

# Oncological standards in the treatment of diffuse inflammatory diseases of the colon

O. I. Poyda<sup>1</sup>, V. M. Melnyk<sup>2</sup>

Bogomolets National Medical University, Kyiv, Ukraine

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colon, ulcerative colitis, Crohn's disease, malignancy, oncoprevention.

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\*E-mail: qwerasd.v@ukr.net

**Aim.** To improve the effectiveness of cancer prevention and the results of surgical treatment in diffuse inflammatory diseases of the colon by identifying and using risk factors for malignancy, improving diagnostic methods, surgical strategy and tactics.

**Materials and methods.** Using generally accepted oncological standards, 36 patients with diffuse inflammatory diseases of the colon were operated on. There were 20 (55.6 %) patients with ulcerative colitis and 16 (44.4 %) with Crohn's disease of the colon. There were 19 (52.7 %) men and 17 (47.3 %) women. The patients' age ranged from 21 to 56 years. When performing surgical interventions, we were guided by the studied risk factors for malignancy, the provisions of the surgical strategy and tactics, that included the indication choice, the surgical intervention extent, and the ensuring of oncoprevention.

**Results.** The use of oncological standards, provisions of surgical strategy and tactics prevented the occurrence of postoperative mortality, malignancy of precancerous conditions, contributed to a decrease in the incidence of early postoperative complications to 5 (13.9 %), locoregional recurrence to 1 (2.8 %).

**Conclusions.** Determination of risk factors for malignancy, improvement of diagnostic methods, surgical strategy and tactics in diffuse inflammatory diseases of the colon contribute to the timely detection of precancerous conditions, malignancy and colon cancer, justification for the feasibility of performing surgical interventions using generally accepted oncological standards. Performing surgical interventions with the use of generally accepted oncological standards, proven provisions of strategy and tactics have made it possible to prevent the occurrence of malignization of precancerous conditions, cases of postoperative mortality, reduce the frequency of early postoperative complications to 5 (13.9 %) and locoregional recurrences to 1 (2.8 %).

## Ключові слова:

товста кишка, виразковий коліт, хвороба Крона, малігнізація, онкопrevenція.

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## Онкологічні стандарти в лікуванні дифузних запальних захворювань товстої кишки

О. І. Пойда, В. М. Мельник

**Мета роботи** – покращити ефективність профілактики раку та результати хірургічного лікування при дифузних запальних захворюваннях товстої кишки шляхом визначення та використання факторів ризику виникнення малігнізації, удосконалення методів діагностики, хірургічної стратегії та тактики.

**Матеріали та методи.** Прооперували 36 пацієнтів із дифузними запальними захворюваннями товстої кишки, спираючись на загальноприйнятні онкологічні стандарти. З приводу виразкового коліту прооперували 20 (55,6 %) осіб, хвороби Крона товстої кишки – 16 (44,4 %). У дослідження залучили 19 (52,7 %) чоловіків і 17 (47,3 %) жінок віком 21–56 років. Під час виконання оперативних втручань керувалися опрацьованими факторами ризику виникнення малігнізації, положеннями хірургічної стратегії та тактики, що полягали у виборі показань, обсягу виконання оперативного втручання, забезпеченні онкопrevenції.

**Результати.** Використання онкологічних стандартів, положень хірургічної стратегії та тактики запобігало випадкам післяопераційної летальності, малігнізації передракових станів, сприяло зменшенню частоти виникнення ранніх післяопераційних ускладнень до 5 (13,9 %), локорегіональних рецидивів – до 1 (2,8 %).

**Висновки.** Визначення факторів ризику виникнення малігнізації, удосконалення методів діагностики, хірургічної стратегії та тактики при дифузних запальних захворюваннях товстої кишки сприяють своєчасному виявленню передракових станів, малігнізації та раку товстої кишки, а також обґрунтовують доцільність виконання хірургічних втручань із використанням загальноприйнятних онкологічних стандартів. Виконання хірургічних втручань відповідно до чинних онкологічних стандартів, опрацьовані положення стратегії та тактики дали змогу запобігти виникненню малігнізації передракових станів, післяопераційній летальності, зменшити частоту виникнення ранніх післяопераційних ускладнень (до 5 (13,9 %) випадків) і локорегіональних рецидивів (в 1 (2,8 %) хворого).

Diffuse inflammatory diseases, in particular, ulcerative colitis and Crohn's disease of the colon, rank third among precancerous conditions after familial adenomatous polyposis and colon polyps [1,9]. Given the predominantly young age of patients, a significant incidence rate of 30–50 and 2–4 cases per 100,000 population a year for ulcerative colitis and Crohn's disease, respectively, their significant prevalence in the specified population, ranging from 37 to 248 patients in the United States [9,10], 4.9 to 505.0 in

Europe [9,10], 35–60 in Ukraine [3,6] with a clear tendency to increase, a significant probability of malignancy in the range of 7.2–11.2 % with a disease duration of 20 years or more [7,8], the need and validity of timely diagnosis, adequate and effective treatment of these diseases should be considered as a significant contribution to the problem of colon cancer prevention.

An important feature of ulcerative colitis and Crohn's disease of the colon is the difficult diagnosing of malignant

foci in the preoperative period before surgery. This is mainly due to the technical difficulties of colonoscopy as a result of existing complications, in particular, colonic stricture caused by scarring deformation of its walls, pseudo-obstruction caused by inflammatory paracolic infiltrates [4,5]. Most likely, this is the reason why foci of malignancy in 10.5–20.3 % of patients are detected retrospectively only during macroscopic and pathological examination of removed colon macropreparations [1,5].

These circumstances need the improvement of diagnostic methods, surgical strategy and tactics in diffuse inflammatory bowel disease, especially in the case of their prolonged course and a significant risk of chronic complications.

## Aim

To improve the effectiveness of cancer prevention and the results of surgical treatment in diffuse inflammatory diseases of the colon by identifying and using risk factors for malignancy, improving diagnostic methods, surgical strategy and tactics.

## Materials and methods

The implementation of the colon cancer prevention program was carried out by identifying and using the following risk factors for malignancy:

- disease duration of 8 years or more;
- chronic continuous course;
- chronic recurrent remitting course;
- resistance to conservative therapy (including hormone-dependent and hormone-resistant forms);
- severe dysplasia (intraepithelial neoplasia);
- total damage to the colon;
- severe lesions (III degree) in the mucous membrane according to endoscopic examination and endosonography, irreversible changes in the colonic wall;
- the presence of colonic strictures;
- the presence of primary sclerosing cholangitis;
- immunohistochemical examination: increased proliferative activity of epithelial cells, decreased apoptosis in ulcerative colitis, low level of apoptosis in Crohn's disease.

The above risk factors for malignancy indicated the aggressiveness of the disease course, the presence of significant irreversible morphological changes in the mucous membrane and other layers of the colonic wall, insufficient effectiveness and futility of further conservative treatment. That is why in case of prolonged course of diffuse inflammatory diseases of the colon, more than 8 years, in the presence of one or, especially, several of the above risk factors, patients were monitored annually with mandatory colonoscopy and biopsy for timely detection of malignant foci.

In addition, an algorithm for the prevention of colon cancer as a chronic complication of inflammatory diseases was developed and implemented in clinical practice. This algorithm included the following measures:

1. Timely and up-to-date diagnosis and differential diagnosis of inflammatory bowel disease;
2. Effective, disease-modifying, anti-relapse therapy as primary chemoprevention of colon cancer;

3. Endoscopic and morphological monitoring of the colon, especially in the presence of risk factors for malignancy;

4. Timely determination of indications and adequate (using oncological standards) surgical treatment.

The study was conducted at the Coloproctological Center of Ukraine – the main clinical base of the Department of Surgery No. 1 of Bogomolets National Medical University.

For the diagnosis of ulcerative colitis and Crohn's disease of the colon, general clinical examination methods were used: analysis of complaints and medical history, results of objective examination methods, including palpation, percussion, auscultation; clinical and biochemical laboratory tests in blood, urine, and faeces.

Special methods of examination of the colon included proctological examination, namely, examination of the perianal area, digital rectal examination, anoscopy, rectomanoscopy; colonoscopy; pathological examination of biopsies; irrography in the phase of filling the colon with contrast and in the phase of emptying; esophagogastroduodenoscopy, capsule enteroscopy, balloon enteroscopy; abdominal ultrasound, endo-ultrasound examination; abdominal CT or MRI, CT or MRI enterocolonography, if indicated. Indications for CT or MRI enterocolonography were mostly cases of impossibility to perform colonoscopy and biopsy for technical reasons, in cases of complications, in particular, long tubular strictures of the colon.

Methods of endoscopic microscopy, in particular, laser confocal endomicroscopy, spectral color imaging, zoom (magnifying) endoscopy, which provide 1000-fold magnification and a significant resolution of up to 0.7 microns, the possibility of examining the surface and sub-surface structures of the intestinal canal wall, high-quality visualization of intramural blood vessels of small diameter, diagnosis of neoplasia without biopsy are quite informative in the practice of diagnosing diffuse inflammatory diseases of the colon and their complications. However, chromocolonoscopy and photodynamic colonoscopy were of great importance as topical diagnostic methods that help to determine the areas of localization of the most marked morphological changes. These methods were often used to identify foci of dysplasia and malignancy. This made it possible to perform a biopsy from the lesions and thus to increase the diagnostic accuracy with a significant reduction in the number of biopsies.

X-ray examinations were performed using a universal X-ray radiographic complex INDlagraf, ultrasound examinations were performed using a TOSHIBA Nemio XG apparatus, computed tomography – using a GENERAL ELECTRIC Maxima 128-slice digital computed tomography scanner, magnetic resonance imaging – using a PHILIPS ACHIEVA magnetic resonance imaging system (1.5 MRI).

Endoscopic examinations, in particular, video enteroscopy was performed using an EndoCapsule video capsule (Olympus), two-balloon enteroscopy – using an Olympus endoscopic system, esophagogastroduodenoscopy – GIF-HQ 190 (Olympus), colonoscopy – CF-HQ 190L (Olympus).

Pathological examinations were performed using a SIGETA BIOGENIC 40x–2000x LED Trino Infinity microscope.

In cases when it was impossible to objectify the state of the mucous membrane using endoscopic diagnostic methods, as well as CT, MRI colonography, with indications

for surgical intervention, the above risk factors for malignancy were guided by the above risk factors for malignancy. The use of risk factors for malignancy contributed to the justification of the expediency for using generally accepted oncological standards in surgical treatment.

These oncological standards include a high cross-section of the arteries of the right half of the colon: ileal and middle mesenteric arteries at the branches from the superior mesenteric artery; separate ligation of the inferior mesenteric artery in the immediate vicinity of the aorta and inferior mesenteric vein at the level of the lower edge of the pancreas, removal of the transverse, descending, sigmoid colon, mesorectum together with lymphatic collectors without damaging the fascial sheaths of these parts of the colon (mesocolon and mesorectumectomy).

## Results

In most cases, the use of general clinical examination methods, clinical and biochemical laboratory tests, and special methods made it possible to establish the diagnosis of ulcerative colitis or Crohn's disease of the colon, to conduct a differential diagnosis between these diseases, as well as with other types of colitis: specific bacterial, HIV-associated, ischemic, and pseudomembranous.

In chronic variants of diffuse inflammatory diseases, timely diagnosis of precancerous conditions, in particular, severe forms of dysplasia and malignancy, was of great importance. When performing traditional colonoscopy, dysplasia was diagnosed in 3.8 % and malignancy in 1.4 % of the examined patients. The use of topical methods, including chromocolonoscopy, contributed to a significant improvement in the quality of diagnosis. The above pathological conditions were diagnosed in 18.6 % and 7.2 % of the examined patients, respectively. However, the largest number of dysplasia and malignancy cases, in 29.7 % and 12.6 % of patients, respectively, were diagnosed retrospectively, based only on the results of macroscopic and pathological examination of removed colon macropreparations. In the vast majority of patients, foci of dysplasia and malignancy were found in areas of existing colon stricture inaccessible for colonoscopy.

Over the past 10 years, 36 patients were operated on using oncological standards. Ulcerative colitis was treated in 20 (55.6 %) and Crohn's disease in 16 (44.4 %). There were 19 men (52.7 %) and 17 women (47.3 %). The patients' age ranged from 21 to 56 years. Among the complications of the underlying disease, T3-4N0-1M0-1 stage colorectal cancer were diagnosed in 3 (8.3 %) patients in the preoperative period. Of these, 2 had Crohn's disease of the colon and 1 had ulcerative colitis. Foci of malignancy were detected in 9 (25.0 %), severe mucosal dysplasia – in 20 (55.6 %), and colonic stricture – in 8 (22.2 %). Concomitant diseases were diagnosed in 14 (38.9 %) patients. Of these, hypertension was diagnosed in 4, coronary heart disease in 3, diabetes mellitus in 3, varicose veins of the superficial veins of the lower extremities in 2, and duodenal ulcer in 2.

The radical stage of surgical intervention in 19 (52.8 %) patients consisted of colectomy, ultra-low resection of the rectum, mucosectomy of the surgical anal canal, in 7 (19.4 %) patients – colectomy with rectal extirpation, in 10 (27.8 %) – segmental resections of the colon. One patient

with liver metastases underwent a cytoreductive colectomy and rectal extirpation. Segmental resections of the colon were performed exclusively for Crohn's disease, in particular, resection of the ileocecal junction in 3 patients, right-sided hemicolectomy in 2, resection of the transverse colon in 2, left-sided hemicolectomy and sigmoidectomy in 2 and 1 patient, respectively. When performing these local resections, only the areas of existing complications were removed: malignancy according to oncological standards, strictures, severe forms of dysplasia.

In the early postoperative period, complications occurred in 5 (13.9 %) patients: pelvic cavity abscess (abscessing hematoma) – 2, surgical wound suppuration – 1, pneumonia – 1, acute pyelocystitis – 1. Complications were treated in accordance with generally accepted standards. No cases of postoperative mortality were observed. These complications due to effective treatment did not significantly affect the quality of rehabilitation of the operated patients. In the late postoperative period, owing to staged monitoring, an implantation metastasis in the walls of the presacral area was timely diagnosed in 1 (2.8 %) patient, which was removed from the perineum. In 1 (2.8 %) patient, metastatic liver disease progressed. As a result, she was treated with symptomatic therapy. No locoregional recurrences were observed in patients with established foci of malignancy in the period before surgery, as well as in patients operated on with existing risk factors for malignancy.

## Discussion

The surgical treatment of patients with diffuse inflammatory diseases of the colon was guided by the provisions of the developed surgical strategy and tactics. The concept of surgical strategy included the performance of surgical interventions before the onset or under conditions of high risk for complications that could pose a threat to patients' life, the performance of sufficiently radical surgical interventions, if possible, with a primary reconstructive and restorative stage, organ-preserving surgical interventions in Crohn's disease. The strategy principle was to refuse unreasonable extensive resections in Crohn's disease, since the risk of this disease recurrence in other anatomical parts of the intestinal canal and the risk of complications, the need for repeated surgical interventions in this regard was quite plausible.

The surgical tactics included the following provisions, namely diagnosis of ulcerative colitis and Crohn's disease, differential diagnosis with other types of colitis, justification of indications for surgical treatment depending on the disease clinical course, in particular the occurrence of complications, choice of method and extent of the radical stage of surgery, justification of the feasibility of performing and choosing a method of reconstructive and restorative stage, prediction and prevention of postoperative complications, adequate management of the postoperative period.

An important component of the surgical tactics was the justification of the feasibility of performing a surgical intervention. In that case, we used proven relative and absolute indications. The relative indications included irreversible morphological changes in the colonic wall in the form of "ulcerative lakes" of significant size in ulcerative colitis and deep ulcers in Crohn's disease; severe dysplasia (D III) – intraepithelial neoplasia; variants of chronic disease for 8

years or more, as well as recurrent with signs of progression and continuous, refractory to conservative therapy, especially steroid-dependent and steroid-resistant forms that significantly limit or make it impossible to use steroid drugs; total colon involvement; systemic complications with skin, eye, joint, internal organ damage; growth and developmental delay in adolescents. These relative indications were considered a priority, as their presence indicated the absence of life-threatening complications and, at the same time, the inappropriateness of further conservative treatment and the most favorable conditions for surgical interventions.

Absolute indications for surgical treatment indicated the presence of life-threatening complications or a sufficiently high risk of their occurrence. Absolute indications included acute complications, in particular, peritonitis and profuse bleeding into the intestinal lumen; toxic dilatation of the colon, mainly in ulcerative colitis, as well as chronic complications: colon cancer, paracolic inflammatory infiltrates, colonic stricture with signs of chronic obstruction, perianal lesions with anal sphincter destruction. Absolute indications also included aggressive variants of diffuse inflammatory diseases: acute (fulminant) attack of colitis with total colon damage, with ineffective conservative therapy for 7–10 days, as well as severe recurrent colitis with total damage and no effect from complex (basic) treatment for 3–4 weeks.

The choice of the radical stage extent of surgical interventions in diffuse inflammatory diseases of the colon depended on the disease diagnosis, the nature of its clinical course, namely, the occurrence of acute or chronic complications, the severity of morphological changes in the digestive tract walls. The standard radical stage of surgical treatment for ulcerative colitis and Crohn's disease with total colon involvement was considered to be colectomy, ultra-low resection of the rectum, and mucosectomy of the surgical anal canal. Colectomy with rectal extirpation and monoileostomy were performed in the above diseases with total colon involvement, as well as destruction of the anal sphincters, or an existing tumor or malignancy in the lower ampullary rectum. Colectomy with resection of the rectum, monoileostomy were performed in acute complications of ulcerative colitis and Crohn's disease when the primary reconstructive and restorative stage of surgery was impossible. Segmental resections such as removal of the ileocecal junction, right-sided hemicolectomy, resection of the transverse colon, left-sided hemicolectomy, sigmoidectomy were performed for complicated Crohn's disease with localized damage to the relevant parts of the colon.

Crucial importance was attached to the performance of reconstructive and restorative surgical interventions after large-scale radical operations, in particular, colectomy with ultra-low resection of the rectum by mucosectomy of the surgical anal canal, as well as after colectomy and rectum extirpation. After these operations, more advanced author's pelvic small bowel reservoirs and ileo-endoanal anastomoses, as well as retaining reservoir and retaining non-reservoir lifelong ileostomies were used. The reconstructive and restorative stage of surgery slowed down the transit of the small intestine contents, increased the time of its contact with the mucous membrane surface, thus improving the process of intestinal digestion and absorption, as well as contributed to a decrease in the frequency of stool

approaching the physiological norm, and the manifestations of post-colectomy syndrome. The use of more advanced ileo-endoanal anastomoses compared to reservoir-anal anastomoses helped to reduce the load on the anal sphincter apparatus and improve the function of anal retention. These reconstructive and restorative surgical interventions promoted a significant improvement in the functional outcomes and quality of life of the operated patients.

## Conclusions

1. Determination of risk factors for malignancy, improvement of diagnostic methods, surgical strategy and tactics in diffuse inflammatory diseases of the colon contribute to the timely detection of precancerous conditions, malignancy and colon cancer, justification of the feasibility of performing surgical interventions using generally accepted oncological standards.

2. Surgical interventions using generally accepted oncological standards, developed strategy and tactics allowed to prevent the occurrence of precancerous condition malignant transformation, cases of postoperative mortality, reduce the incidence of early postoperative complications to 5 (13.9 %) and locoregional recurrence to 1 (2.8 %).

**Prospects for further research.** Improvement of diagnostics and surgical treatment for complicated forms of diffuse inflammatory bowel disease.

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## Information about the authors:

Poyda O. I., MD, PhD, DSc, Professor, Head of the Department of Surgery 1, Bogomolets National Medical University, Kyiv, Ukraine.  
ORCID ID: 0000-0001-9443-6304

Melnyk V. M., MD, PhD, DSc, Professor of the Department of Surgery 1, Bogomolets National Medical University, Kyiv, Ukraine.  
ORCID ID: 0000-0003-4788-546X

## Відомості про авторів:

Пойда О. І., д-р мед. наук, професор, зав. каф. хірургії № 1, Національний медичний університет імені О. О. Богомольця, м. Київ, Україна.

Мельник В. М., д-р мед. наук, професор каф. хірургії № 1, Національний медичний університет імені О. О. Богомольця, м. Київ, Україна.

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