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Translation of the article

PREDICTORS OF COLECTOMY IN PATIENTS WITH «EXTREMELY SEVERE» ULCERATIVE COLITIS

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AIM: to identify predictors of colectomy in patients with «extremely severe» ulcerative colitis.
PATIENTS AND METHODS: Seventy-four patients with severe ulcerative colitis in 2017 were included in the study. The patients were divided into the groups of colectomy (54 pts) and conservative treatment (20 pts).
The predictors such as serum albumin, C-reactive protein, hemoglobin, endoscopic picture, and clinical data were analyzed.
RESULTS: The groups were homogeneous by gender, age and duration of the disease. Mean albumin and hemoglobin levels were significantly lower (28 g/l and 96 g/l) in the colectomy group. The endoscopic picture of «extensive ulcer defects merging among themselves» was significantly more common in the operated patients – 78%, compared with 5% in the conservative treatment group (p<0.0001). The risk of colectomy in the presence of an endoscopic picture was 85%, and when combined with an albumin level of less than 31 g/l and hemoglobin of less than 107 g/l, the risk increased to 100%.
CONCLUSION: The endoscopic picture of «extensive, merging ulcerative defects» in combination with an albumin level of less than 31 g/l and hemoglobin less than 107 g/l are predictors of colectomy with high predictive value.

[Key words: ulcerative colitis, colectomy, predictors of colectomy]

CONFLICTS OF INTERESTS: The authors declare no conflicts of interest.

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INTRODUCTION

Among all forms of ulcerative colitis (UC), a severe attack is observed in 25% of patients [1]. Of them, 40% of patients undergo surgery, while according to a number of papers, the mortality rate in this group of patients reaches 6.3% [2,3]. Treatment in such cases begins with conservative treatment, and only if it is ineffective, colectomy is resorted to [4].

It should be noted that untimely surgery leads to severe metabolic disorders, infectious postoperative complications, and increases the risk of death [5,6].

Selecting a group of high-risk patients who are indicated for early surgery would allow to avoid unnecessary drug therapy and to perform colectomy with a minimal incidence of complications and to avoid death [6]. However, at the moment there are no clear criteria that answer the question of which category of patients needs early surgery. The generally accepted Truelove-Witts classification takes into account only the severity of the disease, and colectomy is considered only when life-threatening complications occur [4].

Despite the fact that the Russian national clinical guidelines identified extremely severe UC, treatment approach for this group of patients meet the standards of treatment of severe attack, and does not provide indications for early colectomy [4].

In our opinion, it is necessary to develop criteria that would allow us to identify a group of patients at high risk of adverse outcomes to determine indications for surgery at an early time.

Thus, the purpose of this study was to determine the predictors of colectomy in patients with extremely severe UC.

Table 1. *Characteristics of patients with severe UC*

Factors	Colectomy, *n*=54	Without colectomy, *n*=20	*P*
Age, median (min-max)	36 (18-75)	32 (23-66)	0.33
Gender, abs, % Males Females	 28 (52%) 26 (48%)	 12 (60%) 8 (40%)	0.6
Disease duration, median, months (min-max)	12 (0-200)	31 (1-200)	0.14
Acute course of the disease, abs, %	16 (29%)	5 (25%)	0.77
Biological therapy, abs, %	10 (18%)	10 (50%)	0.001
Albumin, mean, g/l (±SD)	28 (±5,2)	34 (±4,8)	0.0002
C-reactive protein, median, mg/l, (min-max)	67 (1-200)	35 (1-120)	0.01
Hemoglobin, mean, g/l (±SD)	96 (±19)	118 (±18)	<0.0001
Extensive ulcerative defects in colonoscopy, abs, %	42 (78%)	1 (5%)	<0.0001

Table 2. *The results of single-factor and multi-factor analyses*

Factor	Single-factor analysis		Multi-factor analysis	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Albumin	0.8 (0.71-0.91)	0.001	0.67 (0.48-0.9)	0.017
C-reactiveprotein	1.01 (0.99-1.02)	0.053		
Hemoglobin	0.94 (0.91-0.97)	0.0005	0.88 (0.79-1.0)	0.018
Endoscopic picture	83.6 (9.9-699.8)	0.000045	2926 (17.1-499021.5)	0.0023

PATIENTS AND METHODS

A retrospective study included 74 patients with severe UC attack, who were treated at the clinic in 2017 (Fig. 1).

All the patients were diagnosed with a severe ulcerative colitis, based on the Truelove-Witts criteria. All the patients were examined and treated conservatively, according to the current national clinical guidelines for the diagnosis and treatment of UC, among them 54/74 (73%) underwent surgery.

Colectomy was performed when conservative treatment was ineffective. The ineffectiveness of conservative treatment was understood as the development of hormonal resistance or dependence when it is impossible to prescribe biological therapy, due to the high risk of life-threatening complications; as well as loss of response against the background of therapy with second-line drugs.

These patients underwent colectomy or proctocolectomy depending on the severity of the rectal lesions and the planned ileal pouch.

As predictors of colectomy, the following factors were studied: the level of serum albumin, hemoglobin, C-reactive protein and the endoscopic picture (presence of extensive ulcerative defects), as well as clinical data.

The level of hemoglobin and serum albumin was assessed based on laboratory data, regardless of the fact of blood transfusion and its components.

It is worth noting that extensive ulcerative defects were understood as an endoscopic picture, in which we observed pronounced inflammatory changes in the mucosa of the colon with the formation of extensive, merging with each other, deep, up to the muscle layer,

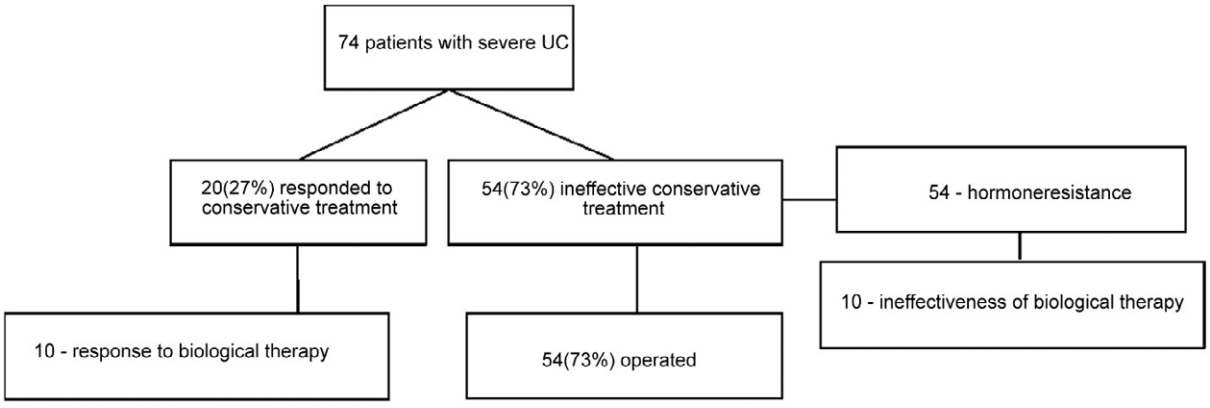

Figure 1. *Characteristics of hospitalized patients*

ulcerative defects with «islands» of the remaining mucosa, or even its absence.

It should be mentioned separately that colonoscopy (sigmoscopy) and laboratory tests were performed for all the patients when they were admitted to the clinic. Further, the laboratory parameters were re-evaluated on the 3rd and 7th days of hormone therapy, as well as urgent when the patients' condition worsened, including repeated sigmoscopy without bowel cleansing.

The analysis of predictors of colectomy was mainly based on examination data obtained at the time of determining the ineffectiveness of conservative therapy and setting indications for surgery, regardless of the duration of therapy.

Statistical Analysis

For normal distribution, the comparison was made by an unpaired Student's *t*-test, for abnormal distribution-by the Mann-Whitney test. The methods of logistic regression and ROC analysis were used to build a predictive model.

The statistical analysis was performed using the software «Statistica 13.3» and «RStatistica».

RESULTS

By gender, age, duration of the disease history, and the number of patients with disease debut the groups were homogeneous (Table 1). The biological therapy in the history was significantly more common in the group of patients without colectomy, p=0.001.

Among the patients who underwent colectomy, the mean values of albumin and hemoglobin levels were significantly lower compared to the group without colectomy (p=0.0002 and p<0.0001, respectively).

An additional analysis was performed based on laboratory data, and it was found that in the colectomy group, albumin level within the normal range were found in 7/54 (13%), which is significantly lower than in the group without colectomy – 10/20 (50%), p=0.0016; as well as the level of hemoglobin within the reference values was observed only in 8/54 (15%) patients in the colectomy group and in 8/20 (40%) – in the group without colectomy, p=0.01.

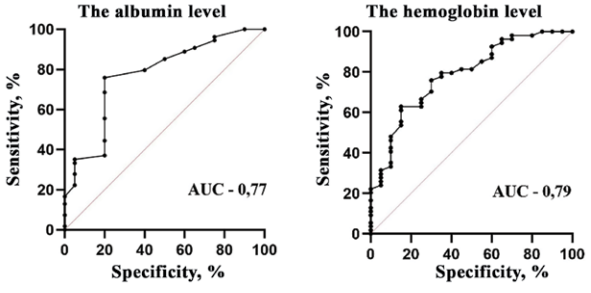

Figure 2. *ROC analysis of albumin and hemoglobin levels*

The median of C-reactive protein level was twice as high in the colectomy group, p=0.01. When analyzing the endoscopic picture, in the colectomy group 42/54 (78%) patients had extensive ulcerative defects, while in the group without colectomy – only 1/20 (5%), p<0.0001.

A single-factor analysis of all the patients with a severe ulcerative colitis revealed that albumin levels, the presence of extensive ulcerative defects, and hemoglobin levels were associated with colectomy during hospital stay.

A multi-factor analysis showed, that all of the above factors are independent predictors of colectomy (Table 2).

A ROC analysis was performed (Fig. 2), during which the threshold values associated with colectomy were determined: for albumin <31 g/l (sensitivity – 76%, specificity – 80%, p=0.0003) and for hemoglobin <107 g/l (sensitivity – 76%, specificity – 70%, p=0.0002).

Based on the obtained binary predictor data, a logistic regression was performed, as a result of which it turned out that all the factors have a statistically significant impact on the risk of colectomy.

A nomogram predicting the probability of colectomy in patients with a severe ulcerative colitis was constructed (Fig. 3). Based on the model, it was found that if the patient had extensive ulcerative defects during colonoscopy and the values of albumin and hemoglobin were higher than the established thresholds, the risk of colectomy was 85%.

If the endoscopic picture was combined with any of the above laboratory parameters, the risk of colectomy increased to 100%.

This logistic model has a statistically significantly high predictive value (AUC=0.93, p=0.006) (Fig. 4).

DISCUSSION

For a long time, the literature has repeatedly attempted to identify a group of patients at high risk of colectomy in severe UC.

However, to date, there are still no uniform criteria for stratification of this category of patients.

According to the American national guidelines, «fulminant» colitis is distinguished as an acute course of UC, the severity of which does not fit into the traditional Truelove-Witts classification.

«Fulminant» colitis is characterized by metabolic disorders and progressive deterioration that requires intensive therapy.

According to the latest revision of the American clinical guidelines, such a course of UC is an indication for an early colectomy within 24 hours after hospitalization [7].

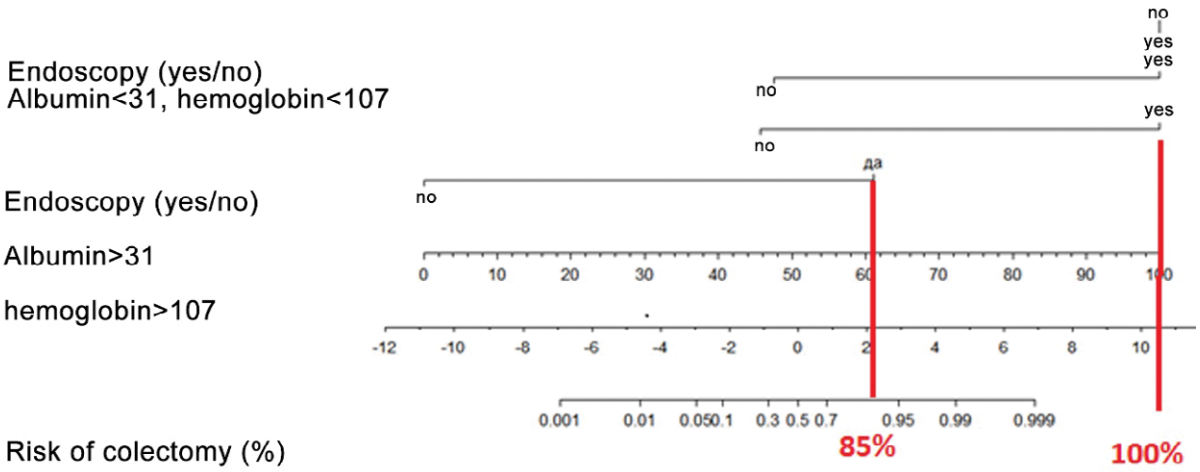

Figure 3. *Nomogram of the probability of colectomy in patients with severe UC*

The European Crohn's and Colitis Organization (ECCO) distinguishes «acute severe» colitis, but the treatment approach corresponds to the therapy of a severe attack, and surgery is recommended when there is a threat of complications [8].

In Russia, according to the latest version of clinical guidelines, a special category of patients with extremely severe UC is allocated. This form of severe UC is identical in its essence to «fulminant» colitis, but the treatment approach in relation to this type of patients remained the same and involves steroids for 7 days with an assessment of the response and a subjective decision of the gastroenterologist on the advisability of prescribing the 2nd – line therapy [4].

However, in all cases where there are groups of colectomy high risk, the severity of UC in them is taken into account only on the basis of the Truelove-Witts classification.

To date, there are no «new» objective criteria that can be used to review existing clinical recommendations.

As demonstrated in the study, one of these criteria is an endoscopic picture in the form of «extensive, deep, merging ulcerative defects with the formation of «islands» of the mucous layer».

The probability of colectomy in its presence was 85%. However, it is worth noting that along with the endoscopic picture, it is possible to use laboratory indicators such as albumin and hemoglobin. As the analysis showed, when combining laboratory parameters with an endoscopic picture, the risk of colectomy increased to 100%.

Similar data were obtained in a study conducted by Xie T. et al. When the UC endoscopic severity scale was over 7 points (UCEIS>7 points), the risk of colectomy exceeded 80% (OR=4.37 (95% CI 1.17-9.05), p<0.001) [9].

Objectively, this is not enough to make a decision about colectomy and, in order to increase the diagnostic value of the endoscopic criterion in real clinical practice, it is advisable to supplement it with laboratory indicators.

The increase in prognostic value when predictors of colectomy are combined was confirmed by Dalal R.S. et al., who included the results of treatment outcomes of 440 patients with severe UC in the analysis.

The combination of a pronounced endoscopic and clinical picture with an albumin level less than 28 g/l significantly correlated with subsequent colectomy (AUC=0.93 (95% CI: 0.92-0.95), p<0.01) [10].

Delayed surgery increases the morbidity rate, which was demonstrated in the analysis of the national database of UC patients in the United States for 2017.

The results of treatment of 2,650 patients who underwent colectomy for severe UC were analyzed.

The rate of postoperative complications was 44.5% in the group of early colectomy performed within 24 hours, which was significantly lower compared to 51.6% in the group of late surgery performed after 24 hours of admission, p=0.003.

The authors also showed that performing surgery at a

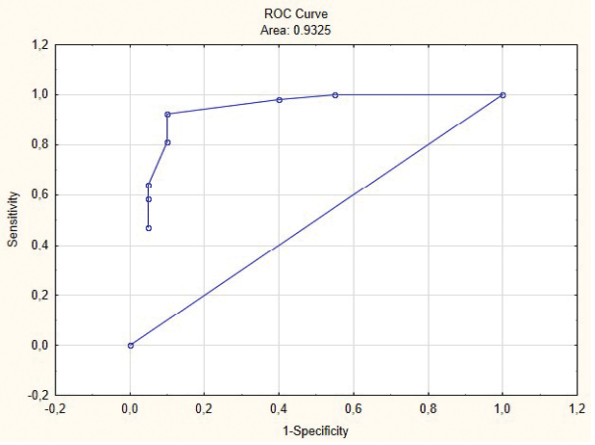

Figure 4. *ROC – curve of the logistics model (AUC=0.93)*

later date is associated with a significant increase in financial costs.

Thus, the postoperative hospital stay was 8 days in the early surgery group and 16 days in the late surgery group, $p<0.001$.

The cost of treatment was significantly lower in the early surgery group: $20,948 vs. $33,666, respectively ($p<0.001$) [6].

In our opinion, initially pronounced inflammatory changes in the colon, low nutritional status, accompanied by severe metabolic disorders in this special group of patients, during conservative therapy inevitably lead to adverse outcomes.

As shown by the results of the study by Geoffrey C. et al., hypoalbuminemia <30 g/l is accompanied by adverse outcomes in patients with severe UC.

Postoperative mortality in these patients is statistically significantly higher in the group of patients with albumin less than 30 g/l, compared to the group of normal albumin levels: 5.6% and 0.1%, respectively, $p<0.01$.

Postoperative complications are also significantly more often in the group of severe hypoalbuminemia: 28% and 15%, respectively, $p<0.01$, (OR=2.08; 95% CI: 1.75-2.48).

The patients in this group showed a significant increase in the risk of deep anterior abdominal wall infection, intra-abdominal infection, pneumonia, sepsis, and septic shock, and they also had a higher risk of developing cardiac, neurological, and other complications [5].

In light of all the above, it is worth noting that the predictors of colectomy identified in our study demonstrated high predictive value in relation to the need for surgical treatment in patients with severe UC.

These same predictors are objective criteria for extremely severe attack in patients with severe UC, who are also prescribed early surgery.

Undoubtedly, to confirm the results obtained, a multicenter prospective study with a large number of patients is necessary, which will increase the level of their evidence.

CONCLUSIONS

As a result of the study, it was demonstrated that the presence of extensive, confluent ulcerative defects detected during colonoscopy in patients with severe UC in combination with serum albumin less than 31 g/l, hemoglobin less than 107 g/l are predictors of colectomy, while having a high prognostic value.

Our analysis has limitations due to the retrospective nature of the data and the small number of patients.

In this regard, the results obtained by us were used in planning the design of the Russian multicenter observational study «Predictors of colectomy in patients with extremely severe ulcerative colitis», which is currently registered and started to recruit patients (clinical.trial.gov: NCT0394793).

THE PARTICIPATION OF THE AUTHORS:

Concept and design of the study: *Mingazov A.F., Vardanyan A.V.*

Collection and processing of the material: *Mingazov A.F., Shapina M.V.*

Statistical processing: *Mingazov A.F., Ponomarenko A.A.*

Writing of the text: *Mingazov A.F., Ponomarenko A.A.*

Editing: *Achkasov S.I., Veselov V.V.*

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