

NJSC "West Kazakhstan Marat Ospanov Medical University»

Abstract to the dissertation
for the degree
Doctor of Philosophy (PhD)

**Minimally invasive technologies in complex treatment of
gallstone disease complicated by obstructive jaundice**

Specialty "6D110100-Medicine".

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ABSTRACT

Of Aitbaeva Aliya Matzhanovna on the topic "Minimally invasive technologies in the complex treatment of gallstones complicated by obstructive jaundice", presented for the degree of Doctor of Philosophy (PhD) in the specialty "6D110100-Medicine".

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TOPICALITY

Gallstone disease (GD) still relates to the number of widespread diseases that are found in 10-15% of the adult population. The growth rate of cholelithiasis is accompanied by an increase in the number of its complicated forms, the frequency of which reaches 35%. Surgical treatment of jaundice complicated by obstructive jaundice (OJ), represents a topical problem in relation to a relatively high percentage of complications and fatal outcomes, with a different statistical rate of 6% to 6%.

The modern stage of development of abdominal surgery is characterized by extensive introduction into clinical practice of new high-tech diagnostic methods and minimally invasive surgical interventions that reduce the risk of surgical surgery. However, the overwhelming majority of scientific research is devoted to the application of new technologies in uncomplicated forms of gallstone disease.

At the present time, the tactics of treatment of GD complicated OJ, as strange as it is not finally decided. This literature in recent years testifies to the diametrically opposite approaches to the surgical solution of this problem. Thus, the authors give preference to retrograde endoscopic transpapillary interventions, directed to the dissection of the large papilla of the duodenum with the implementation of endoscopic papilloscopycoliosis, lithotripsy, endoprosthesis. nasobiliary drainage, etc., followed by cholecystectomy. Other authors suggest a method when intervention in the common gallbladder and cholecystectomy is performed during surgery, performed with minor traumatic access - laparoscopic or minipalarotomy one.

Thus, the multifaceted nature of the known methods of treatment of complicated forms of GD and ambiguous attitude to it significantly complicates the adoption of the right tactical decision in each specific case. Despite the rapid development of new diagnostic and surgical technologies, they are often used incoherently, giving diverse results. The high percentage of mortality and unsatisfactory results of surgical treatment of patients with gallstone disease, complicated by obstructive jaundice determined the main goal and task of our work.

The purpose of our research was to improve the results of treatment of patients with gallstones, complicated by obstructive jaundice through the use of minimally invasive methods of surgical treatment.

To achieve this, the following tasks were set:

1. To develop an optimal therapeutic tactic with the use of minimally invasive surgical methods in patients with GD complicated by obstructive jaundice.

2. To study the clinical effectiveness of differentiated therapeutic tactics in the surgical treatment of GD complicated by obstructive jaundice with the use of minimally invasive technologies depending on the degree of jaundice.

3. To evaluate the reserve-compensatory capabilities of the organism in the methods of minimally invasive and open surgical interventions in patients with gallstone disease complicated by obstructive jaundice

4. To carry out a comparative analysis of the results of minimally invasive and traditional methods of surgical treatment of patients with gallstone disease, complicated by obstructive jaundice, based on the assessment of the parameters of the system peroxidation of lipids- antioxidant protection

Scientific novelty:

1. Developed a differentiated therapeutic tactic with the use of minimally invasive technologies in GD, complicated by the dependence of the degree of jaundice.

2. Proven clinical efficacy and feasibility of performing stages of treatment, combining endovide-
osurgical techniques, endoscopic and endobiliary interventions in patients with gallstone disease,
complicated by obstructive jaundice.

3. Developed and introduced into clinical practice laparoscopic ductocholedocholithotomy for
gallstone disease complicated by choledocholithiasis (application for patent RK № 2020 / 0531.1
dated 05.08.2020).

4. In the comparative aspect of the assessment of the traumatic nature of the stages of open and
minimally invasive operations in patients with acute and chronic diseases, complicated by the study
of the dynamics of reserve-compensatory capabilities of the body.

5. The positive effect of the use of minimally invasive surgical technologies on the indicators of
LPO- AOD blood of patients with OJ, which was expressed at a higher rate of inhibition of LPO and
enhancement of the activity of enzymes of the AOD in order to compare.

Practical significance:

1. The developed system of a differentiated approach in the complex treatment of cholelithiasis
complicated by obstructive jaundice makes it possible to determine the optimal therapeutic tactics
and objectify the volume of surgical intervention, which significantly improves the results of surgical
treatment of this category of patients.

2. A staged method of treatment with the use of minimally invasive and interventional drainage
technologies for cholelithiasis complicated by obstructive jaundice will allow timely decompression
of the biliary system, significantly reduce intoxication caused by the cytolytic process and cholemia,
and improve liver function, thereby reducing the number of postoperative complications and mortal-
ity compared with the traditional way.

3. The developed laparoscopic method of ductolithotomy is less traumatic and simplifies the
technique of removing calculi from the common bile duct, thereby expanding the possibility of using
minimally invasive interventions for cholelithiasis complicated by choledocholithiasis.

The main provisions for the defense:

1. The optimal treatment tactics in patients with GD complicated by obstructive jaundice is a dif-
ferentiated approach to surgical treatment using minimally invasive technologies, depending on the
severity of jaundice.

2. A staged method of treatment using minimally invasive and interventional drainage technolo-
gies allows stopping intoxication, GD and cytolysis, as well as performing radical surgery in more
favorable conditions, which ultimately leads to improved treatment results in patients with choleli-
thiasis complicated by OJ.

3. The use of minimally invasive surgical technology in the surgical treatment of patients with GD
complicated by OJ significantly reduces the degree of trauma of surgery.

4. Minimally invasive technologies in the surgical treatment of gallbladder complicated by OJ
have a positive effect on the parameters of the LPO-AOD system in comparison with traditional open
surgical interventions.

5. One-stage laparoscopic cholecystectomy with ductocholedocholithotomy is the method of
choice in patients with GD complicated by mild obstructive jaundice with minimal changes in the
LPO- AOD system and reserve compensatory capabilities of the body.

Approbation of work. The main provisions of the dissertation work were reported at an expanded
meeting of the scientific and problem commission of the NJSC «M. Ospanov WKMU".

The results of the study were reported at:

- VI Congress of the Kazakhstan Association of Endoscopic Surgeons (Kazakhstan, Aktobe, 2016
- October);

- The 4th Asian Symposium on Health care without Borders (Japan, Hiroshima, 2017 - August);

- 2nd International Advanced Liver & Pancreas Surgery Symposium (Korea, Seoul, 2018 - Octo-
ber).

- VIII International Scientific and Practical Conference "Topical Issues of Medicine" (Azerbaijan, Baku, 2019 - April);
- III International Scientific and Educational Conference "Internationalization of Continuing Medical Education. A look into the future ", (Kazakhstan, Aktobe, 2019 - April);
- International scientific-practical conference (67th annual), dedicated to the 80th anniversary of TSMU named after Abuali ibni Sino "Medical science of the XXI century - a look into the future" (Tajikistan, Dushanbe, 2019 - November).
- 1st Interdisciplinary Endosurgical Congress of the Caspian countries. (Kazakhstan, Aktau, 2019 - September);

Publications on the topic of the dissertation. On the topic of the dissertation, 10 scientific publications were published, of which 1 article was in the publication indexed in the Scopus information base - "Journal of Global Pharma Technology" (SJR = 0.146 in 2019); 3 articles - in publications recommended by the Committee for Control in the Sphere of Education and Science of the Republic of Kazakhstan; 4 theses - in collections of International conferences (including foreign - 2 and indexed in the Scopus database - 1).

All publications were written by the doctoral student personally under the guidance of the supervisor, who consulted and made corrections. Directly the doctoral student carried out a search and review of literary sources, recruiting patients into study groups. The author was directly personally involved in the treatment process when carrying out surgical interventions to patients. Statistical processing and analysis of the results obtained were carried out by a doctoral student.

Implementation of research results. The research materials were introduced into practical health care - in the work of the surgical departments of the state utility company on the right of economic management "Emergency Hospital" and the state enterprise on the right of economic management "Aktobe medical center", Aktobe.

Structure and scope of work. The thesis is presented on 149 pages of computer text and includes the following sections: introduction, references review, materials and research methods, research results, discussion of the results, conclusions, practical recommendations, bibliography, and applications.

The bibliography includes 248 sources, including 144 foreign and 104 domestic sources of scientific literature. The doctoral dissertation is illustrated with 60 tables and 30 figures, which reflect the essence of the scientific work carried out.

MATERIALS AND RESEARCH METHODS

General characteristics of the research

The study was carried out at the clinical bases of the Department of Surgical Diseases No. 2 of the West Kazakhstan Marat Ospanov Medical University (state-owned enterprise on the right of economic management "Ambulance Hospital" and surgical departments of "Aktobe Medical Center"). Design - open-label prospective controlled clinical study with partial historical control.

To achieve the goal and fulfillment of the assigned tasks, the analysis of the treatment results of 384 patients operated on for gallstone disease complicated by obstructive jaundice was carried out for the period from 2016 to 2019.

The examined patients were divided into 2 groups (main and control), each of which, according to the severity of obstructive jaundice, was divided into 3 subgroups according to the classification of V.D. Fedorov, V.I. Vishnevsky (2000).

The main group (group A) consisted of 220 (57.3%) patients, in whose treatment minimally invasive surgical interventions were used. The first subgroup (A1) of the main group included 79 patients (35,9%) with mild obstructive jaundice. The second subgroup (A2) included 104 patients (47,3%) with moderate obstructive jaundice. The third subgroup (A3) included 37 patients (16,8%) with severe obstructive jaundice.

The control group (group B) consisted of 164 (42,7%) patients treated with traditional (open) surgical interventions.

In turn, the first subgroup (B1) included 56 patients (34,2%) with mild severity, the second subgroup (B2) - 76 patients (46,3%) with moderate severity, and the third subgroup (B3) - 32 patients (19,5%) with severe obstructive jaundice.

Inclusion criteria: patients with cholelithiasis complicated by obstructive jaundice of non-neoplastic genesis (choledocholithiasis, BDS stenosis, stricture of the terminal part of the common bile duct, up to 2.0 cm long); the patient's age is over 18 years old; for the main group - patients in whose treatment minimally invasive technologies were used (endoscopic, puncture under visual control); for the control group - patients treated with traditional (open) surgical methods.

Exclusion criteria: patients with destructive forms of acute cholecystitis, complicated by widespread peritonitis; pregnant women and patients in the early postpartum period; patients with cancer and mental illness; terminal (agonal) states; for the main group - patients who had previously undergone open surgical interventions (upper floor of the abdominal cavity).

The average age of patients in the main group was 55 (48; 66) years, in the control group - 53 (44; 64), $p > 0.05$. In the compared groups, there were no gender differences, while the predominance of the female was observed: in the main group - 129 (58.6%), in the control group - 106 (64.6%). Distribution of patients due to obstructive jaundice: choledocholithiasis in the main group was observed in 151 patients (68.6%), in the control group - in 117 (71.3%), $p = 0.568$; BDS stenosis in the main group was found in 47 patients (21.3%), in the control group - in 33 (20.1%), $p = 0.767$; stricture of the terminal part of the common bile duct in the main group was detected in 8 patients (3.7%), in the control - in 6 (3.6%), $p = 0.991$, and pancreatitis in the main group was found in 14 patients (6.4%), in the control - in 8 (4.8%), $p = 0.536$. Distribution of patients according to the duration of jaundice: in the main group in 66 patients (30%), jaundice lasted up to 7 days, in 116 patients (52.7%) - from 7 to 14 days and over 14 days - in 38 patients (17.3%). In the control group, in 48 patients (29.3%), jaundice lasted up to 7 days, in 80 patients (48.8%) - from 7 to 14 days and over 14 days - in 36 patients (21.9%). Distribution of patients by the nature of the inflammatory process of the gallbladder: in the main group, 77 patients (35%) had acute cholecystitis, 143 (65%) had chronic cholecystitis; in the control - 62 (37.8%) and 102 (62.2%) patients, respectively.

Depending on the variant of surgical treatment of cholelithiasis complicated by obstructive jaundice, the patients were distributed as follows.

In the main group (220 patients) minimally invasive interventions were used, of which:

- 79 underwent a one-stage radical operation (A1): in 21 - laparoscopic cholecystectomy (LCE) with endoscopic papillosphincterotomy (EPST), in 24 - LCE, EPST with endoscopic mechanical lithoextraction of concrements, in 20 - LCE, laparoscopic ductomyotomy common bile duct and in 14 - LCE with drainage of the common bile duct according to Halstead-Pikovsky.

- In 104 patients, the tactics of surgical correction in two stages (A2) was used: the first stage - endoscopic debridement of the common bile duct, the second - laparoscopic cholecystectomy.

- 37 patients underwent a two-stage surgical procedure (A3): the first stage - minimal surgical intervention aimed at eliminating jaundice: nasobiliary drainage (8), stenting (24) and percutaneous transhepatic drainage of the biliary tract (5); the second stage is endoscopic papillosphincterotomy to eliminate stenosis, stricture and LCE (8); removal of calculi from the common bile duct with cholecystectomy using minimally invasive technology (29).

In the control group (164 patients), the patients underwent surgical interventions by the traditional method in one stage in groups B1, B2 and in two stages in group B3. Traditional cholecystectomy, choledocholithotomy, transduodenal papillosphincterotomy were performed and the operation was completed by various methods of external (according to Halstead-Pikovsky, Vishnevsky, Keru) and internal (choledochoduodenoanastomosis) drainage of the biliary tract.

Thus, as can be seen from the data presented, the patients of the compared groups in all parameters (gender, age, causes of obstructive jaundice, duration of jaundice, the nature of the inflammatory process of the gallbladder, concomitant diseases) were identical.

Research methods

The examination of patients of the main and control groups was carried out taking into account the clinical protocols for the diagnosis and treatment of diseases developed by the Ministry of Health of the Republic of Kazakhstan. The patients' condition was assessed taking into account clinical, laboratory and instrumental methods.

The clinical study was carried out according to the generally accepted rules for examining surgical patients.

Hematological parameters were determined in all patients: bilirubin and its fractions, urea, creatinine, total protein and its fractions, albumin-globulin coefficient, specific liver enzymes: cytolysis markers - aspartate aminotransferase (AST) and alanine aminotransferase (ALT), cholestasis markers - gamma-glutamyltransferase (GGT) and alkaline phosphatase (ALP), blood glucose, lactate dehydrogenase (LDH); indicators of coagulation hemostasis - fibrinogen, prothrombin index, activated partial thromboplastin time.

To characterize lipid peroxidation (LPO), the level of malondialdehyde (MDA) was determined. The determination of malondialdehyde was carried out by the method proposed by S. Chevari et al., 1991. To assess the antioxidant defense system (AOD), the level of catalase was determined. Plasma catalase activity was determined by the method of M.A. Korolyuk et al. (1988).

Determination of the level of cortisol in the blood, "stress hormone" in response to surgical trauma. The studies were carried out using an enzyme immunoassay analyzer "SEROZYME - I" manufactured by "SERONO" (Italy) using the test system "CORTISOLSEROZYME");

Laboratory studies were carried out using a BIOSYSTEMA-25 biochemical analyzer, a SYS-MEX-21 KX hematological analyzer, a SIEMENS urinary analyzer, a TS-4000 coagulometer, and a BIORAD immunoassay analyzer.

The study of the reserve-compensatory capacities of the organism (RCCB) was carried out by the method of cardiointervalography on the "Varicard" complex before the operation, during the operation and at the end of the operation.

Verification of the diagnosis of obstructive jaundice was carried out using modern methods of instrumental diagnostics: ultrasound examination (ultrasound), fibrogastroduodenoscopy (FGDS), direct methods of radiopaque examination of the biliary tract, percutaneous transhepatic cholangiography (PTC), computed tomography (CT), magnetic resonance cholangiography.

Statistical methods

The required sample size was estimated based on the methodology proposed by J. Cohen (1988). To determine the standardized difference between the mean values of the studied parameters (Cohen's d) equal to 0.3, with a group size ratio of 3: 4, a power of 0.8 and a type I error rate of 0.05, it is necessary to include 150 and 200 patients in the corresponding groups.

Data analysis and predictive modeling were carried out using the R 3.6.3 statistical computing environment (R Foundation for Statistical Computing, Vienna, Austria) using additional third-party packages: lme4 1.1-21, lmer Test 3.1-1, emmeans 1.4.8, car 3.0-7 and MuMIn 1.43.

As a model for analyzing the effects of surgical interventions depending on the severity of obstructive jaundice in relation to the duration of the operation, we used a linear regression model with a \log_2 transformation of the dependent variable and including age, sex, the nature of the inflammatory process, and the duration of jaundice as corrective covariates. The adjusted coefficient of determination (R^2) was used to assess the quality of the model.

Poisson regression models were used to analyze the duration of the pain syndrome, the need for narcotic analgesics, depending on the type of surgery and severity.

A logistic regression model was used as a model for the analysis of surgical interventions depending on the severity of obstructive jaundice in relation to binary indicators (the development of post-operative complications). And for the analysis of surgical interventions depending on the severity of obstructive jaundice in relation to the length of stay of patients in the hospital, a gamma regression model (with a feedback function) was used with the inclusion of age, sex, the nature of the inflammatory process and the duration of jaundice as corrective covariates.

All generalized linear models included correction covariates: age, gender of the patient, the nature of the inflammatory process, and the duration of jaundice. The pseudo-R² Nagelkerke was used as a quality metric for generalized linear models.

To assess the effect of surgical interventions on the dynamics of laboratory parameters, linear models with mixed effects were used. A unique patient index was included in the model as a random effect. The explanatory variables in the model were included after the log₂ transformation. In addition to the above variables, the log₂-transformed value of the corresponding preoperative laboratory value was used as a correction covariate. The quality of the model was assessed using the marginal coefficient of determination (R²).

The estimation of the statistical significance of the variables included in the regression models was carried out using the analysis of type II deviance - the likelihood ratio test.

RESULTS OF RESEARCHES

In order to objectively assess the results of surgical treatment of cholelithiasis complicated by obstructive jaundice, we conducted a comparative study of clinical and laboratory changes in the compared groups.

The functional state of the liver, pancreas and kidneys, LPO-AOD systems and reserve-compensatory capabilities of the body were assessed. Also, as comparative criteria for the effectiveness of treatment in both clinical groups, the course of the postoperative period, the incidence of postoperative complications, mortality and length of hospital stay were taken into account.

Improvement of the clinical condition of patients was simultaneously accompanied by positive changes in laboratory parameters.

The assessment of the functional state of the liver was dictated by the fact that the development of obstructive jaundice disrupts the work of a number of organs, mainly the liver, with the subsequent development of hepatorenal syndrome.

The severity of the disorder depends in most cases on the severity of jaundice, which was assessed by the values of blood biochemical parameters. In this connection, we conducted a study of the main biochemical parameters of blood, such as bilirubin, ALP, AST, ALT, GGT, LDH, albumin-globulin coefficient, urea, creatinine, glucose.

The parameters of cholestasis and cytolysis on admission in both groups exceeded the norm by several times, depending on the severity of OJ. Thus, the level of bilirubinemia upon admission on average exceeded the reference values by 2-3 times in subgroups with mild OJ, 7-8 times and more than 15 times in subgroups with moderate and severe degrees, respectively.

Thus, in the main group, the level of total bilirubin ($M \pm m$) in patients with mild obstructive jaundice was $65.78 \pm 12.29 \mu\text{mol} / \text{l}$, with moderate obstructive jaundice - $149.36 \pm 24.99 \mu\text{mol} / \text{l}$, and with severe obstructive jaundice - $314,55 \pm 51,75 \mu\text{mol} / \text{l}$. In the control group, the total bilirubin index ($M \pm m$) in patients with mild obstructive jaundice was $63.04 \pm 16.39 \mu\text{mol} / \text{L}$, with moderate obstructive jaundice - $152.93 \pm 24.91 \mu\text{mol} / \text{l}$ and with severe obstructive jaundice - $308.89 \pm 45.74 \mu\text{mol} / \text{l}$. The level of direct bilirubin ($M \pm m$) in patients of the main group with mild obstructive jaundice was $29.2 \pm 9.59 \mu\text{mol} / \text{L}$, with moderate obstructive jaundice - $78.46 \pm 13.65 \mu\text{mol} / \text{L}$ and with severe obstructive jaundice. the severity of obstructive jaundice - $182,06 \pm 26,83 \mu\text{mol} / \text{l}$. In the control group, the indicator of direct bilirubin ($M \pm m$) in patients with mild obstructive jaundice was $32.85 \pm 8.72 \mu\text{mol} / \text{l}$, with moderate obstructive jaundice - $80.83 \pm 12.30 \mu\text{mol} / \text{l}$, and with severe obstructive jaundice - $197.56 \pm 16.65 \mu\text{mol} / \text{l}$.

Statistical processing of the data obtained in a linear regression model with mixed effects revealed differences between the groups in relation to the average concentration of total bilirubin, regardless of its level before surgery, the severity of obstructive jaundice, the age and gender of the patient, as well as the duration of jaundice and the nature of the inflammatory process ($p < 0.0001$). The effect of surgery depended on the severity of OJ ($p < 0.0001$): the greatest differences between the groups were observed in severe obstructive jaundice already in the first 5 days after surgery.

The decrease in the level of total bilirubin in dynamics is statistically significant in the comparison groups of the corresponding subgroups. Thus, in a linear regression model with mixed effects, the

level of total bilirubin is 1.4 times lower in the study group compared to the control group in patients with mild OJ severity on day 5 (0.74 [95% CI: 0.70; 0.79]; $p < 0.0001$), and in the subgroup with an average degree - on day 7 (0.74 [95% CI: 0.70; 0.78]; $p < 0.0001$). By the 14th day after surgery, in the subgroup with severe severity of the OJ bilirubin level is 1.9 times lower in the main group than in the control group (0.52 [95% CI: 0.42; 0.64]; $p < 0.0001$). A similar picture was found for the average concentration of direct bilirubin. Thus, a clear positive dynamics of the level of bilirubinemia in the main group of patients was revealed. A significant decrease in the bilirubin index, mainly due to the direct fraction, indicates an adequate restoration of the liver pigment function.

Upon admission to the hospital in patients of both groups, an increase in enzymes was recorded: AST, ALT - markers of cytolysis, GGT, ALP - markers of cholestasis.

In a linear regression model with mixed effects, statistically significant differences between groups were revealed in relation to the mean serum ALT level, regardless of its level before surgery, the severity of obstructive jaundice, as well as correcting covariates ($p < 0.0001$). The effect of surgery depended on the severity ($p < 0.02$): the greatest differences between the groups were observed in severe obstructive jaundice. A similar picture was observed for the mean serum AST level. Thus, in the postoperative period, the level of ALT and AST indices in the main group compared to the control group was, on average, 1.2 times lower ($p < 0.0001$) in the subgroup with mild OJ severity, 1.1 times ($p < 0.0007$, $p < 0.0002$, respectively) in the subgroup with moderate severity of OJ 1.3 times ($p = 0.0013$) and 1.5 times ($p = 0.0267$) in the subgroup with severe severity OJ, respectively.

Statistically significant, but less pronounced differences between the groups were found in relation to the mean level of serum GGT, regardless of its level before surgery and the value of other covariates. ($p < 0, 0001$).

The effect of surgery was weakly dependent on the severity of OJ ($p = 0.04$). Thus, the level of GGT in patients in the main group in dynamics at all periods of observation was significantly lower, for example, in the subgroup with mild severity of OJ on average, 1.5 times (0.66 [95% CI: 0.62; 0.71] $p < 0.0001$), with an average severity of OJ by 1.4 times (0.73 [95% CI: 0.70; 0.77] $p < 0.0001$) and with a severe severity of OJ by 1.3 times (0.77 [95% CI: 0.62; 0.96] $p = 0.0193$) compared with the control.

The severity of OJ reflects the severity of violations of the protein-synthetic function of the liver. Functional disorders of the liver in patients were characterized by the presence of hypoproteinemia on admission and a decrease in the albumin-globulin coefficient in subgroups with moderate and severe degrees of OJ severity in both groups. In the main group, the level of total protein in A2 was 58.89 ± 2.05 g / l, in A3 - $52,13 \pm 2,31$, the albumin-globulin coefficient in A2 was 1.01 ± 0.11 , in A3 - 0.78 ± 0.07 . In the control group, the level of total protein in B2 was $59,01 \pm 2,43$ g / l, in B3 - $51,0 \pm 2,27$ g / l, the albumin-globulin coefficient in B2 was 1.04 ± 0.15 , in B3 - 0.81 ± 0.03 .

There were no pronounced changes in the protein-synthetic function of the liver with mild OJ. In a linear regression model with mixed effects, differences were found between groups in relation to the average concentration of total protein, regardless of its level before surgery, the severity of obstructive jaundice, as well as correcting covariates ($p < 0.0001$). The effect of surgery did not significantly depend on the severity of obstructive jaundice ($p < 0.8193$). According to the obtained marginal estimates of the average level of total protein in the postoperative period, there is a positive dynamics of the increase in the indicator, while statistically significant differences are noted in subgroups with mild ($p = 0.0089$) and moderate ($p = 0.0001$) degrees of OJ severity, where the rate of increase in the main group it is higher than in the control group, which in turn shortens the recovery time of total protein in the main group.

A similar dynamics was observed in relation to the albumin-globulin coefficient, however, a statistically significant association of the intervention effect on the severity was found ($p < 0.0001$): the most pronounced differences between the groups were observed in the subgroup with moderate and severe severity of OJ starting from 7 days.

The analysis of indicators of the hemostasis system in patients with cholelithiasis complicated by mammary gland was carried out. In a linear regression model with mixed effects, differences between groups were revealed in relation to PI, regardless of its level before surgery, the severity of

obstructive jaundice, as well as correcting covariates ($p < 0.0001$). The effect of surgery was associated with the severity of jaundice ($p < 0.0001$): the greatest differences between the groups were observed in the groups with severe and moderate severity of OJ throughout the observation period. The level of PI before the operation remained within the reference values and in the postoperative period the dynamics of the indicator had a positive tendency to increase, which is due to the absence of pronounced disorders of the functional state of the liver against the background of mild jaundice. However, there were no statistically significant differences between the comparison groups for mild OJ ($p = 0.0640$).

In patients with moderate and severe obstructive jaundice, along with changes in the functional activity of the liver, pronounced disorders of the hemostasis system are observed, which is confirmed by our observations. Upon admission to the subgroup with an average degree of OJ in the main group, the level of PI was $71.93 \pm 3.33\%$, and in the control group - $70.97 \pm 3.48\%$. A decrease in the indicator was also observed in the subgroup with severe severity of the OJ where the average PI indicator was $68.53 \pm 1.4\%$ and $67.44 \pm 4.25\%$, respectively, in the main and control groups. Based on the marginal estimates of the average level of PI after surgery and the results of assessing the size of effects (FC), one can judge an increase in the indicator, while in the main group the rate of increase is higher, which is confirmed by the presence of statistically significant differences starting from 3 days after surgery in subgroups with an average degree (PI in A2 is 1.03 times higher compared to B2, $p < 0.0001$) and severe (PI in A3 is 1.04 times higher than in B3, $p = 0.0083$) of severity of OJ.

A statistically significant effect was found with respect to the average concentration of fibrinogen. Regardless of its preoperative level and the values of other covariates, differences were observed between groups ($p < 0.0001$), and there was also an association between the size of the effect of surgery and the severity of OJ.

The marginal estimates of the mean level of fibrinogen after surgery and the results of assessing the size of effects (FC), obtained by us, indicate the presence of statistically significant changes throughout the observation period in patients with mild severity of OJ so the level of fibrinogen in the main group was 1.04 times (1.04 [95% CI: 1.02; 1.05] $p < 0.0001$) higher compared to the control group. In subgroups with moderate and severe severity of the OJ an increase in the average level of fibrinogen is predicted in dynamics, however, significant differences between the groups are noted on the 5th day after surgery: in subgroup A2 it is 1.02 times higher than in B2 ($p = 0.0002$), and in subgroup A3 - by 1.05 times ($p = 0.0346$).

Taking into account the causal relationship between cholelithiasis (GD) and pancreatitis, we assessed the functional state of the pancreas. The level of blood amylase and urine amylase in the comparison groups at admission remained within the reference values, and statistical analysis in a linear regression model with mixed effects did not reveal statistically significant differences between the groups in relation to the level of blood and urine amylase.

Hyperbilirubinemia, as well as operations on the biliary tract in connection with obstructive jaundice, have long been considered one of the main causes of the development of hepatorenal syndrome. In this connection, in patients in the compared groups, we determined the level of creatinine and urea. In subgroups with mild and moderate severity of OJ in both groups, the indicators remained within the normal range, in the subgroup with severe OJ, an increase in the level of nitrogenous wastes was recorded: creatinine was $208,09 \pm 25,06 \mu\text{mol} / \text{L}$, urea - $23,15 \pm 3,92 \text{ mmol} / \text{L}$ in the main group and in the control group, respectively $197,46 \pm 16,39 \text{ mmol} / \text{L}$, $25,96 \pm 4,01 \text{ mmol} / \text{L}$.

On the part of the average concentration of urea, regardless of its level before surgery, the severity of obstructive jaundice, as well as correcting covariates, there were no statistically significant differences between the groups ($p < 0.1564$), however, the effect of surgery significantly depended on the severity ($p < 0.0001$). The obtained data predict a decrease in the average level of urea after surgery in the observation groups, however, significant differences in the subgroup with an average severity of OJ were recorded up to 5 days ($p = 0.0003$), and in the subgroup with severe up to 7 days ($p = 0.0053$).

In relation to the mean level of creatinine, statistically significant differences were found between the groups ($p = 0.0001$). The effect of surgery depended on the severity of OJ. Statistically significant

differences between the compared groups were revealed throughout the observation period in patients with mild OJ severity ($p = 0.0063$), while in patients with moderate ($p < 0.0001$) and severe ($p = 0.0172$) severity OJ on the 10th day after surgery.

Thus, in the postoperative period, the highest rates of resolution of enzyme and cholestasis, restoration of pigment, protein-synthetic function, disorders in the system of coagulation hemostasis, relief of hepatorenal syndrome were found in the postoperative period in patients of the main group, which confirms the low trauma of minimally invasive methods of decompression of the biliary tract unlike traditional open surgery.

Obstructive jaundice is accompanied by a significant increase in the concentration of primary and secondary products of lipid peroxidation in the blood, which is one of the objective criteria for the impaired functional state of the liver. Therefore, we conducted a study of the indicators of LPO-AOD systems in the main and control groups.

Upon admission, there is a significant deviation in the blood plasma of LPO products: MDA in mild, moderate and severe subgroups of the main group was 4.23 ± 0.29 nmol / ml, 6.72 ± 0.21 nmol / ml and 8.91 ± 0.85 nmol / ml, respectively, at the same time in the control group - 4.41 ± 0.38 nmol / ml, 7.06 ± 0.47 nmol / ml and 9.14 ± 0.76 nmol / ml, which have toxic properties, which contributes to the aggravation of the pathological process.

On the part of the indicators of the antioxidant defense system, a decrease in activity was noted in all groups upon admission. Catalase activity in the main group was 1.78 ± 0.15 McCat / L, 1.21 ± 0.11 McCat / L, 0.76 ± 0.19 McCat / L, and in the control group - 1.83 ± 0.11 McCat / L, 1.18 ± 0.02 McCat / L, 0.87 ± 0.10 McCat / L, respectively, of mild, moderate and severe severity of OJ.

In a linear regression model with mixed effects, differences between groups were revealed in relation to the MDA level, regardless of its level before surgery, the severity of obstructive jaundice, as well as other covariates ($p < 0.0001$). The most pronounced differences between the groups were observed in severe obstructive jaundice already on the first day after surgery.

The obtained marginal estimates of the average MDA level reflect a tendency towards a decrease in the level of this indicator in the postoperative period in both groups, however, the average MDA level in patients of the main group is, on average, 1.2 times lower in subgroups with mild (0.85 [0.80 ; 0 , 0.90]; $p \leq 0.0001$) and medium (0.86 [0.81 ; 0.91]; $p \leq 0.0001$) degrees of OJ severity, and with severe - 1.4 times (0.74 [0.60 ; 0.91]; $p = 0.0051$) compared with the control, which indicates a reduction in the time of normalization of indicators in the corresponding group.

We also found differences between the groups in relation to the level of catalase, regardless of its level before surgery, the severity of obstructive jaundice, as well as correcting covariates ($p < 0.0001$). The effect of surgery depended on the severity of OJ ($p < 0.0001$), the most pronounced differences between the groups were observed in severe obstructive jaundice already on the first day after surgery, the least pronounced differences were recorded in obstructive jaundice of moderate severity.

The increase in catalase activity after surgery in the comparison groups reflects the marginal estimates of the average level of this indicator, but the rate of increase in the main group is higher, which is confirmed by significant differences between the groups in the subgroups with mild ($p = 0.0003$) and severe ($p \leq 0, 0001$) by the severity of OJ throughout the observation period. In patients with severe OJ the difference is more pronounced, so in the main group, catalase is on average 1.3 times (1.27 [95% CI: 1.15 ; 1.41]; $p \leq 0.0001$) higher than in the control group.

Thus, minimally invasive interventions in the surgical treatment of cholelithiasis complicated by obstructive jaundice have a more pronounced corrective effect on the parameters of the LPO-AOD system, which was expressed in a higher rate of LPO inhibition and an increase in the activity of AOD enzymes, compared with traditional (open) surgical interventions.

Using the method of cardiointervalography, we studied the effect of minimally invasive and traditional surgical interventions on the indices of reserve-compensatory capacities of the body (RCCB) in patients with cholelithiasis complicated by OJ. One of the highly sensitive tests indicating the activation of vegetative homeostasis and allowing judging the state of the RCCB is the stress index (SI, normally from 80 to 150 conventional units). In a linear regression model with mixed effects,

differences were found between groups in terms of stress index regardless of its level before surgery, the severity of obstructive jaundice, and other covariates ($p < 0.0001$).

The dynamics of the stress index after surgery in the observation groups reflects a decrease in the indicator in the main group and its increase in the control group.

Pairwise comparisons of mean stress index values between groups depending on the severity showed a statistically significant difference in the subgroups after surgery.

Thus, in the subgroup with a mild severity of OJ the stress index is 1.9 times (0.52 [95% CI: 0.43; 0.62]; $p \leq 0.0001$) lower in the main group, in the subgroup with an average degree - 2, 1 time (0.46 [95% CI: 0.38; 0.55]; $p \leq 0.0001$) and in the subgroup with severe - 3.4 times (0.29 [95% CI: 0.14; 0.57]; $p = 0, 0005$) compared to the control. We associate this fact with the significant surgical aggression of traditional surgical interventions.

Also, in order to determine the body's response to surgical trauma, we conducted studies of glucose and cortisol in the blood of operated patients before the operation and for the first time 5 days after the operation. Thus, before surgery, the levels of glucose and cortisol in patients in the compared groups were within the reference values. We found differences between groups in relation to serum glucose levels, regardless of their level before surgery, the severity of obstructive jaundice and other covariates ($p < 0.0001$). At the same time, the effect of surgical intervention statistically significantly depended on the severity of jaundice ($p = 0.0093$), so the most significant differences between the groups were observed with mild OJ severity in the first 4 days after surgery.

Differences were found between groups in terms of serum cortisol levels, regardless of its level before surgery, the severity of obstructive jaundice, and corrective covariates ($p < 0.0001$). The greatest differences between the groups were observed in mild and moderate obstructive jaundice, the least pronounced differences were recorded in severe obstructive jaundice.

The obtained marginal estimates of the average level of cortisol reflect a downward trend in this indicator. At the same time, in the main group, the indicator is significantly lower by 1.3 times (0.77 [95% CI: 0.69; 0.85] $p \leq 0.0001$) and 1.4 times (0.70 [95% CI: 0.64; 0.78] $p \leq 0.0001$) compared with the control in subgroups with mild and moderate severity of the OJ respectively ($p \leq 0.0001$). There were no statistically significant differences in the subgroup with severe OJ severity ($p = 0.4485$).

The study of RCCB in patients with gallstone disease complicated by OJ showed that the use of a staged approach using endovideoscopic surgical interventions reduces the overstrain of the adaptation mechanisms of RCCB in patients, thereby producing a lower degree of surgical aggression.

For a comparative assessment of the course of the postoperative period, we studied the following clinical indicators: the period of disappearance of pain syndrome, the use of narcotic analgesics, restoration of motor activity and motor function of the intestines in the postoperative period. The duration of surgery and the duration of hospital stay were also determined.

The duration of the operation in both groups of patients was assessed based on the study of the protocols of operations. A comparative assessment of the obtained data in the regression model revealed differences between groups in the duration of surgery, regardless of the severity of OJ, as well as correction covariates ($p < 0.0001$), the severity was also a significant predictor of the duration of surgery ($p < 0,0001$).

Significant differences in the effect of surgical intervention from the severity of jaundice were revealed ($p = 0.004$): the greatest decrease in the duration of surgery was observed in patients with moderate severity of jaundice.

Marginal estimates of the average duration of surgery in the main group with mild OJ were 75.58 [95% CI: 70.53; 80.99] min, with the average - 61.94 [95% CI: 58.64; 65.42] min and with severe - 76.36 [95% CI: 56.30; 103.56] min, while in the control group 100.65 [95% CI: 93.13; 108.78] min, 99.35 [95% CI: 93.54; 105.52] min and 108.12 [95% CI: 99.17; 117.87] min, respectively.

In a pairwise comparison, significant differences were obtained in the compared groups. The average duration of surgery in the main group with a mild degree of OJ is 1.3 times less (0.75 [95% CI: 0.69; 0.82], $p \leq 0.0001$), with an average - 1.6 times (0.62 [95% CI: 0.58; 0.67], $p \leq 0.0001$) and in severe - 1.4 times (0.71 [95% CI: 0.51; 0.98], $p = 0.0377$) compared with the control.

Thus, the use of minimally invasive surgical interventions in the treatment of cholelithiasis complicated by mammary gland significantly reduces the duration of surgical intervention in comparison with traditional (open) operations.

As you know, in the postoperative period, pain can largely neutralize the success of surgery and worsen the results of treatment.

In this regard, we carried out a comparative analysis of the duration of pain syndrome. So, in the Poisson regression model, differences were revealed in relation to the average duration of pain syndrome and the average duration of use of narcotic analgesics between the study groups, regardless of the severity of obstructive jaundice, as well as correcting covariates ($p < 0.0001$). Severity was a statistically significant predictor of pain duration ($p < 0.004$). The effect of surgery depended on the severity ($p = 0.0072$): the greatest differences between the groups were observed in moderate obstructive jaundice. However, in relation to the duration of the use of narcotic analgesics, the severity was not associated with this outcome and the effect of surgery did not depend on the severity ($p = 0.9701$). The obtained marginal estimates indicate the duration of the pain syndrome on average in the main group up to 2 days, while in the control group up to 4 days, which was reflected in the duration of the use of narcotic analgesics: in the main group during the first day, in the control group - 2 days. Pairwise comparison showed a significant decrease in the duration of pain in the main group with a mild severity of OJ in the main group by 2.1 times (0.46 [95% CI: 0.37; 0.57], $p \leq 0.0001$) and with an average degree in 3.4 times (0.29 [95% CI: 0.23; 0.36], $p \leq 0.0001$) compared with the control. In the subgroup with severe severity of the OJ there is an insignificant decrease in the duration of pain in the main group by 1.9 times (0.52 [95% CI: 0.18; 1.46], $p = 0.2122$) compared with the control.

An important indicator of hospital activity continues to be the average length of stay of patients in the hospital. This indicator, on the one hand, determines the economic aspects of the hospital's work, and on the other hand, it clearly indicates the results of the treatment of the disease. In this connection, we have analyzed the duration of hospital stay in the compared groups. According to the results obtained in the gamma regression model, differences were revealed in the average length of hospital stay between the study groups, regardless of the severity of obstructive jaundice, the age and sex of the patient, as well as the duration of jaundice and the nature of the inflammatory process ($p < 0.0001$), with severity also being a statistically significant predictor ($p < 0.0001$). The effect of surgical intervention depended on the severity ($p < 0.0001$): the greatest differences between the groups were observed with severe OJ severity.

The average length of hospital stay in the study group with mild OJ was 7.23 [95% CI: 7.50; 6.98] bed-days, with an average of 13.17 [95% CI: 13.63; 12.74] bed-days and with severe - 8.75 [95% CI: 10.21; 7.65] bed-days, in the control - 11.82 [95% CI: 12.40; 11.29], 16.56 [95% CI: 17.24; 15.93] and 17.15 [95% CI: 18.10; 16.29] bed-days, respectively. There is a decrease in the length of hospital stay in patients in the study group compared to the control group, so with a mild severity of OJ by 1.6 times, with an average - by 1.3 times and in severe cases - 1.9 times. According to the data presented, there are significant differences in the compared groups.

Thus, the use of minimally invasive interventions in patients significantly reduces the length of hospital stay in comparison with patients who underwent traditional operations.

Evaluation of the effectiveness of treatment of cholelithiasis complicated by OJ was also carried out according to the presence and severity of postoperative complications and deaths.

The binary logistic model revealed differences in the risk of postoperative complications between the study groups, regardless of the severity of obstructive jaundice, as well as correcting covariates ($p = 0.0115$), while the severity of OJ was also a statistically significant predictor of this outcome. ($p = 0.0005$).

The marginal assessment of the likelihood of postoperative complications in the study group with mild OJ severity was 0.07 [95% CI: 0.17; 0.03], with an average - 0.15 [95% CI: 0.25; 0.09] and in severe cases - 0.14 [95% CI: 0.80; 0.01], in the control - 0.15 [95% CI: 0.31; 0.07], 0.27 [95% CI: 0.41; 0.17] and 0.56 [95% CI: 0.74; 0.37], respectively.

The analysis shows that the use of endovideoscopic surgical interventions in the main group reduces the risk of postoperative complications in subgroups with mild, moderate and severe OJ compared to the control group.

To determine the clinical efficacy and prognostic significance of the proposed surgical tactics, the NNT index was calculated (NNT - number needed to treat). In our case, the NNT index = 7.6 ($NNT = 1 / (FCG - FMG)$; FMG (frequency of events in the main group) = $29/220 = 0.1318$; FCG (frequency of events in the control group) = $43/164 = 0.2621$; $NNT = 1 / (0.2621 - 0.1318) = 7.6$). Taking into account the NNT index (NNT) = 7.6 obtained in our case, it is possible to predict a more significant benefit of using the proposed surgical tactics to improve the results of treatment.

A decrease in postoperative complications affected mortality in patients in the compared groups. The causes of deaths in the groups: acute pancreatitis, pulmonary embolism, myocardial infarction, rear wall damage of duodenum and progressive hepatic renal failure.

In patients with gallstone disease with mild OJ severity, in the main group, the mortality rate was 1.2%, and in the control group - 1.8%, in patients with moderate OJ severity - 2.8% and 5.2%, respectively. In patients with severe severity of OJ in the main group - 5.4%, and in the control group - 9.3%. Comparative study of the results of surgical treatment of patients with cholelithiasis complicated by OJ reflects the advantage of using minimally invasive technologies, which reduces the risk of postoperative complications and reduces mortality by almost 2 times.

Thus, in patients with cholelithiasis complicated by OJ as a result of the development of jaundice and the threat of progression of liver failure, traditional operations are too traumatic; therefore, it is considered necessary to use low-traumatic interventions, dividing their use in time. The tactics of using minimally invasive interventions and their sequence depends on the severity of OJ.

In patients with cholelithiasis complicated by the mild severity of obstructive jaundice, a radical treatment tactic should be used: one-stage laparoscopic cholecystectomy with ductocholedocholithotomy and external drainage of the common bile duct, except for patients in whom the development of jaundice was caused by stenosis or entrapment of the concrement in the large duodenal concrement. In this case, LCE and endoscopic papillosphincterotomy with choledocholitholite extraction were performed simultaneously. However, simultaneous interventions (laparoscopic cholecystectomy and ductocholedocholithotomy) used in this group of patients are feasible only in the uncomplicated stage of the disease. The duration of laparoscopic ductocholedocholithotomy makes it unacceptable for the treatment of patients with high operational risk. Therefore, in patients with cholelithiasis with moderate and severe obstructive jaundice, a different tactic was followed. In these patients, as a result of severe hepatic failure, the implementation of radical one-stage operations is considered dangerous. In this regard, the main task of treating such patients is to perform a drainage operation, which makes it possible to prepare them for subsequent radical interventions, i.e. use of two-step tactics. At the first stage, endoscopic, endobiliary interventions (EPST, choledocholitholite extraction) are used, after 5-7 days, the second stage is laparoscopic cholecystectomy.

In case of severe OJ, drainage operations are preferably performed using minimally invasive interventions (percutaneous transhepatic drainage of the biliary tract, stenting or nasobiliary drainage of the biliary tract, cholecystostomy). Drainage operations reduce the level of serum bilirubin and level the degree of liver failure. After the resolution of fermentemia and cholestasis, restoration of the pigment, protein-synthetic function of the liver, relief of hepatorenal syndrome, the extrahepatic bile ducts are simultaneously sanitized using endobiliary interventions and laparoscopic cholecystectomy 21-28 days after decompression of the bile ducts.

The use of this treatment tactics in patients with cholelithiasis complicated by obstructive jaundice can significantly expand the possibilities of surgical intervention.

CONCLUSION

Based on the results obtained, the following conclusions were drawn:

1. The developed differentiated treatment tactics in the surgical treatment of cholelithiasis complicated by obstructive jaundice using minimally invasive technologies, depending on the severity of jaundice, makes it possible to choose the optimal surgical intervention in patients with this pathology.
- 2A. Differentiated treatment tactics in the surgical treatment of cholelithiasis complicated by obstructive jaundice using minimally invasive technologies, depending on the severity of jaundice, can reduce the level of bilirubin with mild OJ severity by 1.7 times ($p \leq 0.0001$), with an average - by 1, 4 times ($p \leq 0.0001$) and in severe - 1.9 times ($p = 0.0017$), the level of enzymes - markers of cytolysis (transaminase) 1.2 times ($p < 0.0001$), 1, 1 time ($p < 0.0007$, $p < 0.0002$) and 1.3 times ($p = 0.0013$, $p = 0.0267$) and cholestasis marker enzymes (GGT) 1.5 times ($p < 0.0001$), 1.4 times ($p < 0.0001$) and 1.3 times ($p = 0.0193$), respectively, compared with traditional surgical interventions, thereby contributing to the accelerated resolution of intoxication, cholestasis and cytolytic process in liver.
- 2B. The use of minimally invasive technologies in the surgical treatment of patients with cholelithiasis complicated by OJ can reduce the duration of pain with a mild severity of OJ by 2.1 times (0.46 [95% CI: 0.37; 0.57], $p \leq 0.0001$), with an average degree - 3.4 times (0.29 [95% CI: 0.23; 0.36], $p \leq 0.0001$), with a severe degree - 1.9 times (0.52 [95% CI: 0.18; 1, 46], $p = 0.2122$), also reduce the length of stay of patients in hospital with mild OJ severity by 1.6 times, with moderate severity - 1.3 times and with severe - 1.9 times ($p \leq 0.0001$) and reduce the number of postoperative complications in all subgroups depending on the severity of OJ ($p = 0.0005$), with a mild severity of OJ from 14.3% to 7.5%, with an average severity from 26.3 % to 14.4% and in severe cases - from 46.5% to 21.6%, i.e. almost 2 times, as well as mortality - from 1.8% to 1.2%, from 5.2% to 2.8% and from 9.3% to 5.4%, respectively, compared with traditional surgical interventions.
3. The tactics of a staged approach of surgical correction using minimally invasive technologies in patients with cholelithiasis complicated by obstructive jaundice due to less trauma makes it possible to reliably reduce the stress index in the subgroup with mild OJ severity by 1.9 times ($p \leq 0.0001$) after surgery. in the subgroup with the average - 2.1 times ($p \leq 0.0001$) and in the subgroup with severe - 3.4 times ($p = 0.0005$), as well as the level of cortisol in 1.3 and 1.4 times with mild and moderate severity of OJ ($p \leq 0.0001$) in comparison with open surgical interventions, thereby reducing the overstrain of adaptation mechanisms and prevents the suppression of the reserve-compensatory capabilities of the body.
4. Minimally invasive surgical interventions in the complex treatment of cholelithiasis complicated by mammary glands have a positive effect on the LPO-AOD parameters in the blood of patients, which was expressed in a significant acceleration of the inhibition of MDA formation (in subgroups with mild and moderate severity of the mammary gland, 1.2 times ($p < 0, 0001$), with severe - by 1.4 times ($p < 0.0001$)) and increased catalase activity (in subgroups with mild and moderate severity of OJ by 1.1 times ($p < 0.0001$), with severe - 1.3 times ($p < 0.0001$) compared with traditional methods of surgical treatment.

PRACTICAL RECOMMENDATIONS

1. To select the optimal surgical tactics in patients with cholelithiasis complicated by obstructive jaundice, a differentiated approach should be used with the use of minimally invasive surgical technologies, depending on the severity of jaundice.
2. Patients with cholecystectomy complicated by the mild severity of obstructive jaundice, minimal changes in the LPO-AOD system and reserve-compensatory capacities of the body, it is necessary to apply simultaneous laparoscopic cholecystectomy with ductocholedocholithotomy in the absence of concomitant cardiopulmonary pathologies. In the presence of cicatricial-sclerotic changes and an embedded OBD stone, simultaneous laparoscopic cholecystectomy with ductocholedocholithotomy with intraductal manipulations should be performed.
3. Patients with gallstone disease complicated by the moderate severity of obstructive jaundice, need to use a two-stage treatment strategy: stage 1 - EPST with intraductal manipulations from the transpapillary approach, stage 2 in 5-7 days - laparoscopic cholecystectomy.

4. Patients with cholelithiasis complicated by the severe severity of OJ with pronounced changes in the LPO-AOD system and a decrease in the reserve-compensatory capabilities of the body should be performed drainage operations on the biliary tract (percutaneous transhepatic drainage of the biliary tract, stenting or nasobiliary drainage of the biliary tract) at the first stage, then after 21-28 days (second stage) - simultaneous sanitation of the extrahepatic bile ducts using endobiliary interventions and laparoscopic cholecystectomy.