortality rate, rate of surgical intervention due to complication of first treatment. The quality of non-randomized trials was evaluated by using the Newcastle-Ottawa Scale (NOS) criterion [41], which allocates a maximum of 9 points to each study. A score ⩾ 6 indicated good quality [42].

The quality of included studies was determined by examining three factors: patient selection, comparability of the study groups and assessment of outcomes. Risk of bias of non-randomized trials was evaluated using the ROBINS-I [43]. If the mean and standard deviation (S.D.) were not provided, they were calculated using the method described by Wan et al. [44]. Inter-study heterogeneity was assessed by Chi^2 test and I^2 statistics as a measure describing degree of heterogeneity in which $P < 0.05$ was taken to indicate the presence of significant heterogeneity. Odds ratio was used as the treatment effect measure for comparing results. Combined overall effect measures were calculated for a random effect model and were presented with 95% coincidence interval. All p values < 0.05 were considered statistically significant. All analyses were performed using the Review Manager 5.3 software. The registration number in the International Prospective

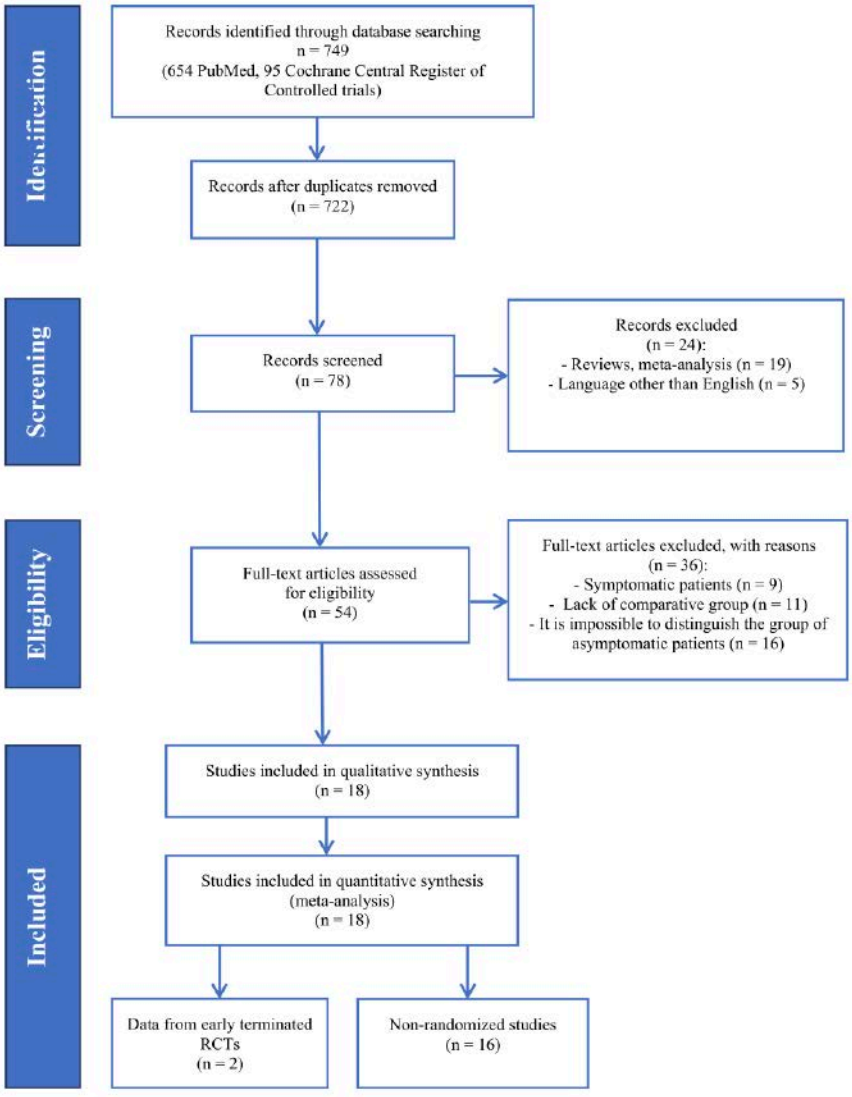

Figure 1. *Block diagram of literature search for a systematic review on PRISMA*

Table 1. The baseline characteristics of the included studies

First author, year of publication	Country	Years of the study	Study type	Patients (n)		NOS
				PTR	Chemo/RT	
Scoggins 1999 [17]	USA	1985–1997	RC, single	66	23	6
Ruo 2003 [12]	USA	1996–1999	RC, single	127	103	6
Michel 2004 [18]	France	1996–1999	RC, single	31	23	6
Benoist 2005 [19]	France	1997–2002	MCC, single	32	27	7
Galizia 2008 [13]	Italy	1995–2005	MCC, single	42	23	6
Seo 2010 [20]	Korea	2001–2008	PC, single	144	83	6
Cetin 2013 [21]	Turkey	2006–2010	RC, multi	53	46	6
Boselli 2013 [22]	Italy	2010–2011	RC, multi	17	31	6
Yun 2014 [23]	Korea	2000–2008	RC with PSM, single	113	113	8
Matsumoto 2014 [24]	Japan	2005–2011	RC, single	41	47	7
Watanabe 2014 [25]	Japan	2002–2009	RC, single	46	112	6
Ahmed 2015 [14]	Canada	1992–2005	RC, multi	521	313	6
Niitsu 2015 [26]	Japan	2007–2013	RC, single	42	15	7
Wang 2016 [15]	China	2011–2013	PC, single	118	73	7
Urvay 2020 [16]	Turkey	2009–2016	RC, multi	139	76	6
Doah 2021 [27]	Korea	2001–2018	RC, single	98	48	7
Park 2020 [45]	Korea	2013–2016	Early terminated RCT, multi	26 (23)*	22 (21)**	8
Kanemitsu 2021 [46]	Japan	2012–2019	Early terminated RCT, multi	81	84	8

*Note: PTR — primary tumor resection; chemotherapy/radiotherapy — chemo/RT; n — number of patients ; PC — prospective cohort study; RC — retrospective cohort study; MCC — Matched Case-Control study; RCT — randomized controlled trial; single — single-centre study; multi — multi-centre study; NOS — Newcastle-Ottawa scale; PSM — propensity score matching; * lost to follow-up n = 3; ** lost to follow-up n = 1*

Register of Systematic Reviews (PROSPERO) was CRD42022325629.

RESULTS

Study Characteristics

A total of 749 articles were identified at the initial literature search. After full text review of the remaining54 articles, 36 were excluded as they did not match the inclusion and exclusion criteria of this meta-analysis. Among these excluded studies, some were excluded due to the lack of comparative group, the others because they included data from patients with both symptomatic and asymptomatic primary tumors or it was not possible to distinguish the group of asymptomatic patients. Finally, 18 studies [12–27,45,46] were included in the meta-analysis (Fig. 1), with a total of 2,999 patients, of whom 1,737 were treated with PTR followed by chemotherapy (the PTR group) and 1,262 patients were first managed with chemo/RT alone (the chemo/RT group). There were 2matched case-control studies [13,19], 2 prospective cohort studies [15,20], 12 retrospective cohort study [12,14,16–18,21–27], and 2 studies with data from early terminated RCTs [45,46]. The baseline characteristics of the included studies are shown in Table 1. Heterogeneity of the studies ranged from 0% to 66%. The quality assessments of all NRCTs were evaluated using NOS and the results ranged from 6 to 8 stars, which corresponded to good quality. Risk of bias in the included studies was evaluated by using the ROBINS-I scale. All the included studies had an overall risk of bias: «low» — 3 studies, «moderate» — 12 studies, «severe» — 3 studies, «critical» — 0 studies.

Patients' Characteristics

The baseline characteristics of patients are reported in Table 2,3 and the information about available outcomes is demonstrated in Table 4,5. The rate of surgical intervention due to complications of first treatment was reported in 14 studies (Table 4). Gender, age, site of primary tumor and distant metastasis, ECOG/WHO PS of patients in the PTR and the chemo/RT groups were comparable in those studies. There were 571/952 (60%)

Table 2. *The baseline characteristics of patients*

First author	Age (Mean ± SD/median)		Gender (M/F)		ECOG/WHO PS 0-1/ ⩾ 2		Site of primary tumor C/(R or RS)		*Site of distant metastasis* (liver ± other location/ extra hepatic disease	
	PTR	Chemo/RT	PTR	Chemo/RT	PTR	Chemo/RT	PTR	Chemo/RT	PTR	Chemo/RT
Scoggins [17]	64 ± 13	64,75 ± 12,25	NA	NA	NA	NA	52/14	12/11	56/10	20/3
Ruo [12]	64 ± 10,83	61 ± 10,5	81/46	57/46	NA	NA	90/37	66/37	97/30	53/50
Michel [18]	59.8*	58.9*	17/14	16/7	25/6	21/2	28/3	15/8	31/0	23/0
Benoist [19]	60 ± 13	61 ± 12	19/13	18/9	NA	NA	23/9	23/4	32/0	27/0
Galizia [13]	62 ± 13	59 ± 14	28/14	15/8	31/11	17/6	35/7	18/5	42/0	23/0
Seo [20]	58*	56*	94/50	52/31	133/11	70/13	71/73	56/27	109/35	67/16
Cetin [21]	55 ± 11,25	52 ± 12,75	29/24	27/19	NA	NA	39/14	26/20	53/0	46/0
Boselli [22]	70 ± 7,5	73 ± 6,75	NA	NA	14/3	23/8	11/6	13/18	17/0	31/0
Yun [23]	59 ± 10,67	60 ± 8,67	73/40	68/45	NA	NA	70/43	79/34	96/17	100/13
Matsumoto [24]	66 ± 9,98	62,3 ± 8,39	25/16	33/14	38/3	44/3	29/12	36/11	NA	NA
Watanabe [25]	63 ± 10	60 ± 8,83	25/21	71/41	NA	NA	39/7	88/24	34/12	93/19
Ahmed [14]	69 ± 11,83	71 ± 9,5	297/224	186/127	419/102	200/113	365/156	196/117	400/121	243/70
Niitsu [26]	61.5 ± 4,13	59,8 ± 5,25	8/34	7/8	42/0	15/0	31/11	4/11	NA	NA
Wang [15]	57 ± 9,17	58 ± 8,5	65/53	43/30	103/15	61/12	73/45	42/31	NA	NA
Urvay [16]	59 ± 10,5	62 ± 9,83	85/54	51/25	101/38	44/32	NA	NA	NA	NA
Doah [27]	68 ± 14,29	67,8 ± 9,92	49/49	29/19	NA	NA	68/30	27/21	72/26	31/17
Park [45]	62.3 ± 11,8	58.8 ± 12,1	21/5	12/10	25/1	20/2	17/9	18/4	NA	NA
Kanemitsu [46]	64,3 ± 7,54	65 ± 9,04	45/36	45/39	81/0	84/0	75/6	78/6	60/21	60/24

*Note: PTR — primary tumor resection; chemotherapy/radiotherapy — chemo/RT; SD — standard deviation; ECOG/WHO PS — Eastern Cooperative Oncology Group/ World Health Organization Performance Status; M — male; F — female; C — colon; R — rectum; RS — rectosigmoid colon; NA — not available; * — median*

males in the PTR group and 486/804 (60%) in the chemo/RT group ($p = 0.89$; test for heterogeneity: df = 12 (P = 0.50), $I^2 = 0\%$) in 13 studies, data were not available in 1 study. In 12 studies the mean difference of age between the two groups was 0.90 (95% CI: -0.30 to 2.10; $p = 0.14$; test for heterogeneity: df = 11 (P = 0.23), $I^2 = 22\%$; $n = 1564$). There were 309/1,018 (30%) patients with rectal or rectosigmoid colon tumors in the PTR group and 243/827 (29%) in the chemo/RT group in 14 studies ($p = 0.46$; test for heterogeneity: df = 13 (P = 0.005), $I^2 = 57\%$). In 11 studies patients with metastatic liver disease were prevalent in both groups: 682/833 (82%) and 543/685 (79%) in the PTR and the chemo/RT groups, respectively ($p = 0.71$; test for heterogeneity: df = 6 (P = 0.007), $I^2 = 66\%$), data were not available in 3 studies. In 7 studies with available ECOG/WHO PS scores, most patients in both groups had scores from 0 to 1: 436/483 (90%) patients in the PTR group and 317/355 (89%) in the chemo/RT group(P = 0.22; test for heterogeneity: df = 5 (P = 0.53), $I^2 = 0\%$). Thirty-day mortality rate was assessed in 16 studies (Table 4). Gender, age, site of primary tumor and distant metastasis, ECOG/WHO PS was similar between the two groups in these studies. There were 579/994 (58%) males in the PTR group and 493/819 (60%) in the chemo/RT group in 14 studies ($p = 0.6$; test for heterogeneity: df = 13 (P = 0.29), $I^2 = 15\%$), but data were not available in 2 studies. In 14 studies the mean difference of age between the two groups was 0.77 (95% CI: -0.36 to 1.91;

Table 3. *The baseline characteristics of patients. Chemotherapy regimens*

First author	PTR	Chemo/RT
Scoggins [17]	NA	5-FU-based CT ± RT
Ruo [12]	NA	5-FU ± leucovorin ± RT
Michel [18]	Oxaliplatin/irinotecan	Oxaliplatin/irinotecan ± RT
Benoist [19]	5-FU ± leucovorin ± irinotecan	5-FU ± leucovorin ± irinotecan
Galizia [13]	5-FU ± oxaliplatin/irinotecan	5-FU ± oxaliplatin/irinotecan
Seo [20]	5-FU ± oxaliplatin/ irinotecan	5-FU ± oxaliplatin/ irinotecan
Cetin [21]	IFL + bevacizumab/XELOX + bevacizumab/ FOLFIRI + bevacizumab	XELOX + bevacizumab/FOLFIRI + bevacizumab
Boselli [22]	FOLFOX ± bevacizumab	FOLFOX ± bevacizumab
Yun [23]	Oxaliplatin-based CT ± targeted agents/ irinotecan-based CT ± targeted agents/ 5-fluorouracil-based CT ± targeted agents	Oxaliplatin-based CT ± targeted agents/ irinotecan-based CT ± targeted agents/ 5-fluorouracil-based CT ± targeted agents
Matsumoto [24]	FOLFOX/FOLFIRI/oxaliplatin + S-1 (SOX)/ CPT-11 + UFT/LV/simplifiedLV5FU2/UFT/LV	FOLFOX ± bevacizumab/FOLFOX ± cetuximab/ FOLFIRI ± bevacizumab/irinotecan + S-1 (IRIS)/ oxaliplatin + S-1 + bevacizumab ± RT
Watanabe [25]	5-FU/ IFL/ FOLFOX/FOLFIRI + SOL/FOLFOX + sunitinib regimen + bevacizumab/FOLFIRI + bevacizumab	5-FU/ IFL/ FOLFOX/FOLFIRI + SOL/ FOLFOX + sunitinib regimen + bevacizumab/ FOLFIRI + bevacizumab
Ahmed [14]	5-FU + leucovorin/oxaliplatin-based CT ± bevacizumab/irinotecan-based CT ± bevacizumab	5-FU + leucovorin/oxaliplatin-based CT ± bevacizumab/irinotecan-based CT ± bevacizumab ± RT
Niitsu [26]	mFOLFOX6 ± bevacizumab or cetuximab or panitumumab/XELOX ± bevacizumab or cetuximab or panitumumab/FOLFIRI	mFOLFOX6 ± bevacizumab or cetuximab or panitumumab/XELOX ± bevacizumab or cetuximab or panitumumab/FOLFIRI
Wang [15]	FOLFOX/XELOX/FOLFIRI + bevacizumab	FOLFOX/XELOX/FOLFIRI + bevacizumab ± RT
Urvay [16]	(FOLFIRI or FOLFOX or XELOX) ± (bevacizumab or cetuximab or panitumumab)	(FOLFIRI or FOLFOX or XELOX) ± (bevacizumab or cetuximab or panitumumab)
Doah [27]	Fluorouracil/capecitabine/(fluorouracil ocapecitabine) + (irinotecan or oxaliplatin) ± (bevacizumab or cetuximab)	Fluorouracil/capecitabine/(fluorouracil or capecitabine) + (irinotecan or oxaliplatin) ± (bevacizumab or cetuximab)
Park [45]	(FOLFIRI or FOLFOX) ± (cetuximab or bevacizumab)	(FOLFIRI or FOLFOX) ± (cetuximab or bevacizumab)
Kanemitsu [46]	mFOLFOX6 + bevacizumab/CapeOX + bevacizumab/ irinotecan/TAS-102/ EGFR antibodies/ S-1	mFOLFOX6 + bevacizumab/CapeOX + bevacizumab/ irinotecan/TAS-102/ EGFR antibodies/ S-1

Note: PTR — primary tumor resection; chemotherapy/radiotherapy — chemo/RT; NA — not available; FOLFIRI = 5-FU + leucovorin + irinotecan; FOLFOX = 5-FU + leucovorin + oxaliplatin; S-1 = tegafur + gimeracil + oteracilpotassium; CapeOX = capecitabine + oxaliplatin

$p = 0.18$; test for heterogeneity: df = 13 (P = 0.18), $I^2 = 25\%$; $n = 1{,}669$). There were 326/1,077 (30%) patients with rectal or rectosigmoid colon tumors in the PTR group and 272/873 (31%) in the chemo/RT group in 16 studies ($p = 0.16$; test for heterogeneity: df = 15 (P = 0.0005), $I^2 = 62\%$). The information about extent of metastatic disease was available in 12 studies: patients with metastatic liver disease were 699/850 (82%) and 574/716 (80%) in the PTR and the chemo/RT groups, respectively ($p = 0.71$; test for heterogeneity: df = 6 (P = 0.007), $I^2 = 66\%$). In 9 studies with available ECOG/WHO PS scores, most patients in both groups had scores from 0 to 1: 492/542 (91%) in the PTR

Table 4. *Outcomes: rate of surgical intervention due to complication of first treatment, 30-day mortality*

First author	Patients (n)		Surgical intervention due to complication of first treatment (%)		30-day mortality (%)	
	PTR	Chemo/RT	PTR	Chemo/RT	PTR	Chemo/RT
Scoggins [17]	66	23	3	8,7	4,6	0
Ruo [12]	127	103	4,7	29	1,6	0
Michel [18]	31	23	0	21,7	0	0
Benoist [19]	32	27	0	14,8	0	0
Galizia [13]	42	23	0	17,4	0	0
Seo [20]	144	83	2,8	4,8	0	0
Cetin [21]	53	46	5,7	4,4	0	0
Boselli [22]	17	31	NA	NA	29,4	19,3
Yun [23]	113	113	0,9	0	0,9	2,7
Matsumoto [24]	41	47	0	38,3	0	0
Watanabe [25]	46	112	0	16	0	0
Ahmed [14]	521	313	NA	NA	4,8	NA
Niitsu [26]	42	15	NA	20	0	0
Wang [15]	118	73	5,1	6,6	2,5	0
Urvay[16]	139	76	NA	NA	NA	9,2
Doah [27]	98	48	0	27,1	0	0
Park [45]	26	22	0	18,2	3,8	0
Kanemitsu [46]	81	84	1,2	13	4	0

Note: PTR — primary tumor resection; chemotherapy/radiotherapy — chemo/RT; NA — not available; n — number of patients

group and 355/401 (89%) in the chemo/RT group (P = 0.17; test for heterogeneity: df = 6 (P = 0.65), I^2 = 0%).

Two-year overall survival was assessed in 7 studies (Table 5). The groups were comparable in terms of sex, age, site of primary tumor and distant metastasis. There were 299/484 (62%) males in the PTR group and 196/324 (60%) in the chemo/RT group (p = 0.75; test for heterogeneity: df = 5 (P = 0.25), I^2 = 24%) in 6 studies, data were not available in 1 study. In 7 studies the mean difference of age between the two groups was 0.13 (95% CI: -2.05 to 2.31; p = 0.91; test for heterogeneity: df = 6 (P = 0.07), I^2 = 49%; n = 897). There were 121/411 (29%) patients with rectal or rectosigmoid tumors in the PTR group and 92/271 (34%) in the chemo/RT group (p = 0.48; test for heterogeneity: df = 5 (P = 0.12), I^2 = 43%) in 6 studies, data were not available in one study. In 4 studies patients with metastatic liver disease were prevalent in both groups: 227/267 (85%) and 123/176 (70%) in the PTR and the chemo/RT groups, respectively (p = 0.3; test for heterogeneity: df = 1 (P = 0.09), I^2 = 65%), data were not available in 3 studies. There were significant differences between the two groups in the comorbidity in 4 studies with available ECOG/WHO PS scores: 260/325 (80%) patients in the PTR group and 142/194 (73%) in the chemo/RT grouphad scores from 0 to 1 (p = 0.03; test for heterogeneity: df = 3 (P = 0.72), I^2 = 0%). Though in most studies fluorouracil-based chemotherapy regimens combined with targeted agents was used, the protocols of systemic treatment varied in great degree (Table 3). Because in most studies median follow-up was reported without range, it was impossible to calculate the mean and standard deviation using the method described by Wan and colleagues [44].

Table 5. Outcomes: overall survival (OS), median survival

First author	Patients (n)		Follow-up mean ± SD/ median (months)	OS (%)		Median survival (months)		P value
	PTR	Chemo/RT		PTR	Chemo/RT	PTR	Chemo/RT	
Scoggins [17]	66	23	NA	17 (2-year)	18 (2-year)	14,5	16,6	0,59
Ruo [12]	127	103	NA	25 (2-year)	6 (2-year)	16	9	0,001
Michel [18]	31	23	NA	NA	NA	21	14	0,718
Benoist [19]	32	27	24*	44 (2-year)	41 (2-year)	23	22	0,753
Galizia [13]	42	23	16*	38 (2-year)	17 (2-year)	15,2	12,3	0,03
Seo [20]	144	83	49*	NA	NA	22	14	NS
Cetin [21]	53	46	NA	NA	NA	23	17	0,322
Boselli [22]	17	31	7*	17,6 (1-year)	19,4 (1-year)	4	5	NS
Yun [23]	113	113	16 ± 26,5	4,9 (5-year)	3,5 (5-year)	17,2	14,4	0,16
Matsumoto [24]	41	47	21,3*	NA	NA	23,9	22,6	NS
Watanabe [25]	46	112	26*	NA	NA	19,9	19	NS
Ahmed [14]	521	313	NA	NA	NA	19,7	8,4	< 0,0001
Niitsu [26]	42	15	19,2/13,4**	NA	NA	23,9	13,4	0,093
Wang [15]	118	73	20*	NA	NA	22,5	17.8	< 0,01
Urvay [16]	139	76	24,6 ± 17,4	57 (2-year) 19 (5-year)	30 (2-year) 8 (5-year)	29,6	14,2	< 0,001
Doah [27]	98	48	18*	NA	NA	18	15	0,15
Park [45]	23	21	15*	69,5 (2-year)	44,8 (2-year)	NA	NA	0,058
Kanemitsu [46]	81	84	22,1*	32,9 (3-year)	33 (3-year)	25,9	26,4	0,72

*Note: PTR — primary tumor resection; chemotherapy/radiotherapy — chemo/RT; NA — not available; n — number of patients; OS — overall survival; NS — no significant differences (P > 0,05); SD — standard deviation; * — median; ** — 19,2 months in the PTR group and 13,4 in Chemo/RT group (median)*

The median follow-up of the studies ranged from 15 to 24.6 months.

Five-year overall survival was assessed in 2 studies (Table 5). Gender, age, follow-up of patients in the PTR and the chemo/RT groups were similar in those studies. There were 158/252 (63%) males in the PTR group and 119/189 (63%) in the chemo/RT group (P = 0.93; test for heterogeneity: df = 1 (P = 0.27), I^2 = 18%). The mean difference of age between the two groups in those studies was — 1.92 (95% CI: -3.87 to 0.03; P = 0.05; test for heterogeneity: df = 1 (P = 0.30), I^2 = 8%; *n* = 441). The mean difference of follow-up between the two groups was 0.00 (95% CI: -3.98 to 3.98; P = 1.00; test for heterogeneity: df = 1 (P = 1.00), I^2 = 0%; *n* = 441). Only 1 study reported the data site of primary tumor and distant metastasis of patients: 43/113 (38%) patients were with rectal tumor in the PTR group and 34/113 (30%) in the chemo/RT group (P = 0.52), 96/113 (85%) patients in the PTR group and 100/113 (88%) in the chemo/RT group had metastatic liver disease (P = 0.43). Only 1 study had the data comorbidity available, most of the patients had ECOG PS 0-1: 101/139 (73%) patients in the PTR group and 44/76 (58%) in the chemo/RT group (P = 0.12).

Outcomes: rate of surgical intervention due to complications of first treatment and 30-day mortality rate

There were 14 studies [12,13,15,17–21,23–25,27,45,46] that evaluated the rate of surgical intervention due to complications of first treatment (1,018 patients in the PTR group and 827 patients in the chemo/RT group) and 16 studies [12,13,15,17–27,45,46] that reported 30-day mortality rate (1,077 patients in the PTR group and 873 patients in the chemo/RT group) (Table 4).

There were significant differences between the two groups in the rate of surgical intervention due to complications of first treatment (2.3% vs.14.53%; OR 0.18; 95%CI 0.08 — 0.40; P < 0.0001; test for heterogeneity: df = 13 (P = 0.02), I^2 = 50%; *n* = 1,845) (Fig. 2A). One hundred and fourteen patients (13.8%; OR 0.19; 95%CI 0.09 — 0.40; P < 0.0001) in the chemo/RT group underwent surgery for symptoms related to the primary tumor (Fig. 2B). There were no significant differences between the two groups in the 30-day mortality rate (1.7% vs. 1%; OR 1.92; 95% CI 0.79–4.68; P = 0.15; test for heterogeneity: df = 6 (P = 0.71), I^2 = 0%; *n* = 1,950) (Fig. 2C).

Outcomes: 2-year and 5-yearoverall survival

Two-year overall survival was reported in 7 studies [12,13,15–17,19,45], including 547 patients in the PTR group and 346 patients in the chemo/RT group (Table 5). There were significant differences between the two groups in 2-year OS (38.2%vs. 21.1%; OR 0.42; 95% CI 0.28 — 0.64; P < 0.0001; test for heterogeneity: df = 6 (P = 0.20), I^2 = 29%; *n* = 893) (Fig. 3A). Five-year overall survival was assessed in 2 studies [16,23], including 252 patients in the PTR group and 189 patients in the chemo/RT group (Table 5). There were significant differences between the two groups in 5-year OS (12.7% vs. 5.3%; OR 0.45; 95%CI 0.21 — 0.97; P = 0.04; test for heterogeneity: df = 1 (P = 0.49), I^2 = 0%; *n* = 441) (Fig. 3B).

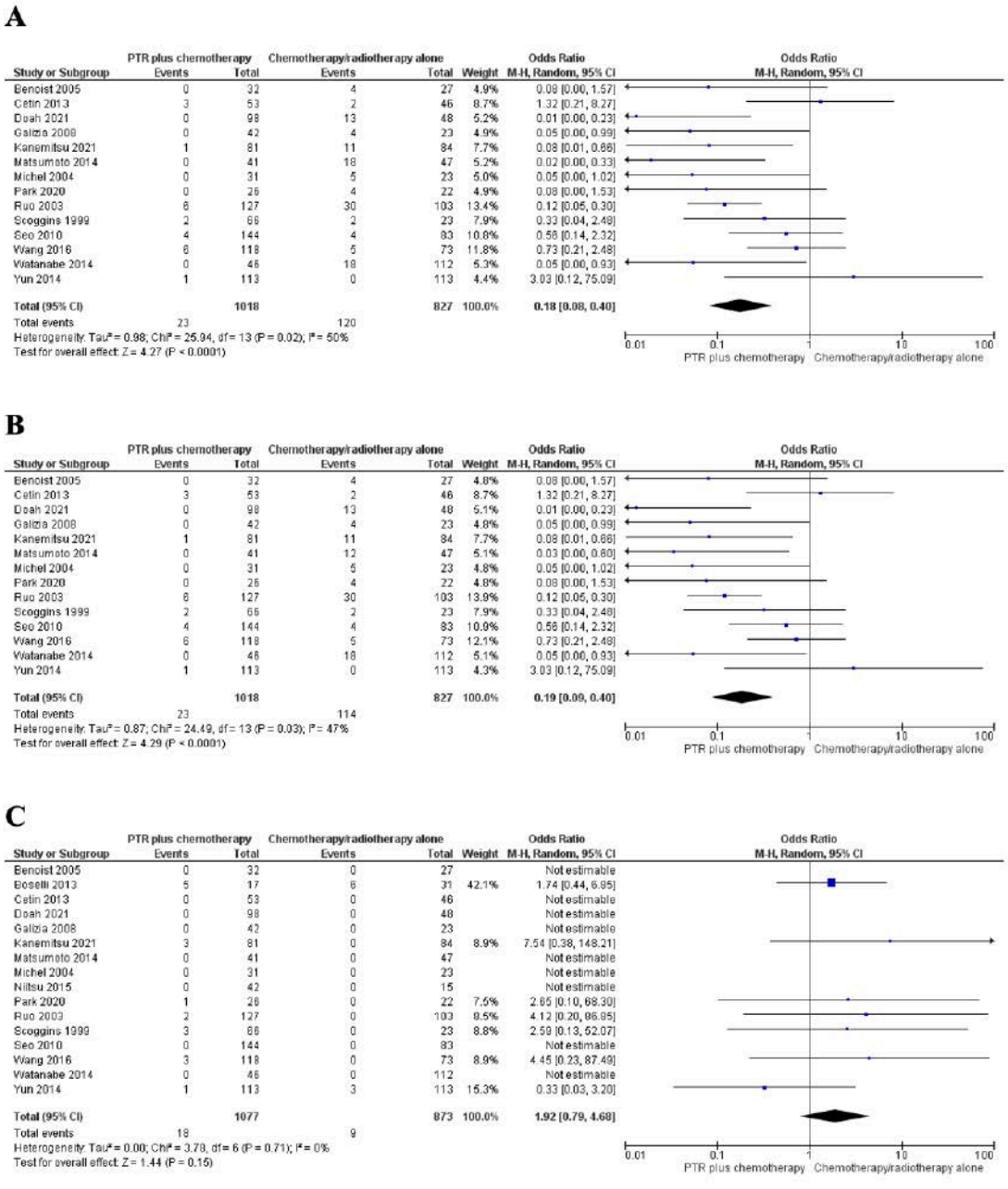

Figure 2. *Forest plots of odds ratios of: rate of surgical intervention due to complications of first treatment (A), rate of surgical intervention due to complications of first treatment, included only patients underwent surgery for symptoms linked to the primary tumor in the chemo/RT group (B) and 30-day mortality rate (C)*

Table 6. *Randomized controlled trials (RCTs)*

RCT name	Country	RCT №	Primary outcome	Simple size	Study start year/ estimated study completion year	Status
SYNCHRONOUS [7]	Germany	ISRCTN30964555	3 years OS	800 → 392	2011-2019	Ongoing/no longer recruiting
CAIRO4 [8]	Netherlands	NCT01606098	5 years OS	360	2012-2020	Recruiting
CCRe-IV [9]	Spain	NCT02015923	2 years OS	336	2013-2018	Ongoing/ no longer recruiting
CLIMAT [10]	France	NCT02363049	2 years OS	278	2014-2018	Recruiting
PTR Trial [47]	Korea	NCT01978249	2 years OS	480	2013-2016	Early terminated*
China multicenter [11]	China	NCT02149784	3 years OS	480	2015-2019	Recruiting
JCOG1007 [48]	Japan	UMIN000008147	3 years OS	770 → 280	2012-2020	Early terminated*

*Note: * — trial was early terminated because of the difficulties of participant enrolment.*

DISCUSSION

The necessity of palliative PTR for asymptomatic or minimally symptomatic patients with CRC and synchronous unresectable metastases is controversial. Currently, only results of non-randomized studies are available on this issue. Several RCTs were initiated comparing PTR followed by chemotherapy with chemo/RT alone in patients with unresectable disseminated metastatic CRC, but not completed yet (Table 6).

Two RCTs [47,48] were terminated early because of the complicated enrolment of patients. Kanemitsu et al. [46] published an interim analysis of early terminated RCT for165 enrolled patients (81 in the PTR and 84 in the chemo/RT groups) and reported that PTR had no benefits in terms of survival, but resulted in higher postoperative mortality rate. Three-year OS was 32.9% in the PTR group and 33% in the chemo/RT group. Median OS was 25.9 months in the PTR group and 26.4 months in the chemo/RT group. Three patients (4%) died due to complications within 30 days after surgery in the PTR group. However, the patients in the chemo/RT group had a higher rate of complications requiring operation after first treatment compared with palliative primary tumor resection (13%vs.1.2%). The study was terminated early by a decision of the Data and Safety Monitoring Committee, and thus the planned statistical power of70% in the

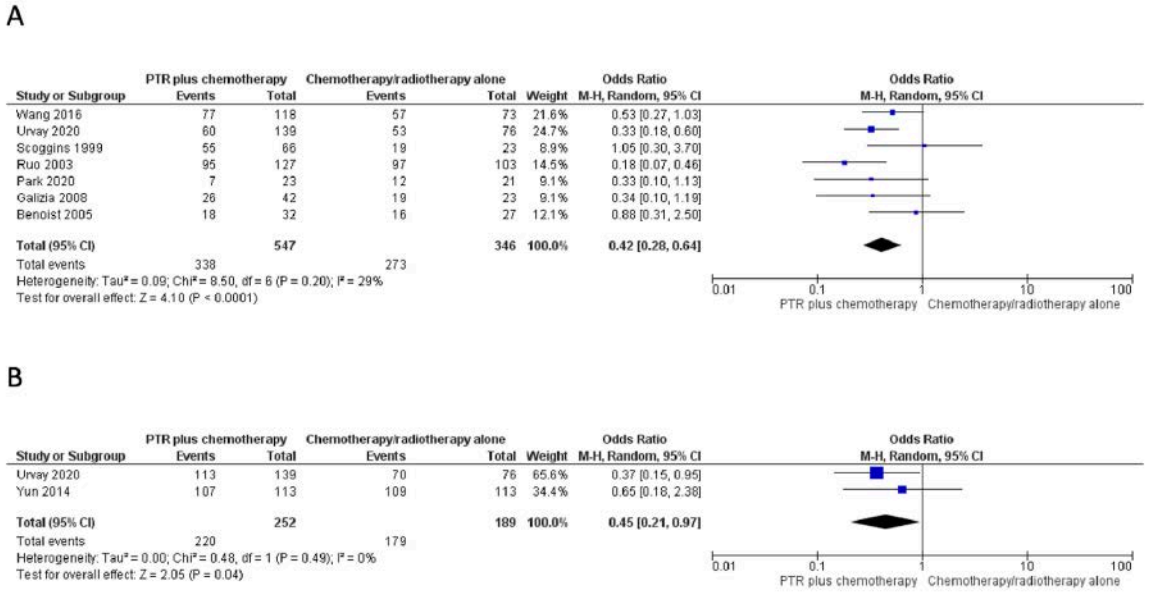

Figure 3. *Forest plots of odd ratios of 2-year overall survival (A) and 5-year overall survival (B)*

planned sample size of 280 patients was not achieved.

Another RCT was terminated early because of the lack of patient enrolment and cessation of funding. Park et al. [45] published an interim analysis with a sample size of 44 patients (23in the PTR group and 21 in the chemo/RT group), whichwasapproximately10-fold smaller than the planned sample size of 480 patients. The researchers found that PTR followed by chemotherapy had only benefit for 2-year cancer-specific survival over chemotherapy alone (72.3%vs. 47.1%; P = 0.049). Although 2-year OS was higher by 25% in the PTR group (69.5% vs. 44.8%), the difference did not reach statistical significance (P = 0.058), which indicates that the study was obviously underpowered. The complications requiring operation after first treatment were found only in the chemo/RT group and the rate was 18.2%, though palliative PTR was associated with a postoperative mortality rate of 3.8%.

Most previous meta-analyses evaluating the role of PTR for patients with CRC and synchronous unresectable metastases included data from patients with both symptomatic and asymptomatic primary tumors [36–39]. The first meta-analysis including only asymptomatic patients was published by Cirocchiet al. in 2012 [49]. The authors included only seven non-randomized trials with 1,086 patients and reported that PTR in asymptomatic patients with unresectable advanced CRC did not improve OS comparing to chemo/RT alone and did not prevent surgical interventions due to complications related to primary tumor. Nevertheless, the authors did not find an association of high postoperative mortality with PTR. Our outcomes are not corresponding to this meta-analysis except the data on postoperative mortality. It can be explained by several new studies published on this issue since 2012 which may change the outcomes. In addition, the authors reported survival outcomes in only 4 studies with 443 patients. Hendren et al. [29] reported that postoperative complications in patients with CRC who underwent surgical resection of the primary tumor were independently associated with a delay in adjuvant chemotherapy, which, in turn, may lead to the progression of the disease and decrease survival. However, Cochrane systematic review, published by Claassen et al. [50] and based on 3 RCTs (351 participants), showed that immediate treatment with chemotherapy did not provide a clear survival benefit compared to delayed chemotherapy for asymptomatic incurable metastatic colorectal cancer (HR = 1.17; 95% CI 0.93–1.46). To date, several cohort studies analyzing the data from national registries have also been published. Some published comparative studies showed survival benefit of PTR over chemotherapy alone [51,52,53], while other studies found no advantages [54]. We did not include these papers into our meta-analysis because it was impossible to distinguish the group of asymptomatic patients in these population-based studies.

In this meta-analysis heterogeneity of the studies ranged from 0% to 66%. There was no significant heterogeneity between the included studies in gender, age, ECOG/WHO PS in analysis rate of surgical intervention due to complications of first treatment and 30-day mortality rate. Nonetheless, there was significant heterogeneity between the studies in term of primary tumor location (colon and rectal/rectosigmoid) and site distant metastasis (hepatic and extrahepatic) in analysis rate of surgical intervention due to complications of first treatment: df = 13 (P = 0.005), I^2 = 57%; df = 6 (P = 0.007), I^2 = 66%, respectively. Significant heterogeneity also was seen in site of primary tumor location (colon and rectal/rectosigmoid) and distant metastasis (hepatic and extrahepatic tumor burden) in analysis of 30-day mortality rate: df = 15 (P = 0.0005), I^2 = 62%; df = 6 (P = 0.007), I^2 = 66%, respectively. There was no significant heterogeneity between the included studies in gender, age, comorbidity, site of primary tumor and distant metastasis in analysis of 2-year OS. In contrast, significant heterogeneity among the studies in terms of gender, age, follow-up was detected in the analysis of 5-year OS. It was impossible to assess the heterogeneity between the included studies in comorbidity, site of primary tumor and distant metastasis because data were available in only 1 of 2 studies. The results of the presented meta-analysis demonstrate that asymptomatic or minimally symptomatic patients with stage IV CRC have benefits from palliative primary tumor resection followed by chemotherapy over chemotherapy and/or radiotherapy alone, such as improvement of the overall survival rate: for 2-year OSOR 0.42,

95%CI 0.28 — 0.64(P < 0.0001) and for5-year OS OR 0.45; 95%CI 0.21– 0.97 (P = 0.04). Also, PTR has advantage as prophylaxis of primary tumor related complications: OR 0.19; 95%CI 0.09– 0.40 (P < 0.0001).

There are some limitations in this meta-analysis. Most included patients had good performance status (ECOG PS 0-1), and therefore were good candidates for both aggressive chemotherapy and surgical palliation. In all included studies patients with metastatic liver metastatic disease were prevalent; however, an extent of metastases, their number and size varied in a great degree, which influenced oncologic outcomes. The chemotherapy protocols between the included studies were heterogeneous among patients, though most patients received fluorouracil-based combination chemotherapy regimens with monoclonal antibodies. The current analysis was also limited by unavailable data in some studies. We did not contact the authors to achieve additional data which were not published, although it would potentially improve the quality of the meta-analysis. But the main drawback was the lack of RCTs. SYNCHRONOUS (ISRCTN30964555), CAIRO4 (NCT01606098), CCRe-IV (NCT02015923), CLIMAT (NCT02363049) and China multicenter (NCT02149784) are still in progress, and acquisition of data allows to elucidate the role of PTR in treatment of disseminated CRC.

CONCLUSION

The results of this meta-analysis have demonstrated that PTR in patients with asymptomatic or minimally symptomatic CRC and synchronous unrespectable metastases significantly improves overall survival, allows to prevent surgical intervention due to complications related to primary tumor and is not associated with increased postoperative mortality rate comparing to systemic chemotherapy and/or radiotherapy as a treatment of first line. The current data are based on non-randomized comparative studies and data from early terminated RCTs and further well-designed RCTs are required.

AUTHORS CONTRIBUTION

Concept and design of the study: *Evgeny G. Rybakov, Iuliia V. Alimova*

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Parastomal hernias: the current state (review)

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ABSTRACT *Every year there is an increase in the number of patients with intestinal stoma, which leads to an increase in the incidence of parastomal hernias (PSH). More than 50% of ostomy patients develop a parastomal hernia two or more years after radical surgery. To date, there are many surgical options for PSH, however, a unified algorithm for choosing an operational technique has not been evolved.*
The purpose of this review is to study modern surgical methods for the treatment of PSH and their late results, to determine the optimal approach and benefits.
The review of the literature showed that in all cases of surgical treatment of PSH it is necessary to use mesh implants. The optimal technique for PSH hernioplasty is the laparoscopic version of Sugarbaker due to the low risk of recurrence and technical simplicity. In patients with large and giant PSH or hernia recurrence, STORRM is the technique of choice; classical stoma transposition is not used due to the high risk of recurrence. The use of Pauli/ePauli technique demonstrates a low recurrence rate, but there are no late results in this category of patients.

KEYWORDS: *Parastomal hernia, Sugarbaker, Pauli, eTEP*

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INTRODUCTION

Due to the successful development of the oncological service and the improvement of the quality of surgical treatment of colorectal cancer, the life expectancy of stoma patients increases, which, in turn, leads to an increase in the number of parastomal hernias (PSH). More than 50% of ostomy patients, two years or more after radical surgery, have a parastomal hernia [1].

According to the data provided by SAGES (Society of American Gastrointestinal and Endoscopic Surgeons), 87,000 ileostomy and 135,000 colostomy surgeries are performed annually. According to experts of the European consensus of 2018, the incidence of PSH in ostomy patients is over 30% by 1 year after surgery, 40% by 2 years, 50% or more with further follow-up [2]. To diagnose PSH, computed tomography, ultrasound, magnetic resonance imaging, and physical examination are used [3,4].

The problem of surgical treatment of PSH is certainly relevant, due to the high rate of occurrence of this type of hernias after large intestine surgery [5]. To date, there are many surgical techniques; however, a single standard in the treatment of parastomal hernias has not been established.

AIM

The purpose of this review is to study modern surgical methods for the treatment of parastomal hernias and their late results, to determine the optimal access and surgical aid.

Table 1. *2018 EHS clinical classification of parastomal hernias*

PSH type	Characteristic
I	Isolated PSH < 5 cm
II	PSH < 5 cm + Ventral hernia
III	Isolated PSH > 5 cm
IV	PSH > 5 cm + Ventral hernia

RESULTS AND THEIR DISCUSSION

Classification

To date, there are many classifications of PSH, but from the point of view of the choice of surgical approach, it is most appropriate to use the modified classification by Szczepkowski, M. (2011), adopted by the European Association of Herniologists (EHS) in 2018 (Table1).

The PSH classification is based on the size of the anterior abdominal wall lesion and the presence of concomitant ventral hernia. According to this classification, there are 4 types of PSH: type I — isolated parastomal hernia up to 5 cm, type II — parastomal hernia up to 5 cm in combination with ventral hernia, type III — isolated parastomal hernia of over 5 cm, type IV — parastomal hernia of over 5 cm in combination with ventral hernia [2].

Prevention

There are surgical techniques that allow to avoid the parastomal hernia during colostomy or ileostomy. The following methods of prevention of PSH are distinguished: the transrectal formation of a stoma, the use of mesh implants in the removal of intestinal stoma, the use of SMART techniques (stapled meshstom are in for cement technique) [6].

A meta-analysis conducted by Carne et al. (2003) showed that only in 4 out of 24 publications, the authors demonstrated a lower percentage of the development of parastomal hernias during the formation of a transrectal stoma compared with lateral removal of the stoma [7]. In 2016, a randomized controlled trial (RCT) of PATRASTOM was conducted, which included 2 groups of patients with PSH with previously formed transrectal or lateral stoma. The incidence of parastomal hernias did not differ between the lateral group (5 out of 27) and the transrectal (4 out of 29; P = 0.725) [8]. Thus, the conclusions obtained from these studies demonstrated the absence of a significant difference in the development of PSH when comparing transrectal and lateral stoma.

In a meta-analysis by Lopez-Cano et al., the authors demonstrated that the prophylactic use of a mesh implant in 451 patients with terminal colostomy significantly reduces the rate of PSH formation (RR 0.43, 95% CI 0.26–0.71; P = 0.0009) [9]. In the ROCSS RCT, the authors found that the preventive use of a biological mesh implant during the closure of the stoma is associated with a lower percentage of PSH development in a two-year period, compared with the group of patients where prevention was not carried out (12% vs 20%) [10]. In 2019, a multicenter STOMAMESH RCT was performed, which included patients who underwent open colorectal surgery, followed by the creation of a permanent terminal colostomy, and divided into 2 groups depending on the installation of a mesh implant. Patients were observed for 1 year after the surgery. The results showed no connection between the preventive use of mesh implants and a lower percentage of the development of parastomal hernias in the analysis of clinical (p = 0.866) and radiological (p = 0.748) data [11]. Thus, despite the contradictory research results, it can be assumed that the preventive use of mesh implants is appropriate and reduces the likelihood of PSH formation.

Another method of preventing the formation of PSH is the SMART technique, which was first proposed by Williams, N.S. et al. in 2011 [6]. The technique consists in using a circular stitching device to strengthen the muscular-aponeurotic lesion in the intestinal stoma using a mesh implant. In a prospective study by Chen, M.Z. et al. in 2021, the authors

demonstrated that using the SMART technique, the PSH in 53 patients in a two-year period was observed in only 8% of the study group [12]. In a 2018 study by Canda et al., it was shown that a high percentage of PSH was observed in the group of patients without the use of the SMART technique (39.5% vs 13.8%, $p = 0.029$) in comparison with the group where the SMART technique was used [13].

Surgical Methods of Treatment

The main method of eliminating PSH is hernioplasty. There are 3 groups of methods of surgical treatment of PSH: hernioplasty using the patient's own tissues, intestinal stoma transposition, and hernioplasty using mesh implants. According to the European consensus of 2018, PSH hernioplasty using the patient's own tissues is not recommended due to the high risk of recurrence [2]. All modern surgical methods of PSH treatment involve combinations of treatment options and differ in the following parameters: type of access (open, laparoscopic, extraperitoneal), type of mesh implant (biological, polytetrafluoroethylene (ePTFE), polyvinylidene fluoride (PVDF), polypropylene (PP)), as well as the choice of anatomical space for implant placement (onlay, inlay, sublay, IPOM — intraperitoneal technique) [14].

Stoma transposition is a technically simple method of surgical treatment of PSH. However, currently this technique is used less and less. According to the data of the European consensus on the prevention and treatment of PSH in 2018, the classic variant of stoma transposition is not recommended, since when moving the stoma, the risk of developing a hernia of a new localization reaches 70% [2]. The optimal method for stoma transposition is the STORRM surgery (Stapled Transabdominal Ostomy Reinforcement with Retromuscular Mesh), proposed by Majumder, A. in 2018. The technique consists in the transposition of the intestinal stoma, a combination of the SMART technique and TAR (Transversus Abdominal Release) separation. The STORRM surgery is used in patients with large, giant parastomal hernias or with recurrent PSH. According to the results of the study, the recurrence rate of PSH with this technique is 17%, while with the use of classical stoma transposition, the recurrence rate is 24–35% [15].

Hernioplasty using a mesh implant is the most common and effective method of treating PSH. However, there is currently no generally accepted surgical standard in the use and location of a particular mesh implant [2]. According to the results of a study by Slater, N.J. et al. in 2011, it was shown that the use of biological mesh implants is associated with a high recurrence rate. The review included four retrospective studies involving 57 patients. In all the studies, patients underwent PSH hernioplasty with the installation of a collagen biological mesh implant. Recurrence of a parastomal hernia occurred in 15.7% (95% CI 7.8–25.9) patients [16]. Implants without an anti-adhesive coating, as a rule, are not considered for IPOM plastics due to the high risk of developing adhesions, intestinal fistulas and strictures [2]. A retrospective cohort study demonstrated a higher incidence of intestinal obstruction when using PVDF implants compared to polyester composite implants (11.5% vs 0%) [17]. In a systematic review by Hansson et al. in 2012, depending on the location of the mesh implant, the following rates of PSH recurrence were observed: onlay — 17.2% (95% CI 11.9–23.4), sublay — 6.9% (95% CI 1.1–17.2), IPOM — 7.2% (95% CI 1.7–16.0). The results of the study demonstrated that the location of the Sublay or IPOM implant is preferable [18]. Hernioplasty with the installation of mesh implants Onlay and Inlay in PSH is currently not recommended due to the high percentage of complications and recurrences (25–70%) [2].

Due to the rapid development of endovideosurgery, laparoscopic and robot-assisted surgical methods of PSH treatment are being actively introduced into daily practice. Paul Sugarbaker in 1985 first described PSH hernioplasty with the installation of a mesh implant by the IPOM method. The technique is carried out by performing the mobilization of the stomated intestine, dissection of the hernial sac and suturing of the hernial lesion (Fig. 1, Fig. 2). Next, the large intestine is lateralized by fixing the latter to the abdominal wall (Fig. 3). The next step is to install a composite mesh implant that overlaps the eliminated hernial lesion and the

lateralized part of the large intestine (Fig. 4) [19]. In recent years, this technique has been actively used in the laparoscopic version [20]. The advantages of this surgery are reliable fixation with the help of a valve mechanism (abdominal pressure ensures reliable fixation of the intestine under the mesh implant) and a low risk of recurrence (11.6%). The main disadvantages of the technique are the large contact area of the implant with the intestinal loops, which, despite the anti-adhesive properties of the implant, leads to the development of the adhesive process; dissection of the intestine during mobilization, as well as the use of braces for fixing the implant, increases the risk of intestinal injury with the development of perforation and peritonitis [19].

Another variant of the IPOM technique is the Keyhole hernioplasty, developed by BME Hansson in 2003 [21]. The technique of the surgery is to eliminate the hernial lesion and create a stomal intestinal tunnel. The next step is the installation of a mesh implant with its cutting around the stoma intestine. Thus, the lesion is closed and a kind of a "keyhole" is created. The advantage of this technique is the qualitative overlap of the lesion and technical simplicity. The intra-abdominal location of the implant is the same disadvantage as with Sugarbaker hernioplasty [22].

The Sandwich method, described by Berger in 2007, is a combination of the two techniques presented above [23]. First, a mesh implant is installed according to the "keyhole" type, which is then covered with a second mesh implant according to the Sugarbaker technique. This technique is recommended for use in large parastomal hernias. The advantage of this surgery is: reliable fixation with the help of double overlap of implants. The main drawback is the technically complex execution of this technique, the location of the stoma intestine between the

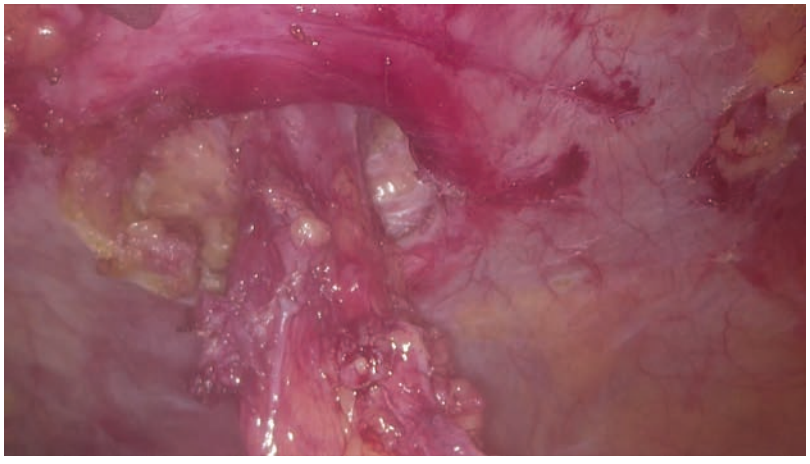

Figure 1. *Performed dissection of the hernial sac*

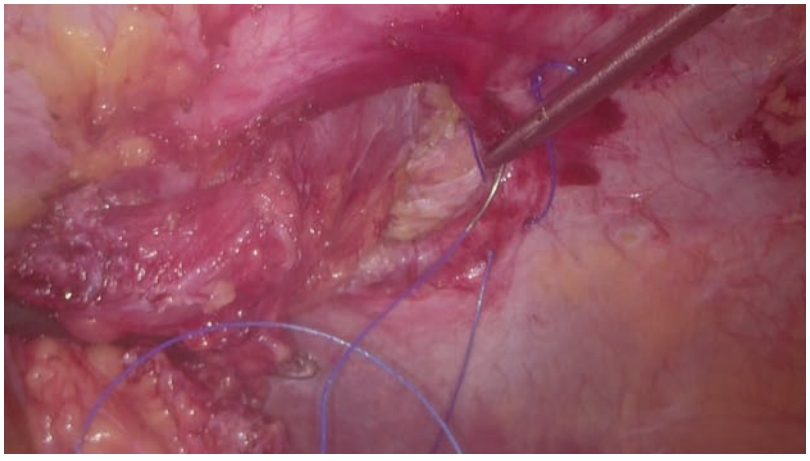

Figure 2. *Sewing of the hernial defect*

implants, as well as the large area of contact of the intestine with the mesh implant [24].

The solution to the disadvantages of the IPOM-hernioplasty in PSH was proposed by Eric Pauli. His hernioplasty (PPHR-Pauli parastomal hernia repair, 2016) consists in a combination of TAR separation and the Sugarbaker hernioplasty with the installation of a mesh implant retromuscularly. This technique is carried out by performing laparotomic access followed by TAR separation behind the stoma intestine. Thus, an additional space is created for the intersection of the posterior leaf of the aponeurosis with the peritoneum and the lateralization of the excreted intestine is performed. The next step is to suture the posterior leaf of the aponeurosis with the placement of the mesh implant extraperitoneally. The advantages of the PPHR hernioplasty are the absence of the influence of intra-abdominal pressure on the migration of the mesh implant and the absence of contact with the contents of the abdominal cavity. The disadvantages of the Pauli surgery include the implementation of open surgical access and the complexity of technical execution [25].

The endoscopic version of the surgery was named after the author — ePauli hernioplasty. In the European Consensus of 2018, this surgical technique is not considered. In addition to conferences and congresses, ePauli is mentioned only in publications by Belyansky, I. as the Pauli-eTEP hernioplasty [26].

A study conducted by Huiyong Jiang et al. in 2021demonstrated that the use of eTEP access during the ePauli surgery is technically complex and requires a lot of surgical experience. With the completed learning curve, the surgery is safe and effective. The recurrence rate requires

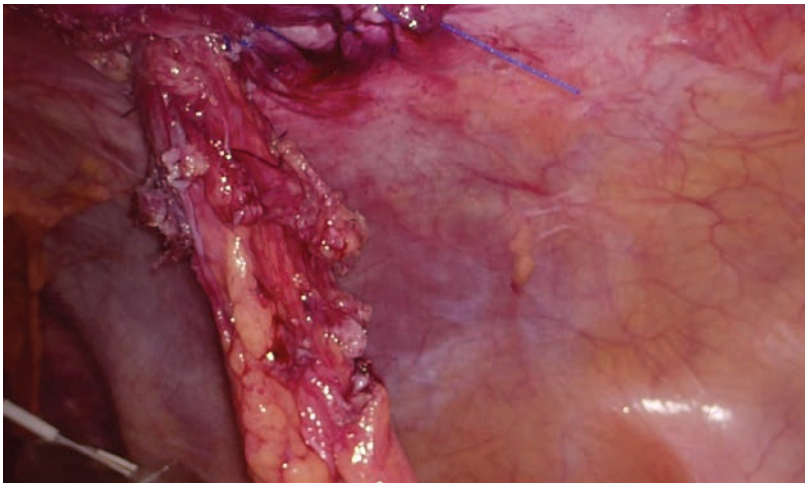

Figure 3. *Lateralization of the colon was performed*

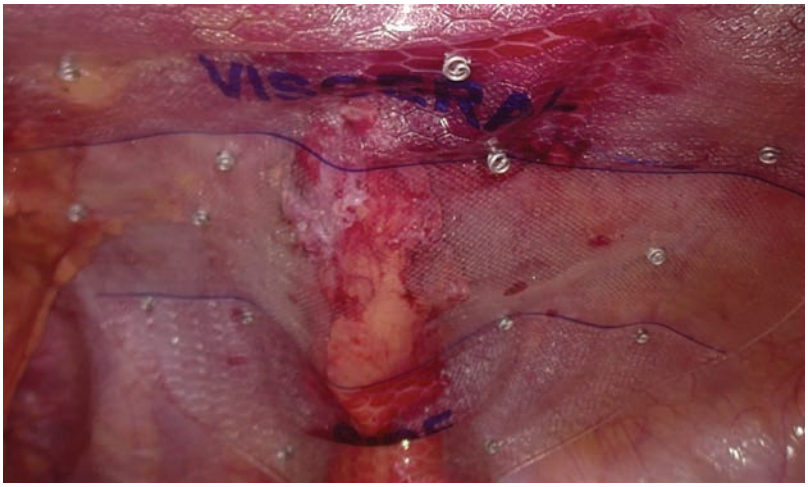

Figure 4. *Fixed composite mesh implant*

further evaluation. However, short-term results in terms of postoperative complications are comparable with the results of the laparoscopic Sugarbaker technique [27]. In a study conducted by Lambrecht, J.R., the author points out that despite the low recurrence rate (6%) 1 year after surgery, the use of the ePauli hernioplasty in primary PSH or recurrence as a surgery of choice is a controversial issue and requires long-term follow-up results [28].

Based on the obtained surgical experience and in-depth study of the problem, E. Pauli proposed a surgical algorithm for the treatment of PSH [29]. Based on the classification of parastomal hernias in 2018 [2], the author recommends using a laparoscopic or robotic version of the Sugarbaker technique for type I of PSH. In type II of PSH, PPHR or Sugarbaker IPOD ventral hernioplasty is recommended. In type III of PSH, a laparoscopic or robotic version of the Sugarbaker technique is used, or PPHR in open, laparoscopic and robotic versions. In case of type IV of PSH or recurrence, Pauli recommends the STORRM technique or PPHR [29].

CONCLUSION

Analyzing the data of late results of RCT and meta-analyses, it was found that in all cases of surgical treatment of PSH it is necessary to use mesh implants. Completing the planned surgical treatment for colorectal cancer by removing a permanent stoma, it is possible to prevent PSH by installing a mesh implant in the retromuscular space around the stoma or using the SMART technique. Due to the development of minimally invasive surgical techniques, preference is given to endovideosurgical hernioplasty methods. Among the existing set of options for surgical treatment of PSH, the laparoscopic option of the Sugarbaker surgery can be called the method of choice due to the low risk of recurrence. If patients have large, giant PSH or a recurrence, it is recommended to resort to the STORRM technique; classical stoma transposition is not recommended due to the high risk of recurrence. Currently, based on the results of research by foreign authors, among all accesses, preference is given to extraperitonal methods of surgical treatment of PSH. However, due to the small experience and complexity of the technical performance of surgeries, the lack of long-term observation results, it cannot be unequivocally stated that extraperitoneal access is superior to other methods.

AUTHORS CONTRIBUTION

Concept and design of the study: *Victor A. Kashchenko, Alexander A. Bogatikov, Nikita R. Kopteev*

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Statistical processing: *Timofey S. Ovchinnikov*

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Minimally invasive treatment of pilonidal sinus disease (a systematic review and meta-analysis)

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ABSTRACT *AIM: to estimate the effectiveness of minimally invasive methods for treatment of chronic inflammation in pilonidal sinus disease by systematic review.*
PATIENTS AND METHODS: fifty-two clinical trials were selected from 2,576 papers in databases for systematic review. It included the following methods: the fibrin glue, the sinusectomy, the video-assisted pilonidal sinus treatment, the laser coagulation and the chemical destruction using crystallized phenol or its solution. Regarding the last two methods, a meta-analysis was carried out.
RESULTS: the meta-analysis demonstrated the high effectiveness of phenol and laser coagulation for pilonidal sinus disease. When comparing the results of phenol use and excisional techniques, there was a significant difference in higher frequency complications rate after excisional techniques (HR 0.42; 95% CI: 0.05–3.71), while the recurrence rate was the same (HR 0.98; 95% CI: 0.45–2.16). The probability of recurrence was significantly higher than after excision techniques in compare with SiLaC (HR 4.02; 95% CI: 1.13 14.3, p = 0.03). However, there was no significant differences in complication rate after SiLaC and excisional techniques (HR 0.63; 95% CI: 0.29–1.34).
CONCLUSION: the chemical destruction and laser coagulation are the most effective methods for pilonidal sinus treatment.

KEYWORDS: *Pilonidal sinus disease, PD, pilonidal cist, minimally invasive treatment, laser coagulation, EPSiT, VAAFT, SiLaC, phenol, fibrin glue*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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INTRODUCTION

Pilonidalsinus (PS) is a narrow channel under the skin, lined with epithelium from the inside, containing hair follicles and sebaceous glands, reaching 10 cm long and blindly ending in soft tissues in the coccyx area. PS communicates with the skin surface by several (from 1 to 6) point primary fistula openings located in the inter-gluteal fold along the midline. As a result of chronic inflammation of the PS, 1 or more secondary fistula openings may appear, located on the skin of the sacrococcygeal or adjacent areas [1].

The estimated incidence of PSD is 26 per 100,000 people. In male patients, the disease occurs 4 times more often than in women, while PS inflammation rarely occurs before puberty or in old age, mainly developing in young persons [2]. There is no consensus in the literature regarding the etiology of PSD. Currently, there are several theories of the development of chronic inflammation of the pilonidalsinus: neurogenic, ectodermal invagination, invert hair growth, etc. In Russia, the innate theory of the origin of this disease has become the most widespread [3]. According to foreign literature, it is believed that this disease is associated with the proliferation and hyperfunction of

hair follicles in the sacrococcygeal area, followed by blockage of the sebaceous glands and the development of the inflammatory process. Features of the anatomy and biomechanics of the gluteal area can cause a vector violation of hair growth, which in turn also contributes to the blockage of hair follicles. As a result, a pathological sinus is formed under the skin of the inter-gluteal fold, followed by the addition of inflammatory reactions [4].

To date, the choice of the method of surgical treatment of chronic inflammation of the pilonidal sinus remains controversial. Over the past 30 years, a fairly large number of techniques have appeared, which had the peak of their popularity at the moment when they were proposed, and their effectiveness was studied. Most of the methods aimed to reduce or completely close the wound lesion with a relatively low risk of the disease recurrence. So, recently, there are a number of very popular techniques for reducing a postoperative wound such as: by stitching its edges to the bottom [5,6], the layer-by-layer suturing of the wound tightly [7], options for plastic closure of the wound using a laterally displaced skin-fat flap according to Karidakis [8] or Bascom 2 [9], excision of PS with plastic surgery of a wound lesion with a displaced rhomboid skin-fat flap (Limberg's procedure), and variants of Z, Y plasty [10–12]. Nevertheless, gradually the methods accompanied by radical excision of PS began to yield the palm to more gentle approaches. The surgery which can be conditionally called a "bridge" between radical excision and minimally invasive techniques was sinusectomy or subcutaneous excision of the pilonidalsinus [13,36]. Already, experience has accumulated in world practice, demonstrating that in the case of uncomplicated PSD, its treatment options associated with tissue excision are significantly inferior to minimally invasive ones. The optimal method of PSD treatment should meet the following criteria: be simple, cost-effective, with the possibility of outpatient treatment, including under local anesthesia, cause minimal discomfort and do not affect performance, as well as have a low recurrence rate. All surgical methods are far from ideal, as they are usually performed under general or spinal anesthesia, require hospital stay and cause temporary loss of patients' working capacity [8]. In this regard, the application of minimally invasive techniques in clinical practice is relevant. However, the data of the world literature on the effectiveness and indications for the use of a minimally invasive method vary significantly. As part of the evaluation of the effectiveness of minimally invasive techniques, a literature review was performed, including an analysis of the results of such methods as: EPSiT (endoscopic pilonidal sinus treatment), VAAPS (video-assisted ablation of pilonidal sinus) [13–15], the use of fibrin glue [16,17], laser thermocoagulation of the fistula (SiLaC — Sinus Laser Coagulation) [18–20], sinusectomy [5,6], the use of phenol [21–25]. In addition, taking into account the absence of meta-analyses evaluating the effectiveness of PSD treatment methods associated with the use of phenol and laser coagulation (SiLaC), the availability of publications characterizing the experience of their application accumulated in the world practice, a meta-analysis of data on their effectiveness was done.

MATERIALS AND METHODS

A literature search was performed in the Medline, Cochrane library, Google Scholar, and E-library databases. A total of 2,576 articles were found for a query containing the following terms: "pilonidal sinus", "sacrococcygeal sinus", "sacrococcygeal", "pilonidal". Restrictions on the date of publication of articles and language restrictions were not applied. Statistical data processing when comparing binary indicators was carried out in the Review Manager 5.3 program. For dichotomous data, the odds ratio (OR) with 95% CI was calculated. After screening, 52 articles were selected on evaluating the effectiveness of minimally invasive techniques in the treatment of PSD. Of these, fibrin glue was used in 5 studies for the treatment of PSD [17], EPSiT/VAAPS technique was used in 14 studies [26], phenol applications were used in 13 [26–28,31], sinusectomy was used in 9 [28], SiLaC was used in 11 [18,19,29–31] articles (Fig. 1).

EPSiT (endoscopic pilonidal sinus treatment) is a minimally invasive method of PSD treatment, first described in 2013 by Mainero, P. et al. The technique of this surgery consists in

removing the contents of the fistula passage under the control of vision through a special rigid fistuloscope followed by ablation of the sinus walls with a monopolar electrode [17,36]. This technique is based on a technology similar to the technique of treating anal fistula VAAFT (video-assisted anal fistula treatment).

Milone M., et al. in 2016 in their randomized study compared the effectiveness of EPSiT with radical excision of PS. The primary point in the study was the duration of disability, which was 1.6 ± 1.7 days in the EPSiT group, which was significantly less than with PS excision — 8.2 ± 3.9 days (p = 0.001) [14]. There was also a marked decrease in pain syndrome when using EPSiT (p = 0.001). However, the complication rate was comparable in both groups (p = 0.1). These studies indicate the obvious advantage of minimally invasive technique over radical excision of PS in such important aspects of treatment as the duration of the period of disability and the intensity of pain syndrome in the postoperative period with comparability of the frequency of complications. A comparative analysis of the recurrence rate after surgery was not performed in the study, which significantly complicates the final assessment of all the advantages and disadvantages of the EPSiT method [14].

In another later publication in 2019, Milone, M. and co-authors compared the results of EPSiT with sinusectomy. With comparability of the complication rate, the intensity of pain syndrome and the duration of the period of disability, a significantly lower recurrence rate was observed after the use of EPSiT (7.5% vs. 25%; p = 0.035) [33]. In the work by Foti, N. et al. (2021), which included 42 patients, the results of video-assisted technologies for PSwere demonstrated.

In the first week of the postoperative period, the level of pain syndrome on a visual-analog scale was 2.1 ± 1.3 points. Complications occurred in 8.7% of cases, the period of disability was 3.8 ± 1.4 days. The most often complication was prolonged non-healing of the wound. The recurrence rate was 10.9%. When analyzing all 14 studies included in the review, the complication rate ranged from 0% to 11.5%, with the most frequent complication being bleeding from a postoperative wound. The recurrence rate of the disease was shown in 5 out of 14 studies and ranged from 0% to 26.9%.

A small number of papers devoted to the evaluation of the results of the use of video-assisted PSD treatment and the fragmentation of the data presented do not allow for its full

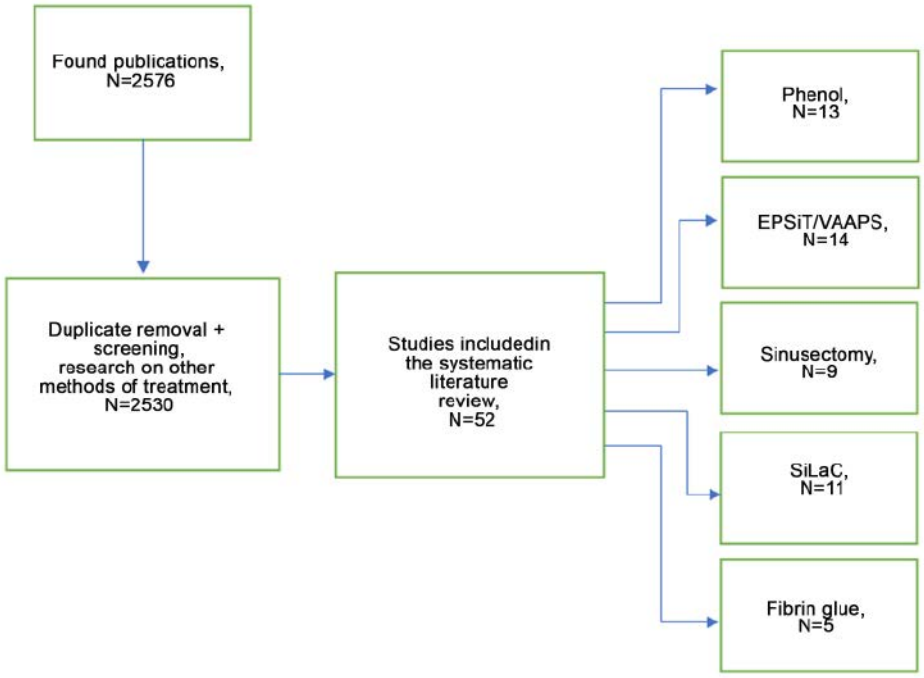

Figure 1. *Literature search diagram*

assessment and aggregation of data in the form of meta-analysis.

Sinusectomy is a minimally invasive technique, which consists in subcutaneous excision of the pilonidalsinus with preservation of the skin bridge between the fistula openings [6]. The method was first described by Soll, Ch. et al. in 2011 [15,37]. Enriquez-Navascues, J.M. et al. (2014) in their meta-analysis, which included 25 studies, compared the effectiveness of sinusectomy and PS excision [28]. Such indicators as the period of wound healing, the recurrence rate, and the time to return to work did not differ significantly between the groups (HR 0.6; 95% CI 0.17–2.38; $p = 0.856$). Thus, the authors revealed that the effectiveness of sinusectomy was completely comparable with radical excision of the PS; however, the analysis of the data obtained did not reveal advantages in the form of accelerated wound healing and faster return to working capacity [28]. In total, when evaluating the results of 9 studies, it was found that the complication rate after the use of the technique ranged from 3.6% to 18.7%, and the recurrence rate–from 4.1% to 14.7%. The most often complications were bleeding from the wound and destruction of the skin bridge. It should be noted that according to some authors, sinusectomy has a number of technical limitations. Thus, according to a study conducted at the RNMRC of Coloproctology, it was found that subcutaneous excision of the PS is most convenient to perform with its length not exceeding 5 cm and when there is no history of surgeries for PSD, which makes it applicable only in some patients [35].

Fibrin glue (a mixture of fibrinogen and thrombin) is used to fill the fistula passage, which promotes its healing without the need for excision of the fistula canal [36]. In analyzing the effectiveness of the technique, the meta-analysis data by Lund, J. et al. are of interest. (2017), which included 253 patients [17]. In this paper, the effectiveness of the use of fibrin glue in the treatment of PSD is compared, both in the form of monotherapy and as an adjunct to the plastic closure of a wound lesion according to the methods by Limberg and Karidakis. So, in the case of using fibrin glue during PS excision surgery with plastic closure of the wound lesion with a displaced diamond-shaped flap along as per Limberg, the glue was applied to the wound surface, after which the wound lesion was covered with a displaced skin-fat flap. This combination allowed the authors to reduce the healing time by an average of 13.9 (95% CI -16.7–11.1) days compared to the classical Limberg surgery. The intensity of the pain syndrome, on average, decreased from 4 to 2 points according to VAS ($p < 0.001$), and the time of return to working capacity from 17 to 8 days ($p < 0.001$). It was also demonstrated that filling the wound with fibrin glue as an addition to the plastic of the wound lesion after excision of the PS by lateral displacement of the skin-fat flap according to the Karidakis method reduces the duration of hospital stay to an average of 2 days compared to 3.7 days in the classic version of the Karidakissurgery ($p < 0.001$). The effectiveness of using fibrin glue in mono mode was compared with the results by Bascom 1 surgery. With isolated use of fibrin glue, the pain syndrome estimated by VAS was, on average, 2.5 points lower (95% CI-4.03 — -0.97), and the time to return to normal life, on average, was 34.8 days less compared with the Bascom 1 surgery (95% CI -66.8 — -2.78). The recurrence rate in the groups did not differ significantly. Nevertheless, the technique of filling the PS channel with fibrin glue has not found wide popularity, the range of its use is limited only to the addition to plastic methods of closing a wound lesion as a cementing agent that improves the fusion between the wound surface and the flap [17].

Phenol is a single-substituted aromatic hydrocarbon with antiseptic, analgesic and sclerosing properties. For the first time, the use of phenol in the treatment of PSD was described by Maurice, A. and co-authors back in 1964 [24]. But the technique has gained the greatest popularity since the 2000s. The analysis of the literature data revealed technical differences in the use of phenol in the treatment of PSD. Thus, applications of crystalline phenol were used in 9 studies [19,26,31,40–45], and in 4 studies a phenol solution was used [27,28,46,47]. In addition, some authors have used a combination of phenol applications

with other minimally invasive methods of PSD treatment. So, Gecim, I. et al. (2017) in their study applied crystalline phenol after fistuloscopy and removal of detritus and hair from the fistula passage through the fistuloscope channel [15].

As part of the evaluation of the effectiveness of phenol in the treatment of chronic inflammation of the pilonidalsinus, a systematic review of the literature was performed, which included 13 studies.

In total, the results were evaluated in 682 patients with PSD, in the treatment of which phenol was used. The overall recurrence rate when using phenol in the treatment of chronic PS inflammation, taking into account all the studies, was 8.7% (60/682) (Table 1).

During the meta-analysis, which included 4 studies, the recurrence rate after the use of phenol and radical excision of PS was compared. So, Ates, A. et al. (2017) in their work compared the results of the technique with the use of phenol withthe PSexcision, accompanied by suturing the wound tightly.

Calikoglur, I. et al. (2017) and Pronk, A. et al. (2019) compared the use of phenol with the PS excision and open wound management. Bayhan, Z. et al. (2015) compared the technique ofthe PS excision with plastic closure of a wound lesion with a displaced diamond-shaped flap along as per the Limberg method.

When evaluating the results of these studies, it was found that the probability of recurrence did not significantly differ statistically between the methods accompanied by excision of the pilonidal cyst and methods with phenol application (OR 0.98; 95% CI: 0.45–2.16) (Fig. 2).

The complication rate with the use of phenol was described in 8 studies. The overall rate of complications after its use in the treatment of PSD was 9.7% — 53 cases among 546 patients. The main complications arising after the use of phenol were chemical burns and abscessing.

Chemical burns in most cases did not affect the results of the treatment, while abscessing was associated with a high risk of ineffective therapy and the likelihood of the disease recurrence. After the PS excision, complications were bleeding from wounds and divergence of sutures. (Table 3).

When performing the meta-analysis of the data, it was revealed that the overall probability of complications with the use of phenol did not differ statistically significantly from the methods in which radical PS excision was performed. However, there was a tendency towards the possibility of a statistically significant difference in the direction of a higher incidence of

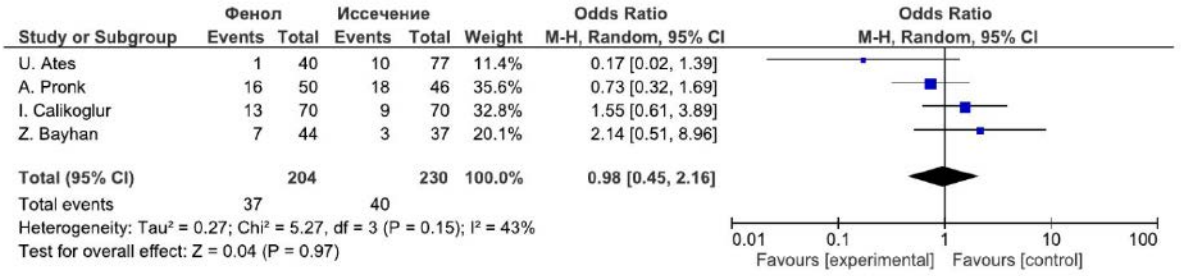

Figure 2. *Forrest plot of the analysis of the reccurence rate when using phenol and pilonidal sinus exision*

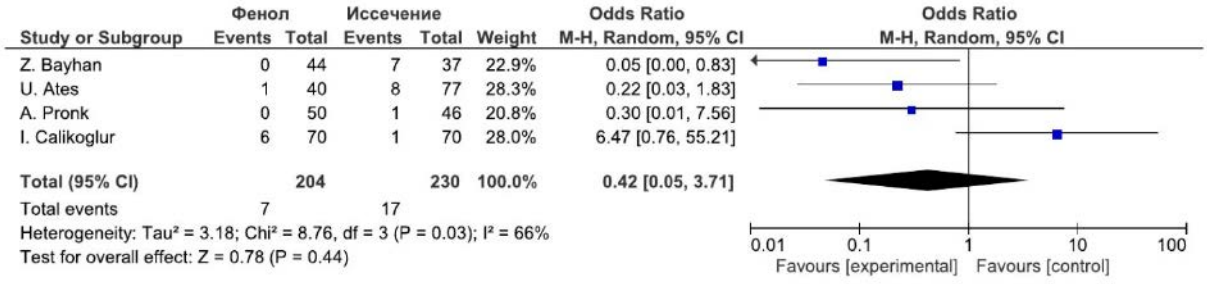

Figure 3. *Forrest plot of the analysis of the complication rate in groups where phenol and pilonidal sinus excision were used*

complications after PS excision, provided that the sample of patients increased (OR 0.42; 95% CI: 0.05–3.71) (Fig. 3).

SiLaC (Sinus Laser Coagulation) — is one of the most popular methods of treatment of chronic PS inflammation today, consisting in coagulation of the walls of the fistula passage with a diode laser [45–49]. The technique has proven itself well due to its low traumatism, the possibility of coagulation of the walls of the sinus with a small laser light guide in diameter, regardless of the PS length, low pain syndrome after the surgery, as well as rapid recovery of working capacity. Dessily, M. et al. were among the first to start using this technology in 2014 [22,33,34]. When analyzing the results of recent studies, it was found that the rate of healing after the application of the technique is in the range of 87–95%. So, Dessily, M. et al. (2017) gave data on the treatment of 200 patients by SiLaC according to which the authors achieved PSD healing in 94% of cases [30]. Similar results were demonstrated in the work by Pappas, I. et al. in 2021, which included an analysis of the results of treatment of 237 patients. The healing rate after the SiLaC application in this study was 90.3% [47]. Nevertheless, a small number of publications devoted to the results of the application of the SiLaC technique does not allow us to develop clear indications and contraindications for its use [23,35,53]. To date, there are no data summarizing the world experience in the treatment of chronic PS inflammation using laser coagulation in the literature.

In this regard, a meta-analysis of the literature data was carried out, in which SiLaC was compared with radical excision of PS by several indicators [35,50].

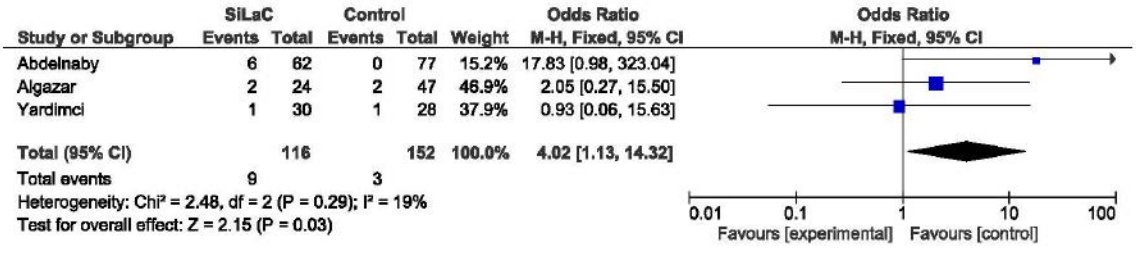

Figure 4. *Forrest plot, showing a comparative analysis of the recurrence rate in groups where the SiLaC technique and pilonidal sinus excision were used*

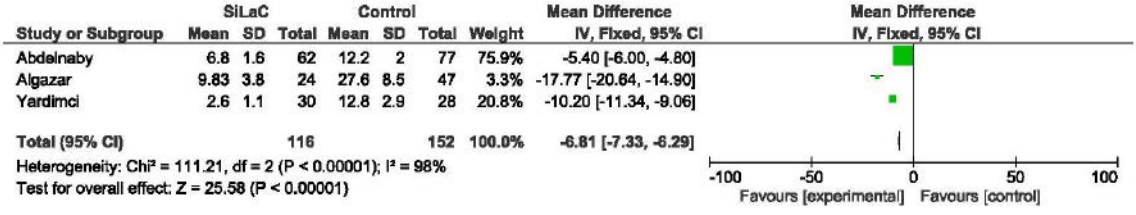

Figure 5. *Forrest plot, showing a comparative analysis of the duration of the period of disability in groups where the SiLaC technique and pilonidal sinus excision were used*

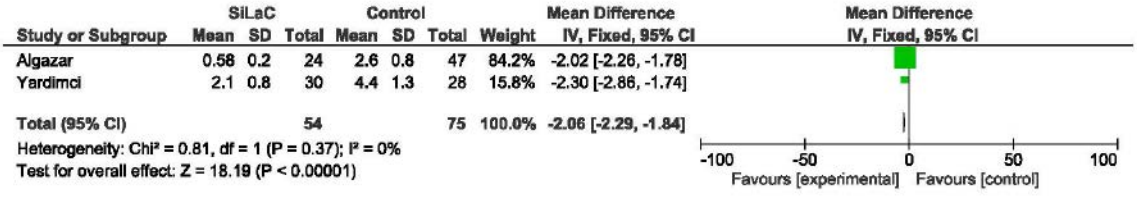

Figure 6. *Forrest plot, showing a comparative analysis of the intensity of pain on the day of discharge (VAS) in groups where the SiLaC technique and pilonidal sinus excision were used*

In total, 3 studies were found in which laser coagulation of PS (SiLaC) was compared with surgical excision of PS. In the studies by Algazar, M. et al. (2021) and Yardimci, V. et al. (2020) in the control group, PS excision was performed with plastic replacement of the wound lesion according to Karidakis and Limberg, respectively. And in the work by Abdelnaby, M. et al. (2021) in the control group, PS excision was performed without suturing the wound [21,31,33]. The methodology of laser coagulation according to all the authors coincided with the technique proposed by Dessily M. et al. (2017), who first described this technology in the treatment of PSD [18]. In the original, a diode laser with a wavelength of 1,470 nm was used for this technique, a light guide with radial energy radiation was used.

It should be noted that Dessily, M. et al. (2017) used a 10 W diode laser in their study, while Yardimci, V. et al. (2020) — 12–14 W, Algazar, M. and co-authors (2021) — 13.5 W, and Abdelnaby, M. and co-authors (2021) in their article do not indicate the exact power of the laser used. In all the studies, the expansion of primary and secondary holes was performed by a sharp way and with the help of a clamp; Yardimci, V. et al. (2020) supplemented the procedure with circular excision of the skin around the holes using a biopsy needle (derma-punch). The results of the analysis comparing the effectiveness of SiLaC with techniques accompanied by excision of PS are presented below (Tabl. 6,7). In the meta-analysis of comparative studies included in the systematic review, we found that the probability of the disease recurrence was statistically significantly higher after the use of SiLaC than after PS excision techniques [OR 4.02 (95% CI: 1.13 14.3, p = 0.03)] (Fig. 4).

However, the comparative analysis of the duration of the period of disability revealed that after using the SiLaC technique, the return to work occurs, on average, 6.8 days earlier than after radical excision of the PS (95% CI: -7.33 — -6.29, p = 0.000001) (Fig. 5).

In the comparative analysis of the intensity of pain syndrome using a visual-analog pain scale (VAS) in 2 papers (Yardimci, V. et al., 2020; Algazar, M. et al., 2021), it was demonstrated that the level of pain after SiLaC, on average, was 2.06 points lower than after excision of PS (95% CI: -2.29 — -1.84, p = 0.00001) (Fig. 6).

According to the analyzed publications, it was found that the complications that developed after the use of SiLaC were not of a specific nature and were mainly represented by purulent-inflammatory processes in the surgery site and bleeding. The meta-analysis included 2 comparative studies, with no statistically significant differences in the incidence of complications between SiLaC and radical excision of PS (OR 0.63 (95% CI: 0.29–1.34)) (Fig. 7). As in the case of evaluating the results of phenol use, after SiLaC there was a tendency towards a decrease in the complication rate. However, the probability of achieving statistical significance could be realized with a larger sample of patients.

DISCUSSION

Inflammation of the pilonidal sinus, despite its benign course and favorable prognosis, is a socially significant disease, which is due to the predominant morbidity among the young able-bodied population [2]. The main method of PSD treatment currently continues to be radical surgical excision of the PS. Surgery for a long time can reduce the

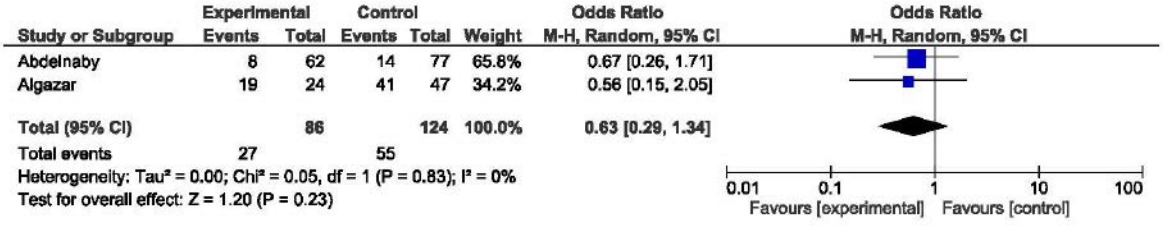

Figure 7. *Forrest plot, showing a comparative analysis of the rate of complications in groups where the SiLaC technique and pilonidal sinus excision were used*

quality of life of the patient, as well as affect his ability to work. Plastic closure of a wound lesion does not always lead to a faster recovery of the patient and is associated with the risk of purulent-inflammatory complications. The emergence of new minimally invasive techniques in the treatment of PSD is aimed at preserving the effectiveness of surgical treatment — minimizing the recurrence and complication rate [8].

Despite the variety of methods of minimally invasive treatment of chronic inflammation of the pilonidal sinus, there is currently no universal method that could become the "gold standard".

Each of the techniques, along with the presence of significant advantages due to less injury, also carries limitations and disadvantages. For example, the use of EPSiT technology is associated with pronounced technical difficulties and the need to use expensive video endoscopic equipment. In addition, despite the comparable effectiveness of the EPSiT method with PS excision, the complication rate was also identical. The use of fibrin glue is practically not considered as an independent technique and is currently regarded by most authors as a satellite of other surgical techniques (Bascom 2, Limberg, Karidakis surgeries). Sinusectomy, despite the satisfactory immediate results of the treatment and a good cosmetic effect, does not have significant advantages over PS excision in terms of wound healing. Also, a significant limitation of the technique is the complexity of its application when the length of the fistula is over 5 cm.

The use of phenol is one of the least traumatic minimally invasive techniques in the treatment of PSD.

During the analysis of the literature data, we found that the use of phenol in the treatment of PSD is an effective technique with a recurrence rate of 8.7%. There was no statistically significant difference in the risk of disease recurrence when using phenol compared with radical surgical excision of PS (OR 0.98 [95% CI: 0.45–2.16]).

Moreover, the incidence of complications (9.7%) not only did not differ statistically significantly between the methods, but also tended to decrease with the use of phenol (OR 0.42 [95% CI: 0.05–3.71]) (Fig. 2). Thus, the use of phenol is a reliable minimally invasive method of PSD treatment, not accompanied by a high risk of complications.

The use of SiLaC in the treatment of chronic inflammation of PS, despite the greater risk of recurrence compared with excision of the PS (OR 4.02 [95% CI: 1.13 14.3, p = 0.03]), carries a number of advantages in the form of a pronounced reduction in pain syndrome and accelerated recovery of the patient's ability to work. The low traumatization of tissues during the surgery, as well as the possibility of its use for various PS lengths, makes SiLaC the method of choice in the treatment of the disease. An important advantage when using SiLaC is the preservation of the possibility of using any more radical surgical techniques in the event of a return of the disease.

CONCLUSION

The data analysis has demonstrated that the use of minimally invasive methods has a number of advantages, such as: low tissue injury, less impact on the quality of life and ability to work of the patient, low intensity of pain syndrome, which makes the techniques promising for wide application. Taking into account the literature data, 2 methods have proven themselves most well: chemical coagulation of PS using phenol and laser coagulation of PS. However, a small number of comparative studies, especially randomized ones, makes it difficult to fully evaluate the effectiveness of these techniques, as well as to develop clear indications and contraindications for their use. To identify the advantages and disadvantages of using phenol and SiLaC in the treatment of PSD, further randomized studies are necessary.

AUTHORS CONTRIBUTION

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Collection and processing of the material: *Sabina B. Kozyreva, Ivan V. Kostarev, Leonid A. Blagodarny, Vadim V. Polovinkin*

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Writing of the text: *Sabina B. Kozyreva, Ivan V. Kostarev*

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Колоректальный рак: эпидемиология, канцерогенез, молекулярно-генетические и клеточные механизмы резистентности к терапии (аналитический обзор)

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РЕЗЮМЕ *В этой статье анализируются статистические данные о колоректальном раке в России и в мире, включая заболеваемость, смертность и выживаемость. Рассматриваются основные пути канцерогенеза колоректального рака, молекулярные подтипы и их влияние на различие при поражении проксимальных и дистальных отделов толстой кишки. В статье приводится обзор ведущих препаратов для химио- и таргетной терапии при колоректальном раке, а также основные причины развития терапевтической резистентности, в том числе изменение клеточного микроокружения опухоли.*

КЛЮЧЕВЫЕ СЛОВА: *колоректальный рак, распространенность, канцерогенез, терапия, лекарственная резистентность*

КОНФЛИКТ ИНТЕРЕСОВ: *авторы заявляют об отсутствии конфликта интересов*

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Colorectal cancer: epidemiology, carcinogenesis, molecular subtypes and cellular mechanisms of therapy resistance (analytical review)

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ABSTRACT *This article analyzes the statistical data on colorectal cancer in Russia and in the world, including incidence, mortality and survival. The main pathways of colorectal cancer carcinogenesis, molecular subtypes and their influence on the difference in lesions of the proximal and distal large intestine are presented. The paper provides an overview of the leading chemotherapy agents and targeted therapy in colorectal cancer, as well as the main reasons for the development of therapeutic resistance, including changes in the cellular microenvironment of the tumor.*

KEYWORDS: *colorectal cancer, prevalence, carcinogenesis, therapy, drug resistance*

CONFLICT OF INTEREST: *The authors declare no conflict of interest*

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Рост заболеваемости колоректальным раком стал одной из основных проблем общественного здравоохранения. Колоректальный рак является третьим по распространенности раком у мужчин и вторым по распространенности раком у женщин во всем мире [1], а также занимает второе место по смертности от онкологических заболеваний в мире [2]. По данным Global Cancer Statistics 2020, рак легких остается ведущей причиной смерти от рака: по оценкам, умерло 1,8 миллиона человек (18%), а за ним следует колоректальный рак (9,4%) [3]. В 2020 году в мире зарегистрировано более 1,9 миллиона новых случаев колоректального рака (включая анус) и 935000 смертей [3]. Эпидемиология колоректального рака значительно отличается в разных регионах мира, а также между различными возрастными, гендерными и расовыми группами. В эту изменчивость вовлечено множество причин, включая воздействие факторов риска, демографические вариации и различные генетические мутации, а также их влияние на прогноз и ответ на лечение [2]. Показатели заболеваемости примерно в 4 раза выше в странах с развитой экономикой в сравнении со странами с развивающейся экономикой, однако различия в показателях смертности менее выражены из-за более высокой смертности в странах с развивающейся экономикой. Уровень заболеваемости раком ободочной кишки различается примерно в 9 раз по регионам мира, с самыми высокими показателями в Европе, Австралии/Новой Зеландии и Северной Америке, при этом Венгрия и Норвегия занимают первое место среди мужчин и женщин, соответственно (Рис. 1) [3]. Показатели заболеваемости раком прямой кишки имеют аналогичное региональное распределение, но в Восточной Азии — максимально высокие. Показатели заболеваемости раком ободочной и прямой кишки, как правило, низкие в большинстве регионов Африки, Южной и Центральной Азии (Рис. 1).

Колоректальный рак можно считать маркером социально-экономического развития, и в странах, переживающих серьезный переходный период, уровень заболеваемости имеет тенденцию к равномерному росту по мере увеличения индекса человеческого развития [4,5]. Показатели заболеваемости неуклонно растут во многих странах Восточной Европы, Юго-Восточной, Южной и Центральной Азии, и Южной

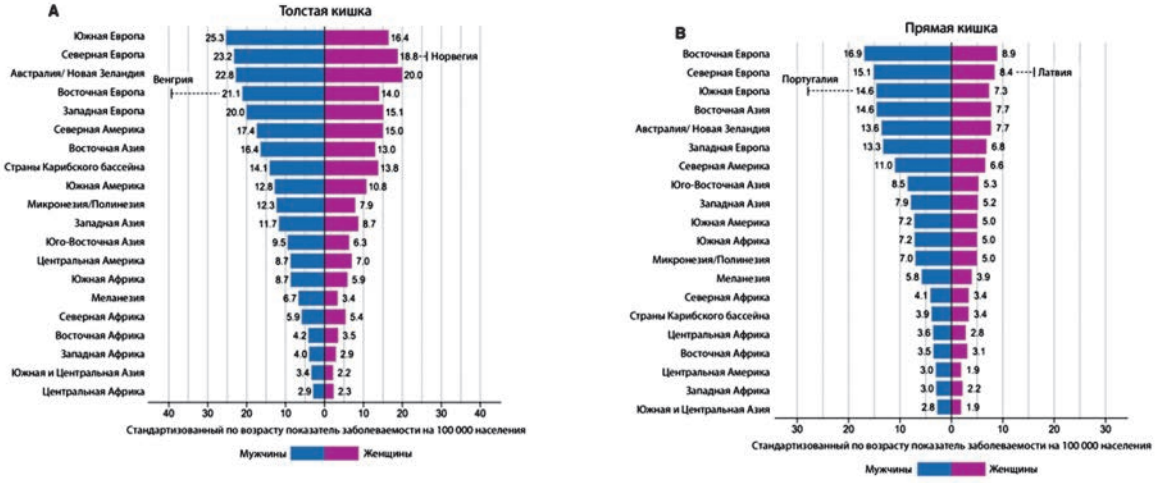

Рисунок 1. *Стандартизированные по возрасту показатели заболеваемости в зависимости от пола и региона проживания пациентов с раком (A) ободочной и (B) прямой кишки в 2020 г. — представлены в порядке убывания стандартизированного по возрасту мирового показателя (W) [5]*
Figure 1. *Age-standardized incidence rates by sex and region of residence of patients with cancer of the colon (A) and (B) rectum in 2020 are presented in descending order of the age-standardized world rate (W) [5]*

Америки [3,6,7]. В Российской Федерации, по данным Федеральной службы государственной статистики за 2019 год, заболеваемость раком ободочной кишки выше у женщин, чем у мужчин (56% и 44%, соответственно), а заболеваемость раком прямой кишки, ректосигмоидного соединения, ануса находится приблизительно на одинаковом уровне в процентном соотношении среди женщин и мужчин (49% и 51%, соответственно) (Рис. 2) [8].

Динамика показателей заболеваемости населения России колоректальным раком за период 2010–2020 гг. неуклонно растет. Среднегодовой темп прироста составил 2,62% для рака ободочной кишки; 1,62% для рака прямой кишки, ректосигмоидного соединения, ануса [9]. Увеличение заболеваемости в странах с более низким индексом человеческого развития, вероятно, отражает изменения в факторах образа жизни и рациона питания, т. е. сдвиг в сторону увеличения потребления продуктов животного происхождения и более малоподвижного образа жизни, что приводит к снижению физической активности и повышенной распространенности избыточной массы тела, которые независимо связаны с риском колоректального рака [10]. Дополнительные факторы риска развития колоректального рака включают чрезмерное употребление алкоголя, курение, потребление красного мяса и мясных полуфабрикатов, тогда как продукты питания и напитки, богатые кальцием, адекватное потребление цельнозерновых продуктов, клетчатки, молочных продуктов, по-видимому, снижают риск [11]. Первичная профилактика остается ключевой стратегией для снижения растущего бремени колоректального рака. Затраты на организацию массового скрининга в большинстве стран с низким и средним уровнем дохода в настоящее время не оправданы, учитывая значительные затраты на колоноскопию и неадекватное предоставление диагностических и лечебных услуг [3]. Некоторые данные, однако, свидетельствуют о том, что скрининг колоректального рака с использованием более доступных и менее инвазивных методов (гваяковая проба на скрытую кровь, фекальные иммунохимические тесты) может быть более рентабельным, по крайней мере, в некоторых странах с развивающейся экономикой [12,13]. Снижение заболеваемости колоректальным раком в некоторых странах с высокой заболеваемостью объясняется изменениями на уровне населения в сторону более здорового образа жизни (например, отказом от курения) [6,14]. Хотя ускорение прогресса с начала 2000-х годов в основном связано с большей доступностью скрининговой колоноскопии и удалением предраковых аденом [15,16]. В последние годы общая заболеваемость колоректальным раком, особенно раком прямой и дистальной части толстой кишки, снизилась у лиц старше 50 лет, но увеличилась у лиц моложе 50 лет [17]. Необходимы исследования для выяснения конкретных причинных факторов, поскольку информация о факторах риска в настоящее время основана почти исключительно на данных старших когорт. Американское онкологическое общество снизило рекомендуемый возраст для начала скрининга для лиц со средним риском с 50 до 45 лет в 2018 г. [15]. Что касается показателей 5-летней и 10-летней выживаемости при колоректальном раке, то они составляют 65% и 58%, соответственно [17]. Показатели заболеваемости и смертности от колоректального рака также различаются в зависимости от расы и этнической принадлежности: они самые высокие у чернокожих неиспаноязычного происхождения и самые низкие у американцев азиатского происхождения/жителей островов Тихого океана [10].

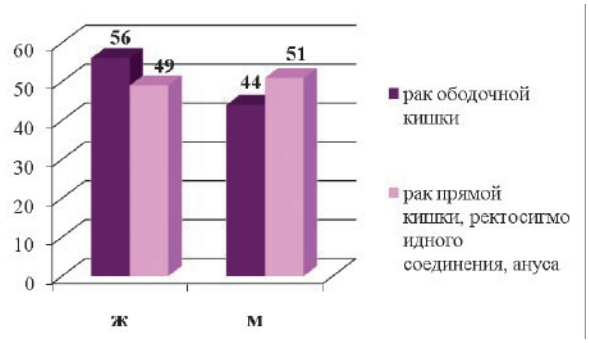

Рисунок 2. *Заболеваемость раком ободочной кишки/ раком прямой кишки, ректосигмоидного соединения, ануса среди мужчин и женщин в Российской Федерации 2019 г. [8]*
Figure 2. *The incidence of colon cancer / rectal cancer, rectosigmoid junction, anus among men and women in the Russian Federation in 2019 [8]*

Пути канцерогенеза

Традиционной моделью канцерогенеза колоректального рака, встречающейся в большинстве случаев (70–90%), является модель последовательной хромосомной нестабильности (модель «аденома-карцинома-метастазы») (Рис. 3) [18]. В данной модели эволюция колоректального рака начинает свое происхождение сначала как аберрантная крипта, которая затем развивается в доброкачественный аденоматозный полип, который в конечном итоге трансформируется в спорадический колоректальный рак. При этом опухолевая прогрессия происходит обычно в течение длительного периода времени (приблизительно 10–15 лет) [19]. Данные фенотипические переходы связаны с накоплением специфических сигнатурных генетических событий «*APC-KRAS-TP53*», известных как модель колоректального онкогенеза человека,

предложенная Vogelstein et al. [20]. Данная модель описывает последовательную инактивацию опухолевого супрессора (инициирование *APC* мутации), активацию онкогена *KRAS* с дальнейшей потерей функции *TP53*. Новые данные, представленные Атласом ракового генома (TCGA), пересмотрели последовательность генных событий как «*APC-TP53-KRAS*» [21,22]. Как показано на рисунке 3, появление аденомы совпадает с инактивирующей мутацией или делецией *APC*, аденокарцинома поддерживает инактивирующие мутации или делецию *TP53* с дисфункцией теломер и двухцепочечным разрывом ДНК, приводящим к индукции хромосомной нестабильности (CIN), а при инвазивном/метастатическом заболевании часто обнаруживают активирующие мутации в онкогене *KRAS* [21].

Альтернативным путем канцерогенеза колоректального рака (около 10%) является так называемый путь зубчатой неоплазии [18]. Характеризуется одним из двух проявлений прогрессирования: (1) сидячий зубчатый путь, при котором микровезикулярный гиперпластический полип прогрессирует в сидячую зубчатую аденому (зубчатое образование на широком основании), а затем либо в микросателлитно нестабильную (MSI), либо микросателлитно стабильную (MSS) карциному или (2) традиционный зубчатый путь, при котором гиперпластический полип, богатый бокаловидными клетками, прогрессирует в традиционную зубчатую аденому, а затем в микросателлитно стабильную карциному (MSS) [23]. Путь зубчатой неоплазии ассоциирован с более высокой частотой мутацией в генах *BRAF* и *KRAS*, повышенным метилированием островков CpG (CIMP) [18], но редко мутациями *APC* [23].

Другой путь развития колоректального рака — рак, ассоциированный с колитом (CAC), чаще всего появляется у пациентов с воспалительным заболеванием кишечника и составляет около 2% случаев [18].

Колоректальный рак можно классифицировать в зависимости от молекулярного подтипа. Известно 4 молекулярных подтипа колоректального рака (consensus molecular subtypes, CMS 1-4): MCH иммунный (CMS1), канонический (CMS2), метаболический (CMS3) и мезенхимальный (CMS4) [24,25]. Опухоли с микросателлитной нестабильностью (MSI), в основном консенсусного молекулярного подтипа 1 (CMS1), имеют характерный паттерн, связанный с огромным числом соматических мутаций и гиперметилированием, опухоли с хромосомной нестабильностью (CIN), в основном относятся к молекулярным подтипам 2-4 (CMS 2-4), развиваются по традиционной модели, предложенной Vogelstein [26]. Считается, что переход от канонического канцерогенеза CMS2 к CMS3 происходит с мутациями *KRAS* и событий, связанных с увеличением числа копий, вызывающих метаболическую дерегуляцию как доминирующий признак на уровне экспрессии генов. В опухолях с CMS4 активация трансформирующего фактора роста-β (TGFβ) из стромально-обогащенного воспаленного микроокружения функционирует как основной фактор эпителиально-мезенхимального перехода (Рис. 4) [24].

Правосторонний и левосторонний колоректальный рак

Правосторонний рак толстой кишки и левосторонний колоректальный рак имеют значительные различия в эпидемиологии, клинических особенностях, дифференцировке опухоли, ответе на лечение, прогнозе

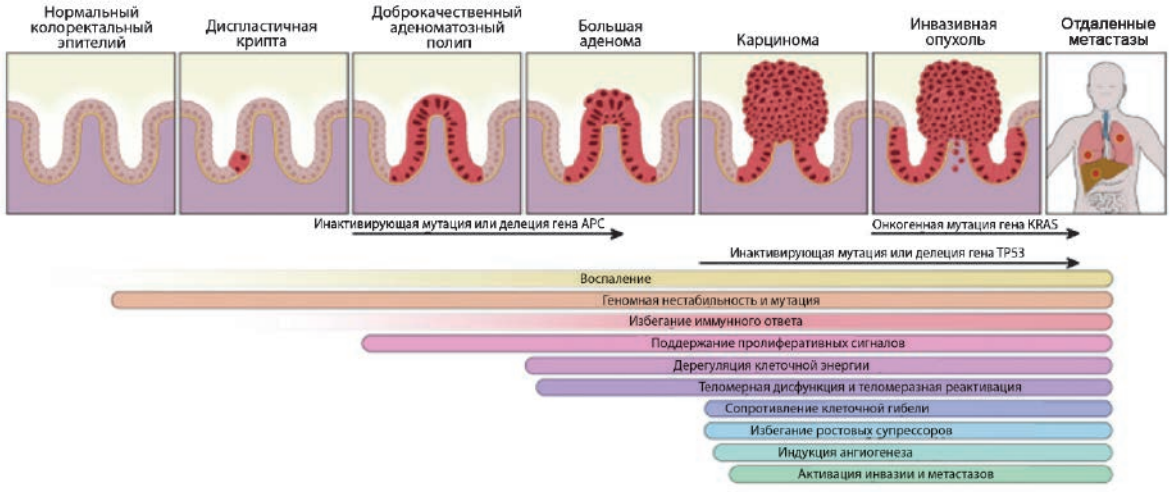

Рисунок 3. *Модель колоректального рака «традиционная аденома-карцинома-метастаз» и соответствующие признаки рака [18]*

Figure 3. *Colorectal cancer "conventional adenoma–carcinoma–metastasis" model and corresponding cancer hallmarks [18]*

и молекулярных характеристиках [27]. Что касается эмбриогенеза кишечника, проксимальная часть (правая) толстой кишки (слепая кишка, восходящая и поперечная ободочная кишка) происходит из эмбриональной средней кишки, тогда как дистальная часть (левая) толстой кишки (селезеночный изгиб, нисходящая ободочная кишка, сигмовидная кишка и прямая кишка) происходит из задней кишки эмбриона [28]. Правосторонний рак толстой кишки имеет более низкую распространенность, чаще развивается у женщин (51–62% случаев) [29] и у афроамериканцев [30], чаще характеризуется низкой дифференцировкой опухоли, сильной инвазией, плохим прогнозом и слабым ответом на ингибиторы рецептора эпидермального фактора роста, имеет тенденцию к высокому уровню метилирования островков CpG (CIMP), проявляет микросателлитную нестабильность (MSI), чаще возникают мутации онкогенов *KRAS* и *BRAF* [19,31,32]. Таким образом, проксимальные поражения более часто представлены иммунным (CMS1) и метаболическим типом (CMS3) [33]. Напротив, дистальные колоректальные опухоли с большей вероятностью проявляются хромосомной нестабильностью (CIN) и имеют более благоприятный прогноз [34]. Левосторонние поражения представлены, в основном, CMS2 и CMS4. К тому же, левосторонние и правосторонние поражения имеют тенденцию к различной симптоматике. Проксимальные опухоли часто проявляются малозаметными признаками и симптомами, такими как микроцитарная анемия и потеря веса, в то время как при дистальном поражении более выражены симптомы ректального кровотечения и нарушения стула [35]. Таким образом, считается, что первичная локализация колоректального рака тесно связана с прогнозом, действуя как независимый прогностический фактор для терапевтической эффективности [36].

Терапия колоректального рака

Химиотерапия

Стандартными методами лечения колоректального рака являются оперативные вмешательства, химиотерапия и лучевая терапия, которые могут использоваться в комбинации в зависимости от локализации и течения заболевания [37,38]. Около 66% и 61% пациентов с раком ободочной и прямой кишки II и III стадии получают адъювантную химиотерапию и/или лучевую терапию, соответственно [39]. Однако эти методы лечения имеют много побочных эффектов из-за их неспецифичности и цитотоксичности по отношению к любым клеткам, включая нормальные клетки, которые растут и делятся. Кроме того, у 54% пациентов рецидивы возникают даже после неоадъювантного лечения [40]. К тому же, у пациентов с неметастатическим колоректальным раком (до 50%) в конечном итоге развивается метастатический колоректальный рак [41]. Таким образом, крайне важно использовать альтернативные и более эффективные методы лечения пациентов с колоректальным раком [42].

Существуют следующие схемы химиотерапии при колоректальном раке: схема FOLFOX (комбинация 5-фторурацил (5-ФУ) и оксалиплатина), схема IFL (иринотекан, болюсный 5-ФУ и лейковорин), схема FOLFIRI (фолиновая кислота (лейковирин), инфузионный 5-ФУ, иринотекан) [43]. 5-фторурацил был первым препаратом для химиотерапии с доказанной активностью против колоректального рака. 5-ФУ — стандарт лечения метастатического

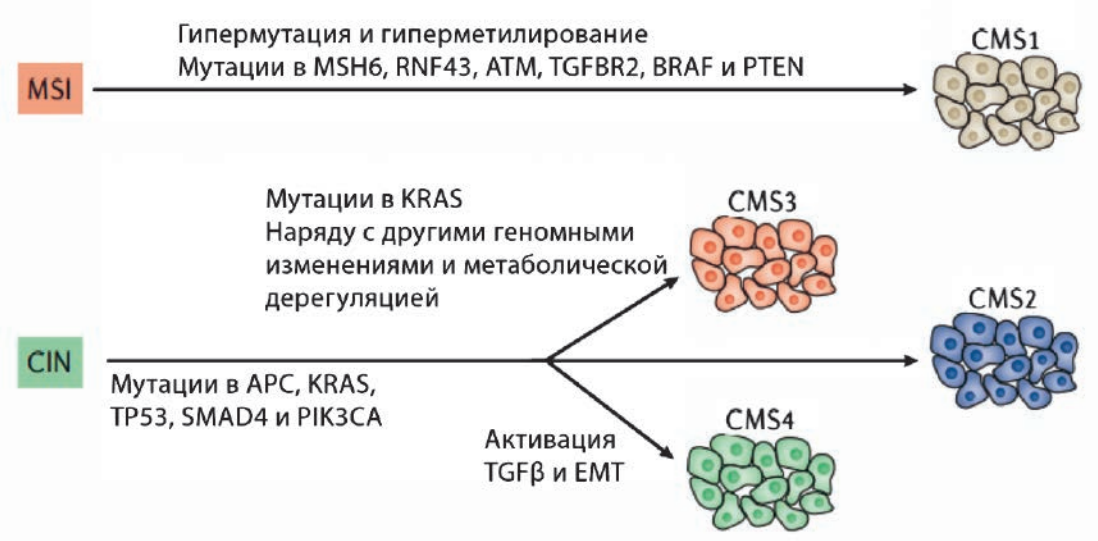

Рисунок 4. *Колоректальный канцерогенез и молекулярные подтипы [24]*
Figure 4. *Colorectal carcinogenesis and molecular subtypes [24]*

колоректального рака с медианой общей выживаемости приблизительно от 8 до 9 месяцев [44]. Пациенты с метастатическим колоректальным раком обычно получают несколько линий терапии, в том числе применяется химиотерапия в сочетании с биопрепаратами в зависимости от особенностей опухоли.

Блокаторы ангиогенеза

Ангиогенез — образование сети новых кровеносных сосудов, — представляет собой удивительный биологический процесс, который способствует росту, пролиферации, организации и выживанию нормальных клеток. Однако он также поддерживает рост и выживание раковых клеток и способствует распространению метастазов [45]. Ангиогенез имеет различное значение при различных видах рака. Например, семейный почечно-клеточный рак зависит от ангиогенеза, но при метастатическом колоректальном раке и большинстве других видов рака ангиогенез способствует, но не является определяющим фактором прогрессирования заболевания [43]. Это опосредуется балансом между проангиогенными и антиангиогенными факторами и рецепторами, включая фактор роста эндотелия сосудов (VEGF), фактор роста тромбоцитов и фактор роста фибробластов [46]. К первому биологическому препарату — блокатору ангиогенеза, одобренному для лечения метастатического колоректального рака [47], относится бевацизумаб. Данный препарат представляет собой гуманизированное моноклональное антитело иммуноглобулина G (IgG), направленное против VEGF-A. Считается, что его потенциальные механизмы действия включают истощение сосудистой сети опухоли, а также временную нормализацию паттерна сосудистой сети опухоли для улучшения доставки препаратов для химиотерапии [48]. Впоследствии, при добавлении бевацизумаба к химиотерапии, была получена более высокая выживаемость [49,50]. Исследования показывают, что бевацизумаб чаще всего используется в первой линии у пациентов с метастатическим колоректальным раком в сочетании с химиотерапией на основе оксалиплатина. Другим разработанным препаратом является афлиберцепт (Залтрап), который представляет собой полностью гуманизированный растворимый рекомбинантный белок, который нацелен на ангиогенез, блокируя VEGF-A, VEGF-B и плацентарный фактор роста. Афлиберцепт обладает более высокой аффинностью связывания с VEGF-A, чем бевацизумаб [51]. Его одобрение во второй линии в комбинации с FOLFIRI основано на результатах двойного слепого исследования VELOR 3 фазы, в котором 1226 пациентов, ранее получавших оксалиплатин, были рандомизированы для получения FOLFIRI плюс афлиберцепт или FOLFIRI плюс плацебо [52]. Добавление афлиберцепта значительно улучшило медиану общей выживаемости до 13,5 месяцев по сравнению с 12,06 месяца в группе плацебо (P = 0,0032) [52]. Рамуцирумаб представляет собой полностью человеческое моноклональное антитело IgG1, нацеленное на внеклеточный домен рецептора 2 фактора роста эндотелия сосудов. Пациенты с прогрессированием после терапии первой линии бевацизумабом, оксалиплатином и фторпиримидином получали рамуцирумаб плюс FOLFIRI или плацебо плюс FOLFIRI. Медиана общей выживаемости была больше в группе рамуцирумаба (13,3 против 11,7 месяцев; P = 0,0219) [53]. Таким образом, как и афлиберцепт, рамуцирумаб также одобрен для использования во второй линии в сочетании с FOLFIRI или иринотеканом. Наконец, современный препарат — регорафениб является ингибитором тирозинкиназы с ингибирующей активностью в отношении многочисленных протеинкиназ, включая киназы, участвующие в ангиогенезе опухоли (VEGFRl,-2,-3, TIE2), онкогенезе (KIT, RET, RAF-1, *BRAF*), метастазировании, а также в противоопухолевом иммунном ответе (CSF1R) [54]. Благодаря этому, регорафениб блокирует пролиферацию опухолевых клеток, в дополнение к тем, которые участвуют в развитии ангиогенеза [54]. Другим препаратом, одобренным для пациентов с рефрактерным метастатическим колоректальным раком без ответа на предшествующую системную терапию (совместно с регорафенибом) [55], является TAS-102 (типирацила гидрохлорид), представляющий собой пероральный препарат, который сочетает в себе два агента, трифлуридин и типирацила гидрохлорид. Трифлуридин встраивается в ДНК, и этот процесс может приводить к противоопухолевым эффектам препарата. Типирацила гидрохлорид помогает поддерживать концентрацию трифлуридина в крови путем ингибирования фермента, расщепляющего трифлуридин. В доклинических исследованиях TAS-102 продемонстрировал противоопухолевую активность в отношении линий раковых клеток, устойчивых к фторурацилу [56].

EGFR препараты

Прежде чем рассматривать назначение анти-VEGF терапии, необходимо проводить исследование на мутации в генах RAS и RAF (*KRAS, NRAS* и *BRAF*) [57]. Рецептор эпидермального фактора роста (EGFR) принадлежит к семейству рецепторных тирозинкиназ ErbB29 и связывание лиганда с его внеклеточным доменом приводит к фосфорилированию тирозинкиназного домена, который активирует сигнальные пути для клеточной пролиферации, ангиогенеза, миграции, выживания и адгезии [58]. К анти-EGFR

препаратам относятся: цетуксимаб и панитумумаб. Цетуксимаб представляет собой химерное мышиное IgG1 mAb31 антитело человека, которое связывается с внеклеточным доменом EGFR, что приводит к подавлению проонкогенной передачи сигналов. Связывание цетуксимаба с естественными клетками-киллерами также может запускать иммуноопосредованный противоопухолевый ответ, приводящий к антителозависимой клеточно-опосредованной цитотоксичности [59]. Цетуксимаб и панитумумаб оба нацелены на EGFR, но их различия не ограничиваются структурой антитела (цетуксимаб является химерным антителом, тогда как панитумумаб является полностью человеческим антителом). Утверждается, что в стандартных дозах панитумумаб вызывает более интенсивную угревую сыпь на коже, чем цетуксимаб. Интенсивность сыпи является клиническим маркером эффективности этого класса препаратов [60], и панитумумаб был разработан после того, как это было установлено, поэтому выбранная доза (6 мг/кг) в некоторой степени основывалась на интенсивности сыпи. Стратегия повышения дозы до максимального развития сыпи использовалась с цетуксимабом в исследовании EVEREST [60], и дозировка при ухудшении акне увеличивала общую частоту ответа, но не влияла на общую выживаемость. Другим различием между двумя препаратами является заметно более высокий риск реакций гиперчувствительности, наблюдаемый при применении цетуксимаба (3,5–7,5%) по сравнению с панитумумабом (0,6–3%) [62].

BRAF-таргетная терапия

Мутации *BRAF* обнаруживаются в 8–12% случаев метастатического колоректального рака, а мутация p.V600E, в частности, обусловливает худший прогноз [63]. Данные опухоли агрессивны и не дают хорошего ответа на системную терапию. Доклинические испытания показали, что ингибирование *BRAF* может вызывать гиперактивацию EGFR и что анти-EGFR терапия может сделать ранее резистентные клеточные линии чувствительными к ингибитору *BRAF* [64]. К *BRAF* таргентной терапии относится препарат вемурафениб — ингибитор BRAF-киназ с активирующими мутациями в кодоне p.V600E. Во 2-й фазе исследования SWOGS140658 была установлена комбинация вемурафениба, иринотекана и цетуксимаба или панитумумаба в качестве последующей терапии метастатического колоректального рака с мутацией *BRAF* V600E. Сто шесть пациентов с опухолями RAS дикого типа с мутацией *BRAF* V600E (которые ранее получали 1 или 2 линию химиотерапии без цетуксимаба) получали иринотекан и цетуксимаб с вемурафенибом или без него. Вемурафениб удлинял медиану выживаемости без прогрессирования заболевания (mPFS) (4,4 против 2,0 месяцев; P < 0,001) и улучшал показатели контроля заболевания (67% против 22%; P = 0,001) [65]. Наиболее распространенные токсические эффекты, связанные с ингибированием *BRAF*, включают сыпь, артралгию, утомляемость и диарею [66].

Ингибиторы иммунных контрольных точек

Несмотря на недавние успехи в ингибировании иммунных контрольных точек при лечении многих видов рака, его преимущества при метастатическом колоректальном раке ограничены [67]. Для 3–7% пациентов с дефектными белками репарации ошибочно спаренных нуклеотидов (dMMR)/микросателлитной нестабильностью (микросателлитная нестабильность — MSI) одобрены ингибиторы PD-1, такие как ниволумаб, пембролизумаб [68]. У этих пациентов обычно имеются низкодифференцированные проксимальные опухоли с обильными опухоль-инфильтрирующими лимфоцитами [67]. Высокий уровень микросателлитной нестабильности (MSI-H) или дефицит белков системы MMR (dMMR) являются предикторами низкого ответа на терапию препаратами фторурацила [69], но определяют вероятность положительного эффекта от иммунотерапии [70]. В случае опухолей с dMMR иммунотерапия назначается как терапия первой линии в адъювантном и неоадъювантном режиме при неметастатическом поражении [71]. Пембролизумаб и ниволумаб представляют собой моноклональные антитела IgG4, которые связываются с PD-1. Токсичность ингибиторов иммунных контрольных точек в значительной степени обусловлена активностью Т-клеток в отношении любой ткани хозяина с последующим аутоиммунным воспалением. Наиболее часто поражаются органы: кожа (сыпь), желудочно-кишечный тракт (колит) и эндокринная система (например, диабет, дисфункция щитовидной железы и гипофизит) [72].

HER2-таргетная терапия

Амплификация Her2 наблюдается в 2–11% случаев метастатического колоректального рака, чаще встречается при левостороннем колоректальном раке и при опухолях прямой кишки и, как считается, придает резистентность к терапии, направленной на EGFR [73]. К HER2-таргетной терапии относятся препараты: трастузумаб и лапатиниб.

Резистентность к терапии

Резистентность к терапии и метастатическое прогрессирование являются двумя критическими факторами неблагоприятного клинического исхода при раке. Несмотря на улучшение показателей ответа

с различными стратегиями подбора терапии, пятилетняя выживаемость при метастатическом колоректальном раке лишь незначительно больше 12 процентов [74]. Это связано с появлением лекарственной устойчивости. Почти половина пациентов с метастатическим колоректальным раком устойчивы к препаратам на основе 5-ФУ [75]. Устойчивость к 5-ФУ тесно связана с экспрессией тимидилатсинтазы (ТС). Так как ТС является основной мишенью 5-ФУ, пациенты с низким уровнем экспрессии ТС имеют лучший ответ на 5-ФУ и более высокую общую выживаемость, чем пациенты с более высокой экспрессией ТС в опухолевой ткани [76]. В случае высокой активности ТС, допустимых концентраций препарата 5-ФУ может быть недостаточно для эффективного ингибирования, то есть токсический эффект 5-ФУ будет неоправданно высоким при назначении необходимой дозы. Тимидинфосфорилаза (ТФ), уридинфосфорилаза (УФ), оротатфосфорибозилтрансфераза (ОФРТ) и дигидропиримидин дегидрогеназы (ДПД) участвуют в метаболизме и деградации 5-ФУ. Высокие уровни экспрессии ТФ, УФ и ОФРТ продемонстрировали в нескольких исследованиях повышенную чувствительность к терапии 5-ФУ [77,78]. Поскольку ДПД способствует деградации 5-ФУ, то уровень его экспрессии обратно пропорционален и коррелирует с химиочувствительностью [78].

Как писалось ранее, другим препаратом, одобренным для лечения колоректального рака, является иринотекан (CPT-11). Иринотекан представляет собой полусинтетическое производное камптотецина, которое селективно ингибирует топоизомеразу I (Топо I). В клетке иринотекан подвергается внутриклеточным модификациям, таким как удаление группы С10 посредством катализа карбоксилэстеразой, а затем метаболизируется, превращаясь в 7-этил10-гидроксикамптотецин (SN-38). SH-38 обладает противораковой активностью в 100–1000 раз выше, чем CPT-11 [79]. Иринотекан или его активный метаболит SN-38 образует комплекс топоизомераза-ингибитор-ДНК, влияющий на функцию ДНК. Следовательно, чем выше концентрация Topo I, тем более чувствительными становятся клетки к иринотекану [80]. Карбоксилэстераза (CES), уридиндифосфатглюкуронозилтрансфераза (UGT), ферменты цитохрома P-450 печени CYP3A, ß-глюкуронидаза и АТФ-связывающий кассетный транспортер (ABC) участвуют в поглощении и метаболизме иринотекана. Следовательно, они определяют лекарственную устойчивость [81,82]. Эпигенетические изменения также принимают участие в развитии резистентности к иринотекану. Изменение ацетилирования гистонов, такое как ацетилирование H4K16, связано с устойчивостью к иринотекану. Комбинированная терапия ингибиторами гистондеацетилазы (HDAC) может преодолеть резистентность к иринотекану [83]. Оксалиплатин, химиотерапевтический препарат на основе платины, также применяется в схемах лечения колоректального рака. Чаще всего его комбинируют с 5-ФУ и лейковорином, фолиновой кислотой. Различие химической структуры между оксалиплатином и другими химиотерапевтическими препаратами на основе платины заключается в том, что оксалиплатин имеет 1,2-диаминоциклогексановый лиганд (DACH). DACH при его соединении с платиной затрудняет репарацию ДНК, тем самым улучшает потенциал уничтожения опухолевых клеток [74]. Устойчивость к оксалиплатину связана с путем эксцизионной репарации нуклеотидов (NER). Уровни экспрессии генов ERCC1, XRCC1 и XDP коррелируют с устойчивостью к оксалиплатину и могут использоваться в качестве предиктора чувствительности к лекарственным средствам [84]. В дополнение к NER, белок WBSCR22 представляет собой новый биомаркер устойчивости к оксалиплатину, а также возможную мишень для терапевтической разработки лекарств [85]. Трансформирующий фактор роста-ß1 (TGF-ß1) обильно секретируется множеством клеток внутри опухолевого микроокружения. Считается, что TGF-ß1 способствует индукции резистентности к оксалиплатину посредством эпителиально-мезенхимального перехода (EMT) [86].

В дополнение к вышеописанным механизмам внутри клеток колоректального рака существует большая гетерогенность. Открытие раковых стволовых клеток и их устойчивости к терапии, а также их способности к самообновлению привлекли внимание к этой своеобразной клеточной популяции. В исследованиях говорится, что эта специфическая подгруппа опухолевых клеток имеет прогностическое значение для пациентов [87]. На сегодняшний день известно, что стволовые клетки колоректального рака имеют специфические поверхностные маркеры, такие как CD133, EphB2high, EpCAMhigh, CD44+, CD166+, ALDH+, LGR5+ и CD44v6+ [88]. Помимо поверхностных маркеров, раковые стволовые клетки можно охарактеризовать по молекулярным особенностям, к примеру — гиперактивированный путь ß-катенина, и функциональным признакам, таким как самообновление [89]. Другим функциональным фенотипом является их экспрессия эффлюксных насосов, таких как АТФ-связывающие транспортные белки семейства ABC, включая ABCG2 [90]. Наличие эффлюксных насосов способствует транспортировке препаратов, например химиотерапевтических соединений, за пределы клетки. Следовательно, раковые стволовые клетки частично более устойчивы к химиотерапии.

ВЫВОД

Несмотря на достижения в изучении, лечении и контроле колоректального рака, данное заболевание продолжает занимать второе место по смертности среди онкологических заболеваний во всем мире. В частности, это связано с тем, что большая часть пациентов по-прежнему сталкивается с резистентностью к терапии. В совокупности для лечения колоректального рака в настоящее время применяется множество химиотерапевтических схем, таргетная терапия и иммунотерапия. Однако при этом заболевании проявляются специфические механизмы, обеспечивающие меньший терапевтический эффект за счет возникновения лекарственной устойчивости. Углубленное изучение лекарственной устойчивости и нацеливание на популяцию раковых стволовых клеток, опухолевого микроокружения представляет собой активно развивающуюся область, которая может в конечном итоге повысить общую выживаемость пациентов с данным заболеванием, а также улучшить их качество жизни.

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Consensus on controversial issues of the surgery for Crohn's disease by Delphi method

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ABSTRACT *AIM: to establish the consensus on controversial issues of the surgery for Crohn's disease by Delphi method.*
METHODS: a cross-sectional study was conducted by the Delphi method. 62 experts voted intramural and anonymous (31.03.23). 5 statements from the current edition of clinical guidelines were selected for correction by working group and further voting [2]. Based on the practical experience of the working group and literature data, 3 new statements were created also. Statements that do not reach the required level of agreement (80% or more) will be subjected to Round 2 of the Delphi method.
RESULTS: all experts took part in the anonymous voting. The panel of experts is represented by 8 different areas of practical medicine and the median of the professional experience of the respondents was 30 (12–49) years. Of the 8 statements submitted for voting, consensus (80% or more) was reached on 6 out of 8. 2 statements have been revised by working group for the distance 2nd round of the Delphi study. Consensus (more than 80%) was reached on both.
CONCLUSION: a cross-sectional study by the Delphi method provided the opinions of a panel of experts on controversial issues in the surgical treatment of Crohn's disease. Statements that reach consensus will be included by the working group in a new edition of clinical guidelines of Crohn's disease.

KEYWORDS: *Crohn's disease, clinical guidelines, surgery, Delphi method*

CONFLICT OF INTEREST: *the authors declare no conflict of interest*

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INTRODUCTION

Crohn's disease (CD) is a disease located in the plane of contact of a large number of medical specialties. Diagnosis and treatment of CD are associated with significant difficulties and represent one of the most pressing problems of modern medicine. Special attention should be paid to the fact that the provisions of the majority of clinical guidelines published in the world on certain CD issues are based only on the opinion of experts, which corresponds to the lowest level of evidence [2,7,21]. Due to the impossibility of large clinical trials, mainly on surgical issues, the authors of many clinical guidelines resort to the help of a panel of experts to consolidate expert opinions [5,8,23].

To achieve consensus on certain issues, the Delphic method is widely used, which allows structuring the process of collecting and consolidating expert opinions. Thus, the Delphi method in modern medicine is widely used in the process of writing clinical guidelines for various specialties [12,26]. In this matter, the methodologically strictly planned Delphic method is able to increase the level of evidence on certain controversial statements, in the absence of relevant literature. To this aim, the working group on the development of a new version of Russian Clinical Guidelines for the diagnosis and treatment of Crohn's disease made this cross-section of experts' opinions on surgical treatment using the Delphic method.

MATERIALS AND METHODS

A cross-sectional study (a cross-section of expert opinions) was done using the Delphi method, by anonymous voting. The completed opinion section is the 1st round of the Delphic Study. The study was done through the successive stages presented below.

The First Stage. The working group has carried out an audit of the current version of the clinical guidelines. In total, 33 statements-recommendations are reflected in the *surgical treatment* section, 19 (57.6%) of which correspond to the level of evidence 5, that is, they are based on the described clinical cases or expert opinions [2]. According to 19 statements, the working group made a literary

Table 1. *Statements of the current version of clinical guidelines 2020 which were selected for voting*

3.2.1 Indications for Surgical Treatment of CD In patients with a complicated CD, when threatening symptoms are detected (peritoneal symptoms, free gas in the abdominal cavity according to abdominal X-ray), emergency surgery is recommended, which in such a situation may be limited to resection of the affected part with anastomosis or stoma [9].	EL — 5
3.2.3 Surgical Treatment of Large Intestine CD If possible, abdominal-perineal extirpation is not recommended in patients with severe perianal lesions [14].	EL — 5
3.2.4 Surgical Treatment of CD with Lesions of the Upper Gastrointestinal Tract In patients of this group, a bypass anastomosis is recommended only in exceptional cases, since the risk of bacterial overgrowth in the diverted part of the small intestine is high, and cancer may also develop. At the same time, extended resections cause the short bowel syndrome [10].	EL — 5
3.2.4 Surgical Treatment of CD with Lesions of the Upper Gastrointestinal Tract In patients of this group, in the presence of single or multiple short strictures, the surgery of choice may be various options for dissection of cicatricial strictures of the small intestine (strictureplasty) [13].	EL — 4
3.2.5 Treatment of CD with Perianal Lesions (Perianal CD) In patients with perianal manifestations of CD, in the presence of stricture of the low rectum or anal canal stenosis, proctosigmoidectomy (or proctectomy) or intersphincteric rectal resectionis recommended [15].	EL — 5

Table 2. *New statements were created by working group*

3.2.2 Surgical Treatment of CD in the Form of Terminal Ileitis or Ileocolitis In patients with a penetrating CD with abdominal abscess, it is recommended to drain it under the control of ultrasound or CT with subsequent conservative treatment (antibacterial, steroids and biotherapy) as an alternative to surgical resection [7,11].	EL — 3
3.2.2 Surgical Treatment of CD in the Form of Terminal Ileitis or Ileocolitis In a patient with a clinical picture of acute appendicitis, upon revision of the abdominal cavity and detection of a macroscopically unchanged appendix and terminal ileitis, is recommended to avoid appendectomy, as well as intestinal resection or ileocecal resection of the intestine [7].	EL — 5
3.2.3 Surgical Treatment of Large Intestine CD In the surgical treatment of large intestine CD with purulent-septic process in the ischioanalregion and perineum, rectal resection is recommended to be performed in the volume of total mesorectumectomy [16].	EL — 3

search, including revision of the statements-recommendations in the latest versions of the world clinical guidelines [3,7,21].

The Second Stage. After a literary revision of 19 statements, 4 theses-recommendations were selected without new level of evidence (5). One statement was allocated by the expert group additionally to reach consensus on the new wording and has the level of evidence (EL) 4 (Table 1).

The Third Stage. All selected statements and recommendations were discussed by the working group in order to clarify new formulations for voting. At this stage, experts also proposed 3 new statements-recommendations for inclusion in the relevant sections of clinical guidelines. It is worth noting that 2 new theses were formulated based on the experience and opinion of experts, and 1 statement has the EL — 3 (Table 2). Thus, at this stage, 8 theses — recommendations for voting have been finalized.

The Fourth Stage. A list of experts involved in the treatment of CD in their clinical practice was compiled for face-to-face voting. Sixty-two experts of different medical specialties were included to achieve one of the principles of the Delphi method — heterogeneity of voters (Table 3).

The Fifth Stage. All 62 experts participated in a secret ballot (31.03.23) on each of the 8 theses-recommendations. The answers to the final formulation of the thesis were as follows: “I agree”, “Partially agree”, “Disagree”, “I find it difficult to answer.”

The prevailing majority of experts participated in the voting in person — 47 (75.8%), online — 15 (24.2%) respondents. Consensus on the thesis was considered achieved with the consent of at least 80% of experts.

RESULTS

Voting was completed on all 8 selected statements, the panel of the experts participated in full (Fig. 1).

Statement No. 1
3.2.1 Indications for Surgical Treatment of CD
In patients with a complicated form of CD, when threatening symptoms are detected (peritoneal symptoms, free gas in the abdominal cavity), emergency surgery is recommended, which in such a situation may be limited to resection of the affected part with the formation of an intestinal stoma.

Agree with the proposed statement — 37 (59.7%), partially agree — 6 (9.7%), disagree — 6 (9.7%), find it difficult to answer — 13 (20.9%). Thus, a consensus of the experts on this issue has not been reached.

Table 3. *Descriptive of voted experts*

Specialty:	***n***
Gastroenterology (internal diseases)	25 (40.4%)
Coloproctology	16 (25.8%)
Surgery, oncology	8 (12.9%)
Pediatric surgery	4 (6.5%)
Pediatrics	3 (4.8%)
Endoscopy	2 (3.2%)
Obstetrics and gynecology	2 (3.2%)
Healthcare organization	2 (3.2%)
Academic degree:	
– Doctor of Medical Sciences – Candidate of Medical Sciences – No degree	46 (74.2%) 14 (22.6%) 2 (3.2%)
Academic title:	
– Academician of the Russian Academy of Sciences – Corresponding Member of the RAS – Professor – Associate Professor – No	7 (11.3%) 4 (6.5%) 19 (30.6%) 11 (17.7%) 21 (33.9%)
Median medical experience, *(min–max), years*	30 (12–49)

Statement No. 2
3.2.4 Surgical Treatment of CD with Lesions of the Upper Gastrointestinal Tract
In patients of this group, it is recommended to resort to the formation of a bypass anastomosis only in exceptional cases, since the risk of bacterial overgrowth in the diverted part of the small intestine is high, and cancer may also develop. At the same time, extended resections cause the short bowel syndrome.

Agree with the proposed statement — 50 (80.6%), partially agree — 3 (4.8%), disagree — 0, find it difficult to answer — 9 (14.6%). A consensus of the experts has been reached.

Statement No. 3
3.2.3 Surgical Treatment of Large Intestine CD
Abdomino-perineal resection (extirpation) is not recommended for patients with severe perianal lesions.

Agree with the proposed statement — 51 (82.2%), partially agree — 1 (1.6%), disagree — 1 (1.6%), find it difficult to answer — 9 (14.6%). A consensus of the experts has been reached.

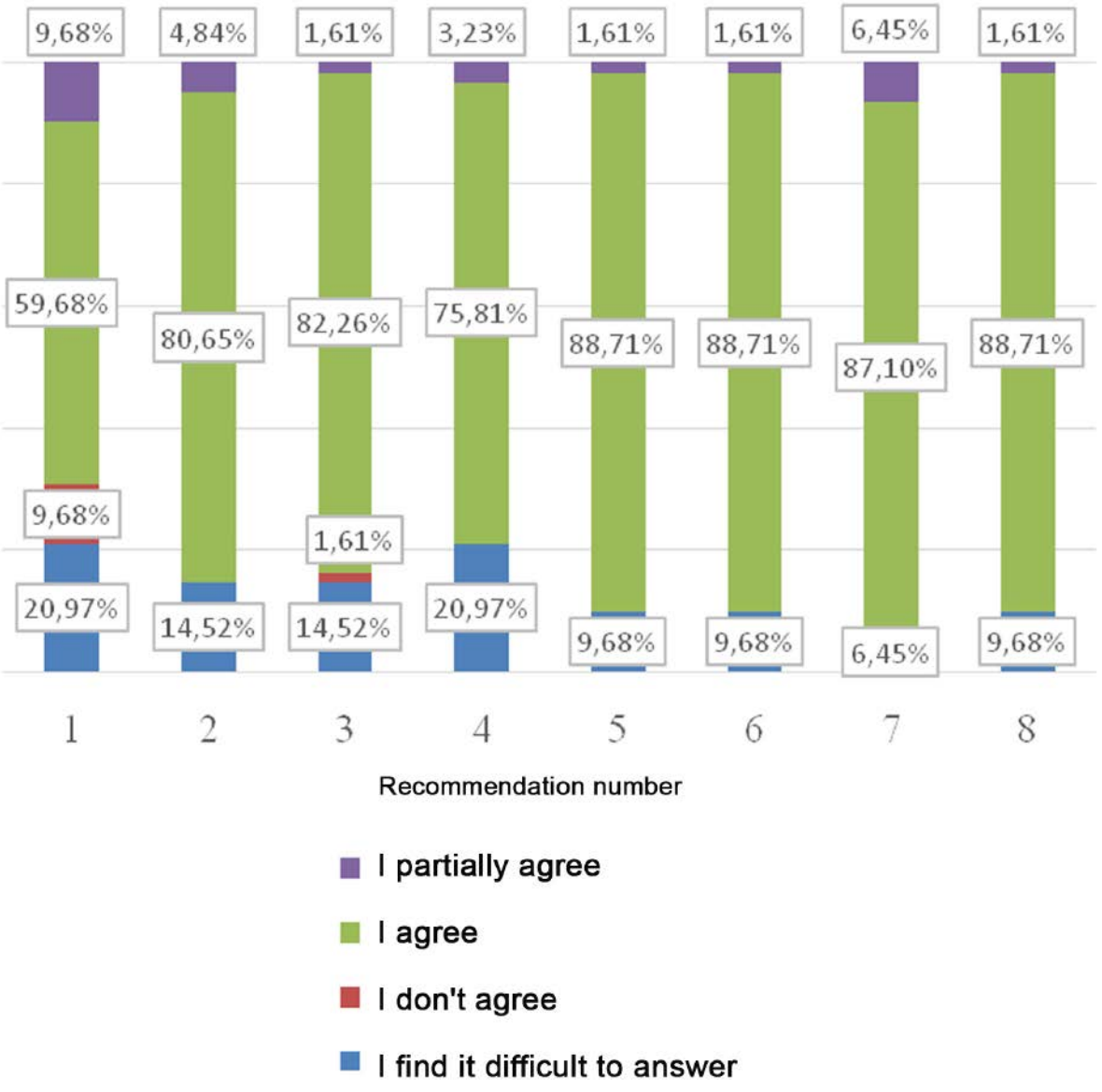

Figure 1. *Histogram of first voting results*

Statement No. 4
3.2.4 Surgical Treatment of CD with Lesions of the Upper Gastrointestinal Tract
In patients of this group, in the presence of strictures, it is recommended to perform various options for dissection of cicatricial strictures of the small intestine (strictureplasty), as an alternative to intestinal resection.

Agree with the proposed statement — 47 (75.8%), partially agree — 2 (3.2%), disagree — 0, find it difficult to answer — 13 (21%). A consensus of the experts was not reached due to the share of those who agreed less than 80%.

Statement No. 5
3.2.5 Treatment of CD with Perianal Lesions (Perianal CD)
Patients with perianal lesions in CD, accompanied by evacuatory disorders and anal incontinence, leading to a significant decrease in the quality of life, are recommended to undergointersphincteric rectal resection.

Agree with the proposed statement — 55 (88.7%), partially agree — 1 (1.6%), disagree — 0, find it difficult to answer — 6 (9.7%). A consensus of the experts has been reached.

Statement No. 6
3.2.2 Surgical Treatment of CD in the Form of Terminal Ileitis or Ileocolitis
In the penetrating form of CD with abdominal abscess, it is recommended to drain it under the control of ultrasound or CT with subsequent conservative treatment (antibacterial, steroid therapy and biotherapy) as an alternative to surgical treatment by resection.

Agree with the proposed statement — 55 (88.7%), partially agree — 1 (1.6%), disagree — 0, find it difficult to answer — 6 (9.7%). A consensus of the experts has been reached.

Statement No. 7
3.2.2 Surgical Treatment of CD in the Form of Terminal Ileitis or Ileocolitis
In a patient, with a clinical picture of acute appendicitis during the revision of the abdominal cavity and the detection of a macroscopically unchanged appendix and terminal ileitis, it is recommended to avoid appendectomy, as well as small intestine resection or ileocecal resection.

Agree with the proposed statement — 54 (87.2%), partially agree — 4 (6.4%), disagree — 0, find it difficult to answer — 4 (6.4%). A consensus of the experts has been reached.

Statement No. 8
3.2.3 Surgical Treatment of Large Intestine CD
In the surgical treatment of large intestine CD with purulent-septic process in the ischioanal region and perineum, rectal resection is recommended to be performed in the volume of total mesorectumectomy.

Agree with the proposed statement — 55 (88.7%), partially agree — 1 (1.6%), disagree — 0, find it difficult to answer — 6 (9.7%). A consensus of the experts has been reached.

DISCUSSION

The cross-sectional study made it possible to reach a consensus of the panel of experts on 6 statements out of 8. To obtain a consensus, a consensus value of 80% or more was chosen. At the same time, to date, there is no unambiguous threshold value of the frequency of consent of respondents in the literature. A systematic review by Diamond, R., et al., summarizing 98 studies on the Delphi method, demonstrated a median frequency of expert consent — 75% [12]. Along with this, for a full assessment, it is extremely important to objectify the degree of expert consent. For this purpose, the Likert scale is most often used in the literature [8]. In this study, no such assessment was made, since the main purpose of the vote was to obtain only a cross-section of experts' opinions on controversial issues for further full-fledged rounds of the Delphic Study. It is important to note that the entire methodology of the study is based on a set of literary data combined in a systematic review and published guidelines by Spranger, J., et al., as well as in the domestic study by Zabolotskikh, I.B., Grigoriev, S.V., et al. [1,26].

An important aspect in the results obtained is that in the absence of any response from the expert, it was recorded as "I find it difficult to answer."

A similar situation is registered in less than 10% of all responses. Fixing the omissions, as the answer "I find it difficult to answer," made it possible to eliminate the bias of the results towards the positive and objectify the result of the vote, reducing the proportion of consenting experts. No consensus was reached by the panel of experts on the 2 statements presented.

Statement No. 1. Section 3.2.1 Indications for Surgical Treatment of CD *In patients with a complicated form of CD, when threatening symptoms are detected(peritoneal symptoms, free gas in the abdominal cavity), emergency surgery is recommended, which in such a situation may be limited to resection of the affected part with the formation of an intestinal stoma.*

Intestinal perforation is recorded in no more than 3% of patients with Crohn's disease. Perforation is one of the rare complications in the natural course of CD. However, it may be the first manifestation of the disease in one quarter of these patients [27]. It is known that more often perforation in CD develops in the small intestine, which leads to acute peritonitis, which is most often generalized and requires emergency surgery [22].

It has been shown that postponement of surgery by more than 6 hours in patients with septic shock due to gastro-intestinal perforation is accompanied by zero 60-day survival [6]. At the same time, there is currently no consensus on the optimal volume of surgery. There is no convincing evidence that intestinal resection with the formation of an anastomosis in stable patients with intestinal perforation significantly increases the rate of postoperative complications and mortality. In some situations, especially in the case of an unstable condition of the patient, it is impossible to perform resection or exteriorization of the bowel loop with a perforated segment due to a severe infiltrative process. In this regard, Statement No. 1 needs to be corrected in its wording for subsequent rounds of Delphi.

Statement No. 4. Section 3.2.4 Surgical Treatment of CD with Lesions of the Upper Gastrointestinal Tract

In patients of this group, in the presence of strictures, it is recommended to perform various options for dissection of cicatricial strictures of the small intestine (strictureplasty), as an alternative to intestinal resection. As it is known, surgeries for strictures in Crohn's disease include strictureplasty or segmental resection of the intestine [25]. There are many different types of strictureplasty, the choice of each of which depends on the extent of the stricture. The most commonly performed plastic surgery is the Heinecke-Mikulicz method, in which a longitudinal incision is made along a narrow section of the stricture and sutured in the transverse direction. According to the literature, it has been established that this type of strictureplasty can be performed with a stricture length of no more than 10 cm [2]. With a longer length of strictures, it is possible to perform procedures by Finneyor Michelassi [7]. It should be noted that in the Russian literature there are only isolated publications on the topic of strictureplasty, which may indicate insufficient experience in performing such procedures in the country. In addition, the presented statement looks rather generalized, does not contain specific criteria for selecting patients to perform strictureplasty. All this probably caused the lack of the required level of consent of respondents and Statement No. 4 will be adjusted before the next round of the Delphic study.

Of course, special attention should be paid to the new statements formed by the working group based on the clinical practice and literature data.

In the surgical treatment of colorectal CD with purulent-septic process in the ischioanalregion and perineum, rectal resection is recommended to be performed in the volume of total mesorectumectomy.

Recently, evidence has accumulated that in CD, the mesentery of the intestine plays a key role in the pathogenesis of the inflammatory process in the intestinal wall. Thus, according to de Groof et al., mesorectum contains an increased number of activated CD14 + macrophages producing anti-TNF, as well as a reduced concentration of the wound healing marker CD206 compared to similar tissue in ulcerative colitis. These fundamental data are also of practical importance, since the performance of total mesorectumectomy, in comparison with the resection of the rectum along the wall with the preservation of adipose tissue in the pelvic cavity, is accompanied by a lower rate of postoperative complications in the perineum, including recurrence of CD: 17.6% and 59.5%, $p = 0.007$ [16]. It is important to note that we are talking about Crohn's disease with pronounced perianal lesions, purulent-septic process in the perineum. The decision on the need to perform mesorectumectomy in other situations remains at the discretion of the operating surgeon.

In the penetrating form of CD with abdominal abscess, it is recommended to drain it under the control of ultrasound or CT with subsequent conservative

treatment (antibacterial, steroid therapy and biotherapy) as an alternative to surgical resection.

The selection of this statement is mainly based on the practical experience of the authors of the working group, as well as on the data of publications on the surgical treatment of CD [21]. Drainage of the abdominal abscess and subsequent conservative treatment serve as a bridge to resection, allowing to reduce the extent of surgery due to the reduction in the size of inflammatory changes. It is also important to note that the conservative treatment after drainage reduces the likelihood of failure of intestinal anastomosis, the formation of external intestinal fistulas and the need for the formation of an intestinal stoma after elective intestinal resection [18,22]. In particular, in the meta-analysis by He, X., et al. a significant decrease in the probability of postoperative complications was revealed (OR = 0.44; 95% CI, 0.23–0.83; p = 0.03) [17]. In the case of primary resection of the intestine in conditions of infiltration and abscess of the abdominal cavity in CD, the extent of resection increases, which can subsequently lead to the short bowel syndrome [19].

It is important to emphasize that according to a systematic review by Clancy, S., et al., abscess drainage in combination with conservative treatment allowed to avoid resectional surgery in more than 30% of patients [11].

In a patient with a clinical picture of acute appendicitis, during the revision of the abdominal cavity and the detection of a macroscopically unchanged appendix and terminal ileitis, is recommended to avoid appendectomy, as well as small intestine resection or ileocecal resection.

Sometimes the onset of Crohn's disease in the form of terminal ileitis can occur under the guise of acute appendicitis, which leads to hospitalization of the patient in a general surgical hospital and often to appendectomy and unjustified resection of the affected ileum [4,20]. In the clinical guidelines of the Russian Society of Surgeons in 2020, this situation is described as "secondary appendicitis". In this case, it is strongly recommended to refrain from performing appendectomy in the absence of macroscopic signs of secondary inflammation in the appendix.

There are no prospective studies on this topic. In 2021, a systematic review by Quaresma, A.B. was published, based on data from 6 retrospective studies, most of which are descriptions of clinical cases. As a result of the review, the authors do not recommend appendectomy and primary resection of the ileum in uncomplicated CD [24]. It is important to note that this statement is consistent with the consensus position of the panel of experts of the European Organization for the Study of UC and CD (ECCO) and the European Association of Coloproctologists (ESCP) [3,7].

CONCLUSION

The study using the Delphi method allowed us to obtain a cross-section of the opinions of a panel of experts on controversial issues of surgical treatment of Crohn's disease. The statements that initially reached consensus will be included by the working group in the new edition of clinical guidelines for the diagnosis and treatment of CD. Statements that have not reached the required level of agreement will be corrected and an additional round of Delphic Research will be conducted. In conclusion, it should be noted separately that the methodology used to achieve consensus on certain controversial issues demonstrates itself as one of the useful methods for increasing the level of evidence credibility in future versions of clinical recommendations.

SECOND ROUND OF DELPHI VOTING

According to the results of the voting on April 31, 23, two statements did not reach the required level of agreement of experts (80%). In this regard, statements were subjected to a second revision and correction by the working group in order to conduct the 2nd round of the Delphic voting in order to reach a consensus.

In the period from 05 May 2023 to 16 May 23, absentee voting was held using a questionnaire in the form of an online form with the participation of representatives of the previous panel of experts. New formulations of statements are presented in the online form. To objectify the 2nd round of voting, an assessment of the level of agreement of the expert on the Likert scale was added (from 1 — "strongly disagree" to 9 — "strongly agree"). The level of agreement to reach consensus was chosen as the previous one — 80%,

and the value on the Likert's scale was determined to be at least 8 points.

3.2.1 Indications for surgical treatment of CD
In patients with a complicated CD, in case of perforation of the small/colon into the free abdomen, with the development of acute peritonitis, emergency surgical intervention is recommended with resection of the affected intestine and, preferably, with the formation of an intestinal stoma [30].
EL — 4.
Comment: *The formation of an intestinal stoma, as an alternative to primary anastomosis, in complicated CD and contamination of the abdominal cavity due to perforation into the free abdominal cavity, reduces the risk of septic complications and recurrence of CD.*

Agree with the proposed statement — 91.3%, partially agree — 2.9%, disagree — 0, find it difficult to answer — 1.4%. The median of the Likert's scale is 9 (8, 9). A consensus of the experts has been reached.

3.2.4 Surgical treatment of CD with lesions of the upper GI
In patients of this group in the presence of isolated strictures of the small intestine, it is recommended to perform various types of strictureplasty as an alternative to bowel resection [28,29].
EL — 2
Comment: *In the case of a stricture of the small intestine less than 10 cm, the Heineke-Mikulich's strictureplasty should be chosen. With a greater length of strictures or the presence of multiple consecutive stenosises, it is preferable to perform bowel resection or Finney's, Michelasi's strictureplasty, if there is appropriate surgical experience.*

Agree with the proposed statement — 89.9%, partially agree — 8.7%, disagree — 0, find it difficult to answer — 1.4%. The median of the Likert's scale is 9 (9, 9). A consensus of the experts has been reached.
As a result of the 2nd round of the Delphi voting, a panel of experts reached a consensus on the new statements. Thus, the submitted abstracts will be included by the working group in the new edition of clinical guidelines for the diagnosis and treatment of Crohn's disease.

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ЮБИЛЕЙ
СЕМИОНКИН Евгений Иванович

18 июня 2023 года доценту Семионкину Евгению Ивановичу исполняется 75 лет со дня рождения.

Евгений Иванович — высококвалифицированный хирург-колопроктолог, около 50 лет ведет врачебную, педагогическую и научную деятельность. В 1972 году окончил Рязанский медицинский институт. После прохождения целевой ординатуры с 1974 по 1979 гг. работал врачом-ординатором хирургического отделения медико-санитарной части в системе 3-го Гл. Управления Минздрава СССР в г. Уч-Кудуке Узбекской ССР, закончил заочную аспирантуру по хирургии, защитил кандидатскую диссертацию.

С 1980 года его жизнь связана с Рязанским государственным медицинским университетом. Ассистент, с 2001 года получил статус доцента, куратор отделения колопроктологии областной клинической больницы. Своими Учителями по колопроктологии считает основоположников колопроктологии на Рязанской Земле — лауреата Всероссийской профессиональной медицинской премии «Призвание» в номинации «За верность профессии» Аллу Ильиничну Левушкину и Анатолия Тимофеевича Хубезова, а также заслуженного деятеля науки РФ, профессора Валентина Павловича Петрова. В настоящее время отделение располагает 40 койками, в год выполняется более 1000 операций, широко используются лапароскопические технологии; при раке прямой кишки около 80% составляют сфинктеросохраняющие операции. В отделении проводится преподавание колопроктологии студентам медицинского вуза и колледжа, врачам ординаторам, курсантам постдипломной подготовки.

Семионкин Е.И. — автор и соавтор более 120 научных публикаций по проблемам колопроктологии, онкологии, хирургии, пособий для студентов на русском языке и французском языках. Известен как автор первого учебника в России по колопроктологии для медицинских ВУЗов: «Колопроктология: учебник». В центральных медицинских издательствах Москвы и Санкт-Петербурга им изданы большим тиражом три учебных пособия и Атлас колопроктологических заболеваний.

За учебное пособие «Колопроктология» (М: ИД МЕДПРАКТИКА — М, 2004, 224 с.) Евгений Иванович награжден дипломом программы «300 лучших учебников для высшей школы» (Санкт-Петербург, 2006 г.); за учебник «Колопроктология» (СПБ.: Эко-Вектор, 2018, 285 с.: ил.) — награжден дипломом победителя II степени в VI Международном конкурсе в сфере образования, г.Саратов, 2022.

В 2022 году им опубликована монография «Оптимизация хирургического лечения рака толстой кишки», по международному обмену читал лекции по колопроктологии в Витебском государственном медицинском университете (Беларусь).

Награжден Почетной грамотой Министра Здравоохранения РФ, нагрудным знаком «Отличник здравоохранения», юбилейной медалью «К 70 -летию Рязанской области».

Член Ассоциации колопроктологов России, член общества хирургов колопроктологов и гастроэнтерологов.

Коллектив Рязанского государственного медицинского института им. акад. И.П. Павлова, Областная клиническая больница г. Рязани, а также редакционная коллегия журнала «Колопроктология» горячо поздравляют юбиляра и желают здоровья, активного долголетия и дальнейших творческих успехов.

Общероссийская общественная организация «Ассоциация колопроктологов России», созданная 3 октября 1991 г. по инициативе врачей-колопроктологов РФ, является уникальной в своей сфере и одной из старейших общественных медицинских организаций. На данный момент в Ассоциации состоит более 800 колопроктологов практически из всех субъектов РФ

ОСНОВНЫЕ ЦЕЛИ И ЗАДАЧИ ОРГАНИЗАЦИИ

- совершенствование и улучшение лечебно-диагностической помощи больным с заболеваниями толстой кишки, анального канала и промежности;
- профессиональная подготовка, специализация врачей-колопроктологов, повышение их профессионального, научного и интеллектуального уровня;
- защита профессиональных и личных интересов врачей-колопроктологов в государственных, общественных и других организациях в РФ и за рубежом;
- разработка и внедрение новых организационных и лечебно-диагностических технологий и более рациональных форм организации помощи колопроктологическим больным в практику работы региональных колопроктологических центров, отделений и кабинетов;
- издание научно-практического медицинского журнала «Колопроктология», входящего в перечень рецензируемых журналов и изданий ВАК Министерства образования и науки РФ;
- международное сотрудничество с организациями и объединениями колопроктологов и врачей смежных специальностей, участие в организации и работе различных зарубежных конференций;
- организация и проведение Всероссийских Съездов колопроктологов, а также общероссийских межрегиональных и региональных конференций, симпозиумов и семинаров по актуальным проблемам колопроктологии.

ПРЕИМУЩЕСТВА ЧЛЕНСТВА В АССОЦИАЦИИ

- более низкие регистрационные взносы на участие в Общероссийских научно-практических мероприятиях;
- преимущества при зачислении на цикл повышения квалификации;
- информационная поддержка и юридически-правовая защита членов Ассоциации;
- членам Ассоциации выдается сертификат установленного Правлением образца.

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Членами Ассоциации могут быть граждане РФ и иностранные граждане, имеющие высшее медицинское образования, прошедшие специализацию по колопроктологии, работающие в области колопроктологии не менее 3-х лет, признающие Устав организации и участвующие в ее деятельности

ОБУЧЕНИЕ КОЛОПРОКТОЛОГОВ НА БАЗЕ ФГБУ «НМИЦ КОЛОПРОКТОЛОГИИ ИМЕНИ А.Н. РЫЖИХ» МИНЗДРАВА РОССИИ

Ординатура по специальности:

- Анестезиология-реаниматология
- Ультразвуковая диагностика
- Гастроэнтерология
- Колопроктология
- Эндоскопия

Профессиональная переподготовка:

- Колопроктология
- Эндоскопия

Повышение квалификации:

- Колопроктология
- Эндоскопия
- Колоноскопия. Теория и практика выполнения
- Обеспечение анестезиологического пособия колопроктологическим больным
- Лапароскопические технологии в колопроктологии
- Функциональные методы диагностики и лечения болезней толстой кишки
- УЗ-методы диагностики в колопроктологии
- Гастроэнтерология
- Дополнительная профессиональная программа повышения квалификации «Колопроктология: симуляционный курс по отработке практических навыков»

НАУЧНО-ОБРАЗОВАТЕЛЬНЫЙ ОТДЕЛ:

123423, г. Москва, ул. Саляма Адиля, д. 2, каб. А002 (цокольный этаж)
Заведующая учебной частью –
Шадина Наталья Евгеньевна
тел.: +7 (499) 642-54-41 доб. 2002
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Главный бухгалтер:
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Реквизиты для уплаты членских взносов:

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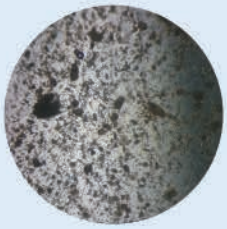
Детралекс® — микронизированная очищенная флавоноидная фракция[1]

Детралекс®[3]



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1 2 3 4 5 6 7 дни

по 1 таблетке 3 раза в день

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Стадия геморроя	1	2	3	4
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ДЕТРАЛЕКС®	✓	✓	✓	✓
Нехирургические амбулаторные процедуры		✓	✓	
Оперативное лечение			✓	✓

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Детралекс®: краткая информация по безопасности

Состав*. Очищенная микронизированная флавоноидная фракция 500 мг: диосмин 450 мг, флавоноиды в пересчете на гесперидин 50 мг. Очищенная микронизированная флавоноидная фракция 1000 мг: диосмин 900 мг, флавоноиды в пересчете на гесперидин 100 мг. **Показания*.** Терапия симптомов хронических заболеваний вен (устранение и облегчение симптомов). Терапия симптомов венозно-лимфатической недостаточности: боль, судороги ног, ощущение тяжести и распирания в ногах, «усталость» ног. Терапия проявлений венозно-лимфатической недостаточности: отеки ног, трофические изменения кожи и подкожной клетчатки, венозные трофические язвы ног. Симптоматическая терапия острого и хронического геморроя. **Способ применения и дозы*.** Венозно-лимфатическая недостаточность — 1000 мг в сутки. Острый геморрой — до 3000 мг в сутки. Хронический геморрой — 1000 мг в сутки. **Противопоказания*.** Гиперчувствительность к действующему веществу или любому из вспомогательных веществ, входящих в состав препарата. **Особые указания*.** Назначение препарата не заменяет специфического лечения заболеваний прямой кишки и анального канала. Если симптомы геморроя сохраняются после рекомендуемого курса терапии, следует пройти осмотр у проктолога, который подберет дальнейшую терапию. **Взаимодействие*. Беременность*/Лактация*.** Не применять препарат. **Фертильность*. Влияние на способность управлять транспортными средствами, механизмами*. Побочное действие*.** Часто: диарея, диспепсия, тошнота, рвота. Нечасто: колит. Редко: головокружение, головная боль, общее недомогание, кожная сыпь, кожный зуд, крапивница. Частота неизвестна: боль в животе, изолированный отек лица, губ, век. В исключительных случаях — ангионевротический отек. **Передозировка*. Фармакологические свойства*.** Детралекс® обладает венотонизирующим и ангиопротективным свойствами. Препарат уменьшает растяжимость вен и венозный застой, снижает проницаемость капилляров и повышает их резистентность. **Форма выпуска*.** * Для получения полной информации, пожалуйста, обратитесь к общей характеристике лекарственного препарата или получите консультацию специалиста.

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