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THE ROLE OF HUMORAL IMMUNITY IN THE COMPLEX DIAGNOSIS OF DESTRUCTIVE FORMS OF ACUTE CHOLECYSTITIS

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The incidence of acute cholecystitis, to date, remains at the same level and amounts to 1.6 cases per 100,000 people. Mortality in this pathology ranges from 4 to 26%. There is no doubt that changes occur in any pathology, both in the local and in the general link of immunity, acute cholecystitis is no exception. The most significant deviations are observed in humoral immunity. Based on this, these criteria can be used to improve the diagnosis of acute destructive cholecystitis. The aim. To evaluate changes in the humoral link of immunity in patients with acute destructive cholecystitis. Materials and methods: A single-stage study of 105 patients with various clinical and morphological variants of acute calculous cholecystitis (acute catarrhal cholecystitis (n=35); acute phlegmonous cholecystitis (n=35); acute gangrenous cholecystitis (n=35)), comparable in age, gender and concomitant pathology and time of surgical intervention, was conducted. When patients were admitted to the hospital with suspected acute cholecystitis, the activity of the following immunogram parameters was determined in the first 2 hours: IgA, IgG, IgM and total immunoglobulin. Statistical processing of the obtained results was carried out using the SPSS Statistics 10.0 program in compliance with the principles of statistical analysis adopted for research in biology and medicine. The results. As a result of the study, an increase in the level of IgA in a subgroup of patients with acute gangrenous cholecystitis (subgroup № 3) to 139.5 IU/ml was found, which is 1,3 times higher than the reference level ($p < 0,05$), 1.1 times less ($p < 0,05$) than the values of the clinical comparison group, and 1.1 times higher ($p \leq 0,05$) values obtained in subgroups with catarrhal (subgroup № 1) and phlegmonous (subgroup № 2) acute cholecystitis. It was revealed that the concentration of IgG in subgroup № 3 reaches 196,6 IU/ml, which exceeds the indicators in other groups, relative to the norm values by 1,4 times ($p \leq 0,05$), comparison group by 1,4 times ($p \leq 0,05$), subgroup № 1 by 1,6 times ($p \leq 0,05$), subgroup № 2 1,2 times ($p \leq 0,05$). In the subgroup with acute gangrenous cholecystitis, it was found that the concentration of IgM is 190,4 IU/ml, which is higher than in other groups: the clinical comparison group by 1,6 times ($p \leq 0,05$), subgroup № 1 by 1,5 times ($p \leq 0,05$), subgroup № 2 by 1,2 times ($p \leq 0,05$). Conclusions. The study found that in destructive forms of acute cholecystitis, an increase in IgG was recorded by 1,6 times in comparison with the group of patients with non-destructive cholecystitis ($p < 0,05$), as well as IgM by 1,3 times in comparison with the group of patients with non-destructive cholecystitis.

Keywords: cholelithiasis, acute cholecystitis, prognosis, destructive forms, cholelithiasis, diagnosis, humoral immunity, IgA, IgM, IgG.

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Acute cholecystitis still remains an important and still unresolved issue of emergency surgery. The continuing high incidence of this nosology (1,6 cases per 100 thousand) and postoperative mortality (0,9-1%) explain the need to search for new prognostic criteria that will increase the sensitivity and specificity of known and publicly available diagnostic methods for acute destructive cholecystitis [9].

Undoubtedly, changes in local and general immunity accompany the pathology of the organs of the hepato-pancreato-duodenal zone, affecting the cellular and humoral link [1,2,3]. At the same time, a number of both domestic and foreign authors indicate that in patients with calculous cholecystitis, which is accompanied by stagnation and thickening of

bile, there is an increase in the concentration of immunoglobulins [2, 5]. In her study, N.M. Kozlova points out that the pathology of the biliary system is characterized by an increase in all classes of immunoglobulins [4]. The liver serves as the main source of utilization of serum IgA, which is captured by hepatocytes and secreted into bile, which explains the increase in this immunoglobulin in bile "sludge" [6,8,10]. In the works of L.G. Levkoeva, G.A. Eliseeva, devoted to the study of the level of CEC in blood plasma in patients with chronic cholecystitis, no significant changes were found [6]. At the same time, there are no data in the literature that reliably show changes in humoral immunity in acute destructive cholecystitis.

The aim. To evaluate changes in the humoral link of immunity in patients with acute destructive cholecystitis

Materials and methods. A simultaneous study of 105 patients with various clinical and morphological variants of acute calculous cholecystitis (acute catarrhal cholecystitis (n=35); acute phlegmonous cholecystitis (n=35); acute gangrenous cholecystitis (n=35)), comparable in age, gender and concomitant pathology and time of surgical intervention (Tab.1.). The study group included patients operated on (laparoscopic cholecystectomy) about acute calculous cholecystitis at the age of 30 to 70 years. Exclusion criteria from the study group: patients suffering from cholelithiasis complicated by mechanical jaundice, aged <30 years and > 70 years. The clinical comparison group consisted of 35 patients suffering from chronic calculous cholecystitis aged 30 to 70 years, whose examination revealed no pathology of the stomach, duodenum, operated by the standard method of laparoscopic cholecystectomy. Exclusion criteria from the clinical comparison group: patients suffering from chronic calculous cholecystitis, acute calculous cholecystitis, aged <30 and >70 years, whose examination revealed pathology of the stomach, duodenum.

During admission to the hospital with suspected acute cholecystitis, the activity of the following immunogram parameters was determined in the first 2 hours: IgA, IgG, IgM. The immunoglobulin content was assessed using a set of reagents "Diagnostic monospecific sera against IgG (H+L), IgA (H), Ig M(H) human, dry".

Statistical processing of the obtained results was carried out using the SPSS Statistics 10.0 program in compliance with the principles of statistical analysis adopted for research in biology and medicine. The results are given in an average value with an average quadratic error ($M \pm m$). To study the relationships between the studied parameters, a paired Pearson correlation analysis was performed. The distribution of degrees of freedom was evaluated by the chi-square criterion for evaluating qualitative data in three or more independent groups. When comparing the average values of a quantitative trait in three or more independent groups, with a normal distribution of data in all groups, a one-factor analysis of variance (ANOVA) was performed. The Friedman criterion was used to compare three or more related samples, the data in which do not obey the law of normal distribution. The Mann-Whitney criterion was used for paired comparison of independent samples [7].

Distribution of patients depending on age and gender / Distribution of patients depending on age and gender

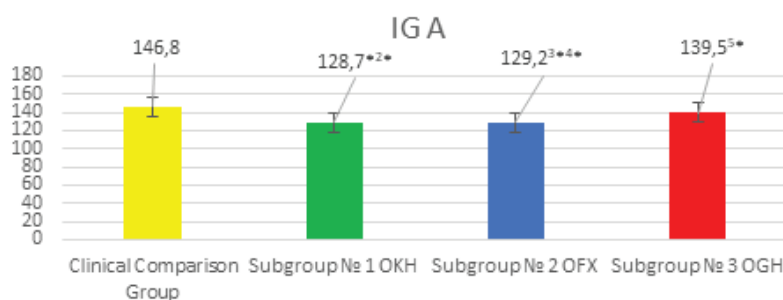
Patient subgroups	Quantity people, %					
	Up to 30 years old		30 to 50 years old		Over 50	
	M	AND	M	AND	M	AND
Acute catarrhal cholecystitis (n=35)	3 (8,6)	5 (14,3)	4 (11,4)	16 (45,7)	1 (2,9)	6 (17,1)
Acute phlegmonous cholecystitis (n=35)	2 (5,7)	7 (20)	5 (14,3)	14 (40)	3 (8,6)	4 (11,4)
Acute gangrenous cholecystitis (n=35)	4 (11,4)	3 (8,6)	7 (20)	13 (37,1)	1 (2,9)	7 (20)
Chronic calculous cholecystitis (clinical comparison group) (n=35)	2 (5,7)	4 (11,4)	4 (11,4)	17 (48,6)	3 (8,6)	5 (14,3)
Total (n=140)	11 (7,9)	19 (13,5)	20 (14,3)	60 (42,9)	8 (5,7)	23 (15,7)

The results. As a result of the study, there was no pronounced increase in Ig A indicators in subgroups of patients with destructive forms of acute cholecystitis. In patients of the clinical comparison group, the average concentration of Ig A reached the level of 146,8 IU/ml, which exceeds the average reference value by 1,4 times ($p < 0,05$). At the same time, in the subgroup of patients with acute catarrhal cholecystitis, the IgA index in blood plasma was 128,7 IU/ml, which is 1,2 times higher ($p < 0,05$) than the average value of the norm and 1,2 times lower ($p < 0,05$) than the level of this immunoglobulin in the clinical comparison group. In the subgroup with acute phlegmonous cholecystitis, the average concentration of IgA was 129,2 IU/ml, which corresponds to the concentration in patients with acute catarrhal cholecystitis, but at the same time, it is 1,2 times lower than similar indicators in the clinical comparison group ($p < 0,05$) and 1,2 times higher than the average reference index ($p < 0,05$). In the subgroup of patients with

acute gangrenous cholecystitis, the IgA index was 139,5 IU/ml, which is 1,3 times higher than the reference level ($p < 0,05$), 1,1 times less ($p < 0,05$) than the values of the clinical comparison group, and 1,1 times higher ($p < 0,05$) than the values obtained in the subgroups with catarrhal and phlegmonous acute cholecystitis (Figure 1).

When assessing the sensitivity of this criterion, it was revealed that the highest sensitivity and specificity in the diagnosis of: acute catarrhal cholecystitis has an Ig A index of <130 IU/ml (Sensitivity 71,4% [CI 66,1-76,7]; Specificity 97,1% [CI 94,4-99,8]); acute phlegmonous cholecystitis – <130 IU/ml (Sensitivity 65,7% [CI 58,8-72,6]; Specificity 97,1% [CI 94,4-99,8]); acute gangrenous cholecystitis – >150 IU/ml (Sensitivity 40% [CI 27,7-53,3]; Specificity 68,6% [CI 62,2-75]) (Figure 2).

It was revealed that when a destructive process appears in the gallbladder, IgG indicators increase. In the clinical comparison group, the indicator was 138,4 IU/ml, which does not exceed the



* $p < 0,05$ chi-square criterion in subgroup №. 1 and subgroup №. 3,
 2* $p < 0,05$ chi-square criterion in subgroup №. 1 and clinical comparison group,
 3* $p < 0,05$ chi-square criterion in subgroup №. 2 and clinical comparison group,
 4* $p < 0,05$ chi-square criterion in subgroup №. 2 and subgroup №. 3,
 5* $p < 0,05$ criterion chi-squared in subgroup №. 3 and clinical comparison group,

Fig. 1. Ig A index in the study group (IU/ml)

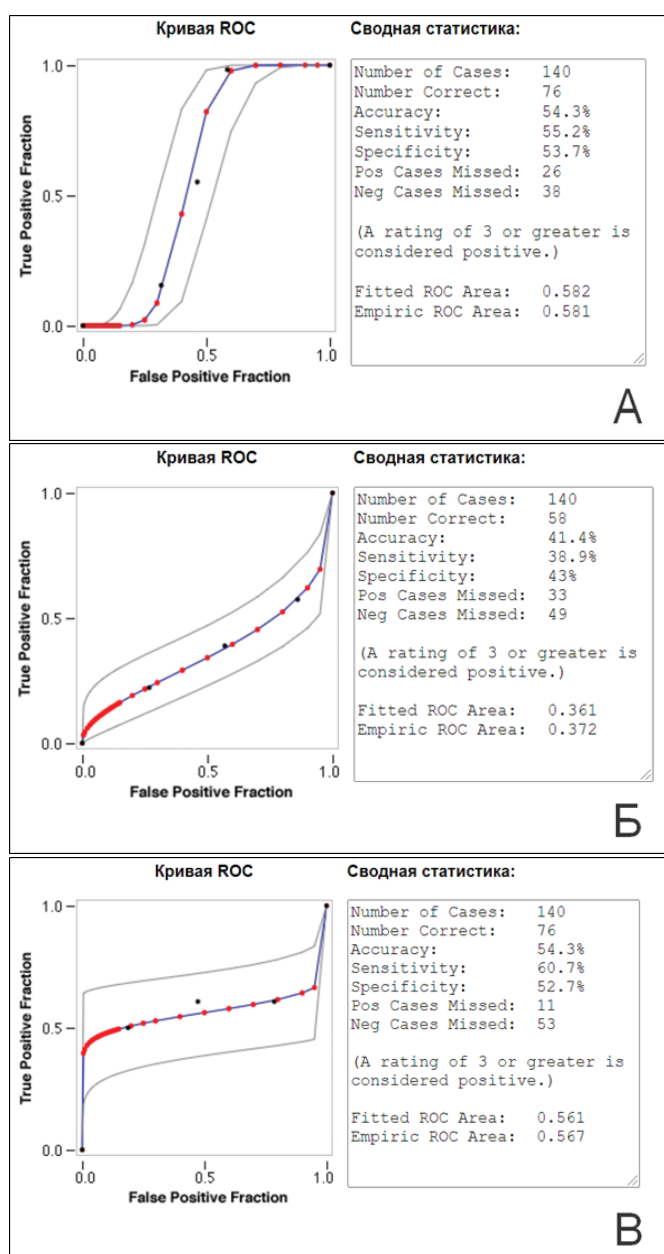


Fig. 2. ROC curve of IgA indices obtained in patients with acute calculous cholecystitis: A - <130 IU/ml; B- 130-150 IU/ml; C->150 IU/ml

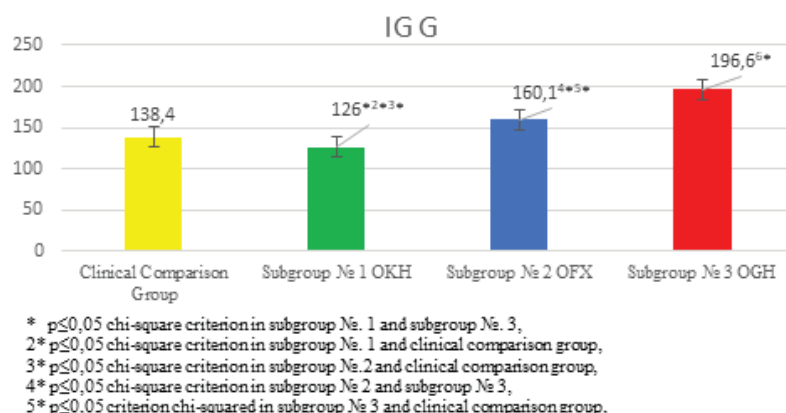


Fig. 3. Ig G index in the study group (IU/ml)

norm. At the same time, in a subgroup of patients with acute catarrhal cholecystitis, the IgG concentration corresponds to 126 IU/ml, which does not exceed the norm. In patients with acute phlegmonous cholecystitis, this indicator is 160,1 IU/ml, which is 1,1 times higher ($p < 0,05$) than the reference value, 1,2 times higher ($p < 0,05$) than the indicators in the clinical comparison group and 1,3 times higher ($p < 0,05$) than the values obtained in the subgroup of acute catarrhal cholecystitis. In subgroup № 3, the IgG concentration reaches 196,6 IU/ml, which exceeds the indicators in other groups, relative to the norm values by 1,4 times ($p \leq 0,05$), the comparison group by 1,4 times ($p \leq 0,05$), group № 1 by 1,6 times ($p \leq 0,05$), group № 2 by 1,2 times ($p \leq 0,05$) (Figure 3).

It was found that the highest sensitivity and specificity in the diagnosis of acute catarrhal cholecystitis is IgG - 100-130 IU/ml (Sensitivity 65,7% [CI 58,8 -72,6]; Specificity 68,6% [CI 62,2-75]); acute phlegmonous cholecystitis - 160-200 IU/ml (Sensitivity 45,7% [CI 38,8-52,6]; Specificity 91,4% [CI 86,1-96,7]); acute gangrenous cholecystitis - 160-200 IU/ml (Sensitivity 62,9% [CI 55,1-70,7]; Specificity 91,4% [CI 86,1-96,7]) (Figure 4).

As a result of the study, it was found that when destruction occurs in the gallbladder, Ig M indicators also increase. In patients in the clinical comparison group, the indicator was 117,5 IU/ml, and in subgroup No. 1 -131 IU/ml, which is within the normal range. At the same time, in the subgroup with acute phlegmonous cholecystitis, this indicator was 161,3 IU/ml, which is 1,2 times higher ($p < 0,05$) than the average norm, 1,4 times higher ($p < 0,05$) than in the clinical comparison group and 1,2 times higher ($p < 0,05$) than the concentration of this immunoglobulin in a subgroup with acute catarrhal cholecystitis. In the subgroup with acute gangrenous cholecystitis, the concentration of IgM is 190,4 IU/ml, which is higher than in other groups: the clinical comparison group by 1,6 times ($p \leq 0,05$), subgroup №. 1 by 1,5 times ($p \leq 0,05$), subgroup № 2 by 1,2 times ($p \leq 0,05$) (Figure 5).

Sensitivity and specificity in the diagnosis: acute catarrhal cholecystitis has an IgM index from 100-130 g/l (Sensitivity 54,3% [CI 49,7 – 58,9]; Specificity 5,7% [CI 0-12,6]); acute phlegmonous cholecystitis - 160-200 g/l (Sensitivity 54,3% [CI 49,7 – 58,9]; Specificity 97,1% [CI 94,4-99,8]); acute gangrenous cholecystitis - 160-200 g/l (Sensitivity 71,4% [CI 66,1-76,7]; Specificity 97,1% [CI 94,4-99,8]) (Figure 6).

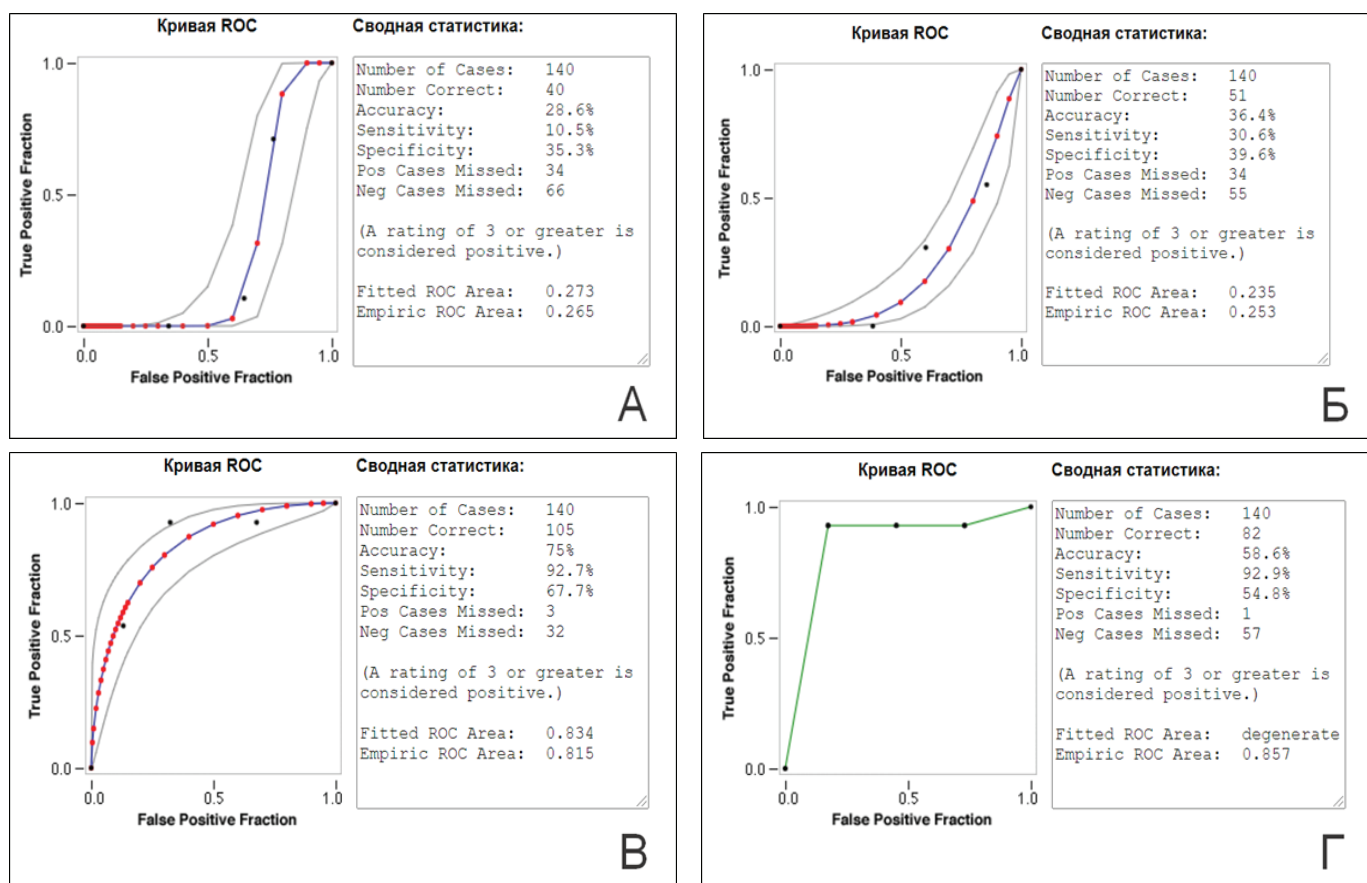


Fig. 4. Sensitivity and specificity of IgG indicators obtained in patients with acute calculous cholecystitis: A- 100-130 IU/ml; B- 130-160 IU/ml; C-160-200 IU/ml; D- >200 IU/ml

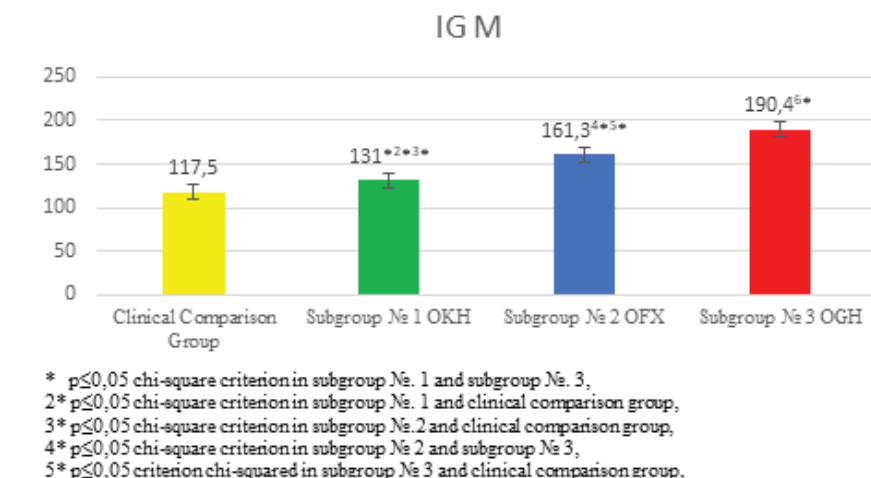


Fig. 5. Ig M index in the study group (IU/ml)

Conclusions: The study found that in destructive forms of acute cholecystitis, there is an increase in IgG by 1,6 times in comparison with the group of patients with non-destructive cholecystitis ($p < 0.05$), as well as an increase in the level of Ig M by 1,3 times in comparison with the group of patients with non-destructive cholecystitis. There was no change in IgA indicators in patients with destructive cholecystitis in the study.

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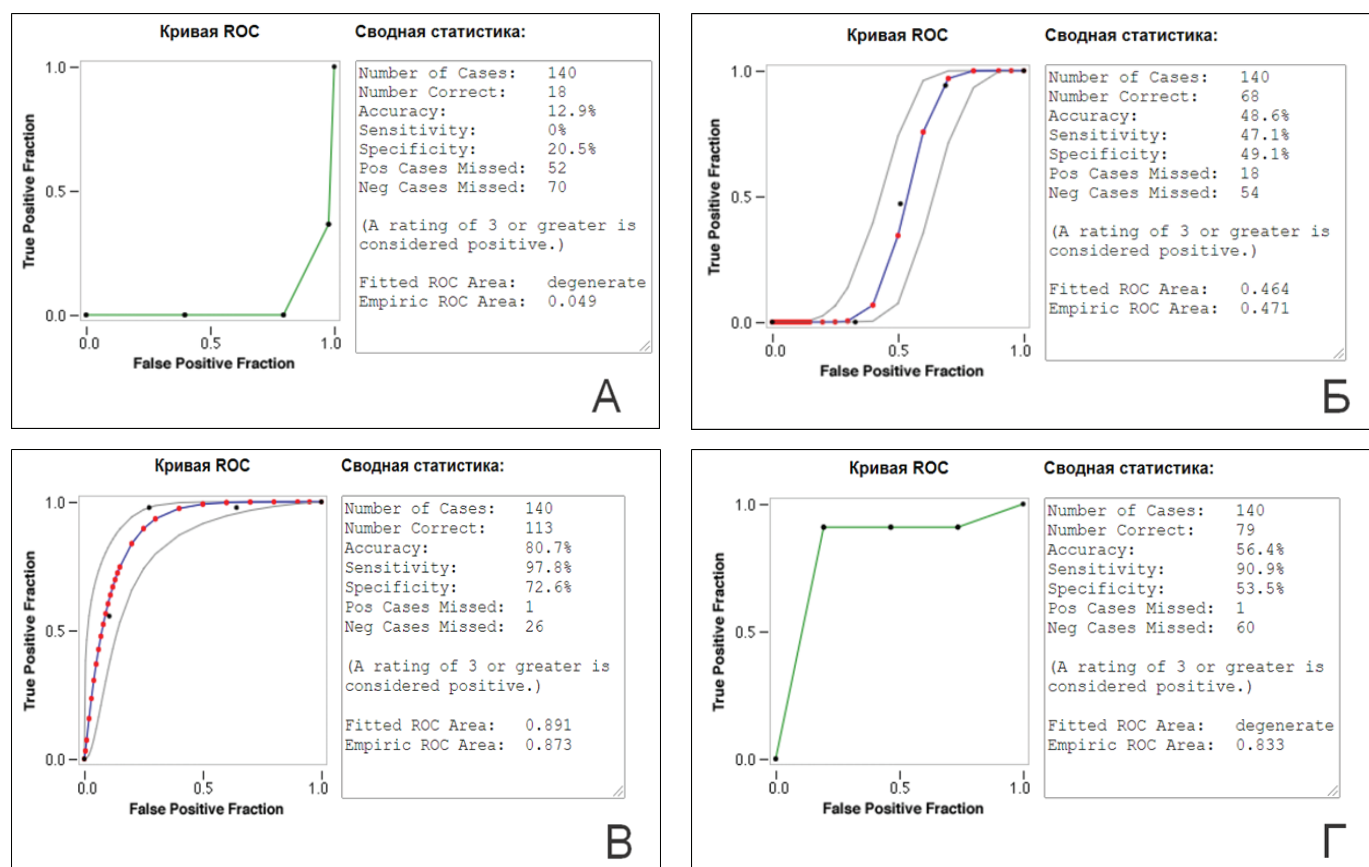


Fig. 6. Sensitivity and specificity of IgM indicators obtained in patients with acute calculous cholecystitis: A- 100-130 IU/ml; B- 130-160 IU/ml; C- 160-200 IU/ml; D- >200 IU/ml

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