

## ORIGINAL ARTICLE

# CLINICAL FEATURES OF GASTROINTESTINAL ULCERATIVE BLEEDING IN ELDERLY PATIENTS COMPLICATED BY CARDIO-VASCULAR PATHOLOGY

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## ABSTRACT

**The aim:** To determine clinical and endoscopic features of gastroduodenal hemorrhages in elderly patients with concomitant cardio-vascular pathology in a way by studying, main indicators of the immune system for drawing up further tactics.

**Material and methods:** The study included 609 patients with ulcerative gastroduodenal bleeding, complicated by cardio-vascular system pathology in 2017-2019 years. The observed patients were distributed into the groups: I – patients, who received treatment according to the standard system of cardiovascular pathology treatment (n=541), II – “double” therapy (n=68). Control group consists of 20 relatively healthy patients were similar to the research group.

**Results:** Blood lost of a big amount and massive blood lost were noticed in 113 (18.56%±1.58) and 121 (19.87%±1.62) patients respectively. Active bleeding (F I) was revealed in 38 patients (6.24%±0.98), a high risk of hemorrhage relapse was determined in 486 patients (79.80%±1.63). Signs of recent hemorrhage were absent in 85 patients (13.96%±1.40). A high level of pro-inflammatory cytokines IL-6, TNF-α and a low activity of the anti-inflammatory mediator IL-10 define the process activity, their long-term circulation in patients with ulcerative hemorrhages of the gastro-intestinal tract are associated with unfavorable prognosis. In 5 cases conditionally-radical surgical interventions were performed. Palliative surgery – 3 patients (p>0.05).

**Conclusions:** The patients of second group (“double therapy”) with big and massive blood loss was 2.7 times higher than similar indices in patients of the first group (standard therapy). The patients who received “double therapy” had 3.3 times more active hemorrhage percentage than the patients who received standard therapy (p<0.05).

**KEY WORDS:** ulcer bleeding, Forrest scale, cytokines

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## INTRODUCTION

Gastroduodenal hemorrhages remain one of the most essential issues in urgent abdominal surgery. This group is presented by patients both with chronic pathology of the cardio-vascular system and acute myocardial infarction, arrhythmias with different origins, angina pectoris, conditions after coronary artery bypass grafting and stenting. For the last 3 years, there had been a growth in the number of acute ulcerative hemorrhages from the upper parts of the gastrointestinal tract I-IV degrees, especially in the elderly patients with concomitant cardiovascular pathologies [1]. Despite of using the modern minimally invasive methods (endoscopic hemostasis and hemorrhage relapse prevention), the mortality remains high and reach 10-20%, and post-operative mortality reaches 50% according to Fomin P. D., Shepetko E. M., Mennuni M.G., Halperin J. L., Kral J.B [2,3,4].

## THE AIM

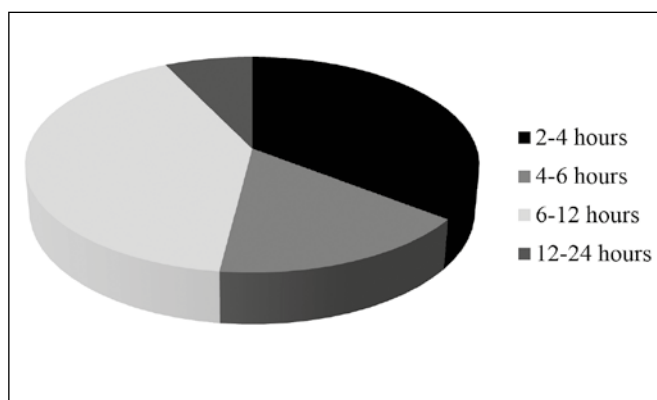
To determine the clinical features of gastroduodenal hemorrhages in elderly patients with concomitant cardio-vascular pathology in a way by studying basic clinical-endo-

scopic indicators, main indicators of the immune system for drawing up further tactics.

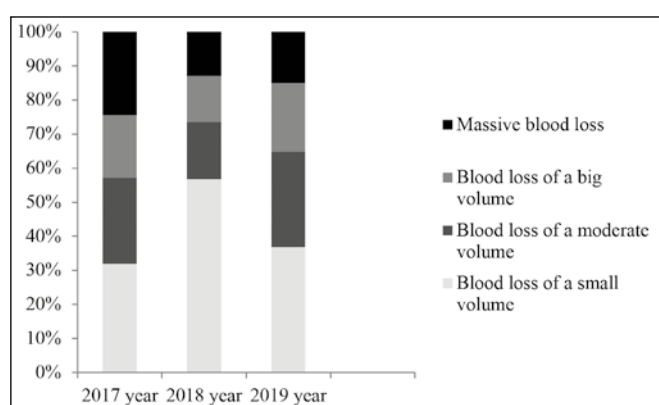
## MATERIALS AND METHODS

Having studied and analyzed the dynamics of the course of gastrointestinal hemorrhages on the background of cardiovascular pathology including acute myocardial infarction, arrhythmias, anginas, conditions after coronary artery stenting, it has been revealed 609 elderly patients (according to the WHO classification – 61-90 years old). Among them males were 322 (52.8%), females – 287 (47.2%). Average age was 71.8 years old. The obtained data were distributed into the groups: I – patients, who received treatment according to the standard system of cardiovascular pathology treatment (n=541), II – “double” therapy (n=68). As the group of control, we selected 20 patients – relatively healthy patients (donors), who by age, gender, methodology of determining main indices were similar to the research group.

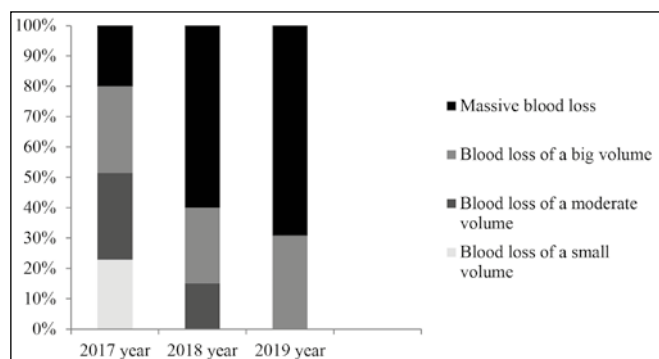
Processing of data was made using laboratory methods – common blood test – to define the degree of blood loss and



**Fig. 1.** Distribution of patients with gastro-duodenal ulcerative hemorrhages depending on the extension of the pre-hospital period during the first day.



**Fig. 2.** Dynamics of distribution degrees of blood lost during the treatment of the background disease according to standard hypotension therapy in 2017–2019 years.



**Fig. 3.** Dynamics of distributing degrees of blood lost during the treatment of the background disease according to "double" scheme of therapy in 2017–2019 years.

main indexes of the immune system – IL-6, IL-10, TNF- $\alpha$ . Quantification of concentration of IL-6, IL-10, TNF- $\alpha$  in blood serum was carried out using enzyme-linked immunosorbent assay by test systems [5].

General clinical method include esophagogastroduodenoscopy for determining the localization, size and condition of the local hemostasis.

Patient distribution analysis was carried out depending on the degree of blood loss according to the classification of American Association of Surgeons (1998) and it was

revealed that severe degrees of blood loss (heavy and massive) were found in 234 patients (38.4%).

At analysis of the condition of the endoscopic hemostasis it was revealed that active hemorrhage F I – was observed in 38 patients (6.24%±0.98). Major part includes patients with signs of unstable local endoscopic hemostasis with a high risk of bleeding relapse – 486 patients (79.80%±1.63), ulcerative defect without signs of hemorrhage – 85 patients (13.96%±1.40).

All input data obtained during the research, with the purpose of optimizing mathematical processing were input in the database, which was built using spreadsheet Microsoft Excel. Statistical processing of the research results was made according to methods of variation statistics, implemented by the standard package of application programs Statistica for Windows 6.0. Descriptive statistics was used for the statistical analysis: M – mean value, m – error in determining the mean, comparison of mean values of variables carried out by the parametric method (Student t-test). Compliance of the type of distribution of characteristics with the law of normal distribution was checked using Shapiro-Wilk method. In other cases non-parametric method (Mann-Whitney U-test) was used. Difference of mean values of indices was considered reliable at  $p < 0.05$ ,  $p < 0.01$ ,  $p < 0.001$  [6].

## RESULTS

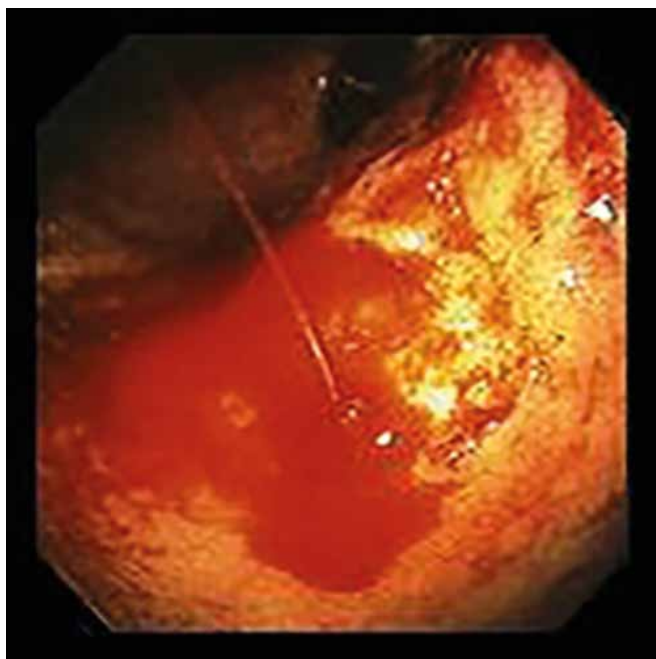
Medical case histories of patients were analyzed. It was determined that from all 609 patients, who were hospitalized into the city center of hemorrhage 314 patients (51.6%) had ulcerative duodenal hemorrhages, 295 (48.4%) – gastric ulcer.

In 375 cases, pre-hospital period were 24 hours. It was revealed that within 2-4 hours 133 (35.47%±2.47) patients had been delivered to the in-patient department, within 4-6 hours – 62 (16.53%±1.92), within 6-12 hours – 153 (40.80%±2.54), within 12-24 hours – 27 (7.20%±1.33) patients.

Blood lost of a big amount and massive blood lost were noticed in 113 (18.56%±1.58) and 121 (19.87%±1.62) patients respectively. Blood lost of middle volume – 139 (22.82%±1.70) cases whereas due to certain reasons the small blood lost was revealed in 236 (38.57%±1.97) patients. Providing analysis the index of severity of blood lost, we determined that it directly depends on therapy, which the patients receive for treating pathologies of the cardio-vascular system.

Having an analysis the degree of blood lost depending on the therapy aimed at a cardio-vascular pathology, in particular in case of receiving standard hypotension therapy (n=541), it is possible to conclude that a small blood loss prevailed 228 (42.14%±2.12) along with moderate blood lost – 126 (23.29%±1.82) cases. Blood lost of a big volume and massive blood lost were 94 (17.38%±1.63) and 93 (17.19%±1.62) patients respectively. In 2018 the blood lost of a small volume was 105 (56.8%) cases, in comparison with 2019 – 34 cases more and it is 20% ( $p < 0.05$ ).

During the "double" therapy (n=68), blood loss of a big volume and massive blood lost were noticed more often



**Fig. 4.** Active hemorrhage. F IA.



**Fig. 5.** Blood leakage. F IB.



**Fig. 6.** Visible thrombosed vessel. F IIA



**Fig. 7.** Signs of recent hemorrhage. F III

– 19 (27.94%±5.44) and 28 (41.18%±5.97) patients respectively. Blood lost of a small volume and blood lost of a moderate volume were 8 (11.76%±3.91) and 13 (19.12%±4.77) cases respectively. Massive blood lost was 69.2% in 2019, which is 9.2% more than that of 2018; blood lost of a small volume was not revealed during this period ( $p>0.05$ ).

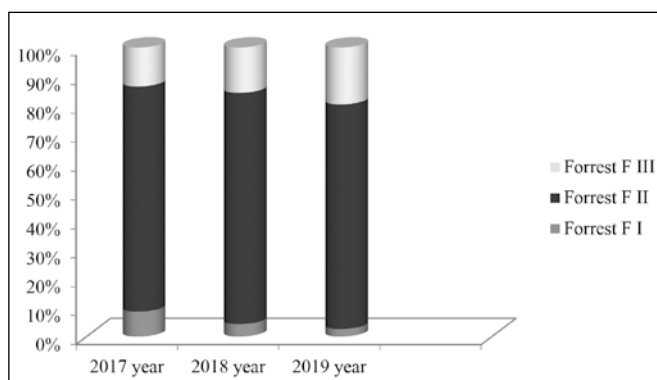
Local endoscopic hemostasis was considered according to Forrest classification. Active increase (F I) was revealed in 38 patients (6.24%±0.98) among them F IA – 18 (2.96%±0.69), F IB – 20 (3.28%±0.72).

A high risk of hemorrhage relapse was determined in 486 patients (79.80%±1.63), at that F IIA – in 161 patients

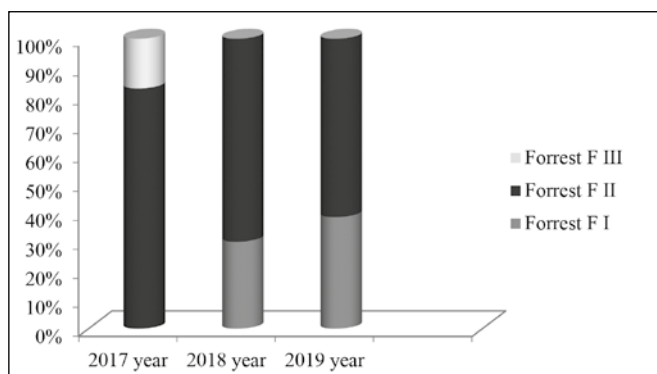
(26.44%±1.79), F IIB – in 191 patients (31.36%±1.88), F IIC – in 134 patients (22.00%±1.68). Signs of recent hemorrhage were absent in 85 patients (13.96%±1.40)

## DISCUSSION

The analysis has shown that the indicators of the local endoscopic hemostasis depends on therapy aimed at treatment of the cardiovascular pathology; it was revealed that within 2017-2019, in case of receiving standard hypotension therapy the endoscopic picture of F III prevailed – 89 (16.4%) cases, and F I was revealed in 27 (5%) patients. In 2019 F III revealed in 19.7% patients, which is 4% more than that of 2018 and 6.2% more than in 2017. Active hemorrhage



**Fig.8.** Dynamics of distributing local endoscopic hemostasis at treatment of the background pathology with the help of the hypotension therapy.



**Fig.9.** Dynamics of distributing local endoscopic hemostasis at treatment of the background pathology with the help of the "double" therapy.

F I, in its turn tends to decrease in 2019 by 6%, than the same indicator in 2017 ( $p < 0.05$ ).

Having analyzed the indices of the local endoscopic hemostasis in patients who receive "double" therapy for treating a cardiovascular pathology, we can conclude that indicator of active hemorrhage significant increased in 2018 in comparison with 2017 – by 30% with consequent gradual increase in 2019 – by 8.5%

Indicator F III remarkable decreased in. Moreover, in 2019 there were no patients with F III ( $p < 0.05$ ).

At all stages of forming specific immune response of the body, the dominant role belongs to cytokines. Increase in the level of cytokines is an essential component of adequate reaction of the body to inflammation [7, 8, 9]. At the same time, over expression of mediators causes changes of physiological processes. The research of cytokines in

patients with gastroduodenal hemorrhage has been carried out Tab.I.

Analysis of the obtained research results has show that patients of the II group have an increased level of IL-6 in blood serum – in 47.9 % ( $p > 0.05$ ), and TNF- $\alpha$  (2.4 times) – in 43.8 % patients ( $p < 0.05$ ). Level of IL-6 in blood serum of the II group of patients was significantly increased 1.8 times, ( $p < 0.05$ ) in comparison with values in the I group of patients. It illustrates the activity of the inflammatory process in patients of the II group. The level of anti-inflammatory IL-10, which slows down the proliferative response of T-cells, was within the norm. The correlation link between levels of IL-6 in blood serum and the level of and polymorphonuclear leukocytes ( $r = +0.4$ ;  $p < 0.01$ ), the intensity of hemorrhage ( $r = +0.29$ ;  $p < 0.05$ ), with the level of TNF- $\alpha$  in blood serum ( $r = +0.64$ ;  $p < 0.01$ ) and the level of IL-10 in blood serum ( $r = +0.45$ ;  $p < 0.01$ ) was determined.

In the II group of patients there was an increase in the level of IL-6 ( $p > 0.05$ ) in blood serum in 28.6 % patients, TNF- $\alpha$  – (1.6 times) in 28.6 % ( $p < 0.05$ ). The number of IL-10 in patients of the II group was within the norm.

The correlation link was determined between the level of IL-10 and inflammation activity ( $r = -0.76$ ;  $p < 0.01$ ), level of IL-6 ( $r = +0.64$ ;  $p < 0.05$ ), level of TNF- $\alpha$  ( $r = +0.76$ ;  $p < 0.01$ ). The level of anti-inflammatory IL-6 correlated with: the level of TNF- $\alpha$  ( $r = +0.86$ ;  $p < 0.01$ ). A high level of pro-inflammatory cytokines IL-6, TNF- $\alpha$  and a low activity of the anti-inflammatory mediator IL-10 define the process activity, their long-term circulation in patients with ulcerative hemorrhages from the upper areas of the gastro-intestinal tract are associated with unfavorable prognosis. In case of imbalance between pro- and anti-inflammatory mediators in favor of the first, the risk for relapsing hemorrhage in the second group increases. Changes in the number of anti-inflammatory cytokines IL-6, TNF- $\alpha$  in peripheral blood could be the reason and one of the realization mechanism of hemorrhage relapse.

During the period 2017-2019 years 10 elderly patients (1.6%) were operated. In 5 cases conditionally-radical surgical interventions were performed. They include excision of the ulcerative defect with pyloroplasty by Heyneke-Mikulicz (30%), by Finney (20%). In this case ulcerative defects were localized in duodenum. Palliative surgery included suturing of ulcerative defect with truncal vagotomy (TV) – 3 patients. Partial gastric resection performed in 2 cases. Ulcerative defects localized in duodenum and

**Table I.** Level of cytokines in patients with gastroduodenal hemorrhages, Me (Q1; Q2).

Indicators, units of measurement	I group (n=541)	II group (n=68)	Control group (n=20)	$p_1$	$p_2$	$p_3$
TNF- $\alpha$ , $\mu\text{g/ml}$	3.5 (0.27; 7.4)	5.4 (1.1; 15)	2.3 (0.3; 3.9)	$p < 0.05$		
IL-6, $\mu\text{g/ml}$	3.7 (0.8; 9.8)	5.38 (3.01; 21.9)	5.60 (1.2; 7.8)			$p < 0.05$
IL-10, $\mu\text{g/ml}$	17.1 (11.4; 25.1)	16.9 (12.8; 24.2)	18.7 (0.4; 21.4)			

Remark:

1.  $p_1$  – significance of differences of the I group of patients in comparison with the control group;
2.  $p_2$  – significance of differences of the II group of patients in comparison with the control group;
3.  $p_3$  – significance of differences between I and II group of patients.

stomach in ratio 1:2 ( $p>0.05$ ). Differences were insignificantly reliable due to small number of patients.

Post-operative complications included the relapse of hemorrhages, suture failures of the stitched area of ulcer. Post-operative mortality was 30%, which testifies in favor of the initially severe condition of patients, complicated by cardio-vascular pathology. Most patients operated on the peak of hemorrhage and could be considered as a “surgery of despair”.

## CONCLUSIONS

1. An essential aspect for choosing the medical tactics include taking into consideration the cardio-vascular pathology.
2. The number of second group patients (“double therapy”) with big and massive blood loss is 2.7 times higher than similar indices in of the first group (standard therapy) ( $p<0.05$ ).
3. According to analysis of the condition of the local endoscopic hemostasis, the indicator of the unstable hemostasis with the high risk for hemorrhage relapse, with stable hemostasis F III in I group is 1.8 times higher than the similar indicator in the II group ( $p<0.05$ ). These data have been the ground of treatment elaboration. As for the index of active hemorrhage F I, the patients who receive standard hypotension therapy have 3.3 times less active hemorrhage than the patients who receive “double therapy” ( $p<0.05$ ).
4. In the group of patients who had hemorrhage relapse and received “double therapy”, indices of body immune reactivity are compared to the group of patients who have got standard hypotension therapy and have smaller hemorrhage relapse rate which coming along more positive tendency of immune status changes.
5. In cases of acute cardiovascular pathology the palliative surgery was performed in 100%. At the same time the part of the conditionally-radical methods, including elements of radicalism and organ-preserving type is increased.

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## Conflict of interest:

The Authors declare no conflict of interest.

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**D** – Writing the article, **E** – Critical review, **F** – Final approval of the article