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COMPREHENSIVE MANAGEMENT STRATEGY FOR PATIENTS WITH CHOLEDOCHOLITHIASIS: DIAGNOSTICS, MINIMALLY INVASIVE TREATMENT, AND SURGICAL RISK PREDICTION



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The monograph presents current data on the technical aspects of performing minimally invasive and open (laparotomic) interventions for chronic benign biliary obstruction (CBBO), as well as developed strategic approaches to the selection of treatment methods.

Based on the analysis of the diagnostic performance of various imaging modalities (ultrasound, multislice computed tomography (MSCT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP),

endoscopic ultrasound (EUS), etc.), the diagnostic value of each modality has been уточнено and a rational sequence for their use in clinical practice has been established.

The importance of the integrated use of preoperative and intraoperative diagnostic methods is demonstrated, including the application of the authors' method entitled "A method for determining the localization and extent of biliary outflow obstruction in the common hepatic or common bile duct," which improves diagnostic accuracy and enables a well-founded choice of surgical strategy.

The high diagnostic value of MRCP and EUS as alternatives to invasive techniques (endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTC)) is substantiated.

Diagnostic algorithms for CBBO and schemes for the differential diagnosis of obstructive jaundice have been developed.

CONTENTS

PREFACE

INTRODUCTION

CHAPTER I. CURRENT CONCEPTS IN THE DIAGNOSIS AND TREATMENT OF CHOLEDOCHOLITHIASIS AND PREDICTION OF POSTOPERATIVE COMPLICATIONS (LITERATURE REVIEW)

- 1.1. Epidemiology, etiology, and main clinical manifestations of chronic benign biliary obstruction (CBBO)
- 1.2. Diagnosis of choledocholithiasis
- 1.3. Treatment modalities for CBBO
- 1.4. Prediction of operative risk and postoperative complications in abdominal surgery

CHAPTER II. CLINICAL FEATURES AND COMPREHENSIVE DIAGNOSIS OF CHOLEDOCHOLITHIASIS

- 2.1. Clinical manifestations of choledocholithiasis
- 2.2. Characteristics of obstructive jaundice syndrome
- 2.3. Laboratory diagnosis of CBBO and its complications
- 2.4. General and biochemical blood tests
- 2.5. Instrumental (imaging) diagnostic methods

CHAPTER III. MANAGEMENT OF PATIENTS WITH CHOLECYSTOCHOLEDOCHOLITHIASIS: MINIMALLY INVASIVE, NOVEL, AND CONVENTIONAL TREATMENT METHODS

- 3.1. Preoperative preparation
- 3.2. Endoscopic transpapillary interventions
- 3.3. Laparoscopic laser choledocholithotripsy

3.4. Combined (antegrade + retrograde) treatment approaches

3.5. Postoperative patient management

Chapter IV. Treatment of Patients with Cholecystochledocholithiasis. Minimally Invasive, Novel and Traditional Treatment Methods

4.1. Preoperative Preparation

4.2. Endoscopic Transpapillary Surgical Interventions

4.3 Laparoscopic laser choledocholithotripsy

4.4 Combined (antegrade + retrograde) treatment methods

4.5. Postoperative management of patients

CONCLUSION

APPENDICES

REFERENCES

LIST OF ABBREVIATIONS

1. **ALT** — Alanine aminotransferase
2. **AOS** — Antioxidant system
3. **BDA** — Biliodigestive anastomosis
4. **MDP** — Major duodenal papilla
5. **BS** — Biliary sepsis
6. **HDS** — Hepaticoduodenostomy
7. **HJS** — Hepaticojejunostomy
8. **DC** — Diene conjugates
9. **DU** — Duodenum
10. **BDT** — Biliary tract
11. **GSD** — Gallstone disease
12. **ANN** — Artificial neural networks
13. **IOC** — Intraoperative cholangiography
14. **CT** — Computed tomography
15. **LT** — Lithotripsy
16. **LTSP** — Laparoscopic transduodenal sphincteroplasty
17. **LC** — Laparoscopic cholecystectomy
18. **LE** — Lithoextraction
19. **MDA** — Malondialdehyde

- 20.**MRI** — Magnetic resonance imaging
- 21.**MRCP** — Magnetic resonance cholangiopancreatography
- 22.**NBD** — Nasobiliary drainage
- 23.**ECD** — External common bile duct drainage
- 24.**OJ** — Obstructive jaundice
- 25.**CBD** — Common bile duct
- 26.**ACC** — Acute calculous cholangitis
- 27.**Pancreas (P)** — Pancreas (*обычно не сокращают, но оставлено по структуре*)
- 28.**ST** — Surface tension
- 29.**EGD** — Esophagogastroduodenoscopy
- 30.**CE** — Cholecystectomy
- 31.**EPD** — Endoscopic papillary dilation
- 32.**EUS** — Endoscopic ultrasonography

PREFACE

Gallstone disease is широко распространена in both developed and developing countries in Europe, as well as in Russia and North America, particularly among elderly and senile patients. The prevalence of gallstone disease in Europe ranges from 10% to 40%, while in Russia it is approximately 15–25% (Balagurov B.A. et al., 2012; Merzlikin N.V. et al., 2015; Pavelets K.V. et al., 2018; Wandling M.W. et al., 2016). The number of surgical procedures involving the gallbladder and bile ducts has nearly doubled every 10 years and has reached approximately 1.5 million operations in recent years, ranking first among abdominal surgical interventions.

The number of patients with choledocholithiasis (CBBO) has also increased; it is detected in 20–30% of patients with calculous cholecystitis. The rate of postoperative infectious complications ranges from 4% to 36.5% (Aslanova K.D. et al., 2017; Korolkov A.Yu. et al., 2019; Okhotnikov O.I. et al., 2020; Parikh M.P. et al., 2018).

Comprehensive evaluation is required for the diagnosis of CBBO and its complications, including ultrasound (US), multislice computed tomography (MSCT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS), endoscopic retrograde cholangiopancreatography (ERCP), percutaneous transhepatic cholangiography (PTC), fiberoptic cholangioscopy, and others (Zagidullina G.T. et al., 2015; Abramova A.G. et al., 2017; Antonyuk O.S. et al., 2019; Khatsko V.V. et al., 2019; Gupta N., 2016).

In recent years, there has been a growing trend toward the widespread use of minimally invasive procedures, mini-access surgery, endoscopic transpapillary interventions, percutaneous transhepatic drainage, balloon dilation, combined antegrade and retrograde interventions, lithotripsy, and stenting (Vozlyublennyy E.I. et al., 2016; Shatalov A.D. et al., 2018; Bykov M.I. et al., 2019; Rinchinov V.B. et al., 2020; Hazey J.W., 2016). The combination of ERCP, PTC, and laparoscopic cholangiography with various methods of biliary decompression (including nasobiliary drainage, among others) has opened new possibilities for the treatment of CBBO and its complications, particularly in patients at high operative risk (Dynko V.Yu., 2017; Kulezneva Yu.V. et al., 2018; Bykov M.I. et al., 2019; Prazdnikov E.N. et al., 2020; Costi R. et al., 2014).

At present, there is no single universally accepted method for the diagnosis of CBBO. Comparative analyses of the diagnostic performance of ultrasound and other imaging modalities remain insufficiently studied. The effectiveness of these methods largely depends on the availability of diagnostic equipment, necessary materials, the severity of the patient's condition, and local anatomical and inflammatory changes. Therefore, further improvement of diagnostic techniques remains an important and practically significant task.

Standardized diagnostic algorithms and practical guidelines for the evaluation and treatment of CBBO—taking into account individual disease course, severity of the patient's condition, and comorbidities—have not yet been fully developed (Kazakov N.M. et al., 2018; Podoluzhny V.I. et al., 2018; Mamoshin A.V. et al., 2019; Monreal-Robles R. et al., 2016).

Several issues related to diagnosis, treatment strategy, and the nature and extent of surgical interventions in obstructive jaundice and purulent cholangitis, especially in elderly patients, remain controversial. In clinical practice, there is no consensus regarding the duration of conservative therapy for obstructive jaundice and cholangitis, the timing of endoscopic and open surgical interventions, as well as their extent and sequence (Tarasenko S.V. et al., 2017; Zubritsky V.F. et al., 2019; Kotovsky A.E. et al., 2019; Ersoz G. et al., 2016).

The relationship between morphological changes in liver tissue and disease duration, alterations in biochemical blood parameters, and lipid peroxidation has not been sufficiently studied. In addition, the potential of modern comprehensive predictive methods in patients with CBBO—allowing objective preoperative assessment of operative risk and postoperative complications, as well as the avoidance of interventions associated with unfavorable outcomes—remains poorly addressed in the literature.

The development of an expert system for predicting operative risk and the postoperative course, enabling individualized treatment strategies, appears to be both relevant and necessary.

Many aspects of diagnosis, surgical treatment, prediction of operative risk, and postoperative complications in patients with CBBO remain insufficiently studied. These considerations formed the basis for the present study.

INTRODUCTION

Choledocholithiasis (CL) is one of the most common forms of complicated gallstone disease, characterized by the presence of calculi in the common hepatic duct and/or the common bile duct. According to various authors, CL is detected in 10–18% of patients with symptomatic gallstone disease and in up to 30% of cases in the presence of concomitant biliary pathology. This condition is associated with a high risk of complications, including obstructive jaundice, acute cholangitis, biliary pancreatitis, and sepsis, which determines its clinical and social significance.

Despite advances in diagnostic and therapeutic technologies, issues related to timely verification of the diagnosis, selection of optimal treatment strategies, and stratification of patients according to surgical risk remain relevant. The key objective

of modern surgery is to minimize the invasiveness of interventions while maintaining their radicality and safety.

In this context, a comprehensive approach to the management of patients with CL is of particular importance, incorporating modern imaging modalities (magnetic resonance cholangiopancreatography [MRCP], endoscopic ultrasound [EUS]), minimally invasive techniques (endoscopic retrograde cholangiopancreatography [ERCP], laparoscopic choledochotomy), as well as objective scoring systems for patient assessment (ASA, APACHE II, POSSUM).

Clinical practice demonstrates that the timely application of stratified treatment algorithms reduces the incidence of complications, shortens hospital stay, and improves treatment outcomes, particularly in elderly patients and those with comorbidities. However, questions regarding the extent and sequence of diagnostic procedures, the timing and methods of biliary drainage, indications for one-stage procedures, and the role of intraoperative imaging remain controversial.

CHAPTER I. CURRENT CONCEPTS IN THE DIAGNOSIS AND TREATMENT OF CHOLEDOCHOLITHIASIS AND PREDICTION OF POSTOPERATIVE COMPLICATIONS (LITERATURE REVIEW)

Gallstone disease (GSD) has been known since ancient times. It is widely распространена in developed and developing countries of Europe, North America, and Russia. The prevalence of GSD ranges from 9% to 42% in Europe, 14–21% in Russia, and 9–26% in the United States. Over the past 25 years, more than 5 million patients have been registered in Germany and over 15 million in the United States. A high prevalence is also observed among approximately 11% of the middle-class population in China, associated with a “Westernized” high-calorie diet and low physical activity. Lower rates are reported among African (4.2%) and Japanese (3.6%) populations.

In the overall structure of morbidity, GSD ranks third after cardiovascular diseases and diabetes mellitus. In recent years, the incidence of GSD has increased, with the number of patients doubling every decade, making it one of the leading abdominal pathologies. According to the 6th World Congress of Gastroenterologists, approximately 10% of the global population is affected; however, due to the often asymptomatic course, the rate of clinical presentation is only 4–5 per 1,000 population. Women are affected approximately four times more frequently than men, and about one-quarter of individuals over 70 years of age have gallstones.

With the increasing incidence of GSD, the number of surgical procedures on the gallbladder and bile ducts has also risen, reaching approximately 1.5 million operations in recent years. According to WHO data, 1–2 million cholecystectomies are performed annually worldwide, including 250,000–300,000 in Russia and more than 500,000 in the United States. In 8–45% of cases, the so-called postcholecystectomy syndrome develops, one of the causes of which is recurrent stone formation in the bile ducts.

One of the main causes of recurrent choledocholithiasis (in 1–7% of cases) is increased lithogenicity of bile after cholecystectomy, particularly in obese patients and in the presence of concomitant conditions not corrected during the initial surgery (e.g., stenosis of the major duodenal papilla). Residual choledocholithiasis accounts for 2–65.1% of cases.

Modern diagnostic methods have not yet achieved 100% accuracy in intraoperative detection of choledocholithiasis. After cholecystectomy without intraoperative cholangiography, residual stones are found in up to 40% of cases; however, the use of intraoperative cholangiography and other diagnostic techniques reduces this rate to 1–1.4%. In the United States, approximately 15,000 patients with residual bile duct stones are identified annually, and worldwide more than 20,000 patients undergo treatment for this condition each year.

Autopsy studies reveal gallstones in the gallbladder or common bile duct in approximately every 10th–11th woman and every 29th man. Accurate epidemiological data on prevalence, morbidity, mortality, and trends are essential for effective healthcare planning. Choledocholithiasis was first described by the Nuremberg physician V. Coiter in 1573.

According to most researchers, the main causes of GSD include changes in bile composition, inflammation of the biliary tract, and bile stasis. The gallbladder is the primary site of stone formation. In 97% of cases, bile duct stones are secondary, migrating from the gallbladder. Primary stone formation in the bile ducts occurs in only 3–5.7% of patients with GSD or in 1–3% of patients with biliary obstruction.

The reported incidence of bile duct stones in patients with cholecystitis and during choledochotomy varies widely—from 4% to 84%—which may be explained by differing surgical approaches and the variable use of intraoperative diagnostic methods. Stones are relatively rarely located in the hepatic ducts; more commonly, they are found in the common bile duct (76–81.1%) and in the region of the major duodenal papilla (6–25%). Ampullary lithiasis occurs in up to 25% of cases. The frequency of intrahepatic lithiasis varies widely, from 0.38% to 18%.

Two principal mechanisms of gallstone formation are described in the literature: the hepatometabolic and the vesicoinflammatory mechanisms. Hepatic dysfunction may result from diets rich in animal fats, neuroendocrine disorders (including hypothyroidism), infectious or toxic liver damage, bile stasis, and physical inactivity. These factors contribute to the production of lithogenic bile. Cholesterol stones form when cholesterol levels are elevated and bile acids are reduced.

In the vesicoinflammatory mechanism, inflammation of the gallbladder leads to physicochemical changes in bile. Bilirubin micelles precipitate from suspension into crystalline form, forming a primary crystallization center (the nucleus of the stone), upon which other bile components, epithelium, and mucus subsequently deposit, resulting in gradual stone growth.

By chemical composition and structure, gallstones are classified as cholesterol, pigment, mixed (combined, conglomerate, incrustated), and calcareous. On section, they typically exhibit a pigmented core and a layered structure.

The clinical presentation of choledocholithiasis is characterized by abdominal pain, jaundice, chills, and fever. Approximately 70–76% of patients experience intermittent pain in the right upper quadrant or epigastrium, with pain-free intervals; less commonly, the pain is constant and severe. Pain often radiates to the right scapula and back and may be accompanied by vomiting. Girdle-like pain is typical in cases of concomitant pancreatitis.

The most severe clinical manifestations are associated with acute pancreatitis caused by obstruction of the distal common bile duct by a stone. However, the clinical

presentation of choledocholithiasis is highly variable. The following forms are described: asymptomatic; peritoneal (with abdominal pain, fever, and signs of peritoneal irritation); and septic (with features of purulent cholangitis).

In clinical practice, most authors distinguish two main forms of choledocholithiasis: non-icteric and icteric. In 7–52% of patients, the disease is complicated by obstructive jaundice, cholangitis, and intoxication syndrome. Obstructive jaundice is the most frequent and severe complication. In 28.5–85% of cases, non-tumor-related obstructive jaundice is caused by choledocholithiasis.

The incidence of complications and adverse outcomes in elderly and senile patients with obstructive jaundice is 4–10 times higher than in younger patients. Postoperative mortality due to hepatic failure in this group ranges from 13.1% to 100%.

In patients with choledocholithiasis, stenosis of the major duodenal papilla, acute cholecystitis, and postcholecystectomy syndrome, the incidence of cholangitis ranges from 23.6% to 96.8%. Cholangitis, initially a manifestation of endogenous infection, may progress to an independent infectious disease. Its course is determined by both local purulent inflammation and systemic infectious responses.

The severity of purulent cholangitis is influenced by synergistic interactions between aerobic and anaerobic microorganisms. In most cases, death results from septic intoxication associated with hepatic and renal failure. Postoperative mortality in cholangitis ranges from 9.3% to 64%.

Duodenal microflora may contribute to the development of cholangitis via reflux through biliodigestive anastomoses.

Thus, gallstone disease is a highly prevalent condition, particularly in economically developed countries, with a prevalence ranging from 9% to 42%. The number of affected patients doubles every decade, and approximately one-quarter of individuals over 70 years of age have gallstones. Annually, 1–2 million cholecystectomies are performed worldwide.

The incidence of bile duct stones varies widely (4–84%), with the gallbladder being the primary site of stone formation. The main mechanisms of stone formation are hepatometabolic and vesicoinflammatory.

The clinical forms of choledocholithiasis are highly polymorphic, ranging from asymptomatic to severe icteric-septic forms, which determines the diversity of diagnostic approaches used before, during, and after surgical intervention.

1.2. Diagnosis of Choledocholithiasis

Preoperative and intraoperative diagnosis of choledocholithiasis presents significant challenges due to the absence of specific signs indicating the presence of calculi within the bile ducts. The greatest diagnostic difficulties arise in atypical and subtle forms of bile duct stones, which are often a source of residual choledocholithiasis.

Highly informative anamnestic indicators of choledocholithiasis include a history of jaundice and cholangitis, as well as early and recurrent episodes of biliary colic.

The following diagnostic methods are used to detect stones in the hepatobiliary ducts: laboratory tests (bilirubin, transaminases, alkaline phosphatase, etc.), ultrasound (US), infusion cholecystocholangiography, endoscopic retrograde cholangiopancreatography (ERCP), hepatobiliary scintigraphy, intraoperative cholangiography (IOC), endoscopic ultrasound (EUS), fiberoptic cholangioscopy, fistulocholangiography, computed tomography (CT), percutaneous transhepatic cholangiography (PTC), magnetic resonance cholangiopancreatography (MRCP), and laparoscopic cholecystocholangiography.

Laboratory diagnostics are mandatory in all patients with choledocholithiasis. However, routine clinical blood tests are not central to the diagnostic algorithm and primarily reflect concomitant pathological processes and complications. Leukocytosis is detected in 18–32% of patients, anemia of varying severity in 12–29%, and elevated erythrocyte sedimentation rate (ESR) in 15–67.5%.

Biochemical blood parameters are more informative. Elevated bilirubin levels may confirm obstructive jaundice. The ratio of direct to indirect bilirubin fractions is an important criterion in the differential diagnosis of jaundice. Reported sensitivity and specificity are as follows: bilirubin—67.3% and 63.5%, alkaline phosphatase—67.3% and 65.0%, alanine aminotransferase (ALT)—52.6% and 52.6%, and amylase—44.2% and 44.0%, respectively.

Nevertheless, laboratory findings in choledocholithiasis are not always conclusive. Increased levels of middle-mass molecules in the blood have been reported, indicating endotoxemia— 0.464 ± 0.159 arbitrary units in cases complicated by cholangitis and 0.379 ± 0.113 in pancreatitis ($p < 0.05$).

Polarizing microscopy of bile is used to detect microcholedocholithiasis. Bile samples for cytological examination are obtained during esophagogastroduodenoscopy (EGD) using a catheter employed for ERCP. The presence of calcium bilirubinate granules and cholesterol monohydrate crystals suggests possible cholelithiasis. The diagnostic accuracy of polarizing microscopy of ductal bile reaches 97%, compared to 85% for conventional microscopy.

Instrumental methods play a key role in the diagnosis of choledocholithiasis. Oral and intravenous cholecystocholangiography fail to provide sufficient information on the hepatobiliary system in 10–41.5% of cases, indicating their low diagnostic value.

Ultrasound is a screening method for gallstone disease and is more informative for detecting gallbladder stones than cholecystography, achieving diagnostic accuracy of 88.7–100%. In obstructive jaundice, ultrasound sensitivity ranges from 90% to 97%, and specificity from 73.8% to 98%.

However, the role of ultrasound in diagnosing choledocholithiasis remains controversial. Reported accuracy varies widely—from 82–98% to as low as 13%. Sensitivity ranges from 55% to 95%, increasing with stone size. For stones smaller than 5 mm, ultrasound may yield false-positive (4.9%) and false-negative (13.6%) results.

Despite these limitations, ultrasound alone may suffice in certain cases, which is advantageous from both clinical and economic perspectives. Its diagnostic capability is limited in 20–25% of cases due to difficulty visualizing the prepapillary segment of the common bile duct. Image quality is highly operator-dependent.

Intraoperative ultrasound increases diagnostic accuracy to 98.2% and may reduce the need for intraoperative cholangiography, although detection of small stones remains challenging. High-frequency probes (7.5 MHz) are increasingly used during laparoscopic procedures. Combined use of IOC and intraoperative ultrasound improves diagnostic performance but increases operative time.

When ultrasound findings are inconclusive, more sensitive methods are employed, including ERCP, EUS, CT, MRCP, PTC, and transduodenal cholangioscopy. Esophagogastroduodenoscopy allows exclusion of gastric and duodenal diseases that may mimic gallstone disease and enables assessment of the major duodenal papilla, detection of parapapillary diverticula, and cannulation feasibility.

Radiological imaging techniques (ERCP, PTC, IOC, fistulography, and drainage cholangiography) play a central role in diagnosing complicated forms of choledocholithiasis. ERCP remains a leading diagnostic modality, particularly for differential diagnosis of jaundice, with an accuracy of 89–93% and overall informativeness of 78–98%. It allows precise localization and removal of stones via endoscopic sphincterotomy.

However, ERCP is associated with complications in 0.8–36% of cases and mortality of 0.4–3.7%, as well as radiation exposure. Therefore, it should be used only under strict indications.

MRCP and EUS are increasingly used as noninvasive alternatives. MRCP demonstrates overall diagnostic accuracy of 89–97%, sensitivity of 81–100%, and specificity of 85–100%. It allows visualization of stones as small as 2 mm and detailed assessment of biliary anatomy without ionizing radiation.

Limitations of MRCP include difficulty in evaluating ducts completely filled with stones, as well as interference from blood clots, pneumobilia, and metallic stents.

CT is useful primarily for differential diagnosis, detecting biliary obstruction in 80–85% of cases and stones in 49.8–93%, although cholesterol stones may be difficult to visualize.

PTC demonstrates high diagnostic efficiency (88.9–98%) and is particularly useful when ERCP is unsuccessful, especially in patients with obstructive jaundice and dilated intrahepatic ducts. However, it is invasive and associated with complications (0.8–7.1%) and low mortality (0.14–0.2%).

Intraoperative diagnostic methods are indicated when biliary hypertension is suspected or when preoperative evaluation is insufficient. These include IOC, EUS, cholangioscopy, duct probing, and others. No single method is universal; therefore, a stepwise approach from simpler to more complex techniques is recommended.

Fiberoptic cholangioscopy provides the highest diagnostic accuracy (up to 97.8%), with sensitivity of 99.2% and specificity of 98%, and allows direct visualization of bile duct pathology.

Fluorescence imaging using indocyanine green (ICG) is an emerging technique that enables real-time visualization of biliary anatomy with high accuracy.

Fistulocholangiography remains a simple and widely available method with diagnostic effectiveness of 95–97% for detecting residual stones.

In summary, there is currently no unified diagnostic protocol for choledocholithiasis. The diagnostic algorithm should include MRCP as a key modality, with EUS used for further clarification when needed. ERCP should be reserved for cases where noninvasive methods are inconclusive.

Such an approach improves diagnostic accuracy, reduces the number of invasive procedures, lowers complication rates, shortens hospital stay, and decreases overall healthcare costs.

1.3. Methods of Treatment of Choledocholithiasis (CHDL)

At the present stage, significant progress has been achieved in the treatment of gallstone disease (GSD), but the question of treatment tactics for choledocholithiasis (CHDL) is still widely debated, considering its frequent complications (obstructive jaundice, cholangitis, acute and chronic pancreatitis, stenosis of the major duodenal papilla, biliary cirrhosis of the liver).

A wide range of therapeutic methods is used in CHDL. Recent decades have been characterized by the emergence and improvement of minimally invasive endoscopic techniques, as well as a gradual reassessment of their role as definitive treatment methods. The issues of optimal timing, nature, and sequence of therapeutic interventions remain unresolved, as evidenced by the diversity of approaches used.

When stones are detected in the bile ducts, the following treatment options are possible:

1. **Endoscopic papillosphincterotomy (EPST):**
 - a) mechanical extraction of stones using Dormia baskets, Fogarty balloon catheters, mechanical lithotripters;
 - b) lithotripsy (mechanical, electrohydraulic, laser) with subsequent flushing of fragments into the duodenum.
2. **Endoscopic balloon papillary dilatation** with or without lithotripsy and stone extraction.
3. **One-stage laparoscopic cholecystectomy (LCHE) with antegrade laparoscopic choledocholithotomy:**
 - a) with mechanical, laser, or electrohydraulic lithotripsy;
 - b) with papillosphincterotomy;
 - c) with balloon papillary dilatation.
4. **Percutaneous transhepatic approach** with antegrade lithotripsy and stone removal or stone displacement into the duodenum via papillary dilation.
5. **“Rendezvous” technique** – simultaneous use of percutaneous transhepatic (antegrade) and endoscopic (retrograde) approaches with combined manipulation in the bile ducts.
6. **Open laparotomy choledocholithotomy** with completion by various methods (external drainage, biliodigestive anastomosis, primary closure of the common bile duct, transduodenal sphincteroplasty; liver resection in intrahepatic lithiasis).
7. **Removal of stones through drainage or fistula (non-operative methods):**
 - a) forceps or catheters;
 - b) laser fragmentation;
 - c) flushing into the duodenum;
 - d) Dormia baskets, Fogarty balloon;
 - e) aspiration.
8. **Litholytic (stone-dissolving) therapy:**
 - a) oral administration;
 - b) through choledochal drainage;
 - c) via endoscopic bile duct catheter;
 - d) percutaneous transhepatic drainage;
 - e) nasobiliary drainage;
 - f) laparoscopic cholecysto- or choledochostomy.

It is also noted that choledochal stones may spontaneously pass into the intestine or dissolve.

Normally, bile is sterile and has bactericidal properties, but in inflammatory conditions it becomes infected by various microorganisms. Most researchers agree that purulent-septic complications after biliary surgery are caused by microorganisms found in bile. Infectious complications and mortality are

significantly higher in patients with infected bile compared to sterile bile: bacteremia increases more than 40 times, wound infection 3–20 times, and mortality more than twice.

In choledocholithiasis and bile duct strictures, bile infection occurs in 30–100% of cases. In obstructive jaundice, intrahepatic bile is infected in 63–89% of cases. Common pathogens include *E. coli*, staphylococcus, streptococcus, clostridia, and *Proteus* species.

Antibiotic therapy

Issues of pathogenetic treatment and prevention of infectious complications in obstructive jaundice and cholangitis remain insufficiently studied. There is no clear consensus on antibiotic indications and administration methods.

Prophylactic antibiotics are recommended only for high-risk patients. They should be administered in adequate doses effective against endogenous flora, 1–6 hours before surgery and no longer than 24–48 hours postoperatively (sometimes up to 72 hours). Prolonged use increases resistance and hospital infections.

In “clean” surgeries, routine prophylaxis is generally not justified unless risk factors exist (e.g., diabetes, immunosuppression). Combination antibiotic therapy is often required due to mixed microflora, especially with anaerobes (metronidazole, ceftriaxone, clindamycin). High doses are necessary in biliary hypertension, although adequate concentrations in bile are often not achieved due to impaired liver excretion.

Pathophysiology and surgical timing

Long-standing gallstone disease leads to structural liver changes. After biliary decompression, liver function improves significantly. Patients with obstructive jaundice should be considered urgent surgical cases.

However, surgery during peak jaundice increases operative risk and postoperative mortality by approximately fourfold compared to surgery after jaundice relief. Therefore, urgent but staged management is often required.

Acute cholangitis with obstructive jaundice remains a major challenge, with mortality reaching 40–70%. There is no consensus on duration of conservative therapy or timing of surgery.

Minimally invasive approaches

Modern trends emphasize minimally invasive techniques to reduce surgical trauma. Endoscopic papillosphincterotomy (first performed in 1973) has become widely

used, achieving duct clearance in 78–95.8% of cases. However, complications include pancreatitis, bleeding, cholangitis, and mortality up to 2.8%.

Limitations include inability to remove large or multiple stones and risk of sphincter dysfunction leading to recurrence (0.3–3%).

Endoscopic papillary balloon dilatation is an alternative preserving sphincter function, but is limited to small stones (<1 cm) and selected cases.

Percutaneous transhepatic methods and rendezvous techniques provide additional options but carry risks such as bleeding, bile leakage, and infection.

Lithotripsy methods (mechanical, electrohydraulic, laser) are effective but vary in cost, complexity, and complication rates. Recurrence after lithotripsy occurs in about 32% of cases.

Laparoscopic and open surgery

Laparoscopic approaches offer advantages over open surgery, including lower morbidity and shorter hospital stay. One-stage laparoscopic procedures are generally preferred, though results vary.

Open surgery remains relevant as a “rescue” method in complex cases or when minimally invasive approaches fail. Postoperative management may include drainage, biliodigestive anastomosis, or primary duct closure.

Biliary drainage and anastomoses

External drainage methods (e.g., T-tube drainage) remain widely used but are associated with complications (8.2–33.6%). Primary duct closure is preferred by some surgeons, while others advocate external drainage or biliodigestive anastomoses.

Internal drainage (e.g., choledochoduodenostomy) is physiologically favorable but controversial due to risks such as reflux cholangitis and biliary cirrhosis. Alternative techniques include hepaticojejunostomy.

Conclusion

Despite advances in surgery, choledocholithiasis remains a complex and unresolved clinical problem. No single standardized method exists. Treatment strategy depends on patient condition, technical resources, and surgical expertise.

Current trends favor individualized, multidisciplinary approaches combining endoscopic, laparoscopic, percutaneous, and open techniques to optimize outcomes and reduce complications and mortality.

1.4. Prediction of Operative Risk and Postoperative Complications in Abdominal Surgery

The history of clinical prognosis spans many centuries. Prognostication represents one of the functions of information systems based on databases. A key requirement is the precise definition of medical terminology used in computer systems, ensuring consistency and unambiguity [125].

The problem of reliable prognosis is based on three main factors:

- accurate reflection of the most important changes in the patient's body;
- selection of an adequate number of parameters (at least 60–70 features);
- proper algorithmization of the prognostic process [28].

In medicine, many types of prognosis are considered: diagnostic prognosis, assessment of diagnostic value of new tests, prediction of one factor's change under the influence of another, etc. Various forecasting methods are known, including moving averages, simple extrapolation, exponential smoothing, average growth rate, and model-based forecasting [61, 125]. However, there is still no universally accepted methodology for predicting pathological processes. More than 150 forecasting methods in surgery have been described in the literature [28].

At present, the problem of creating a reliable operative prognosis for surgical and oncological patients remains unresolved. There are discrepancies in the definition of "operative risk," which complicates the development of predictive models.

Limitations of existing scoring systems

Commonly used quantitative risk assessment systems in surgical practice (APACHE, SAPS, SOFA, MODS) have not fully solved the problem of prediction in elective and emergency surgery. These systems have been repeatedly modified and updated [25], but they still do not reliably predict perioperative complications in individual patients.

Such scoring systems are mainly suitable for scientific research and reporting, but are less effective for clinical decision-making in specific patients [56, 28].

Role of expert systems and artificial intelligence

At the modern stage, expert systems are increasingly used in surgery for:

- differential diagnosis,
- assessment of patient condition,
- selection of surgical strategy in real time [61, 65].

Artificial neural networks (ANNs) are widely used in the development of such systems. They improve classification accuracy and specificity without reducing sensitivity, as they simulate certain functions of the human brain [65, 25].

A significant number of developments exist in pancreatology due to high hospitalization rates and high mortality (24–66%) in infected pancreatic necrosis [86]. For example:

- Andersson et al. [125] selected six key parameters for predicting severity of acute pancreatitis using ANN;
- Korenevsky et al. [88] applied similar methods for acute cholecystitis severity prediction;
- Mironov et al. [86] used ANN to predict outcomes in severe acute pancreatitis.

Modern challenges in abdominal surgery

Despite the development of laparoscopic surgery, complication rates in emergency abdominal operations remain up to 9%. However, traditional scoring systems (SAPS, Ranson, APACHE II) cannot provide individualized predictions.

Expert systems are increasingly used for:

- selection of surgical method [61, 28],
- quantitative risk assessment [56, 88],
- training in surgical education [25].

A key factor in decision-making is the surgeon's experience and ability to assess operative risk. Therefore, modern predictive systems should consider not only clinical and laboratory parameters but also the surgeon's qualification level.

For example, an automated system for assessing outcomes in acute abdominal pathology includes three main components:

1. patient condition,
2. complexity of surgery,
3. surgeon's professional rating [25].

Development of specialized predictive systems

Zharikov et al. [61] developed a computer-based expert system for predicting postoperative peritonitis using 25 parameters grouped into four diagnostic clusters reflecting homeostasis.

A major issue is risk assessment in hepatobiliary surgery. Prediction in gallstone disease (GSD) is still insufficiently studied. Mortality reaches 13% in emergency cases and about 1% in elective surgery [51].

Existing scoring systems are difficult to apply due to:

- inability to integrate multiple parameters into a unified model,
- lack of adaptability to individual clinical situations [93].

AI-based models for operative risk

Dragun et al. [56] developed an automated system for quantitative operative risk assessment (ASQORA) based on neural network and probabilistic-statistical models. It generates a “computer image” of the patient’s condition and provides an integrated risk score.

Zvyagintsev et al. [65] proposed an expert system to predict the complexity of laparoscopic cholecystectomy using coded clinical, sonographic, and laboratory parameters. It helps:

- anticipate surgical difficulties,
- select optimal technique,
- prevent complications,
- adjust surgical team composition.

Current gaps in choledocholithiasis

There are almost no comprehensive predictive models for choledocholithiasis. Considering the frequency of such operations, this is a significant gap. Predictive models could:

- determine the optimal surgical approach,
- define indications for surgery,
- estimate operative risk,
- predict outcomes.

About 100 scoring systems exist for predicting gastrointestinal bleeding recurrence, but none fully meet clinical needs. Many are too complex or use non-routine parameters [25].

Borets et al. [28] developed an expert system (ESPOR) that proved effective in colorectal and combined abdominal pathology, showing the potential of such systems in surgery.

Future directions

Many aspects of operative risk prediction remain controversial and insufficiently studied. The relationship between oxidative stress processes, liver failure stages, and operative risk is still unclear.

Future development should focus on:

- individualized predictive models,
- integration of statistical, neural, and expert approaches,
- use of correlation, factor, and cluster analysis,
- creation of simplified and clinically applicable systems.

Conclusion

The informatization of medical decision-making in abdominal surgery continues to develop rapidly. The main goal of modern predictive systems is to minimize complications and individualize treatment strategies.

Despite progress, there is still no universally accepted method for accurate operative risk prediction in every patient. Therefore, development and clinical implementation of expert systems remain essential for improving surgical outcomes.

CHAPTER II. FEATURES OF THE CLINICAL COURSE AND COMPLEX DIAGNOSTICS OF CHOLEDOCHOLITHIASIS

Materials and Methods of the Study: Characteristics of Clinical Observations

The study is based on the results of examination and treatment of 828 patients with choledocholithiasis who underwent surgical treatment in the Department of Surgery of the V.K. Gusak Institute of Emergency and Reconstructive Surgery from 2011 to 2020.

Among the examined patients, there were 517 (62.5%) women and 311 (37.5%) men, aged from 20 to 88 years. In 363 (43.8%) patients, the age exceeded 60 years (Table 1).

Age (years)	Female patients	Male patients	Total patients
20-30	42	11	53
31-40	73	34	107
41-50	87	28	115
51-60	98	92	190
61-70	116	83	199
71-80	82	54	136
81-90	19	9	28
Всего	517 62,5%	311 37,5%	828 100%

Cholelithiasis was observed 1.7 times more frequently in women than in men (517 and 311 patients, respectively). This ratio varied across different age groups: 21–30 years – 3.8; 31–40 years – 2.1; 41–50 years – 3.1; 51–60 years – 1.07; 61–70 years – 1.4; 71–80 years – 1.5; 81–90 years – 2.1.

The diagnostic characteristics of patients with choledocholithiasis are presented in Table 1.2.

Diagnosis	Total
Chronic calculous cholecystitis, choledochal stones	598 (72,2%)

Chronic acalculous cholecystitis, choledochal stones	43 (5,2%)
Postcholecystectomy syndrome, choledochal stones	187 (22,6%)

Obstructive jaundice was observed in 324 (39.2%) patients, cholangitis in 178 (21.5%), stenosis of the major duodenal papilla (MDP) in 308 (37.3%), intrahepatic lithiasis in 16 (1.9%), and internal biliary fistula in 14 (1.7%) patients.

Out of 828 patients, 187 (22.6%) had previously undergone surgical interventions on the gallbladder or bile ducts, mainly in other hospitals: Donetsk city – 58, Donetsk region – 104, Ukraine – 16, Russia – 7, and in our clinic (severely ill elderly patients) – 2.

Type of primary operation	Total
Cholecystectomy	32
Cholecystectomy, choledochostomy according to Vishnevsky	28
Cholecystectomy, choledochostomy according to Halsted	24
Cholecystostomy	18
Cholecystoduodenostomy	15
Cholecystectomy, primary closure of the common bile duct	23
Laparoscopic cholecystectomy	47

As follows from the data in Table 1.3, the most common primary operations were:

Laparoscopic cholecystectomy (LCE) – 47 cases, cholecystectomy – 32 cases, cholecystectomy with choledochostomy according to Vishnevsky – 28 cases.

Comorbid pathology leads to masking and distortion of symptoms of the underlying disease and to diagnostic errors. Each concomitant disease represents a risk factor for the development of associated complications and may worsen the prognosis. In

the presence of four or more comorbid conditions, especially in the stages of subcompensation and decompensation, the prognosis often becomes unfavorable. Such patients belong to a high-risk group and require intensive therapy. (repeated twice in the original text)

In 386 (46.7%) patients, various comorbid diseases were observed, and 129 of them had two or more such diseases. The following risk factors were identified:

1. cardiovascular system – 74 cases
2. gastrointestinal tract – 42 cases
3. metabolic system – 37 cases
4. respiratory system – 24 cases
5. urinary system – 7 cases
6. central nervous system – 5 cases

In total, 433 comorbid conditions were recorded in 386 patients. In patients under 60 years of age, comorbid diseases were present in 24.7% of cases; from 61 to 70 years – in 53.6%; and over 70 years – in 100% of cases.

Previously, 72 patients underwent surgery for concomitant diseases (gastrectomy, strumectomy, mastectomy, etc.).

According to the main diagnosis, 828 patients with choledocholithiasis (CHD) were divided into 6 groups:

Group I – chronic acalculous cholecystitis, choledocholithiasis (33 patients)

Group II – chronic acalculous cholecystitis, choledocholithiasis, obstructive jaundice (10 patients)

Group III – chronic calculous cholecystitis, choledocholithiasis (341 patients)

Group IV – chronic calculous cholecystitis, choledocholithiasis, obstructive jaundice (257 patients)

Group V – postcholecystectomy syndrome (PCS), choledocholithiasis (130 patients)

Group VI – PCS, choledocholithiasis, obstructive jaundice (57 patients)

Average	age	of	patients	(years):
Group I	–	64.32	±	3.07
Group II	–	60.71	±	2.59
Group III	–	55.03	±	1.84
Group IV	–	59.10	±	1.02
Group V	–	60.07	±	1.90
Group VI – 59.54 ± 1.33				

All patients were divided into 5 groups according to surgical methods:

I – endoscopic transpapillary interventions (617 patients)

II – laparoscopic transcholedochal interventions (46)

III – endoscopic transhepatic interventions (30)

IV – combined (antegrade + retrograde) (23)
 V – laparotomic operations (112)

Table 2.5 shows surgical methods and outcomes in 828 patients with CHD. The highest rate of postoperative complications (16.0%) and mortality (4.5%) was observed after laparotomic operations, while the lowest complication rate was after laparoscopic transcholedochal interventions (10.8%), with no mortality ($p < 0.05$).

Positive trends in treatment outcomes were noted despite the complexity of pathology and multiple risk factors. The use of modern diagnostic methods, surgical techniques, and perioperative prediction systems reduced postoperative complications in Group I from 16.0% to 8.7% and mortality from 4.5% to 2.1% ($p < 0.05$).

Computer-based integral risk factors and graphical prognostic models were developed. Prognostic assessment allows surgeons to optimize preoperative preparation and choose the most appropriate surgical method. Computer-based prediction significantly improves outcomes in choledocholithiasis treatment.

Long-term outcomes (1–5 years) were studied in 483 patients. Modified surgical techniques resulted in 32% more favorable outcomes compared to conventional treatment.

The comparative analysis allowed identification of causes of complications, development of preventive measures, determination of key diagnostic features, formulation of treatment principles, establishment of surgical risk criteria, creation of an expert system for predicting postoperative complications, and development of targeted correction schemes.

3.1. Clinical manifestations of choledocholithiasis

The clinical course of cholelithiasis, particularly choledocholithiasis, is diverse and depends on different forms of the disease. In our observations, choledocholithiasis occurred in four main clinical forms:

1. severe form with pain attacks, jaundice, and cholangitis (76.1%)
2. mild/atypical forms (17.4%)
3. asymptomatic forms (3.7%)
4. atypical forms (2.8%)

Atypical forms were observed in 23 (2.8%) patients and manifested as conditions such as urolithiasis, ischemic heart disease, angina pectoris, pancreatic head tumor, sepsis, intestinal obstruction, and chronic colitis.

Atypical and asymptomatic forms are the most common causes of unsatisfactory treatment outcomes and residual stones.

Clinical manifestations depended on stone size, localization, and number, ranging from latent disease to severe complications (obstructive jaundice, cholangitis, pancreatitis, and hepatic abscesses).

The classical triad (pain, jaundice, and cholangitis) was observed in 278 (33.6%) patients. Pain was present in 761 (91.9%) patients, obstructive jaundice in 324 (39.2%), and cholangitis in 178 (21.5%).

Choledocholithiasis was suspected in 630 (76.1%) patients, while in 198 (23.9%) no clear clinical signs were present.

In young patients (20–35 years), diagnosis was more difficult due to atypical presentation. Women often developed initial symptoms during pregnancy or postpartum ($49.3 \pm 4.2\%$). Pain was more frequently localized in the epigastric region (46.2%) than in the right hypochondrium (24.1%). Only 28.4% had typical localization.

Obstructive jaundice at admission was less frequent in young patients (17.8%) than in middle-aged patients (29.7%).

In elderly patients, choledocholithiasis was often combined with destructive cholecystitis (38.3%) and had a more severe course.

Three clinical syndromes were identified in elderly patients:

1. destructive cholecystitis (17%)
2. pancreatic syndrome (21%)
3. cholangitic syndrome (24%)
4. short but severe biliary colic (38%)

In 29.4% of elderly patients, jaundice was absent. Delayed hospitalization (>3 days) occurred in 38.7% of cases, leading to increased complications and mortality.

3.1.1. Characteristics of obstructive jaundice syndrome

Obstructive jaundice is a key symptom of choledocholithiasis. It is often preceded by biliary colic and may be intermittent, indicating a “ball-valve” stone mechanism.

In 324 patients, obstructive jaundice was recorded. Duration before hospitalization ranged from 7 days to 6 months.

Symptoms included abdominal pain (38.9% acute, 52.6% dull), absence of pain in 8.5%, nausea (91.4%), vomiting (63.6%), weakness (42%), weight loss (28.7%), dark urine (100%), and pale stool (81.8%).

Liver enlargement was present in 41.8% of patients. Serum bilirubin ranged from 36 to 344 $\mu\text{mol/L}$.

Most patients were in moderate condition; 59 were in severe condition. Comorbid diseases significantly worsened the clinical course in 56.7% of cases.

There was no direct correlation between the number of stones and jaundice. Jaundice occurred most frequently (89.1%) when stones were located in the terminal part of the common bile duct and in the major duodenal papilla.

Occurrence of jaundice depending on the number of stones in the bile ducts

Presence of jaundice	Total cases	Number of stones (single)	Number of stones (multiple)
History of jaundice	137	28(20,4%)	109(79,6%)
Jaundice at the time of surgery	324	71(21,9%)	253(78,1%)
No jaundice observed	367	317(86,4%)	50(13,6%)

The longer and more severe the jaundice, the more pronounced the clinical signs of hepatitis and liver failure become (itching of the skin, sleep disturbances, drowsiness, increased bleeding tendency, oliguria, etc.). Clinical symptoms in jaundice correlate with morphological changes in the liver, such as hepatocyte dystrophy up to focal or total necrosis.

In acholia, the absorption of fats and fat-soluble vitamins (A, D, E, K) is primarily impaired. Vitamin K deficiency leads to impaired prothrombin synthesis function of the liver and, as a consequence, to hemorrhagic syndrome (nosebleeds, melena, etc.).

In cases of liver decompensation, its excretory, detoxification, and enzymatic functions are disrupted, resulting in changes in the cardiovascular, nervous, and urinary systems, as well as disorders of protein and electrolyte metabolism.

For clarification of obstructive jaundice (OJ), biochemical blood tests, ultrasound, computed tomography, gastrointestinal radiography, laparoscopy, and endoscopic studies were used. Diagnosis of jaundice remains difficult even with modern diagnostic methods.

Hepatic failure may be considered a breakdown of the liver's compensatory capacity, when it can no longer maintain homeostasis. Acute hepatic failure represents the terminal stage of almost complete hepatocyte destruction. Hypoproteinemia leads to a decrease in oncotic pressure, development of interstitial edema and ascites.

Due to impaired amino acid metabolism, levels of tyrosine, phenylalanine, methionine, and tryptophan increase in the blood and central nervous system tissues, contributing to excessive accumulation of neurotransmitters (serotonin) and toxic metabolites such as mercaptans, which together with hyperammonemia lead to encephalopathy.

Our results show that treatment outcomes in choledocholithiasis largely depend on the severity of liver damage; therefore, improving liver function before surgery and in the early postoperative period should be one of the main surgical objectives.

A pathogenetic classification of hepatic failure was modified and supplemented by our data.

Stage I (compensated stage):

Reflects temporary impairment of liver function due to loss of excretory function, with the possibility of full recovery after removal of obstruction. There is mild jaundice with bilirubin up to $50 \pm 10 \mu\text{mol/L}$ and a transient increase in aminotransferases. Pain syndrome may cause temporary disturbances in systemic and organ hemodynamics, correctable by analgesia and infusion therapy. A hypercoagulable form of thrombohemorrhagic syndrome is observed. Patients present with asthenovegetative symptoms such as fatigue and weakness. Diuresis is normal. Medium molecular substances (MMS) range from 0.22 to 0.26 units. No abnormalities are detected in psychometric testing.

Stage II (subcompensated stage):

There is progression of excretory dysfunction; bilirubin increases up to $150 \pm 40 \mu\text{mol/L}$, ALP up to $5 \pm 1 \text{ mmol/L}$. Protein synthesis disorders develop, with total protein decreasing to 56 g/L and albumin fraction reduction. Aminotransferases increase; metabolic disturbances appear. Hemodynamic changes include hypovolemia with compensatory hyperdynamic circulation. Hyperaldosteronism leads to sodium retention and increased plasma volume. Renal blood flow impairment reduces glomerular filtration. Patients have moderate to severe condition with marked jaundice, pruritus, and fever. Emotional changes include irritability,

sleep disturbances, and behavioral changes such as euphoria or depression. MMS levels range from 0.27 to 0.40 units. Hepatic encephalopathy stage I is detected.

Stage III (decompensated stage):

Progressive accumulation of excretory products leads to severe cholemia. Bilirubin exceeds 300 $\mu\text{mol/L}$, bile acids over 300 $\mu\text{mol/L}$, unconjugated bilirubin up to 100 $\mu\text{mol/L}$. Liver secretory function is markedly reduced; albumin levels decrease to 35%, and enzymatic activity is significantly impaired. Toxic metabolites (ammonia, phenylalanine, methionine) accumulate. Severe cytolysis occurs with release of enzymes (RNase, DNase, aldolase, LDH-5). Homeostatic mechanisms fail to compensate. Severe hemodynamic disturbances (hypovolemia, hypoperfusion), oliguria, and azotemia develop. Urea rises up to 30 mmol/L due to impaired renal excretion. Immune function is suppressed. Coagulation disorders include hypofibrinogenemia and bleeding tendency. Encephalopathy progresses with confusion, lethargy, and behavioral changes. MMS levels reach 0.41–0.5 units (encephalopathy stage II).

Different dominant syndromes may appear: hepatocardiovascular, hepatorenal, hemorrhagic, hepatovisceral, and hepatohormonal.

Stage IV (terminal stage):

Characterized by progressive liver failure, severe intoxication, and breakdown of homeostasis. Patients develop coma with loss of consciousness, motor disorders, pathological reflexes, and bilirubin-enzyme-protein dissociation. MMS reaches 0.6–0.8 units or higher.

Among 9 deceased patients with CHD and obstructive jaundice, 1 had stage II liver failure, 2 had stage III, and 6 had stage IV. A clear correlation was found between mortality and stage of liver failure.

The danger of obstructive jaundice lies in the development of endotoxemia due to accumulation of toxic metabolites and blockade of oxidative enzymes. Treatment success depends on proper preoperative preparation and surgical strategy. Individualized intensive therapy is applied depending on the stage of liver failure.

Active conservative therapy combined with surgery significantly reduces postoperative complications and mortality.

The causes of obstructive jaundice are always serious, as liver failure is associated with high mortality. Surgical treatment includes not only removal of bile duct stones but also optimal completion of choledochotomy and assessment of the hepatopancreatoduodenal zone.

Prognosis improves significantly when urgent surgical tactics are applied in unresolved obstructive jaundice. Not only acute inflammatory changes but also the degree of liver failure should determine surgical timing. Surgery should be performed when liver function is minimally impaired, especially in elderly patients.

After diagnostic evaluation and preoperative preparation, all patients underwent surgery. The main goal was decompression of the biliary tract, elimination of obstruction, or palliative biliary drainage (internal or external).

Currently, minimally invasive techniques are more commonly used (endoscopic papillosphincterotomy, percutaneous transhepatic cholangiostomy, laparoscopic operations).

3.2. Laboratory diagnosis of HCLD and its complications. General and biochemical blood tests

Laboratory diagnostics are mandatory for all patients with cholecystocholedocholithiasis. However, the parameters of the clinical blood test are not the main diagnostic criteria for cholelithiasis and mainly indicate concomitant pathology or complications. Biochemical blood parameters are of greater diagnostic value, especially in the differential diagnosis of jaundice. In cases of impaired bile outflow, an increase in the activity of ALT, AST, and LDH is observed, indicating impaired liver function.

An increase in AST, ALT, and blood amylase levels may suggest HCLD in the absence of obstructive jaundice. In such minimal bile outflow disorders, which are not yet clinically manifested, additional diagnostic methods should be used to confirm or exclude HCLD, especially in atypical forms of the disease. According to our data, endoscopic ultrasonography (EUS) was performed in such cases, which allowed detection of common bile duct (CBD) stones in 23.9% of cases.

We performed a statistical analysis of blood and urine parameters in order to determine mean values, variances, standard errors, coefficients of variation, and statistically significant differences in laboratory parameters in 828 patients with choledocholithiasis.

The following statistically significant differences (95% confidence interval) between groups were identified:

- Groups I–III and V–III: blood glucose was higher in group III
- Groups II–I: erythrocytes and hemoglobin were higher in group I
- Direct and indirect bilirubin were higher in group II
- Groups I–V: no significant differences in studied parameters

- Groups VI–I: erythrocyte count was higher in group I
- Band neutrophils, direct and total bilirubin were higher in group VI
- Groups IV–II: recalcification time and ALP were higher in group II, AST was higher in group IV
- Groups VI–V: erythrocytes and AST were higher in group V, bilirubin was higher in group IV
- Groups IV–VI: total and direct bilirubin were higher in group IV
- Groups IV–I: erythrocytes and band neutrophils were higher in group I; total, direct, and indirect bilirubin, blood glucose, ESR, and γ -globulins were higher in group IV
- Groups IV–V: leukocytes, bilirubin fractions, glucose, ESR were higher in group IV
- Groups II–V: erythrocytes, leukocytes, and hemoglobin were higher in group V; bilirubin and ESR were higher in group II
- Groups IV–III: erythrocytes, hemoglobin, albumin, and prothrombin index were higher in group III; leukocytes, neutrophils, ESR, bilirubin fractions, γ -globulin, AST, ALT, and ALP were higher in group IV
- Groups II–III: erythrocytes, hemoglobin, plasma calcium were higher in group III; ESR, bilirubin, β -globulins, prothrombin index, recalcification time, and ALP were higher in group II

In 23.9% of patients suspected of HCLD without classical symptoms (pain, jaundice, fever), the most frequently elevated biochemical parameters and their mean values were: bilirubin $> 2\times$ normal (63.1%), ALT $> 2.4\times$ normal (48.1%), ALP $> 1.6\times$ normal (69.8%), amylase $> 1.6\times$ normal (36.8%) ($p < 0.05$). AST levels were not diagnostically significant.

Sensitivity and specificity of key biochemical markers of HCLD were determined:

- Total bilirubin: 67.3% and 65.9%
- ALP: 67.3% and 45.0%
- ALT: 52.6% and 52.8%
- Amylase: 46.2% and 44.8% ($p < 0.05$)

With prolonged obstructive jaundice, hepatorenal failure develops (19 cases), caused by vasoconstriction and reduced glomerular filtration. A decrease in diuresis up to anuria and an increase in residual nitrogen and creatinine levels were observed. Such patients had a high operative risk.

Comparative analysis of laboratory parameters showed that hypoalbuminemia is characteristic of functional hepatic insufficiency and acute hepatitis. In bile duct obstruction, the activity of the excretory enzyme alkaline phosphatase (ALP) increases. In mechanical jaundice, cholesterol levels reached up to 7.5 mmol/L, and bilirubin increased mainly due to the direct fraction. Transaminases (AST, ALT)

remained normal during the first 7–10 days of obstructive jaundice and increased later in one-third of patients.

A high leukocytosis with neutrophilia and a left shift confirmed the presence of purulent cholangitis. The study of enzyme activity in blood serum is increasingly important in diagnosing liver diseases, as well as in prognosis and treatment monitoring. Enzyme activity determination can be considered a kind of “enzymological liver biopsy,” guiding clinical decision-making.

The following enzyme activity levels were obtained:

AST – 1.48 ± 0.07 mmol/h·L

ALT – 2.73 ± 0.16 mmol/h·L

ALP – 3.12 ± 0.17 mmol/h·L

LDH – 445.6 ± 2.1 mmol/h·L

GDH – 250.4 ± 1.7

Cholinesterase (ChE) – 656.4 ± 1.6 µg/min

Pseudocholinesterase (PChE) – 287.06 ± 1.34 µg/min

Ceruloplasmin (copper oxidase) – 3.6 ± 0.2 µmol/L

Increases in AST, ALT, ALP, GDH, and ceruloplasmin indicate hepatocyte damage and membrane injury, reflecting necrobiotic processes in the liver during extrahepatic cholestasis. In bile duct obstruction, ALP activity increases. A decrease in PChE reflects impaired hepatocyte function. ALT activity often increases before bilirubin elevation and clinical deterioration, allowing early detection of complications and adjustment of treatment.

Enzymes are widely used to assess treatment effectiveness, recovery dynamics, and prognosis. Lack of changes in enzyme activity during therapy indicates low treatment efficacy. Enzyme activity is more informative than bilirubin levels in assessing hepatic regeneration. Persistent reduction of ChE activity in chronic hepatitis indicates disease progression and poor prognosis.

However, no single biochemical test provides fully reliable results. Only a complex evaluation combined with clinical data allows an accurate assessment of liver parenchyma status in choledocholithiasis, which is important for predicting postoperative outcomes.

Thus, laboratory studies in HCLD are not always decisive. The most significant clinical and laboratory criteria include obstructive jaundice, episodes of cholangitis, and elevated bilirubin, ALT, ALP, and amylase levels. Instrumental methods play a key role in diagnosis.

Morphological examination of liver and gallbladder tissue is essential, as the most adequate understanding of pathological processes is obtained through combined structural and functional assessment. Liver biopsy was performed in 134 patients, and gallbladder specimens in 578 patients. Intraoperative marginal liver biopsy was

used for evaluation of immediate and long-term outcomes. The control group included 16 suddenly deceased individuals.

Liver failure stages were identified as follows: stage I in 57 patients, stage II in 46, stage III in 23, and stage IV in 8. CT scanning revealed focal areas of liver tissue destruction in 32 cases.

Pain syndrome with jaundice was observed in 76 patients, cholangitis in 21, liver enlargement in 65, and liver induration in 23 cases. Patients were divided into two groups: with obstructive jaundice (76 patients) and without jaundice (58 patients).

Microscopic examination revealed inflammatory and dystrophic changes in most patients, especially those with jaundice. Hepatocyte damage manifested as protein and fatty degeneration (46 cases, including 31 with jaundice). Severe morphological changes in the gallbladder correlated with disease duration exceeding 5 years and corresponded to liver pathology severity.

Long disease duration, advanced age, repeated surgery, jaundice, and liver failure led to irreversible liver and bile duct changes and fatal outcomes. In the common bile duct, dilation, mucosal thickening with folds and villous projections, smooth muscle atrophy, and pronounced leukocyte infiltration were observed, sometimes with mucosal ulceration.

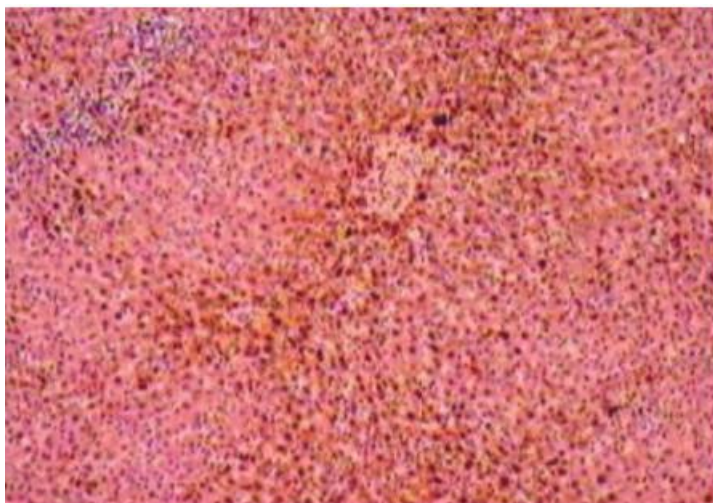


Figure 3.8. Liver biopsy of patient U., 54 years old. Protein (hydropic) degeneration of hepatocytes in obstructive jaundice. Hematoxylin and eosin staining. Magnification $\times 100$.

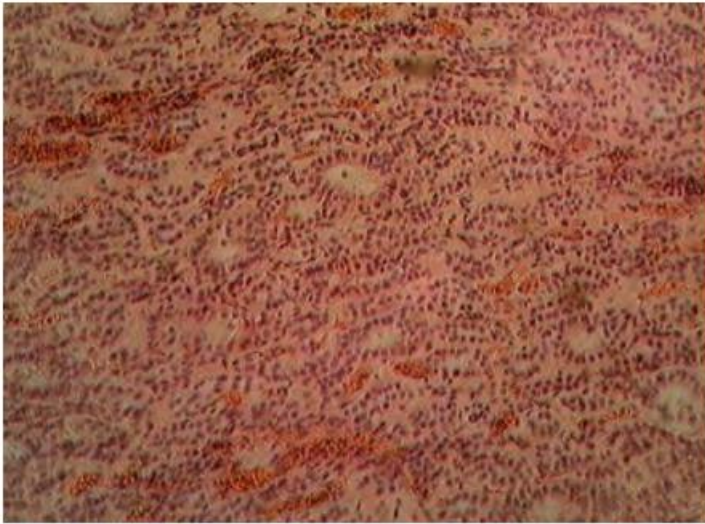


Figure 3.9. Liver biopsy of patient Ya., 63 years old. Lipid accumulation in hepatocytes is present in the form of vacuoles of varying sizes, displacing the nucleus to the periphery. The process is more pronounced in hepatocytes at the periphery of the hepatic lobules. Fatty

degeneration of the liver. Hematoxylin and eosin staining. Magnification $\times 200$.

Figure 3.10. Liver biopsy of patient K., 58 years old. Granular degeneration of hepatocytes. Hematoxylin and eosin staining. Magnification $\times 180$.

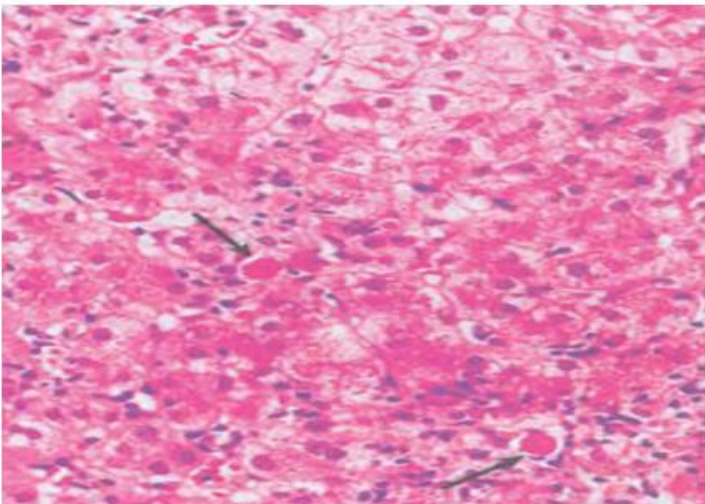


Figure 3.11. Liver biopsy of patient I., 63 years old. Granular and hyaline droplet degeneration of hepatocytes with formation of councilman bodies (arrow). Hematoxylin and eosin staining. Magnification $\times 400$.

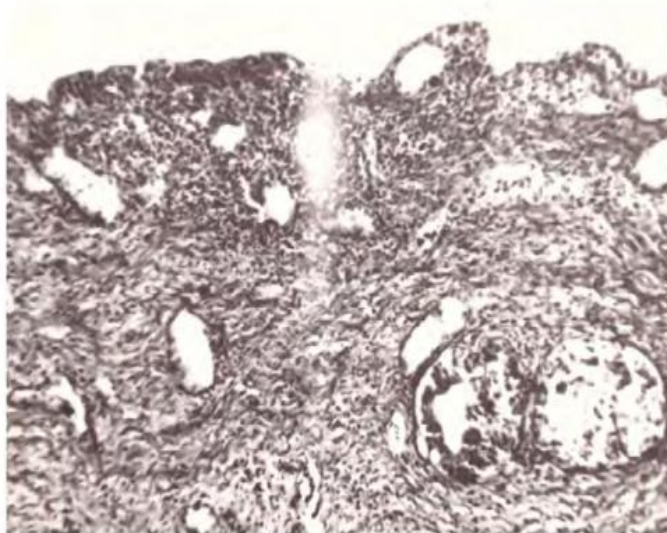


Figure 3.12. Segment of the common bile duct in patient V., 67 years old (autopsy material). Inflammatory infiltration, sclerosis, and atrophy of the mucosa. Hematoxylin and eosin staining. Magnification $\times 180$.

The structural changes in the liver identified were grouped into the following morphological syndromes:

1. chronic cholangiogenic hepatitis (58.5%),
2. chronic cholangiogenic hepatitis with exacerbation (19.4%),
3. chronic cholangiogenic hepatitis with severe hepatocyte degeneration and necrosis (12.8%),
4. chronic cholangiogenic hepatitis with cirrhotic changes (9.3%).

These syndromes were observed in 82.6% of patients with obstructive jaundice and in 17.4% without jaundice (patients who had undergone multiple biliary tract operations or had a history of Botkin's disease).

In the study of early postoperative outcomes, special attention was paid to cases with pronounced clinical signs of hepatic failure (stage III and IV). Such signs were recorded in 31 patients, and in 15 cases functional liver insufficiency was the primary manifestation of an unfavorable postoperative course. In 8 cases, stage IV hepatic failure led to hepatic coma with a fatal outcome.

In the group of patients with obstructive jaundice (76 out of 134 cases), 48 postoperative complications were observed: hepatitis and hepatorenal failure – 12, wound suppuration – 9, pneumonia – 6, cholangitis – 5, peritonitis – 4, pancreatitis – 2, multiple cholangitic liver abscesses – 2, pleural empyema – 1, subdiaphragmatic abscess – 1, hydrothorax – 1, ascites – 1, external biliary fistula – 1, failure of choledochoduodenostomy – 1, thrombosis of small branches of the pulmonary artery with pulmonary infarctions – 1, portal vein thrombosis – 1.

Causes of death in 8 patients included hepatorenal failure (6), peritonitis (1), and pulmonary artery branch thrombosis (1). The most severe morphological liver changes were also observed in this group.

Morphological examination revealed significant hepatic damage: protein and fatty degeneration, hepatocyte necrosis, and pronounced interstitial hepatitis with signs of liver cirrhosis. The severity of morphological changes increased from stage I to IV of hepatic failure.

In one patient (D., 72 years old), liver morphology was studied dynamically during surgery and at autopsy. Progressive activation of the pathological process was revealed, including extensive inflammatory infiltration with varying degrees of fibrous tissue maturity and hepatocyte degeneration up to necrosis. It is likely that the surgical intervention itself acted as a trigger for the rapid activation of destructive and degenerative processes in the liver.

Severe functional decompensation of the liver in the early postoperative period develops more readily in the presence of pronounced structural changes in hepatic parenchyma.

In 9 of 76 patients with obstructive jaundice, no complications were observed. These patients were aged 32–48 years, and the duration of jaundice was up to 20 days. Morphological examination showed less pronounced protein and fatty degeneration, hepatocyte necrosis, cholangitis, and interstitial hepatitis.

In the group without obstructive jaundice (48 patients), the postoperative period was uncomplicated in 36 cases. Thirty-three of these patients were younger than 50 years. In 32 cases, mild protein or fatty degeneration was observed, and in 16 cases, mild interstitial hepatitis was present.

Complications occurred in 7 of 48 patients: wound suppuration – 4, failure of choledochoduodenostomy – 2, pneumonia – 2. Two of these patients had undergone two previous biliary tract surgeries and showed interstitial hepatitis with initial signs of cirrhosis and obesity. One patient had marked hepatocellular degeneration. There were no fatal outcomes in this group.

Thus, significant morphological liver damage in patients with obstructive jaundice serves as a criterion for assessing disease severity, determining treatment strategy, and predicting postoperative outcomes.

In 47 cases, postoperative laboratory tests showed improvement in liver pigment-forming function and protein metabolism. An increase in total serum protein was observed in 39 patients. In 34 cases, this increase was accompanied by correction of protein composition due to an increase in albumin fraction and a decrease in γ -

globulins. In 48 cases, resolution of dysproteinemia was associated with a decrease in bilirubin levels.

According to our data, adequate biliary decompression has a positive effect on the pathological process in the liver. It reduces sinusoidal pressure, improves portal blood–hepatocyte interaction, and increases arterial inflow. However, such favorable outcomes depend on the presence of regenerative potential in hepatic parenchyma.

In some patients, rational biliary decompression may slow disease progression, although the depth of parenchymal destruction may preclude complete recovery of liver function.

After complex treatment, liver function improved significantly but not immediately and not always completely normalized. The severity of liver damage was directly correlated with disease duration and duration of jaundice. The most pronounced morphological changes were observed in patients with jaundice lasting more than 5 years.

3.3. INSTRUMENTAL METHODS OF STUDY

3.3.1. Transabdominal Ultrasound Examination

Over the past 10 years, transabdominal ultrasound examination was performed in 828 patients with choledocholithiasis aged from 20 to 88 years. In addition to stones in the common bile duct, 43 patients had chronic non-calculous cholecystitis, 598 had chronic calculous cholecystitis, 187 had postcholecystectomy syndrome, 324 had obstructive jaundice, and 178 had cholangitis. Ultrasound served as a screening method for diseases of the hepatopancreatobiliary system. The indication for ultrasound in 177 patients was jaundice of unclear etiology. In 434 out of 828 cases, choledocholithiasis was detected for the first time during ultrasound examination. Subsequently, this diagnosis was confirmed by other methods, including computed tomography, MRCP, and intraoperative cholangiography.

Transabdominal ultrasound allowed sufficiently informative visualization of the gallbladder, its contents and wall, assessment of liver and pancreas structure, detection of intrahepatic bile duct dilatation, and mainly proximal portions of extrahepatic bile ducts. The terminal portion of the common bile duct could be visualized only in 70.4% of cases. Stones in a dilated common bile duct (>8 mm) were better visualized as round or oval hyperechoic structures with or without

acoustic shadow (Figures 3.21 and 3.22). Stones smaller than 3 mm could not be detected by ultrasound.

In 828 patients, ultrasound revealed the following findings: diffuse enlargement of the liver with heterogeneous structure – 517 cases; normal-sized liver with homogeneous structure – 316; enlarged pancreas with irregular contours and increased echogenicity – 366; normal-sized pancreas with increased echogenicity – 75; gallbladder stones – 509; intrahepatic lithiasis – 16; echogenic sludge in dilated common bile duct – 226; stones in dilated common bile duct – 375; stone in dilated cystic duct – 19; deformed gallbladder without visible stones – 84; dilated common bile duct – 554; dilated and thickened intrahepatic bile ducts – 140; normal common bile duct without stones – 56; dilated Wirsung duct – 19; right kidney cyst – 19. In 16 out of 828 patients, signs of intrahepatic lithiasis were detected.

In 226 (27.3%) patients, heterogeneous echogenic sludge was found in the common bile duct. In 37 cases with high-level calculous obstruction, echogenic contours and acoustic shadow of the stone were clearly visible on sagittal echograms in the hepatic hilum, in the supraduodenal portion of the common bile duct at the confluence of the dilated hepatic and cystic ducts. In 112 patients, including 42 without signs of cholestasis, stones were located in the terminal portion of the common bile duct. On transverse echograms at the level of the pancreatic head, echogenic contours of the stone facing the transducer and its acoustic shadow were visualized.

In 34 patients, the dilated common bile duct contained diffusely heterogeneous, increased echogenic material. During surgery, these patients were found to have purulent cholangitis with thick, sludge-like bile in the duct. In 29.6% of cases, identification of echogenic structures and assessment of the distal bile duct were difficult.

During surgical treatment, errors of ultrasound diagnosis were confirmed. Non-obstructing duct stones were missed in 27 patients due to obesity, severe intestinal gas, postoperative adhesions, or inflammatory infiltrates. Thus, transabdominal ultrasound allows determination not only of localization, number, and size of stones, but also signs of obstructive cholestasis and inflammatory changes in bile duct contents.

According to our data, the diagnostic accuracy of ultrasound in choledocholithiasis was 47.4%, and sensitivity was 68.7%. The widespread use of ultrasound in clinical practice will likely improve diagnostic accuracy and reduce examination time, especially in cases of unclear cholestasis etiology. However, ultrasound should not be overestimated and, in doubtful cases, must be supplemented with other methods (CT, EUS, etc.). Difficult cases require intraoperative verification and appropriate correction. Ultrasound data can be used to construct diagnostic investigation algorithms.

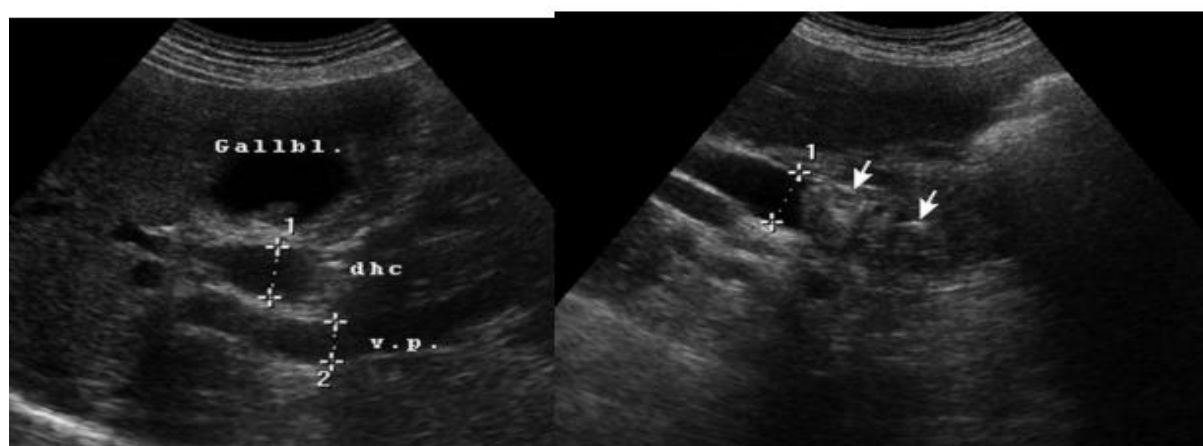


Figure 3.21. Ultrasound examination of patient V., 58 years old (a, b). Echogenic (hyperechoic) calculi are visualized in the dilated common bile duct (CBD). Choledocholithiasis.



Figure 3.22. Ultrasound examination of patient B., 68 years old. The common bile duct is dilated up to 16 mm, containing a calculus measuring up to 14.2 mm in diameter. Choledocholithiasis.

On hepatosonograms, small foci (3–7 mm in diameter) of high echogenicity were visualized within the liver parenchyma, producing a posterior acoustic shadow. In these patients, ultrasound revealed combined calculous involvement of the intrahepatic bile ducts and gallbladder without signs of obstruction of the extrahepatic bile ducts.

Cholangiolithiasis was confirmed by dilation of the lumen of the lobar duct proximal to the site of stone localization, in addition to a hyperechoic focus and a posterior acoustic shadow.

On liver echograms obtained in patients with obstructive jaundice (324 cases), a number of characteristic changes were identified: in 80.7% of cases, the liver was enlarged, its contours were smooth, and the acoustic structure was heterogeneous and mottled. This appearance was due to the alternation of areas of homogeneous parenchyma with elements of the venous system and dilated intrahepatic bile ducts, seen as multiple tubular or sac-like tortuous structures within the liver lobes.

3.3.2. Endoscopic methods

3.3.2.1. Fibrogastroduodenoscopy

At present, fibrogastroduodenoscopy (FGDS) is an essential diagnostic method in patients with diseases of the hepatopancreatoduodenal zone. Endoscopic examination allows assessment of the mucosa of the stomach and duodenum, duodenal lumen width, and patency of biliodigestive anastomoses. It also enables detection of duodenogastric reflux as a sign of duodenal motility disorders.

With FGDS, it is possible to diagnose tumors of the major duodenal papilla (MDP), duodenum, and stomach; visualize an impacted stone in the MDP with absence of bile flow into the duodenum; perform biopsy; and detect comorbid gastrointestinal pathology.

Before FGDS, patient preparation was performed. On the day before the examination, after 18:00, only liquid food and water were allowed. For oropharyngeal anesthesia, a 10% lidocaine solution was used, and for prolonged procedures, intravenous propofol and dormicum were administered.

FGDS was performed prior to endoscopic papillotomy (EPST) using the standard technique in 617 patients with choledocholithiasis (373 women and 244 men) aged 24 to 79 years. Among them, 129 patients had obstructive jaundice, 82 had chronic pancreatitis, and 37 had postcholecystectomy syndrome.

Attention was paid to direct and indirect signs of disease. General endoscopic signs of hepatopancreatoduodenal pathology included changes in the configuration of the duodenal "C-loop," mucosal relief and color alterations, wall deformation, and narrowing of the intestinal lumen.

Indirect signs included: pronounced duodenitis of the descending part; coarse mucosal folds in the postbulbar region; focal duodenitis in the parapapillary zone; duodenal dyskinesia with retroperistalsis; active bile reflux through the MDP or

impaired bile passage; presence of duodenogastric reflux (DGR); bulging of the posterior gastric wall in the fundal region; and isolated gastric varices.

FGDS revealed the following findings: chronic gastritis – 239 cases (atrophic – 143, hypertrophic – 77, erosive – 19); chronic gastroduodenitis – 112 (erosive – 21); esophagitis – 12; duodenogastric reflux – 146; gastric antrum polyp – 24; delayed bile flow through the MDP – 137; duodenal diverticulum with diverticulitis – 53; deformity and narrowing of the duodenal bulb – 23; papillitis – 46.

A clear age-related increase in atrophic gastritis was noted: it was not observed in patients under 30 years, but its frequency increased with age, reaching 57.3% in patients over 65 years.

In chronic gastritis, unfavorable prognostic signs included intestinal content regurgitation and pharmacoresistant pyloric insufficiency. It is considered a mistake to perform cholecystectomy and bile duct surgery in patients with chronic acalculous cholecystitis and duodenostasis, as their condition usually does not improve and they become recurrent hospital patients.

Duodenal erosions were found in 21 patients, mainly in the bulb. In combined erosive lesions of the stomach and duodenum, gastric erosions were more often located in the pyloroantral region (17 patients).

In choledocholithiasis complicated by chronic pancreatitis, diffuse duodenitis (16 patients) was more common, with predominant involvement of the postbulbar duodenum and papillitis.

Persistent peripapillary inflammatory and dystrophic changes of the duodenal mucosa (edema, hyperemia, fragility, whitish deposits, etc.), along with deformation of the posterior-medial wall of the descending duodenum and indentation of the gastric antrum, corresponded to long-term recurrent disease.

A duodenal diverticulum (53 patients) was located on the medial wall of the descending duodenum near the MDP. The endoscopic appearance of diverticulitis depended on the severity of inflammatory and erosive-ulcerative changes.

Papillitis (46 patients) was characterized by marked hyperemia, mucosal edema, thickening of villi, and distortion of the normal papillary pattern, making its contours irregular. The size of the MDP increased up to 1.5 cm.

Endoscopy is a reliable method for assessing the gastric, duodenal, and papillary mucosa, allowing clarification of the location, shape, and size of the papilla and detection of inflammatory changes. Particular attention was paid to the postbulbar duodenum as the site of potential surgical intervention (parapapillary diverticula, papillitis, and signs of possible stone impaction or purulent cholangitis).

If a bile-impregnated obstructed stent is present in a biliodigestive anastomosis, it can be removed during FGDS, which was performed in 3 cases.

Thus, FGDS is an essential diagnostic method in hepatopancreatoduodenal diseases, particularly choledocholithiasis. It allows detection of comorbid gastric and duodenal pathology, parapapillary diverticula, impacted stones in the MDP, selection of appropriate treatment tactics, and performance of therapeutic endoscopic procedures (EPST, lithotripsy, etc.).

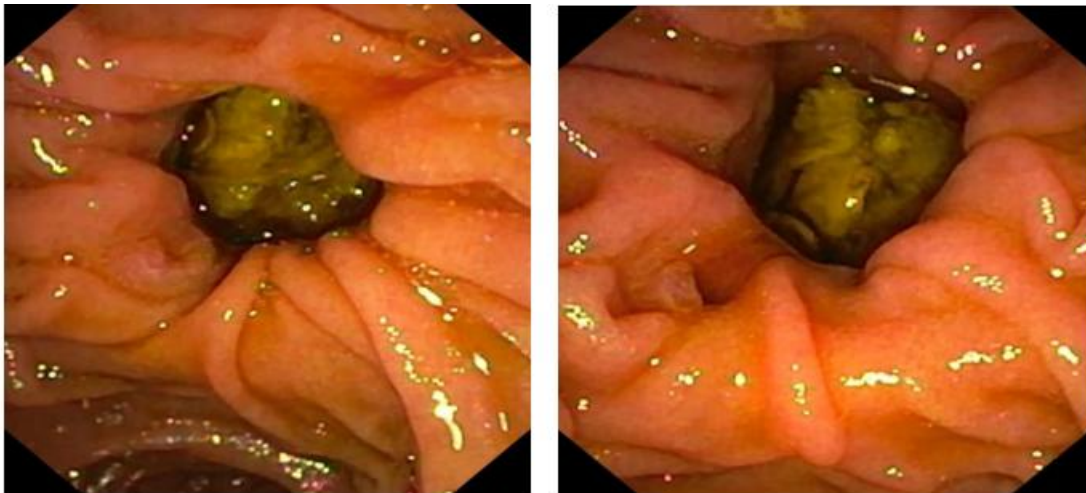


Figure 3.32. FGDS of patient G., 63 years old. Presence of parapapillary diverticula causing alteration of the anatomical relationships within the duodenopancreatobiliary region.

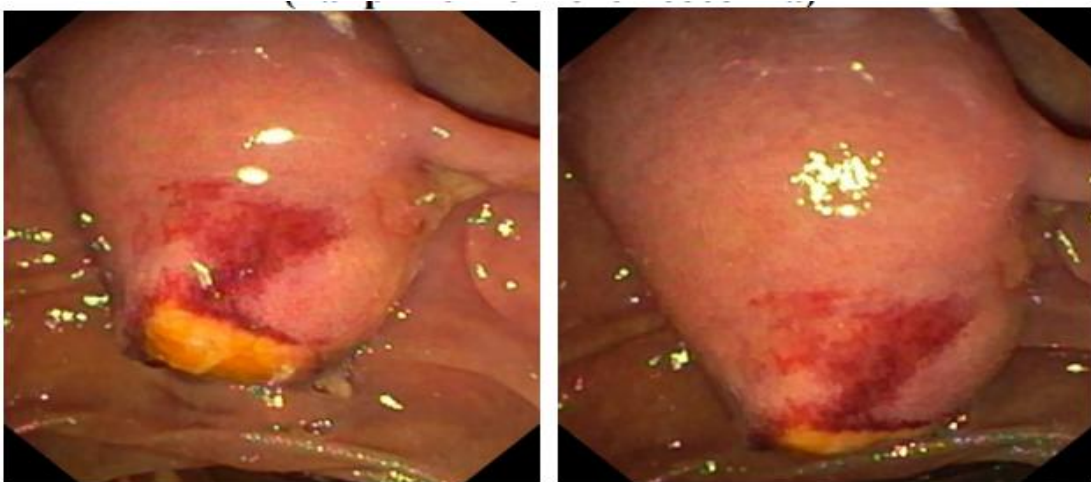


Figure 3.33. FGDS of patient Z., 60 years old. Stone impacted in the major duodenal papilla (papillary tension and edema).

3.3.2.2. Cholangioscopy

Radiological methods do not always fully reflect all possible changes in the biliary system. Fibrocholangioscopy allows direct endoscopic visualization. The disadvantages of previously proposed cholangioscopy devices include limited mobility of the distal end of the instrument, poor image quality, high susceptibility to mechanical damage, and a small diameter of the working channel.

At present, peroral cholangioscopy can be performed using an ultrathin transnasal gastroscope (after papillotomy up to 8 mm in length).

Indications for laparoscopic cholecystectomy followed by laparoscopic cholangioscopy included: dilation of the common bile duct (>1 cm) detected intraoperatively; preoperative diagnosis of choledocholithiasis with unsuccessful attempt at endoscopic papillotomy (EPST); obstructive jaundice; purulent cholangitis; diagnostic uncertainty regarding choledocholithiasis (in the absence of convincing ERCP, MRCP, and other data); and the presence of small gallbladder stones with a wide cystic duct.

Absolute contraindications for laparoscopic choledochoscopy include stroke and acute myocardial infarction. Relative contraindications include severe respiratory and cardiac failure, peritonitis, intolerance to anesthesia, grade III–IV obesity, and previous surgical interventions in the operative field.

Cholangioscopy was performed in the clinic in 231 patients with choledocholithiasis aged 24 to 80 years using a gastrointestinal video endoscope (GIF-XP150N “Olympus”, Japan) with an outer diameter of 5.5 mm (Figure 3.37). There were 144 women (62.3%) and 87 men (37.6%). Fibrocholangioscopy was performed in combination with other intraoperative examination methods: inspection, palpation, cholangiography, and probing.



Figure 3.37. Gastrointestinal video gastroscope “Olympus” used for cholangioscopy.

Sterilization of the device was carried out in formalin vapors followed by treatment with 76% alcohol.

Access through the cystic duct stump is less traumatic, but more often requires dilation and is usually used in cases of a narrow common bile duct and small stones. The disadvantages of the transvesical approach include the impossibility of manipulation in cases of an obliterated cystic duct, the need for bougienage, and the ability to evaluate only the terminal part of the common bile duct.

In cases of high predictive value of choledocholithiasis, dilation of the common bile duct (>8 – 10 mm), large stones, and cholangitis, a choledochotomy approach for laparoscopic fibrocholangioscopy was indicated and used in 76 cases.

During the procedure, the proximal bile ducts were inspected, their patency, elasticity, and the contractility of the sphincter of Oddi were assessed, as well as inflammatory changes of the common bile duct mucosa and the condition of bile. Fibrocholangioscopy provided a more complete picture of cholangitis (mucosal edema, hyperemia, turbid or purulent bile, fibrin deposits).

During cholangioscopy, bile samples were taken for microbiological examination, and irrigation with antiseptic ozonated solutions and antibiotics was performed. If necessary, biopsy of the bile duct or major duodenal papilla mucosa was carried out. In cases of papillary tumors, cholangioscopy with biopsy allowed verification of the process stage and determination of the level of obstruction, which is important for adequate surgical planning.

In 218 patients, choledocholithiasis was clearly identified during cholangioscopy, and the bile duct mucosa was examined. Between 2 and 7 stones were extracted using a Dormia basket. Small stones and sludge were removed by irrigation through the choledochotomy opening.

Under cholangioscopic control, laser lithotripsy was performed in 43 cases. In 34 patients, inflammatory changes of the hepatocolodochus mucosa were detected that were not clinically evident and not diagnosed by other methods. These included hyperemia, edema, vascular injection, and erosions.

The diagnostic value of fibrocholangioscopy is high: sensitivity 99.3%, specificity 98.1%, accuracy 98.6%. Advantages include absence of radiation exposure, surgeon-controlled performance, and low cost.

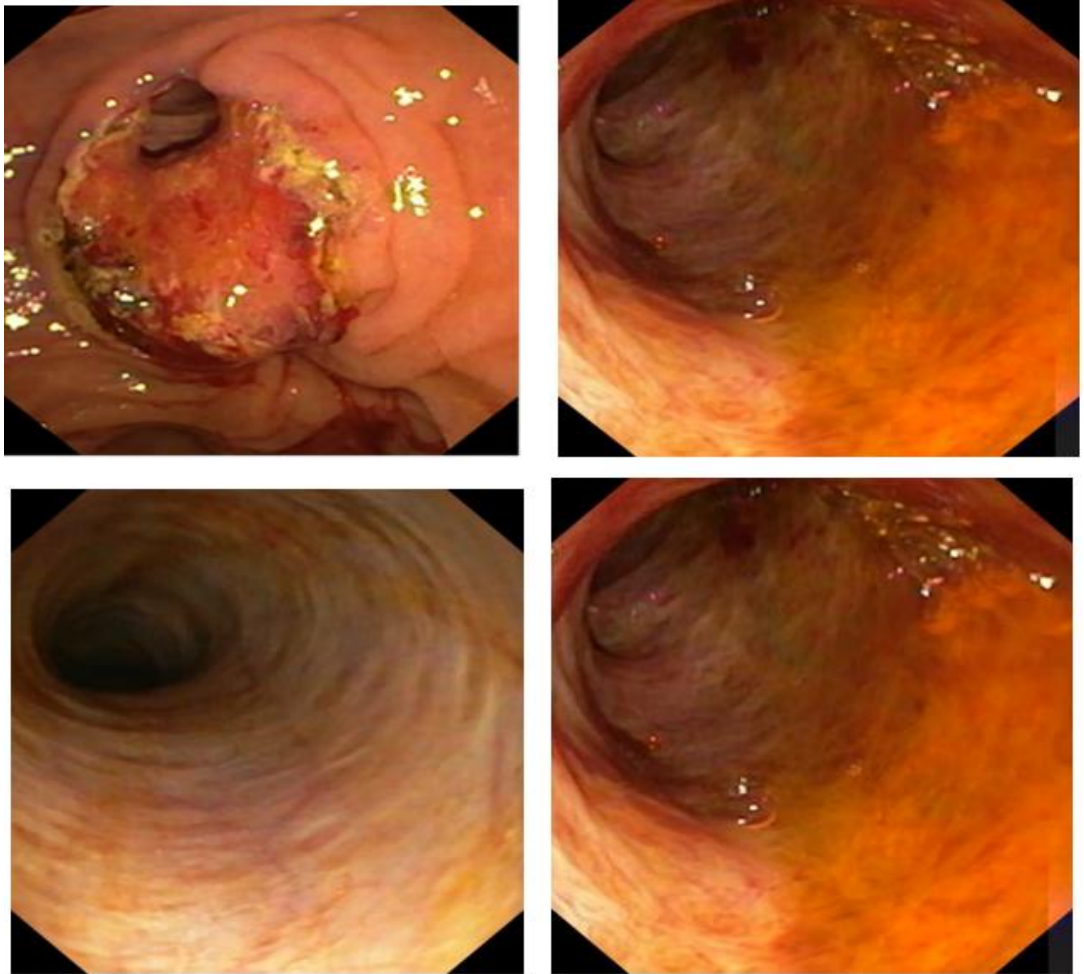


Figure 3.38. Cholangioscopy in patient Ch., 55 years old. Visualization of different segments of the common bile duct (CBD).

Chapter IV. Treatment of Patients with Cholecystochledocholithiasis. Minimally Invasive, Novel and Traditional Treatment Methods

4.1. Preoperative Preparation

Preoperative preparation in patients with cholecystochledocholithiasis was aimed at improving the functional state and compensatory capacities of the liver, other organs, and body systems, as well as eliminating pathological manifestations of concomitant diseases. The goal was to increase the functional reserves of the organism to at least a level sufficient for the patient to tolerate surgery without complications.

However, a clear differentiation of patients is necessary, since they present varying degrees of hepatic and renal dysfunction, bile duct involvement, and changes in other organs. This stratification was performed using a risk scale developed by us.

Preoperative measures included corrective therapy aimed at eliminating the pathological symptom complex and normalizing liver and systemic function. The duration of preparation ranged from 1 day to 2 weeks.

In cases of anemia, hypoproteinemia, and electrolyte imbalance, the operative and anesthetic risk significantly increases. A plasma albumin level below 30 g/L indicates a high surgical risk. It is essential to fully correct water-electrolyte imbalance, protein metabolism disorders, and acid–base disturbances.

Multimodal preoperative preparation (correction of metabolic acidosis, reduction of dehydration and hypovolemia, restoration of diuresis, and improvement of central and peripheral hemodynamics) significantly reduces operative risk.

Special correction is required in elderly patients and in those with obstructive jaundice, cholangitis, obesity, cardiac disease, bronchial asthma, hypertension, and diabetes mellitus.

In patients with obstructive jaundice, complex treatment includes urgent external biliary drainage, reduction of endogenous intoxication (lympho- and hemosorption), and moderate substitution and stimulation therapy to improve liver function.

For detoxification and bilirubin elimination, forced diuresis after hemodilution was used (correction of hypovolemia, electrolyte imbalance, cardiovascular stabilization, and administration of diuretics such as furosemide 40–80 mg, potassium preparations, and osmotic diuretics such as 10% mannitol solution at 1 g/kg body weight combined with 2.4% aminophylline 20 ml).

Supportive measures included gastric and intestinal lavage and dietary management.

To improve liver function, the following were administered intravenously: 10–20% glucose solution (600–800 ml with insulin), aminophylline, novocaine, glucocorticoids (hydrocortisone 250–1000 mg according to indications), hepatoprotectors (LIV-52), and vitamins B1, B6, B12, and C.

Electrolyte and protein correction included potassium, calcium chloride, plasma, albumin, Ringer–Locke solution, reopolyglucin, hemodez, and protein hydrolysates.

Metabolic correction included glutamic acid, lipoic acid, potassium orotate, cocarboxylase, ATP, and trypsin inhibitors.

Immunocorrection included levamisole, gamma globulin, methyluracil, and ultraviolet irradiation of blood.

Cardiovascular stabilization was achieved using cardiac glycosides, antihypertensive agents, and metabolic support.

Anticoagulation and hemostatic correction included calcium chloride, vikasol, dicynone, and fibrinogen.

Antibiotic prophylaxis was administered preoperatively and postoperatively, most commonly ceftriaxone with metronidazole or ampicillin with metronidazole. Short-course high-dose antibiotic regimens were more effective in achieving bactericidal bile concentrations.

Antioxidant therapy was used to inhibit lipid peroxidation processes.

Anabolic hormones were administered to improve myocardial efficiency and metabolic stability.

In patients with external bile fistulas, early bile reinfusion and vitamin supplementation were essential to prevent acholic disease.

A risk stratification scale was developed to guide individualized therapy and surgical planning. Depending on risk grade (I–IV), different treatment strategies and surgical volumes were selected.

At higher risk levels, staged approaches were used, including detoxification methods (hemo- and lymphosorption, dialysis techniques), regional infusion therapy, and minimally invasive biliary decompression (percutaneous transhepatic cholangiostomy, laparoscopic cholecystostomy, or endoscopic papillotomy with nasobiliary drainage).

In severe cases, urgent minimal decompressive surgery was performed to relieve cholestasis.

After adequate preparation, patient condition improved significantly, with reduction of intoxication and partial normalization of biochemical parameters. In many cases, surgery was postponed until bilirubin levels decreased, reducing operative risk.

In recent years, postoperative complications decreased from 28.6% to 9.4%, and mortality from 5.7% to 0.9%.

Treatment and preoperative preparation of patients with choledocholithiasis are best performed in specialized hepatobiliary centers with appropriate multidisciplinary support.

4.2. Endoscopic Transpapillary Surgical Interventions

Endoscopic papillary sphincterotomy (EPST) followed by laparoscopic cholecystectomy (LCE) is one of the leading methods for treating choledocholithiasis in many medical institutions due to its relative minimally invasive nature and acceptable long-term outcomes. It is recognized as an optimal method of biliary decompression in the first stage of treatment of obstructive jaundice.

The following indications for EPST were identified:

- choledocholithiasis with signs of obstructive jaundice and/or cholangitis;
- choledocholithiasis with stenosis of the major duodenal papilla in patients with calculous cholecystitis and high operative risk;
- microlithiasis and stenosis of the major duodenal papilla without gallbladder stones;
- impacted stone in the distal common bile duct with clinical signs of jaundice and cholangitis.

At the Endoscopic Surgery Department of the V.K. Gusak Institute of Emergency and Reconstructive Surgery, 617 EPST procedures were performed over the last 8 years, accounting for 82.3% of patients with complicated choledocholithiasis. There were 189 men (30.6%) and 428 women (69.4%), with a mean age of 54.3 ± 2.1 years.

In 460 patients (74.6%), a two-stage treatment approach was used:

- Stage I – EPST with stone extraction
- Stage II (after 1–3 days) – laparoscopic cholecystectomy.

Obstructive jaundice was present in 439 patients (71.3%), while choledocholithiasis with obstructive jaundice and cholangitis was observed in 90 patients (14.7%). Concomitant diseases (arterial hypertension, ischemic heart disease, diabetes mellitus, post-infarction and atherosclerotic cardiosclerosis, etc.) were found in 335 patients (54.3%), including 175 patients (52.3%) with two or more comorbid conditions.

Before EPST, endoscopic retrograde cholangiopancreatography (ERCP) was performed, which provided more accurate diagnosis of complicated choledocholithiasis (see Section 3.3.4.2). Primary choledocholithiasis was detected in 460 cases (74.6%), residual in 110 (17.8%), and recurrent in 47 (7.6%).

During fibrogastroduodenoscopy, in 25.6% of cases edema and hyperemia of the major duodenal papilla (MDP) and parapapillary region were observed, as well as prolapse of tissues or the stone itself into the duodenal lumen. In such cases, retrograde cannulation of the common bile duct during ERCP was technically difficult.

The presence of fine particulate material in the sphincter of Oddi region (cholesterol crystals, sludge-like masses, fibrin flakes up to 3 mm in size) is defined as **microcholedocholithiasis**.

During FGD, in 158 patients signs of stone impaction in the distal common bile duct were detected (enlarged, edematous, firm papilla), later confirmed by endoscopic ultrasonography (EUS).

A parapapillary diverticulum was identified in 27 cases (4.3%). In 11 patients (1.8%), the MDP was located inside a duodenal diverticulum, confirmed using a side-viewing duodenoscope. These anatomical variations significantly complicated cannulation of the papilla and performance of EPST.

Various atypical endoscopic findings of choledocholithiasis were observed. Of 617 patients, complete visualization of the MDP was achieved in 591 cases (95.7%).

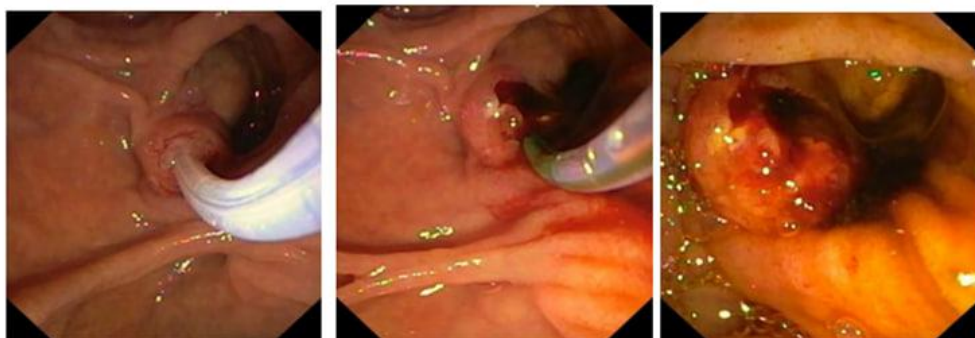


Figure 4.1. Cannulation of the ampulla of the major duodenal papilla (BDS) followed by standard endoscopic papillosphincterotomy (EPST) in patient K with severe papillostenosis.



Figure 4.2. Non-cannulation (atypical) needle-knife papillosphincterotomy in patient B with an impacted stone in the ampulla of the major duodenal papilla (BDS).

We used a fiberoptic gastroduodenoscope with a frontal-viewing optic and a distal cap. In 2 cases (0.3%), access to the major duodenal papilla (ampulla of Vater) was not achieved due to technical difficulties after previous gastric resection with gastrojejunostomy formation. In such patients, it is advisable to plan surgical treatment using an antegrade approach to the biliary ducts.

ERCP allowed a fairly clear assessment of the anatomical features of the distal common bile duct (CBD), the type of obstruction (papillary stenosis, biliary calculi, disruption of the papillary orifice due to a passed stone), and its level (acute blockage of the major duodenal papilla, intramural segment of the CBD).

Three clinical variants of acute papillary obstruction were identified by ERCP in 158 (25.6%) patients (Table 4.2). At the same time, signs of progressive obstructive jaundice were observed in 77 (48.7%) of them, including 15 (20.2%) cases combined with cholangitis. The clinical presentation of the pancreatic type of papillary obstruction was seen in 11 (7.0%) patients, the biliary type in 77 (48.7%), and the mixed type in 70 (44.3%). In 18 (11.4%) cases, microcholedocholithiasis was combined with acute papillitis, which aggravated the course of the disease.



Figure 4.3.

Total endoscopic papillosphincterotomy (EPST) in patient B. A stone and cream-like pus are visible in the major duodenal papilla (ampulla of Vater).



Figure 4.4. Sphincterotomy of the major duodenal papilla in the same patient.

In 81 (13.2%) patients, mechanical biliary lithotripsy was performed with 1 to 3 treatment stages. Difficulties arose in cases of large, impacted, or high-located stones, as well as in choledochal strictures after choledochotomy.

All patients after EPST and nasobiliary drainage underwent

irrigation of the bile ducts with a warmed 0.25% novocaine solution, as well as 5–10 ml of a 1% dioxidine solution.

The adequacy of the performed EPST was assessed by contrast radiography of the common bile duct immediately after the intervention.

In 52 (8.4%) cases, contact laser choledocholithotripsy after EPST was performed using a holmium laser and fiberoptic cholangioscopy. Stone fragments were flushed into the duodenum using antiseptic solutions.

In 198 (32.1%) patients, EPST and retrograde endoscopic stone extraction were technically difficult due to specific anatomical features (an impacted stone in the major duodenal papilla in 192 cases, and multiple stones—more than five—in the common bile duct).

The average duration of EPST was 110.8 ± 35.4 minutes.

In the early postoperative period, complications after EPST occurred in 73 (11.9%) patients: acute pancreatitis in 38 (6.2%), which was resolved by days 3–4 with conservative treatment; bleeding from the papillotomy site in 15 (2.5%); cholangitis in 9 (1.5%); pleuropneumonia in 4 (0.6%); and enzymatic peritonitis in 7 (1.1%).

Bleeding from the papillotomy site was managed endoscopically in 8 cases, conservatively in 5, and in 2 cases, due to failure of conservative hemostatic therapy, laparotomy, duodenotomy, and ligation of the bleeding vessel were performed.

Nine (1.4%) patients died: 8 from progressive severe pancreatic necrosis and 1 from pulmonary embolism.

For complication prevention, anticholinergic agents, ganglion blockers, sedatives, and, when indicated, antibiotics were used in premedication. Patients with risk factors for pancreatitis received somatostatin (octreotide) before and after EPST.

Since acute pancreatitis developed in 38 (6.2%) patients after EPST and 8 patients died from progressive severe pancreatic necrosis, the clinic developed a “Method for diagnosing the stage of pancreatic abscess formation” (UA utility model patent No. 26849, 21.05.2007).

The method includes dynamic transabdominal ultrasound examination with assessment of pancreatic contour, parenchymal structure, surrounding organs, peripancreatic tissue, and the presence or absence of fluid collections.

If a hypoechoic triangular or spindle-shaped area with indistinct borders is detected, the infiltration stage is diagnosed. If a hyperechoic area in the form of a 2–3 mm cavity is present, the sequestration stage is diagnosed. If a hyperechoic capsule with fluid content inside is present, the stage of purulent liquefaction is diagnosed.

Based on these dynamic changes, appropriate intensive complex therapy was administered. Development of pancreatic necrosis was prevented in 30 of 38 patients with post-EPST acute pancreatitis.

Thus, EPST is an effective (98.5%) but invasive procedure in the treatment of complicated choledocholithiasis. It allows elimination of choledocholithiasis, stenosis of the major duodenal papilla, and its manifestations, or preparation of patients for elective surgery.

A two-stage treatment approach (EPST + laparoscopic cholecystectomy) is advisable in specialized surgical centers, especially in elderly and high-risk patients with severe comorbidities.

4.3 Laparoscopic laser choledocholithotripsy

Currently, many surgeons prefer a two-stage approach for the treatment of cholecystocholedocholithiasis, especially when complicated. At the first stage, EPST is performed with various lithotripsy techniques and removal of stones from the common bile duct. At the second stage (after 1–3 days), laparoscopic cholecystectomy (LCE) is performed.

However, the number of complications in two-stage procedures and the rate of unsatisfactory outcomes remain significant. EPST also has several contraindications, including anatomical features of the major duodenal papilla, large or multiple stones in the common bile duct, etc.

At the Department of Surgery of the Institute of Emergency and Reconstructive Surgery named after V.K. Gusak, a single-stage laparoscopic method of intraoperative choledochoscopy and contact laser lithotripsy was developed and implemented.

We used the Dornier Medilas H2O laser system and the Olympus laparoscopic system (Japan). The system is a holmium YAG laser for stone and soft tissue treatment, with a power of 20 W and a wavelength of 2.1 microns, with a pulse duration of 350 milliseconds.

The laser lithotripter is equipped with flexible light guides for laparoscopic and endoscopic procedures.

The indication for laser choledocholithotripsy was the presence of one or more stones in the common bile duct, regardless of size.

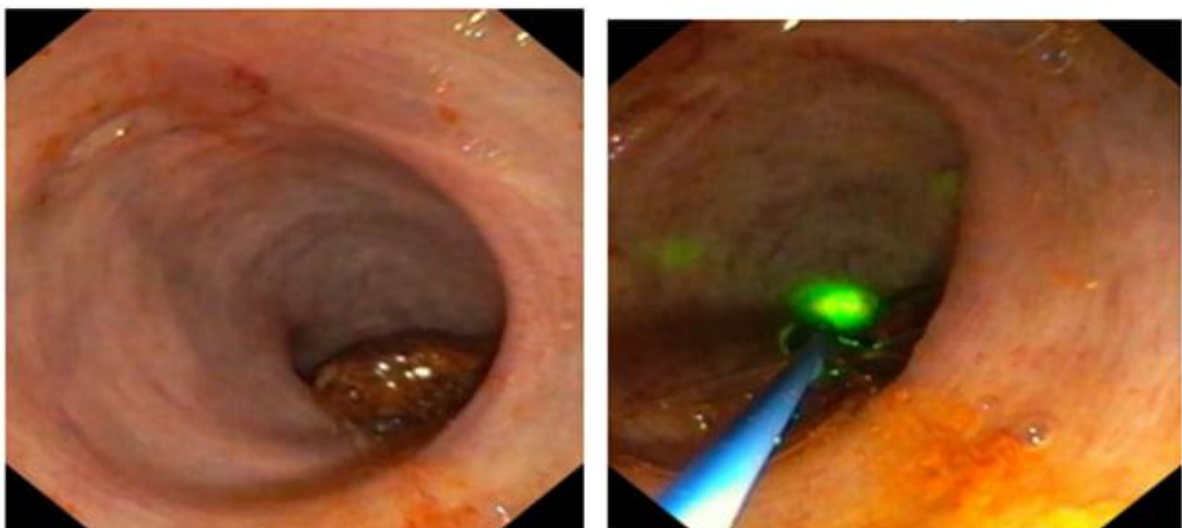


Figure 4.7. Laparoscopic laser choledocholithotripsy of the common bile duct (CBD) in patient M.

The operation was started in the same way as laparoscopic cholecystectomy. After dissection of the gallbladder neck structures, the cystic artery was clipped and transected. The distal part of the cystic duct (from the gallbladder side) was also clipped.

Through the cystic duct stump, the distal part of the “Olympus” CHF P20 choledochoscope (working diameter 4.9 mm, instrument channel 2.2 mm) was introduced into the common bile duct (CBD). If the cystic duct diameter was insufficient, it was mechanically dilated using a dissector. If dilation was not possible, choledochotomy and choledochoscopy were performed.

When a stone was visualized in the CBD, a Dornier Medilas H20 holmium laser was directed to it, and the stone was fragmented into pieces up to 2–3 mm in size. Laser power was adjusted depending on stone density. Stone fragments were flushed into the duodenum, after which patency of the distal CBD was verified. In 2 cases, balloon dilation of the major duodenal papilla (MDP) was performed.

After a final inspection of the bile duct lumen, the choledochoscope was removed from the CBD.

Unlike other laser systems, the holmium laser does not generate visible vapor bubbles, allowing clear visualization of anatomical structures and stones. The vapor bubble diameter is several millimeters and depends on laser pulse energy. The lifetime of the bubble, like the laser pulse itself, is approximately 500 microseconds and is not perceived by the human eye; therefore, the bubbles remain invisible.

In cases of multiple or large stones, lithotripsy was repeated until all fragments were flushed into the duodenum with irrigation fluid. The lithotripsy process was performed in real time.

Using the described technique, 46 patients with cholecystocholedocholithiasis were operated on. Among them, 29 (63.0%) were women and 17 (37.0%) were men, with a mean age of 52.3 ± 1.4 years.

All 46 patients had obstructive jaundice, and 16 (34.8%) had purulent cholangitis. In 37 (80.4%) cases, stones were freely located within the CBD (Figure 4.7), while in 9 (19.6%) cases, stones were impacted in the terminal part of the CBD.

After laparoscopic laser choledocholithotripsy and stone extraction, a control choledochoscopy was performed (Figure 4.8). Biliary drainage was performed through the cystic duct stump in 23 (50.0%) patients and through a choledochotomy incision in 13 (28.3%) patients.

In 10 (21.7%) patients, primary closure of the CBD was performed with drainage, and the cystic duct stump was clipped. External drainage was used in cases of cholangitis, choledochotomy access, and marked preoperative hyperbilirubinemia.

The gallbladder was extracted through an incision above the umbilical ring.

4.4 Combined (antegrade + retrograde) treatment methods

Stone removal from the CBD is often technically impossible using endoscopic methods alone. Non-standard situations occur in patients with biliodigestive anastomoses after Billroth-II gastric resection or total gastrectomy, where endoscopic access to the major duodenal papilla is difficult.

In such cases, combined procedures under ultrasound, radiological, and endoscopic control expand the possibilities of minimally invasive surgery for choledocholithiasis of any localization.

Indications for combined minimally invasive procedures in 23 patients with choledocholithiasis in non-standard situations included:

- Biliary decompression in severe obstructive jaundice to prepare for a second-stage operation – 8 (34.8%)
- Technical inability to cannulate the major duodenal papilla (periampullary diverticulum, impacted stone in the terminal CBD, or stricture of the distal CBD) – 7 (30.4%)
- Severe patient condition making EPST with retrograde extraction unsafe – 4 (17.4%)
- Previous surgical operations preventing endoscopic access to the papilla without additional tools – 2 (8.7%)
- Anatomical peculiarities of the major duodenal papilla with inadvertent guidewire passage into the main pancreatic duct – 2 (8.7%)

In 8 (34.8%) elderly or critically ill patients with severe obstructive jaundice and comorbidities, percutaneous transhepatic biliary drainage (PTBD) was performed with placement of the drain beyond the obstruction into the duodenum to avoid bile loss. This allowed preparation for the next stage—EPST with retrograde stone extraction.

It should be noted that after PTBD and resolution of obstructive jaundice, patients tolerated EPST better.

In 7 (30.4%) patients, the major duodenal papilla was located within or near a duodenal diverticulum. Differentiation of the papillary orifice was achieved only via an antegrade guidewire placed during percutaneous transhepatic cholangiostomy. Subsequently, EPST with stone extraction was performed.



Figure 4.9. FGDS in patient D. Periampullary diverticula. Endoscopic papillosphincterotomy (EPST) performed over a guidewire advanced antegradely (percutaneously via a transhepatic route).

In 2 (8.7%) patients, it was not possible to pass a guidewire or other manipulator in a retrograde manner into the lumen of the common bile duct due to anatomical features of the ampullary region of the major duodenal papilla (MDP). The guidewire immediately entered the main pancreatic duct, making endoscopic papillosphincterotomy (EPST) extremely dangerous. A papillotome was successfully advanced into the common bile duct through the MDP over a guidewire placed via percutaneous transhepatic cholangial drainage (PTCD).

In 2 (8.7%) cases with a history of residual choledocholithiasis, patients had previously undergone Billroth II gastric resection with gastrojejunostomy. Therefore, using a method developed in our clinic, a manipulation catheter was advanced antegradely through PTCD, alongside the stone, into the duodenum, and then with a guidewire into the gastric stump or afferent intestinal loop. After endoscopic visualization of the catheter and guidewire, the guidewire was secured with a Dormia basket introduced through the endoscope channel. Using reverse traction on the guidewire or manipulation catheter, the endoscope was guided to the major duodenal papilla. Retrograde endoscopic lithoextraction and antegrade external or external-internal biliary drainage were then performed.

4.5. Postoperative management of patients

Surgical interventions on the bile ducts for choledocholithiasis are extensive and carry significant risk for the patient. Major tissue trauma and severe disturbances of homeostasis caused by the underlying disease place considerable stress on the body's compensatory mechanisms in the postoperative period.

In the early postoperative period, there is impaired pulmonary ventilation, reduced vital lung capacity, and decreased forced expiration. Therefore, patients require breathing exercises, training in effective coughing techniques, and maintenance of overall physical activity.

Surgical stress induces changes in metabolic processes. Features of postoperative metabolism (days 1–5) include: adrenergic–corticosteroid phase, increased protein breakdown, hypoalbuminemia, azotemia, fluid and sodium retention, oliguria,

increased potassium and magnesium excretion in urine, decreased glucose tolerance, and hyperketonemia [72, 101, 109, 115].

If no preoperative or intraoperative disturbances in water–electrolyte balance, plasma protein concentration, or hemoglobin levels were present, infusion therapy was administered in adequate volumes according to daily fluid and electrolyte requirements (2.5–3 L/day). In patients with severe water, electrolyte, and protein imbalance, full infusion therapy was performed, including plasma, albumin, protein, and rheopolyglucin administration.

To maintain water–electrolyte balance, balanced electrolyte solutions such as Acesol were used at a dose of 1.5 L/m². In cases of oliguria or renal failure, potassium and magnesium were not administered. Significant albumin losses were appropriately corrected postoperatively.

Prolonged mechanical ventilation was used in all cases of acute water–electrolyte imbalance. Transition to spontaneous breathing was performed only after correction of blood volume, water, electrolyte, and acid–base balance, as well as adequate circulating blood volume, hemoglobin, and hematocrit levels.

After surgery, patients were managed in intensive care or resuscitation units. Key physiological parameters were monitored every 1–3 hours using special charts. This allowed timely assessment of postoperative dynamics and prompt correction of therapy.

Well-planned preoperative preparation and carefully performed surgery generally ensured an uncomplicated postoperative course. In essence, postoperative intensive care is a continuation of treatment started before and during surgery.

All postoperative measures were divided into:

1. infection control
2. correction of pathological changes related to the primary disease
3. support of vital organ function
4. parenteral nutrition and infusion therapy

Reduction of pain using adequate analgesia improves respiratory depth, enhances lung ventilation, and stimulates cardiac function.

In elderly and senile patients, infusion-transfusion therapy was performed considering circulatory type, as cardiovascular systems in such patients have reduced tolerance to fluid overload. Rapid infusion may cause right ventricular overload and acute right-sided heart failure. Infusion rates should not exceed 60 drops/min, and in circulatory insufficiency 30 drops/min, at 10–15 ml/kg, with simultaneous cardiotonic and diuretic therapy.

The most dangerous complications in choledocholithiasis patients leading to death include hepatorenal failure, acute pancreatitis, and septic complications of cholangitis (peritonitis, pneumonia, abscesses).

Special attention was given to prevention and treatment of hepatic failure (see section 4.1). Patients admitted already with stage II–III hepatic failure required transfer to intensive care after surgery. They underwent active therapy under continuous biochemical monitoring: infusion via umbilical vein, subclavian vein cannulation with central venous pressure control, staged peritoneal dialysis, hyperbaric oxygenation, lymph drainage, lympho-, hemo- and enterosorption.

Joint management of such severe patients by surgical and intensive care teams significantly improves treatment outcomes.

Management of patients with external biliary fistulas after surgery has specific features crucial for favorable outcomes. The distal end of the drain was connected to a closed sterile bile collection system. Daily bile output reflects the functional state of the liver and biliary system. In early postoperative days, bile output decreased to 300–350 ml, then increased from days 4–6, returning to 500–800 ml by days 9–11.

Early reinfusion of filtered bile into the digestive tract via a duodenal tube was considered essential. A specially designed adjustable stand allowed regulation of bile drainage under fistulocholangiography control. After confirming free bile flow into the duodenum, the drain was removed, usually by the end of the second week after choledochostomy.

Longer drainage was required in patients with obstructive jaundice, purulent cholangitis, destructive cholecystitis, and cholecystopancreatitis.

Systematic bacteriological monitoring of bile was performed to guide antibiotic therapy based on microbial sensitivity.

Postoperative complications include cardiovascular and pulmonary disorders (myocardial infarction, pneumonia, thromboembolism), hepatorenal failure, pancreatitis, wound infection, and biliodigestive anastomotic failure. Treatment is particularly difficult in elderly debilitated patients.

Principles of treatment of purulent cholangitis include:

1. Preliminary minimally invasive biliary decompression (PTCD, cholecystostomy, EPST, laser lithotripsy, nasobiliary drainage).
2. Definitive decompression or biliodigestive reconstruction.
3. Antibiotic therapy guided by microbiology and sensitivity testing.
4. Detoxification therapy (forced diuresis, hemosorption, lymphosorption, thoracic duct drainage, laser blood irradiation, ozonized saline infusion).

5. Percutaneous drainage of liver abscesses under imaging guidance.
6. Cholesterol sorption and laser bile irradiation in severe bacterobilia.
7. Continuous monitoring of bile and blood cultures and laboratory parameters.

Antibiotic therapy must consider intrahepatic bile duct sclerosis causing cholestasis and infection persistence despite restored duct patency.

Combination antibiotic regimens (e.g., morphocycline, metronidazole, lincomycin, gentamicin, trichopol) were used in high-risk patients.

Adjunct therapy included hyperbaric oxygenation, hemoperfusion, and bile duct irrigation with ozonized or antiseptic solutions.

Groups with poor prognosis for conservative treatment include elderly patients with decompensated comorbidities, severe cholangitis with risk of abscess formation or hepatorenal failure, and patients with impacted stones in the major papilla.

Membrane-stabilizing drugs (e.g., legalon, vitamin E) were used in cases of cytolysis. Vitamin E deficiency (average reduction 38%) was observed and correlated with oxidative stress and poor prognosis.

A combined antioxidant–sorption therapy was developed, including vitamin E, multivitamins, sorbents, essential phospholipids, and bile acid binders. This reduced lipid peroxidation markers and improved outcomes.

Modern wound management included laser therapy, UV blood irradiation, immobilized antibiotics, immunocorrection, and sorption techniques.

Postoperative mortality decreased from 6.2% to 0.9% over 5 years despite an increase in elderly high-risk patients.

Individualized treatment based on patient biorhythms and precise metabolic assessment is recommended instead of standardized infusion protocols.

Overall, individualized therapy, meticulous postoperative management, and continuous monitoring significantly reduce complications and mortality and improve recovery.

Conclusions

1. At present, there is no universal diagnostic algorithm for choledocholithiasis (CDL). The diagnostic pathway directly depends on the availability of diagnostic equipment in a medical institution, anatomical and inflammatory changes in the hepatopancreatoduodenal zone, and the patient's condition

severity. The standard set of methods includes: ultrasound, ERCP; if non-informative – CT (MRCP) or laparoscopic cholecystectomy with intraoperative cholangiography, cholangioscopy, and endoscopic ultrasound (EUS).

2. The clinical course of CDL is diverse, and four main forms are identified:
 1. pronounced CDL with pain attacks, jaundice, and cholangitis (76.1%);
 2. mild/atypical forms (17.4%);
 3. asymptomatic (3.7%);
 4. atypical course (2.8%).

A level of middle-mass molecules above 0.6 units in blood plasma in patients with complicated CDL confirms severe endotoxiosis and pronounced hepatic failure. In high-risk patients, increased levels of middle-mass molecules, malondialdehyde, and diene conjugates with decreased vitamin E levels in plasma were observed.

In favorable prognosis cases, interphase dynamic tensiometric markers included: $\downarrow\delta 1$, $\uparrow\delta 3$, $\uparrow\delta 4$, $\downarrow\lambda$; in unfavorable prognosis: $\uparrow\delta 1$, $\downarrow\delta 4$, $\uparrow\lambda$, regardless of the type of surgery.

3. In pronounced pathomorphological and morphometric liver changes, increased enzyme levels (ALT, AST, ceruloplasmin, alkaline phosphatase) and lipid peroxidation products were observed, which significantly worsens postoperative prognosis and increases mortality.
4. The choice of the most rational surgical method for CDL should depend on bile duct pathology, periampullary zone condition, stone size, surgical-anesthetic risk (according to the developed risk scale), and computer-based prognostic results. Laparoscopic cholecystectomy combined with intraoperative choledochoscopy and holmium laser contact lithotripsy proved to be the most effective minimally invasive method for treating cholecystocholedocholithiasis, with minimal complications (10.8%) and no mortality.
5. Using principal component and factor analysis, four regression models and four risk scale gradations were developed. Based on comprehensive data, an expert system for predicting operative risk and postoperative complications (graphical models) was created. Transition between risk levels increases complication and mortality risk. The prediction accuracy was 87.5–97.5%, confirming its reliability and clinical applicability.
6. The improved diagnostic methods and newly developed minimally invasive surgical techniques for choledocholithiasis, along with pathogenetically justified perioperative management using sorption and antioxidant therapy, led to favorable short- and long-term outcomes.
7. Early postoperative complications were lowest after laparoscopic surgery (10.8%) and highest after open laparotomy (16.9%). In group I – 11.9%, group III – 13.3%, group IV – 13.0%. Mortality was absent after laparoscopic

operations. It was 1.4% in group I, 3.3% in group III, 4.3% in group IV, and 4.5% in group V. The proposed methods reduced complications by 3.2–5.3% and mortality by 0.4–2.1%.

Of 382 patients followed long-term after surgery:

- Good outcomes – 58.6% (224 patients)
- Satisfactory – 33.5% (128 patients)
- Poor – 5.0% (19 patients)
- Deaths – 2.9% (11 patients)

Best results were observed after laparoscopic transcholedochal interventions, supporting their wider use in specialized centers.

Practical Recommendations

1. Diagnostic algorithm for choledocholithiasis should include (in various combinations): clinical and laboratory tests, transabdominal ultrasound, endoscopic ultrasonography, FGD, ERCP, percutaneous transhepatic cholangiography, CT, MRCP, intraoperative cholangiography, cholangioscopy, fistulography, a developed method for determining and localizing biliary obstruction, morphological examination of gallbladder and liver tissue (in jaundice/cholangitis), and microbiological bile analysis (in complicated cases).
2. Treatment of complicated gallstone disease should be performed in specialized surgical units equipped for both traditional and endobiliary lithoextraction. Stone size, perampullary condition, and surgical risk determine the treatment approach.
3. Laparoscopic laser choledocholithotripsy with choledochoscopy and stone extraction is an effective method of choice when equipment is available. It is indicated when endoscopic extraction is not possible or when there is high risk, especially with large stones. Antegrade balloon dilation of the major duodenal papilla is safer than EPST and does not cause bleeding or pancreatitis.
4. Holmium laser lithotripsy should start at 0.5 J and 5 Hz; for hard stones, increase to 1.0 J and 10 Hz, avoiding excessive choledochoscope bending and alternating laser sessions to maintain visibility.
5. When laparoscopic equipment is unavailable, endoscopic papillary sphincterotomy followed by laparoscopic cholecystectomy may be used, but it is associated with complications in 11.9% and mortality of 1.4%.
6. Percutaneous transhepatic biliary drainage should be performed urgently in obstructive jaundice lasting more than 7 days or bilirubin levels above 124 $\mu\text{mol/L}$.

7. In high-risk patients, percutaneous transhepatic laser lithotripsy with balloon dilation (Patent UA No. 144478, 23.01.2020) effectively clears the bile ducts while preserving the sphincter and avoiding transpapillary complications.
8. The “rendezvous” technique (combining percutaneous and transpapillary interventions) enables biliary decompression and resolution of biliary pancreatitis.
9. When endoscopic procedures are not possible (distal bile duct stenosis, acute pancreatitis, impacted papilla stones, periampullary diverticula, large stones >2 cm, or post-Billroth II surgery), open surgery is indicated, though it carries higher complication (16.9%) and mortality rates (4.5%) and longer hospitalization (14.2 ± 5.3 days).
10. The developed computer-based expert system with four regression models and four risk grades should be used in clinical practice for assessing surgical-anesthetic risk and predicting postoperative complications.

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