

## ORIGINAL ARTICLE

# FORECASTING THE DEVELOPMENT OF PURULENT-INFLAMMATORY POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH OBSTRUCTIVE BOWEL OBSTRUCTION

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**Julia V. Ivanova<sup>1</sup>, Svitlana M. Gramatyuk<sup>2</sup>, Yuriy O. Vinnyk<sup>3</sup>, Sergii V. Viun<sup>1</sup>, Tetiana I. Viun<sup>1</sup>, Mykola M. Goloborodko<sup>1</sup>**<sup>1</sup>KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE<sup>2</sup>INSTITUTE OF CELL BIOREHABILITATION OF THE MINISTRY OF HEALTH OF UKRAINE, KHARKIV, UKRAINE<sup>3</sup>KHARKIV ACADEMY OF POSTGRADUATE EDUCATION, KHARKIV, UKRAINE

## ABSTRACT

**The aim:** The purpose of the study is to improve the results of treatment of patients with acute intestinal obstruction of tumor origin by developing individualized surgical tactics considering the level of cryoglobulins.

**Materials and methods:** 96 patients with ileus of tumor origin were studied. The mean age of patients was  $54.7 \pm 5.9$  years. 30 patients were diagnosed with colorectal cancer, 35 patients - with sigmoid cancer, 13 patients - with cecum and ascending colon, 11 patients - with transverse colon cancer, and 7 patients with descending colon cancer. Isolation of cryoglobulins from blood serum was performed by the method of A. E. Kalovidoris with modifications. The content of Ig A, Ig M, Ig G, total Ig E in the serum was investigated using enzyme-linked immunosorbent assay systems "Granum-Ukraine", the content of allergen-specific Ig E was investigated using enzyme-linked immunosorbent assay systems produced by "Microgen".

**Results:** As a result of treatment of 96 patients, it was found that the level of development of postoperative purulent complications was significantly influenced by the level of cryoglobulinemia and the volume of surgery (CMU,  $p < 0.05$ ). It was found that in patients with decompensated intestinal obstruction, the initial concentration of cryoglobulins was 16.4% higher than in the group with compensated intestinal obstruction (CMU,  $p < 0.05$ ).

**Conclusions:** Determination of cryoglobulinemia on admission of patients with acute obstructive ileus of tumor origin is a simple and effective method for predicting the development of purulent-inflammatory complications in the postoperative period and can influence the choice of treatment tactics.

**KEY WORDS:** colorectal cancer, surgical treatment, acute obstructive ileus, cryoglobulins

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## INTRODUCTION

Acute intestinal obstruction (AIO) is one of the most common and severe diseases in abdominal surgery, which is accompanied by high mortality. Studies in recent years have revealed a change in the structure of AIO due to a significant increase in the incidence of colorectal cancer [1-3].

In 20% of patients AIO is the first manifestation of the disease [4-8]. To date, there is a large proportion of symptomatic operations in this disease [9-11]. This is also due to the fact that approximately 25% of all patients with colorectal cancer are diagnosed with stage 4 [12], due to untimely treatment of patients with qualified medical care, and often due to the elderly age and severe comorbidities.

AIO is characterized by a large polymorphism of clinical manifestations, quickly leads to severe intoxication, changes in homeostasis, which causes various complications of the pathological process and worsens the patient's condition. Mortality from rectal cancer ranges from 5 to 30%, and with the development of acute intestinal obstruction in the early postoperative period reaches

16.2 - 60.3%, and depends on timely diagnosis, timing of surgical treatment, surgeon's qualifications, age and comorbidities [2, 13-15].

In cases of AIO, emergency surgeons are faced with the dilemma of which treatment tactics to choose: to perform primary radical surgery or to apply two- or three-stage treatment. Staged tactics of AIO treatment help to reduce the level of postoperative complications and mortality, but when it is used, the patient receives specific treatment in the long term basis, or does not receive it at all. Primary radical surgery allows to start such treatment at an early stage, but such tactics are accompanied by high levels (according to some authors 32% of cases) of postoperative purulent-inflammatory complications [16,17].

The probability of developing the failure of the sutures of intestinal anastomoses increases in technically difficult conditions of their formation. Complications such as peritonitis, intraoperative infection, intestinal obstruction call into question the effective functioning of anastomoses. Following two main factors are among the reasons for the

**Table I.** Assessment of patients according to the M-SAPS scale

Patient's condition at the time of admission (n = 96)	Compensated intestinal obstruction	Decompensated intestinal obstruction
Satisfactory ( $\leq 6$ points)	41 (61,1 %)	0
Moderate (from 7 to 12 points)	25 (37,3%)	11 (38,0 %)
Severe ( $\geq 13$ points)	1 (1,5%)	18 (62,0 %)

Note: The calculation was performed using the Simplified Acute Physiology Score (SAPS II) Calculator

**Table II.** Types of cryoglobulinemia depending on the degree of intestinal obstruction

Degree of intestinal obstruction	Type of cryoglobulinemia
Compensated (n=17)	absent
Subcompensated (n=39)	Doubtful, type III cryoglobulinemia
Decompensated (n=30)	type II cryoglobulinemia

**Table III.** Dependence of the postoperative period on the type of cryoglobulinemia

Course of the postoperative period	Type of cryoglobulinemia	
Uncomplicated (n=53)	Absent, doubtful	
Complicated (n=43)	Therapeutic complications (n=4)	II type KGE
	Surgical complications (n=39)	II, III type KGE

failure of anastomotic sutures: circulatory disorders in the area of suturing and infection [18-20].

In recent years, researchers have drawn a lot of attention to the pathophysiological aspects of colorectal cancer and its complications. It is known that in the conditions of the oncological process development in patients the syndrome of cryoglobulinemia is observed. This is an immune-dependent process due to the presence in the serum of pathological proteins (cryoglobulins), which belong to immunoglobulins and can form insoluble complexes - cryoprecipitates, which reduces the ability of tissues to regenerate due to general metabolic changes (anemia, hypoproteinemia, metabolism) and local changes in tissues [20, 21].

In the absence of universal methods for the prevention of leaks of intestinal anastomoses, it is important to find new approaches for finding markers for predicting the risk of intestinal anastomoses in the AIO. This is a prerequisite for choosing the tactics of surgical treatment of patients in order to prevent postoperative complications, rapid recovery of intestinal function and their subsequent effective rehabilitation.

## THE AIM

The purpose of the study is to improve the results of treatment of patients with acute intestinal obstruction of tumor origin by developing individualized surgical tactics considering the level of cryoglobulins.

## MATERIALS AND METHODS

This study is based on our own clinical observations of 96 patients with ileus of tumor origin, who were operated in

the city clinical hospital №17 of Kharkiv and SI "IZNH named after V.T. Zaitsev NAMNU" in the period from 2012 to 2021. The average age of patients was  $54.7 \pm 5.9$  years. The control group consisted of 25 conditionally healthy patients (men and women) aged 35 to 66 years, the metabolic parameters of whom were studied.

Clinical, laboratory-diagnostic and histo-morphological methods diagnosed colorectal cancer in 30 patients, sigmoid colon cancer in 35 patients, cecum colon and ascending section cancer in 13 patients, transverse colon cancer in 11 patients and cancer of the descending colon in 7 patients.

All patients were admitted to hospitals with urgent indications.

According to the classification of E.G. Topuzov, patients with compensated and subcompensated forms of intestinal obstruction accounted for 68.8% (66 patients) and 31.2% (30 cases) were diagnosed with uncompensated intestinal obstruction.

Surgical treatment in a planned manner (after elimination of manifestations of obstruction and stabilization of the patient's condition) was performed in 21 (21.8%) patients, with urgent indications - 42 (43.7%), in an emergency - 33 (34.5%) patients.

In assessing the patient's condition modified scale SAPS (Simplified Acute Physiology Score), proposed by Le Gall Jr. et al. (Table I) was used.

The distribution of patients by the level of invasion of the intestinal wall was as follows: patients with damage to the mucous and submucosal layer occurred on average in 0.63%, while the main percentage was reaches by tumors germinated the muscular membrane - 45.6%, as well as the whole thickness of the intestinal wall (49.4%). The

proportion of tumors with the germination of all layers of the intestinal wall was predominant and amounted to more than 54%.

Comprehensive examination of patients in surgical institutions consisted of three stages: preoperative (including the study of anamnestic and clinical data, physical examination of the patient, general clinical and biochemical parameters, the results of instrumental methods of examination, morphological examination of tumor biopsy), intraoperative (visual assessment of the degree of process) and postoperative (final histological analysis of surgical material and generalization of all data obtained at the stages of diagnosis, treatment and prognosis of survival).

Isolation of cryoglobulins (immunoglobulins of serum, which reverse precipitate at temperatures below 37 °C) from serum was performed by the method of A. E. Kalovidoris with modifications. The concentration of cryoglobulins was evaluated spectrophotometrically on a spectrophotometer SF-46. Control serum cryoglobulins were studied in 25 healthy patients and ranged from 60 to 80 µg/ml, which corresponded to the norms obtained in the works of Ferri C., Zignego A.L. et al. (2002) [21]. The content of immunoglobulins A, M, G (Ig A, Ig M, Ig G), total immunoglobulin E (Ig E) in the serum was investigated using enzyme-linked immunoenzymometric assay systems produced by LLC NVL "Granum-Ukraine", and the content of allergen-specific IgE was investigated using enzyme-linked immunoenzymometric assays produced by NVT "Microgen" Russia.

The obtained data were subjected to statistical processing using the program STATISTICA 6.0. Quantitative indicators are presented as  $X \pm m$ , where  $X$  is the average value, and  $m$  is the standard error of the average value. For indicators that characterize the qualitative characteristics, the absolute number and the relative value in percent (%) were indicated. The Kolmogorov-Smirnov agreement criterion was used to verify the coincidence of the distribution of quantitative indicators with the normal one in the groups. Since the law of distribution of numerical indicators studied was different from normal, in the case of paired independent populations, the statistical significance was checked using the Mann-Whitney U-criteria (MWC). In the case of dependent populations, the Wilcoxon W-criteria (WC) was used. Qualitative characteristics were compared using the criterion "xi" - Pearson's square (CXP). The differences were considered statistically significant at  $p < 0.05$ . To determine the existence of functional relationships between the parameters, the Spearman correlation coefficient  $r$  was calculated, which was considered statistically significant at  $p < 0.05$ .

## RESULTS

All surgeries were performed in an open manner. Surgical interventions performed in patients with AOI by volume were as follows: in 28 cases - resection of the rectum, in 35 - resection of the sigmoid colon, in 13 - right hemicolectomy, in 9 - resection of the lumbar colon and in

6 left hemicolectomy. At the same time, radical surgical interventions were performed in 24 (25%) patients, palliative (obstructive resections) - in 32 (33.3%) patients, and symptomatic surgical interventions (obstructive resections and preventive intestinal stoma) - in 40 (41.7%) patients.

Tumor resectability and intestinal obstruction without peritonitis were indications for the formation of the anastomosis. In 43 (44.8%) patients, one-stage resections of intestinal segments with a tumor were performed, the formed primary anastomosis was located extraperitoneally (in all cases), and the anastomosis was decompressed by leading a probe behind the suture line. Primary anastomosis and preventive intestinal stoma was formed in 27 (28.1%) patients, obstructive resections or preventive stoma were performed in an emergency in 26 (27.0%) patients with uncompensated obstruction.

Surgical complications occurred in 39 patients (40.6%), while complications associated with uncompensated adaptive response (therapeutic complications) accounted for 4 patients (4.2%).

Failure of intestinal anastomoses, according to our study, was a leading purulent-inflammatory postoperative complication. Postoperative complications due to the pathology of intestinal anastomoses were observed in 13 (13.5%) patients, and in most cases (76.9%) they were eliminated by conservative measures and local treatment. On the second place (in 6 (6.3%) cases) there were suppurations of postoperative wounds. The postoperative period was complicated by the development of peritonitis in 3 patients (2 (15.4%) of them died against the background of peritonitis and the progression of endogenous intoxication).

The overall mortality was 5.2% (5 patients died), 2 of them - from PATE (thromboembolism of pulmonary artery) and one patient - on the background of acute heart failure, in 2 patients the cause of death was the progression of endogenous intoxication.

Cryoglobulinemia was detected in the majority - in 59 (62.5%) cases of 96 examined patients with AOI of tumor genesis, the remaining 37 patients (38.5%) did not have CGE (CXP,  $p < 0.05$ ). In most patients (36 (61%)) the content of cryoglobulins was average ( $298.6 \pm 2.5$  mg/l;  $1.3 \pm 0.08\%$ ), which corresponds to type III CGE; high CG content ( $477.3 \pm 48$  mg/l;  $3.4 \pm 0.2\%$ ) was registered in 9 (15.2%), which indirectly indicated type II CGE; with questionable CGE ( $79.4 \pm 1.01$  mg/l) was 14 (23.7%).

The study of concentrations of immunoglobulins of classes G and M, as well as immunoglobulins of class A in cryocomplexes revealed a decrease in Ig G and Ig M concentrations, which according to the immunological concept of pathogenesis of intestinal obstruction of tumor genesis is associated with cryoglobulin fixation in myocirculatory tract and to the intestinal epithelium. On the 7th day of the disease, there was an increase in IgG content by 4.3% and a statistically significant (CV,  $p < 0.05$ ) increase in IgM by 19.4% compared to baseline. The increase in antibody content on the 7th day may be associated with the development of a secondary immune response. In some cases, the increase in the concentration of IgG and

IgM relative to their initial level occurred by the 3rd or 5th day of observation.

As a result of our study it was found that in patients with compensated intestinal obstruction cryoglobulinemia was not detected, doubtful cryoglobulinemia and its type III was determined in most patients with subcompensated obstruction, and the patients with decompensated form of the disease was characterized by type II cryoglobulinemia (Table II). Besides, it was found that in patients with decompensated intestinal obstruction, the initial concentration of cryoglobulins was 16.4% higher than in the group with compensated intestinal obstruction. (MWC,  $p < 0.05$ ).

As a result of the analysis of the treatment results of 96 patients, it was found that the level of postoperative purulent complications was significantly influenced by the level of cryoglobulinemia and the volume of surgery (CMU,  $p < 0.05$ ) (Table III).

The correlation analysis revealed a direct correlation between the initial content of cryoglobulins and the level of postoperative purulent complications ( $r = 0.56$ ,  $p = 0.07$  and  $r = 0.53$ ,  $p = 0.052$ ). The available cryoglobulin concentrations of  $162.5 \pm 32.6 \mu\text{g/ml}$  were observed in patients with postoperative complications directly related to surgery (wound suppuration, failure of intestinal anastomoses). Also noteworthy is the lack of mortality in the group of patients with normal cryoglobulin levels.

## DISCUSSION

According to many authors [3,7,22-23], the integrity of surgical sutures depends on several reasons, both from the anastomosing organs and changes beyond such organs. There are 3 groups of reasons violating the integrity of surgical sutures: first, it is the condition and pathomorphological processes occurring in the sutured organs; secondly, adverse factors in which these sutures are applied, or adverse factors that occur in the postoperative period; and thirdly, the technical features of suturing. The above factors are quite fully analyzed in the scientific literature: violation of general homeostasis, intra-intestinal hypertension and colostasis, infection of the abdominal cavity, impaired blood flow in the tissues of the anastomosis [4].

Of course, the first group of reasons is decisive, because the viability of the organ wall, in the first place, affects functions of the intestinal sutures. These include: active inflammation of tissues, technical errors in the form of excessive mobilization of the organ wall and rough suturing, microcirculatory and general circulatory disorders, increased intra-intestinal pressure, hypoproteinemia, local infection [17].

For quite a long time in surgical science there have been trends in the development of diagnostic methods and criteria for assessing the viability of hollow organs that are part of the anastomosis. The following are among them: Doppler ultrasound, transillumination angio-tensiometry, pulsomotorography, surface oximetry, infrared photoplethysmography, laser Doppler cycling symmetry, laser

Doppler flowmetry, spectrophotometry, transillumination angioscopy; thermometry, angiography, chromoscopy, fluorescence method [19,24-25].

But all these methods are difficult to use, their use is debatable during surgery, because they do not take root in the clinic, and this, in turn, requires further development in this area.

Despite the improvement of the principles of diagnosis of intestinal viability, the tendency to failure of the sutures of intestinal anastomoses is only gaining momentum: from 0.5-1.7% in the late twentieth century to 4.3-69% in 2000-2010 [13,26]. That is why this problem, requiring further development, attracts new analytical data: so the American College of Surgeons in 2015 publishes a metaanalysis, based on several large multicenter studies, on the relationship between increasing cases of anastomosis failure (odds ratio OR = 31.5; 95% CI 2.6- 381.4;  $p = 0.007$ ) congestive heart failure, peripheral vascular disease (OR = 4.6; 95% CI 1.0-20.5;  $p = 0.048$ ), alcohol abuse (OR = 3.7; 95% CI, 1.6-8.3;  $p = 0.002$ ), the use of steroids (OR = 2.3; 95% CI: 1.1-5.0;  $p = 0.027$ ), impaired sodium metabolism (OR = 0.4; 95% CI 0.2-0.7;  $p = 0.002$ ), weight loss (OR = 0.2; 95% CI 0.06-0.7;  $p = 0.011$ ), as well as the location of the anastomosis; in addition, there are data on the influence on this process of the perioperative level of C-reactive protein and indicators of proteolysis, fibrinolysis and lipid peroxidation [20,25].

The restoration of continuity of the gastrointestinal tract is of particular importance in conditions of peritonitis or mesenteric circulation due to severely limited reparative regeneration in this group of patients, accompanied by an increased risk of anastomotic failure [3]. Determination of cryoglobulins during surgery can be chosen as an intraoperative rapid method of determining the viability of the intestine and deciding on the anastomosis formation or completion of the operation by stomating the patient.

According to the existing theory of the autoimmune mechanism of tumor formation, the detected decrease in the level of cryoglobulins on the 2nd day could be associated with their fixation in the microcirculatory tract and the development of immunocomplex inflammation. While the increase in the content of cryoglobulins in the serum on the third day can be caused by their release into the circulatory system from the sites of deposition or fixation, and the development of a secondary immune response [23,24]. Detection of high concentrations of cryoglobulins in the serum of the studied patients suggested the presence of maximum autoimmune changes due to the underlying disease.

Thus, our studies found that patients with cryoglobulinemia operated for acute intestinal ileus of tumor origin, secondary immune deficiency is formed, which is determined by abnormalities in the system of cellular and humoral immunity.

## CONCLUSIONS

Determination of cryoglobulinemia on admission of patients with acute obstruction of tumor origin is a simple

and effective method of predicting the development of purulent-inflammatory complications in the postoperative period and can influence the choice of treatment tactics.

## PROSPECTS FOR FURTHER RESEARCH

Development of an effective rapid method for determining cryoglobulinemia, as well as further study of the informativeness of this indicator depending on the specific clinical situation.

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#### **ORCID and contributionship:**

Julia V. Ivanova: 0000-0003-3660-9558 <sup>A, B, D</sup>

Svitlana M. Gramatyuk: 0000-0003-4238-7031 <sup>A, B, E</sup>

Yuriy O. Vinnyk: 0000-0002-8995-2862 <sup>E, F</sup>

Sergii V. Viun: 0000-0002-7318-0087 <sup>B, C</sup>

Tetiana I. Viun: 0000-0002-7862-349X <sup>A, C, F</sup>

Mykola M. Goloborodko: 0000-0001-9554-928X <sup>C, D</sup>

#### **Conflict of interest:**

*The Authors declare no conflict of interest*

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#### **CORRESPONDING AUTHOR**

**Tetiana I. Viun**

Kharkiv National Medical University  
4 Nauky Avenue, 61022 Kharkiv, Ukraine  
tel: +380669159081  
e-mail: ti.viun@knmu.edu.ua

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