ISBN: 978-93-87643-21-4

OPTIMIZATION OF TACTICAL AND TECHNICAL ASPECTS OF COMPLEX SURGICAL TREATMENT OF BENIGN ACUTE SUPPURATIVE CHOLANGITIS

Author

Arziev Ismoil Alievich

Published by
Novateur Publication
466, Sadashiv Peth, M.S.India-411030
novateurpublication.org

MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN

SAMARKAND STATE MEDICAL UNIVERSITY

Monograph

OPTIMIZATION OF TACTICAL AND TECHNICAL ASPECTS OF COMPLEX SURGICAL TREATMENT OF BENIGN ACUTE SUPPURATIVE CHOLANGITIS

Samarkand - 2026

Arziev Ismoil Alievich. Optimization of Tactical and Technical Aspects of Complex Surgical Treatment of Benign Acute Suppurative Cholangitis. Monograph. Samarkand, 2026. - 122 p.

Reviewers:

Safoyev B.B.	Professor, Department of General Surgery, Bukhara State Medical Institute, Doctor of Medical Sciences
Sherbekov U.A.	Associate Professor, Head of the Department of General Surgery, Samarkand State Medical University, Candidate of Medical Sciences

The monograph presents modern radiodiagnostic methods and describes the tactical and technical aspects of complex surgical treatment developed in accordance with the severity and clinical manifestations of acute cholangitis. Minimally invasive endoscopic transduodenal interventions and diapeutic techniques were introduced into clinical practice, which substantially improved treatment outcomes. A technique for intrahepatic biliary sanitation via the alternating administration of 0.06% anolyte and catholyte solutions of sodium hypochlorite was developed and implemented in surgical practice, enabling a significant reduction in mortality and purulent-septic complications. The monograph is intended for surgeons, master's degree candidates, clinical residents, and students of medical institutions.

UDC: 616.361-002:616-089.

INTRODUCTION

According to data from the World Health Organization, "the development of purulent complications in 46% of cases resulting from inflammatory biliary tract diseases remains an extremely urgent problem to this day, despite ongoing research in this field." The inflammatory process in the biliary tract is characterised not only by local purulent-destructive involvement but also by the rapid development of severe endogenous intoxication and significant impairment of organ function as a result of systemic changes. Such a condition is most commonly assessed as cholangitis, which manifests at various degrees of morphological and clinical severity. The disruption of biliary patency due to increased intraluminal pressure secondary to cholelithiasis, infection of bile, and the ensuing inflammatory process plays a decisive role in the development of suppurative cholangitis. Clinically, signs of mechanical jaundice appear immediately in 87% of patients, subsequently leading to the development of endotoxicosis and progression to biliary sepsis and multiple organ failure.

Worldwide, the principal direction in the management of patients with suppurative cholangitis consists of early decompression of the biliary tract, administration of antibacterial therapy guided by the sensitivity of the biliary microflora, and implementation of detoxification therapy. The first stage of surgical treatment of suppurative cholangitis involves biliary decompression using minimally invasive techniques: endoscopic papillosphincterotomy with nasobiliary drainage placement or percutaneous transhepatic drainage. In the second stage, laparoscopic cholecystectomy or cholecystectomy via minilaparotomy with external drainage of the common bile duct is performed. At the same time, in 36.0-55.5% of cases, the concomitant presence of destructive cholecystitis complicated by infiltrate in the right hypochondriac region, local peritonitis, or cholecystoduodenal fistula necessitates simultaneous open surgical intervention. However, the results of treatment of this condition do not always satisfy surgeons: septic complications are observed in 20.0% of patients, and mortality in 6.25-30.0%.

The increasing number of patients with complications of cholelithiasis, the growing frequency of atypical forms of cholelithiasis, the increasing surgical activity in elderly and aged patients, high-type iatrogenic injuries of the bile ducts, the wide introduction of surgical techniques and direct contrast procedures (percutaneous transhepatic cholangiostomy, endoscopic retrograde pancreatocholangiography) leading to disruption of the integrity of the biliary

system, and the tendency of suppurative cholangitis toward generalisation have further increased the urgency of this problem.

The primary pathogenetic role in the development of acute suppurative cholangitis is occupied by disruption of biliary patency due to rapidly increasing intraluminal pressure and the creation of conditions favourable for microbial proliferation (Karimov Sh.I., 2018). The favourable conditions arising within the biliary system lead to adequate proliferation of aerobic and/or anaerobic micro-organisms in the bile and in the wall of the biliary ducts, which in turn results in the development of cholangivenous and cholangio-lymphatic reflux and the subsequent appearance of systemic bacteraemia and severe intoxication (Hanau L. et al., 2020). The pathogenesis, stages of development, and clinical manifestations of the disease are characterised by three syndromes: cholestasis, endotoxicosis, and multiple organ failure.

Leading experts engaged with this problem emphasise that two anatomico-physiological conditions predisposing to biliary infection play an important role: bile stasis and the emergence of microbial aggression. Stagnant bile thickens, becomes sludge, and is readily infected as a consequence of ascending enteric infection. The principal cause of biliary obstruction is choledocholithiasis. Occasionally, benign strictures of the biliary ducts may also lead to obstruction (Korolkov A.Yu., 2009; Gomi H. et al., 2018). In addition, reflux cholangitis develops as a result of duodenal fluid regurgitation into the biliary tract. However, when biliary patency is unimpaired, pathological reflux does not constitute a significant hazard. In the postoperative period following papillosphincterotomy and biliary stenting, bacterial colonisation of bile occurs in most patients as a result of free reflux of air and duodenal contents into the choledochus; this does not ordinarily lead to the development of cholangitis. This condition may arise as a complication of reconstructive biliary surgery--a clear example of this is the "blind loop" syndrome (Khadzhibaev F.A. et al., 2018).

The current development of non-invasive radiodiagnostic techniques has led specialists to assign endoscopic biliary diagnostic and decompression methods to a secondary priority, since their application may cause complications such as acute pancreatitis and haemorrhage. At the present time, primary attention is being directed toward magnetic resonance cholangiography, and its findings serve as the basis for determining subsequent diagnostic and therapeutic management (Anand G., 2016; Cao J. et al., 2018).

The objective assessment of disease severity and outcome is of particular importance in the development of effective new therapeutic approaches for biliary sepsis, which manifests with heterogeneous clinical features. The accurate assessment of surgical risk constitutes a fundamental task of surgery. Over the past decade, the continuous improvement of minimally invasive surgical techniques and the implementation of staged surgical tactics have resulted in a significant reduction of mortality from suppurative cholangitis--an achievement acknowledged by the majority of clinicians (Shulutko A.M., 2018; Issa H. et al., 2018; Wang D., 2017). Korolkov A.Yu. et al. (2018) recommended lavage of the biliary tract with antiseptic solutions in the postoperative period, concurrent administration of antibiotics in combination with metronidazole, and detoxification therapy.

The unsatisfactory outcomes of treatment of benign acute suppurative cholangitis necessitate the optimisation of the tactical and technical aspects of complex surgical treatment of this condition. The use of minimally invasive surgery in combination with intrahepatic biliary procedures via drainage allows for the elimination of bacterial contamination of the biliary tract, prevention of cholangenic hepatic abscesses and septic conditions, and reduction of endotoxaemia--achieving clinically significant results.

CHAPTER I
CONTEMPORARY ASPECTS OF SURGICAL TREATMENT OF ACUTE SUPPURATIVE CHOLANGITIS

Suppurative cholangitis is one of the most severe and life-threatening complications of biliary tract disease; it represents an acute inflammation of the bile ducts arising as a result of persistent disruption of bile flow. The primary cause of impaired bile flow is cholelithiasis. One in every ten inhabitants of the globe suffers from cholelithiasis; choledocholithiasis, as a complication thereof, is encountered in 20-30% of cases [Stolin A.V., Prudkov M.I., 2009]. Stenosis or benign stricture of the terminal portion of the common bile duct (CBD) as a cause of impaired bile flow is observed in 3-40% of patients [Nazirov F.G. et al., 2011; Bagnenko S.F., 2007; Korolkov A.Yu., 2009]. Rupture of hepatic echinococcosis into the main bile ducts (MBD), complicated by biliary involvement, accounts for 0.4-2% of cases [Akhaladze G.G., 2004; Nichitaylo M.E., 2005; Beburishvili A.G., 2013]. According to published studies, 11-60% of patients with biliary obstruction develop suppurative cholangitis. To date, more than 30 aetiological causes of impaired bile flow have been identified. However, the principal cause of suppurative cholangitis is choledocholithiasis, which in turn holds a leading position among the complications of cholelithiasis and is identified in 8.1-26.8% of patients with CBD pathology (Bagnenko S.F., 2007; Rosing et al. D.K., 2007).

Whereas suppurative cholangitis was previously regarded as invariably accompanied by mechanical jaundice, it is currently recognised as a distinct, autonomous clinical problem. This is attributable to its significant role in the development of cholangiogenic sepsis (Stolin A.V., Nishnevich E.V., Prudkov M.I., 2009) and the resulting high mortality rate (15-60%).

The increasing number of patients with complications of cholelithiasis, the growing frequency of atypical forms of cholelithiasis, the increasing surgical activity in elderly and aged patients, high-type iatrogenic biliary tract injuries, the widespread introduction of surgical techniques and direct contrast procedures (percutaneous transhepatic cholangiostomy (PTCS), endoscopic retrograde pancreatocholangiography (ERCP)) that disrupt the integrity of the biliary system, and the tendency of suppurative cholangitis toward generalisation have further increased the urgency of this problem (Akhaladze G.G., 2004; Nichitaylo M.E., 2005; Galperin E.I., 2009; Korolkov A.Yu., 2009; Beburishvili A.G., 2013).

The clinical significance of suppurative cholangitis is primarily associated with its high mortality (4.7-28.5%) and the rapid ascending spread of infection through the intrahepatic bile ducts, leading to the development of cholangenic hepatic abscess and biliary sepsis [Datsenko B.M., 2009; Rybachkov V.V. et al., 2016; Rumyantsev N.I. et al., 2017]. As early as 1903, Rogers noted the association of suppurative cholangitis with biliary obstruction and hepatic abscess in a patient who died from unsuccessful resolution of cholestasis [2, 4, 24].

The persistently unsatisfactory results of treatment of acute suppurative cholangitis over the past 20 years--including high mortality from multiple organ failure in 3-4 organ systems (11-64%), even when surgery is performed in a timely manner--remain the primary reason for continued attention to this condition. The majority of fatal outcomes are associated with the need to perform emergency surgical interventions (33.0-60.0%) in patients whose condition deteriorates as a result of acute destructive cholecystitis complicated by peritonitis (Grigoryan K.G.).

Without surgical intervention, acute suppurative cholangitis invariably leads to death through the development of biliary sepsis in 100% of cases. According to various authors, postoperative mortality ranges from 13 to 60% (Galperin E.I., 2009; Nazirov F.G. et al., 2011; Bagnenko et al., 2009; Schneider J. et al., 2016). In addition, acute cholangitis in the elderly frequently differs by concurrent occurrence with destructive forms of calculous cholecystitis. Destructive forms of cholecystitis are identified in only 25% of patients under 70 years of age, in 37-57% of patients over 70, and in 67-100% of patients over 80 years of age (Akhaladze G.G., 2013).

Two anatomico-physiological conditions that predispose to biliary infection play an important role: bile stasis and the emergence of microbial aggression. Stagnant bile thickens, becomes sludge, and is readily infected as a consequence of ascending enteric infection. The principal cause of biliary obstruction is choledocholithiasis. Occasionally, benign strictures of the biliary ducts may also lead to obstruction (Nazirov F.G. et al., 2011; Bagnenko S.F., 2007; Korolkov A.Yu., 2009; Beburishvili A.G. et al., 2013). Furthermore, reflux cholangitis develops as a result of regurgitation of intestinal fluid into the biliary ducts. When biliary patency is maintained, however, pathological reflux does not constitute a significant hazard. Following papillosphincterotomy and biliary stenting, bacterial colonisation of the bile occurs in most patients due to

free reflux of air and duodenal contents into the choledochus, which ordinarily does not lead to the development of cholangitis. This condition may arise as a complication of reconstructive biliary surgery; a clear illustration of this is the "blind loop" syndrome (Khadzhibaev F.A. et al., 2018).

Microorganisms of the intestinal microflora are the typical causative agents of cholangitis and most commonly appear in association, a finding confirmed by microbiological culture of bile obtained from patients. Among these, E. coli (50-60%) from the Enterobacteriaceae family is most commonly detected, followed by Klebsiella (8-20%), Serratia, Proteus, Enterobacter, Acinetobacter; Gram-negative organisms Streptococcus and Enterococcus (2-30%); non-spore-forming anaerobes Bacteroides, Clostridium, fusobacteria, peptococci (up to 20%); and Pseudomonas (2-4%). The clear predominance of Gram-negative enteric bacilli in cultures is unquestionable; however, considerable variation in the detection of anaerobes, staphylococci, streptococci, and Pseudomonas aeruginosa has been noted across studies (Ustinov G.G., 2011; Koychuk R.A., 2011).

It should be noted that in 13-18% of patients with clearly pronounced clinical manifestations of acute suppurative cholangitis, bile cultures yield no microbial growth. The principal limitation of microbiological examination of bile for diagnostic and therapeutic purposes in acute suppurative cholangitis is the time required--several days--to obtain results (Akhaladze G.G., 2009; Bagnenko S.F. et al., 2008).

Several classifications of cholangitis exist at present; however, the classification by V.K. Gostishchev, adopted in 2009, is the most convenient for practical use:

Table 1.1

Classification of Acute Cholangitis According to V.K. Gostishchev

№	Criterion	Form
1	By aetiology	- Cholecystogenic - Ascending - Primary
2	By extent of process	- Circumscribed inflammation of the MBD - Ascending cholangitis - Angiocholitis - Cholangenic hepatitis - Cholangenic hepatic abscesses

3	By type of inflammation	- Catarrhal - Suppurative - Fibrinous-suppurative
4	By clinical course	- Acute - Acute suppurative - Acute suppurative obstructive - Chronic - Chronic recurrent
5	By outcome	- Recovery - Cholangenic abscesses and biliary sepsis - Hepatic cirrhosis

According to the Tokyo Guidelines 2013 (TG13) classification, acute cholangitis is divided into 3 grades:

Grade I (Mild)	**Grade II (Moderate)**	**Grade III (Severe)**
Criteria for moderate and severe grade are absent.	No organ dysfunction present; ≥2 of the following criteria: leucocytosis >12,000 or <4,000 /μL; fever >39°C; age >75 years; bilirubin >85 μmol/L; albumin <28 g/L.	Organ dysfunction present in at least 1 system.

The above-listed diagnostic criteria possess high sensitivity (87.6%) and high specificity (77.7%) and may be applied in determining the treatment strategy for acute cholangitis (level of evidence 1b, strength of recommendation B).

Cholangitis was first described in 1877 by J.M. Charcot in the form of the clinical triad: rigors, fever, and jaundice. In severe forms of cholangitis, the Charcot triad may be accompanied by encephalopathy and hypotension (Reynolds' pentad) (Kiriyama S. et al., 2013). Thus, the clinical features of acute suppurative cholangitis (ASC) consist of the Charcot triad or Reynolds' pentad, presenting as malaise, pain in the right hypochondrium, jaundice, altered consciousness, and arterial hypotension. The majority of patients admitted to hospital note the acute onset of the disease and the rapid development of fever

against a background of right hypochondriac pain and jaundice. The location of pain on the skin surface typically corresponds to the area involved in the disease process. Choledochal colic caused by an impacted stone at the major duodenal papilla is extremely severe, arising at the anterior abdominal wall (Chauffard's zone--slightly to the right of and above the umbilicus), radiating to the right (along the biliary tract and liver) or as a girdle (along the pancreatic parenchyma and ducts) (Dibirov M.D., 2011).

Fever is typically observed in 90% of cases, and is accompanied by jaundice in 60% and abdominal pain in 70% of patients, respectively (Hanau L.H., Steigbigel N.H., 2000). High fever with rigors and diaphoresis is characteristic of the disease. Jaundice, which is not markedly pronounced, appears after the pain syndrome.

In the most severe forms of cholangitis, the Charcot triad may be accompanied by manifestations of encephalopathy (10-20%) and hypotension (30%) (Reynolds' pentad) (Kiriyama S. et al., 2013). Peritoneal signs are absent in uncomplicated cholangitis.

Upon development of certain clinical features of ASC, the diagnostic work-up includes laboratory (clinical-biochemical) and instrumental investigations. A variety of radiodiagnostic modalities are currently available in modern hospitals; physicians must select the optimal sequence of diagnostic tests for biliary hypertension and acute cholangitis based on the history, presenting complaints, and laboratory findings. The patient's history, prior biliary surgery, prior episodes of cholangitis, and existing complications of diagnostic and endoscopic therapeutic procedures are important in establishing the diagnosis (Galperin E.I., 2009; K. Wada et al., 2007).

Diagnostic errors in routine clinical examinations for biliary tract disease occur in up to 30% of cases. This is attributable not only to the experience and technical capabilities of the examining specialist but also to an incorrect diagnostic algorithm. For this reason, the development of effective clinical-radiodiagnostic methods for biliary tract disease remains a pressing problem (Zagidullina G.T. et al., 2015; Ratnikov V.A. et al., 2015; Fomicheva N.V., 2014).

The diagnosis of acute cholangitis is well-founded when the following signs are present: hyperthermia, along with leucocytosis of approximately 6-9×10^9/L in the peripheral blood. Leucocytosis indicates migration of endotoxin and inflammatory mediators from the purulent focus (biliary tract) into the

systemic circulation. In cholangitis, these signs are completely resolved through local treatment combined with restoration of bile flow (Bagnenko S.F., 2007; 2009; Korolkov A.Yu., 2009; Li V.K., 2010).

A proportion of patients are admitted in severe condition with clinical criteria of systemic inflammatory response (tachycardia, tachypnoea, hyperthermia with rigors) of varying severity, concomitant with the Charcot triad; the presence of a purulent focus (biliary tract) in these patients signifies the progression of ASC to biliary sepsis (Koychuk R.A., 2011).

Biliary sepsis (BS) develops as a result of the activation and uncontrolled dissemination of mononuclear phagocytes (macrophages), neutrophils, and vascular endothelium. The excessive production of cytokines by these cells leads to the development of systemic inflammatory response syndrome (SIRS). Its basis consists not merely of functional but histostructural (morphological) changes in organs and systems, the escalation of which leads to dysfunction thereof (Beburishvili A.G. et al., 2013; Korolkov A.Yu., 2009; Catenacci M.H., 2008).

Examination of these patients reveals clearly pronounced SIRS parameters (hyperthermia, tachycardia, etc.) and progressively worsening laboratory indicators of intoxication (leucocytosis with marked leftward shift of the differential, appearance of immature forms, elevation of the leucocyte toxicity index). The emergence of hypotension and signs of impaired cerebral and other organ function (most commonly manifesting as hepatorenal insufficiency) in patients reflects the escalation of SIRS. The combination of clinical-laboratory findings with evidence of organ and system dysfunction constitutes the primary indication for the diagnosis of "severe biliary sepsis" (Galperin E.I., 2009; Nichitaylo M.E., 2005; Ilchenko F.N., 2010).

However, it must be stated that leucocytosis with a leftward differential shift in the blood count constitutes a general indicator of undrained abscess; biochemical results (hyperbilirubinaemia, hyperphosphataemia, hypercholesterolaemia) confirm the presence of cholestasis. The development of elevated transaminase activity as a result of acute biliary obstruction also has diagnostic significance (Datsenko B.M., 2009; Ilchenko F.N., 2010).

The initial method of investigation for hepatopancreatoduodenal region pathology is typically ultrasonography, which is straightforward to perform and allows the detection of choledochectasia [Parfenova A.A., 2009; Prizentsov A.A. et al., 2012; Usmanova L.I. et al., 2012; Sainani N., 2008]. However, the

effectiveness of this technique in identifying the aetiology of biliary hypertension is limited. This is related to the difficulty in visualising the distal portions of the common bile duct, the severity of the disease, and the experience and manual skills of the examining specialist [Ilchenko A.A., 2008; Prizentsov A.A., 2012; Fomicheva N.V., 2014; Sainani N.I., 2008]. Ultrasonography practically permits determination of the type of jaundice in 90.3% of cases: dilatation of the biliary tract above the level of obstruction and the presence of signs of biliary hypertension indicate the mechanical nature of cholestasis. However, in transient hypertension, biliary duct diameter may remain within normal values. In such cases, computed tomography of the liver may provide more information.

Characteristic sonographic changes are present in the hepatic parenchyma in ASC. In these cases, the liver parenchyma loses its homogeneity due to the development of focal formations with irregular borders of increased echogenicity (inflammatory infiltrate) or decreased echogenicity (microabscesses) (Kulish V.A., 2011; Koychuk R.A., 2011).

In some cases, the "snow-storm" sonographic syndrome is detected; it arises from the accumulation of markedly echogenic inclusions due to gas bubbles (microbial metabolites) in the intrahepatic bile ducts against a background of hepatic inhomogeneity.

Endoscopic examination is a mandatory instrumental investigation in patients with mechanical jaundice and cholangitis. In the majority of patients with ASC, gastroduodenoscopy reveals inflammatory changes of the duodenal mucosa with papillitis and the absence of bile in the intestinal lumen. The cause of complete biliary obstruction identified at endoscopy is an impacted stone at the papilla or cicatricial stenosis of the papilla (Nichitaylo M.E., 2005; Khadzhibaev A.M. et al., 2006).

When conclusions drawn from ultrasonography are uncertain, endoscopic retrograde cholangiopancreatography (ERCP) is employed; when ERCP is not feasible, percutaneous transhepatic cholangiography (PTHC) is used. During catheterisation of the biliary ducts for cholangiography, bile is aspirated for microbiological examination. The aspirated bile is initially assessed by microscopy: the presence of pus and fibrin confirms ASC. Bacteriological examination of bile is performed to identify the infectious agent and determine its sensitivity to antibacterial agents (Bagnenko S.F., 2008).

Traditional radiological diagnostic methods for biliary hypertension, such as endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic cholangiography (PTHC), continue to be widely used in practice; however, they require high radiation exposure, are invasive, necessitate the administration of iodine-containing contrast agents, and are associated with specific complications. For this reason, their use is currently considered appropriate for therapeutic rather than purely diagnostic purposes [Alentiev S.A., 2010; Bordin D.S., 2012; A. Andriulli et al., 2007].

The current development of non-invasive radiodiagnostic techniques has led specialists to assign endoscopic biliary diagnostic and decompression methods to a secondary priority, since their application may cause complications such as acute pancreatitis and haemorrhage. At the present time, primary attention is being directed toward magnetic resonance cholangiography, and its findings serve as the basis for determining subsequent diagnostic and management strategy (Weber A. et al., 2009; Gadiev S.I., Kurbanova E.M., 2011; Fracanzani A.L. et al., 2012; Goncharova T.P. et al., 2014).

Magnetic resonance cholangiopancreatography (MRCP) allows visualisation of the biliary and pancreatic ductal systems naturally without contrast medium, both in the fasting state and following meal ingestion (Katabathina V.S. et al., 2014).

The clinical implementation of MRCP has brought a new approach to abdominal imaging; in particular, the successful use of MRCP has created the opportunity to study the causes of biliary hypertension associated with obstruction of the distal common bile duct (Y.E. Chung et al., 2011; A. Frydrychowicz et al., 2012). Furthermore, the quality of the images obtained is not inferior to those of radiographic cholangiograms. High correlation of MRCP results with direct biliary contrast data has been demonstrated (Ilchenko A.A., 2011; Fomicheva N.V. et al., 2014; V.S. Katabathina, 2014; T. Patel, 2009). Vasilev and V.A. Ratnikov (2006) acknowledged that MRCP is a complete diagnostic alternative to direct biliary contrast techniques [14], a view shared by other authors [Ikramov A.I., Khodzhibekov M.Kh., Ilchenko A.A., 2011; Katabathina V.S. et al., 2014; Hossary S.H. et al., 2014].

MRCP is based on the acquisition of images using a block method and thin-slice technique (1-2 mm). The primary indication for MRCP is the identification of biliary obstruction, its level, and its aetiology. Many authors rate the diagnostic accuracy of the technique at 91-100% for detecting biliary

obstruction, with a reported accuracy of approximately 85-100% [23, 93, 115, 132, 141]. The accuracy of the technique in determining the aetiology of mechanical jaundice is also high, reaching 94-97% [Zagidullina G.T. et al., 2015; I. Petrescu et al., 2015; K.S. Madhusudhan et al., 2015; S.H. Hossary et al., 2014]. Among the advantages of MRCP is the ability to visualise both the proximal and distal portions of injured bile ducts compared with other contrast modalities (Vasilev A.Yu. et al., 2006). Moreover, MRCP images allow for a holistic assessment of the biliary system (B.M. Yeh et al., 2009).

One of the problems in biliary tract visualisation remains the assessment of the extent of involvement. This requires combining MRCP with optimised conventional MRI and the search for new methodological techniques and approaches, as well as supplementing the algorithm with newer techniques, specifically endosonography (Nechipay A.M. et al., 2013; R. Costi et al., 2014; Griffin N. et al., 2013). Numerous investigators have emphasised the high significance of MRCP in studying the anatomical variants of the gallbladder and biliary tract, as well as the intrahepatic and extrahepatic bile ducts. MRCP plays an important role in analysing variants of their union with the pancreatic ducts.

Overall, MRCP allows the detection of anatomical variants of the biliary system with 98% accuracy and of intrahepatic biliary confluence with 36-95% accuracy (K. Darge et al., 2011). Prior to treatment, MRCP is of particular importance in planning surgical management, including reconstructive biliary surgery. This is relevant because insufficient information about the variant of biliary entry, or the variant of a tributary branch draining into the common hepatic duct, may lead to their inadvertent injury during the procedure (M. Wojcicki et al., 2013; M.T. Perera et al., 2011; T. Patel et al., 2009).

In a number of conditions, including cholelithiasis and its complications, the use of MRCP for examining the gallbladder and both intrahepatic and extrahepatic bile ducts significantly supplements the diagnostic capabilities of contrast imaging. Notwithstanding the high cost of the examination, the information obtained is comparable to that of direct cholangiography, and MRCP is given preference from a cost-benefit standpoint (no ERCP-specific complications, no radiation risk, and non-invasive technique) (C.W. Kim et al., 2013; S.H. Hossary et al., 2014).

Controversy currently exists regarding the management of biliary sepsis--one of the most serious complications of suppurative cholangitis. Despite the active development and continuous improvement of diagnostic and therapeutic

techniques for biliary system disease, sepsis has remained one of the pressing problems of modern medicine for several decades, given the increasing number of patients and the consistently high mortality ranging from 30 to 90% (Rybachkov V.V., 2009; Ilchenko F.N., 2010). Sepsis and septic shock remain among the leading causes of death in intensive care unit patients (Ustinov G.G., 2011).

It should be emphasised that intensive care of a patient with sepsis is five times more costly than the management of any other critical condition and subsequent treatment [Kondratenko P.G., 2007; Bagnenko S.F., 2008; Galperin E.I., 2009; Vincent J.L., 2010; Pulido J.N. et al., 2012]. The concept of biliary sepsis is directly related to the pathogenetic mechanisms of cholangitis development, as biliary septic shock pathogenesis invariably involves the manifestation of acute suppurative or acute obstructive suppurative cholangitis. In essence, one is the consequence of the other, although the generalised infectious process undoubtedly has its own distinctive characteristics. In contemporary literature, the term "biliary sepsis" (BS) denotes the most severe manifestations of suppurative cholangitis (Datsenko B.M., 2009; Grebenyuk V.V., 2010; Ilchenko F.N., 2010; R. Chaudhary, L.J. Moore et al., 2011).

Differences were noted in the rate of development of suppurative cholangitis and in the timing of its progression to biliary sepsis in patients with mechanical jaundice. Thus, sepsis develops rapidly in 39.1% of patients with acute cholangitis (within hours to days) and frequently runs a fulminant course, characterised by the rapid formation of miliary hepatic abscesses and signs of multiple organ failure. In 60.9% of patients with long-standing chronic cholangitis, the course is prolonged and gradually progressive (over weeks to months). In chronic sepsis, abscesses are often solitary and may occasionally coalesce into a single suppurative focus (Catenacci M.H., 2008; Ustinov G.G., 2011).

Although the aetiological causes of acute suppurative cholangitis and biliary sepsis are closely interrelated, morphological changes in the extrahepatic and intrahepatic bile ducts develop primarily in acute suppurative cholangitis. Biliary sepsis is a pathological process based on the generalised (systemic) inflammatory response of the organism to infection. In other terms, acute suppurative cholangitis and biliary sepsis represent different manifestations of the same local and systemic infectious-inflammatory process (Datsenko B.M., 2009; Grebenyuk V.V., 2010; Vincent J.L., 2008).

The objective assessment of disease severity and outcome is of particular importance in developing the prospects for treatment of biliary sepsis, which manifests with diverse clinical features. The objective assessment of surgical risk is a fundamental task of surgery (Korolkov A.Yu., 2009; Bagnenko S.F. et al., 2008).

Established biliary sepsis represents a new pathological condition requiring radically specific approaches to management. Treatment of patients with acute suppurative cholangitis must be initiated immediately upon hospitalisation. It must be remembered that the effectiveness of pharmacological therapy alone is very low in the setting of biliary hypertension accompanying cholangitis (Datsenko B.M., 2009).

The development of complications leads to deterioration of hepatic functional reserve, multiple organ failure, and septic manifestations, which substantially increase the incidence of postoperative complications (Fang Y. et al., 2012; El-Chafic A.H. et al., 2013; Ye X. et al., 2013; Ermolov A.S. et al., 2014). These patients require emergency biliary decompression in combination with substantiated therapeutic measures. Accordingly, in patients at high surgical risk, minimally invasive biliary decompression should precede radical intervention (Labiya A.I., 2007; Galperin E.I., Vetshev P.S., 2009; Wu X. et al., 2012).

In life-threatening conditions, intensive care must be initiated concurrently with immediate decompression. Despite advances in surgical technique and anaesthetic-resuscitation management, conventional operations cause serious trauma, disrupt topographical-anatomical relationships, and generate functional and organic changes. Furthermore, they are associated with numerous complications and high mortality, particularly in elderly patients with severe comorbidities (Stolin A.V., 2009; Kulish V.A., 2011).

It must be acknowledged that mortality from suppurative cholangitis has been declining over recent decades due to the advances made in treating this pathology--a trend attributed primarily to the development of minimally invasive surgical techniques and the implementation of staged surgical tactics, as acknowledged by the majority of clinicians (A.M. Shulutko, V.G. Agadzhanov, 2008; O.V. Babkin, A.Yu. Platonov et al., 2009; K. Uchiyama, Onishi et al., 2003).

The unsatisfactory outcomes of treatment of benign suppurative cholangitis necessitate the optimisation of the tactical and technical aspects of

complex surgical treatment. Effective results in this direction--including elimination of bacterial contamination of the gallbladder and biliary tract, prevention of microabscess formation in the liver, prevention of septic conditions, and reduction of endotoxaemia--can be achieved only through the combined use of minimally invasive surgery and drainage-based intrabiliary procedures.

Over the past decades, mortality from suppurative cholangitis has been decreasing owing to the development of minimally invasive surgical techniques and the implementation of staged surgical tactics (Shulutko A.M., Agadzhanov V.G., 2008; Chumakov A.A., Malashenko V.N., Kozlov S.V., 2008; Babkin O.V., Platonov A.Yu. et al.).

The principal treatment directions for patients with suppurative cholangitis are early biliary decompression, administration of antibacterial and detoxification therapy considering the sensitivity of the biliary microflora, and haemodynamic and respiratory support (Shapkin Yu.G. et al., 2013; Samartsev V.A. et al., 2015; Osipov A.V. et al., 2017; Yoshida H. et al., 2008).

Patients with acute cholangitis must receive preoperative preparation in a ward setting, including infusion-detoxification therapy and antibacterial therapy. Patients with biliary sepsis and severe biliary sepsis should be admitted to the surgical intensive care unit for preoperative preparation. Third-generation cephalosporins are used for antibacterial therapy of biliary sepsis; fourth-generation cephalosporins or carbapenems are used for severe biliary sepsis (Stolin A.V., 2009; L.E. White et al., 2011).

In this respect, there is considerable interest in the use of minimally invasive techniques, primarily endoscopic papillosphincterotomy (EPST), nasobiliary drainage, lithoextraction and mechanical lithotripsy, and transpappillary endoprosthetic stenting of the choledochus. The application of EPST in pancreatobiliary surgery has fully resolved the issues of decompression of the biliary system against a background of mechanical jaundice and acute cholangitis (Khadzhibaev F.A. et al., 2018).

The indication for and choice of decompression technique must be determined individually in each case, considering the clinical situation and the nature and duration of biliary obstruction based on the results of direct radiographic biliary contrast examinations. The use of endoprosthetic stenting in post-traumatic cicatricial stenosis and compressive tumours of the choledochus

ensures its decompression and resolves cholangitis in 90% of cases (Korolkov A.Yu., 2009; Tseng L.J., 2009).

Percutaneous transhepatic cholangiostomy (PTCS) was first described by K.C. Weichel in 1964 and has since been used as a method of preoperative biliary decompression. It must be borne in mind, however, that this procedure may be a source of such complications as sepsis and endotoxic shock. Through PTCS, the drainage may be passed beyond the obstruction or placed transpappillarily, directing bile either externally or into the intestine. PTCS is the method of choice in intrahepatic biliary stenosis and lithiasis causing biliary sepsis. Balloon dilatation of strictures via cholangiostomy, fibrochledochoscopy, and various biliary procedures may be performed through this route (Beburishvili A.G. et al., 2013).

In some patients, a minimally invasive radical operation is performed after urgent decompression of the biliary tract: cholecystectomy, choledochoduodenostomy, etc. In certain cases, external drainage of the biliary tract, with or without minimally invasive technology, represents the definitive treatment. This approach is principally used in oncological patients and those with severe comorbidities (Galperin E.I., 2009; Altiev B.K., 2007).

Prevention of biliary hypertension (one of the causes leading to cholangitis) is insufficient for arresting the inflammatory process in the extrahepatic biliary tract; moreover, biliary decompression does not exert a direct effect on the infectious agent (Melkonyan G.G. et al., 2014).

One of the most important challenges in cholangitis management is the selection of appropriate antibacterial therapy. Following decompression, antibacterial therapy plays a supplementary role. At the same time, it is impossible to guarantee complete bile sterility (in cultures taken from T-tube drainage). It has been established that the titre of microbial bodies in bile does not decrease after decompression without antibacterial therapy. Furthermore, quantification of micro-organisms in bile is a time-consuming task (Shapkin Yu.G. et al., 2013; Samartsev V.A. et al., 2015; Osipov A.V. et al., 2017). Current international guidelines for the management of severe sepsis and septic shock (Surviving Sepsis Campaign) recommend intravenous administration of broad-spectrum antibiotics with high penetration into the suspected site of infection within the first hour (Dellinger R.P. et al., 2008). In patients with cholangiogenic sepsis and septic shock, daily dose adjustment is recommended,

taking into account pathophysiological changes and drug characteristics (Dellinger R.P. et al., 2008).

The treatment of biliary septic shock is considerably more complex. Effective intensive care of biliary sepsis can only be achieved through complete surgical eradication of the infectious focus combined with antibacterial therapy. Inadequate initial antibacterial therapy leads to unfavourable outcomes in patients with biliary sepsis. Additionally, preservation of the patient's life, prevention, and resolution of organ dysfunction are impossible without targeted intensive care (Grebenyuk V.V., 2010; Ustinov G.G., 2011; Kulish V.A., 2011; Catenacci M.H., 2008).

Pathogenetic correction of immune deficiency in this disease can be achieved through the individual or combined use of pharmacological agents. First, by exclusion of the erythrocytic mechanism of immunomodulation--the effect of membrane protectors on the erythrocyte membrane itself; second, by exclusion of the formation of immunosuppressive metabolic compounds in the blood acting upon cells of damaged tissues--through the use of antioxidants (antihypoxants); and finally, through direct stimulatory effects on effector immunocompetent immunomodulator cells. The combined use of these drug groups may influence the normalisation of impaired structural and functional parameters of erythrocytes in suppurative cholangitis (Prokopenko L.G. et al., 2005; Konoplya A.I., 2008; Kulish V.A., 2011).

Thus, the principal treatment directions for patients with suppurative cholangitis are early biliary decompression, administration of antibacterial therapy considering the sensitivity of the biliary microflora, haemodynamic and respiratory support, immunocorrection, and detoxification therapy (Shapkin Yu.G. et al., 2013; Samartsev V.A. et al., 2015; Osipov A.V. et al., 2017; Yoshida H. et al., 2008).

As a general rule, surgical treatment of patients with suppurative cholangitis is carried out in two stages. In the first stage, biliary decompression is performed using minimally invasive techniques: endoscopic papillosphincterotomy (EPST) with nasobiliary drainage (NBD) placement, or percutaneous transhepatic drainage. In the second stage, laparoscopic cholecystectomy (LC) or mini-laparotomy cholecystectomy with external drainage of the choledochus is performed (Korolev M.P. et al., 2017; Kukosh M.V. et al., 2017). However, in approximately 10.0-36.0% of patients, simultaneous conventional open surgery is required due to destructive

cholecystitis complicated by local peritonitis, cholecystoduodenal fistula, or right hypochondriac infiltrate (Borisov A.E. et al., 2003; Kulish V.A., 2011; Chernov V.N. et al., 2013; Korolkov A.Yu. et al., 2017).

Minimally invasive surgical techniques--primarily EPST and PTCS--should be used extensively in surgical practice, as these techniques lead to a reduction in complications and mortality (Khadzhibaev F.A. et al., 2018).

When acute cholangitis with biliary sepsis or severe biliary sepsis occurs concurrently with acute cholecystitis, the surgical method of choice is laparoscopic cholecystectomy with biliary drainage according to the Halsted technique and intraoperative cholangiography. In the postoperative period, EPST is performed for single stones up to 1.5 cm in diameter for stone removal. If multiple stones are present or the diameter exceeds 1.5 cm, conversion is performed with traditional choledocholithotomy and choledochostomy according to Ker (Nichitaylo M.E., 2005; Nazirov F.G. et al., 2011; Kulish V.A., 2011; Khadzhibaev F.A. et al., 2018).

In the postoperative period, the biliary tract is irrigated with antiseptic solutions. Patients are also prescribed antibiotics in combination with metronidazole, and detoxification therapy is administered.

Some authors have noted that elderly and aged patients constitute the principal group among those with severe forms of CBD pathology, and that cholecystectomy combined with opening of the hepaticocholedochal lumen increases mortality 3-4-fold in this group (Palazzo L. et al., 2003; Voegeli D. et al., 2003).

In this context, diapeutic techniques have become widely established in recent years, allowing primary therapeutic measures to be performed at the diagnostic stage. Methods of primary MBD decompression include: percutaneous transhepatic cholangio- and cholecystostomy, endoscopic papillosphincterotomy (EPST), and nasobiliary drainage (NBD) (Maystrenko N.A. et al., 2000; Machulin E.G. et al., 2000; Sakhautdinov V.G., 2001; Kondratenko P.G. et al., 2004). These measures have made it possible to perform conservative operations in a large proportion of patients following mechanical jaundice and acute cholangitis resolution, and in the majority of cases have allowed avoidance of transcholedochal and transduodenal interventions, thereby reducing mortality in this patient category. At the same time, certain difficulties exist in the broad application of these minimally invasive techniques due to their technical complexity and a number of

contraindications (Akhaladze G.G., 2013). Furthermore, there is no consensus regarding radical surgical intervention following the first stage of minimally invasive operations aimed at preventing and relieving mechanical jaundice and acute cholangitis. In this regard, the interval varies from 2 to 30 days or more (Mashinsky A.A., 2003). Treatment outcomes do not always satisfy surgeons. Septic conditions are identified in 20.0% of patients. Fatal outcomes are recorded in 6.25-30.0% of cases (Chernyadev S.V. et al., 2011; Dibirov M.D. et al., 2011; Vorotyntsev S.A. et al., 2011).

Thus, the issues of complex treatment of acute suppurative cholangitis remain urgent and require continued research within this field of modern medical science. The continuation of investigations into various methods of predicting and preventing biliary sepsis in accordance with surgical treatment tactics once again underscores the necessity of identifying new methods and opportunities for addressing the problem. Through the combined use of minimally invasive surgery with drainage-based intrabiliary procedures, it is possible to achieve effective results: elimination of bacterial contamination of the biliary tract, prevention of cholangenic hepatic abscesses and septic conditions, and reduction of endotoxaemia.

CHAPTER II
RESEARCH MATERIALS AND METHODS

§2.1. General Characteristics of Patients Examined

The present study analysed the treatment outcomes of 144 patients with suppurative cholangitis developing as a complication of cholelithiasis, treated in the Surgical Department of the 1st Clinical Base of Samarkand State Medical Institute between 2000 and 2019. Of these, 91 were women (63.2%) and 53 were men (36.8%) aged 33 to 81 years. The mean patient age was 53.2±6.2 years (Table 2.1).

Table 2.1

Distribution of Patients by Sex and Age

Sex	Age Group	Study Group	Comparison Group	Total
Male	31-40	3 (3.6%)	3 (4.9%)	6 (4.2%)
	41-50	5 (6.0%)	4 (6.6%)	9 (6.3%)
	51-60	10 (12.0%)	7 (11.5%)	17 (11.8%)
	61-70	7 (8.4%)	4 (6.6%)	11 (7.6%)
	71-79	5 (6.0%)	4 (6.6%)	9 (6.3%)
	≥80	1 (1.2%)	-	1 (0.7%)
	Total	31 (37.3%)	22 (36.1%)	53 (36.8%)
Female	31-40	7 (8.4%)	5 (8.2%)	12 (8.3%)
	41-50	14 (16.9%)	9 (14.8%)	23 (16.0%)
	51-60	13 (15.7%)	12 (19.7%)	25 (17.4%)
	61-70	11 (13.3%)	8 (13.1%)	19 (13.2%)
	71-79	6 (7.2%)	5 (8.2%)	11 (7.6%)
	≥80	1 (1.2%)	-	1 (0.7%)
	Total	52 (62.7%)	39 (63.9%)	91 (63.2%)
Total		83 (57.6%)	61 (42.4%)	144 (100%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

In accordance with the objectives and aims of the study, patients were divided into two groups. The comparison group comprised 61 patients (42.4%) who underwent surgical intervention between 2000 and 2009 for acute suppurative cholangitis developing as a complication of cholelithiasis. The study

group included 83 patients (57.6%) treated between 2010 and 2019 using the surgical treatment protocol developed within the clinic.

The examinations revealed that patients in both groups were comparable in age, disease severity, and prominence of clinical manifestations. The duration of biliary system disease exceeded 5 years in 112 patients (78%). A total of 106 patients (73.6%)--or three-quarters of all patients--were admitted to hospital more than 3 days after disease onset. The duration of cholangitis was up to 3 days in 38 patients (26.4%), 3-7 days in 78 patients (54.2%), and more than 7 days in 38 patients (26.4%) (Table 2.2).

Table 2.2

Time Interval from Onset of Suppurative Cholangitis to Hospital Admission

Admission interval (days)	Number of patients, abs. (%)		Total
	Study Group	Comparison Group	
≤3	20 (24.1%)	18 (29.5%)	38 (26.4%)
3-7	40 (48.2%)	28 (45.9%)	68 (47.2%)
>7	23 (27.7%)	15 (24.6%)	38 (26.4%)
Total	83 (100%)	61 (100%)	144 (100%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

Pain in the right hypochondrium and epigastric region (89.9%) was characteristic in the early days of the acute cholangitis attack; as more than 4 days elapsed from the onset, the number of patients complaining of pain syndrome decreased substantially (67.3%), while the number of patients with purulent-inflammatory complications of cholangitis increased (83.6%) (Table 2.3).

Table 2.3

Clinical Symptoms Observed in Patients According to Duration of Suppurative Cholangitis

Clinical Symptom	Jaundice ≤3 days (n=89)			Jaundice >3 days (n=55)		
	Study Group	Comparison Group	Total	Study Group	Comparison Group	Total
Pain in right	43	37 (41.6%)	80	20	17 (30.9%)	37

hypochondrium and epigastrium	(48.3%)		(89.9%)	(36.4%)		(67.3%)
Vomiting	31 (34.8%)	27 (30.3%)	58 (65.2%)	14 (25.5%)	12 (21.8%)	26 (47.3%)
Subfebrile temperature	38 (42.7%)	23 (25.8%)	61 (68.5%)	5 (9.1%)	4 (7.3%)	9 (16.4%)
Temperature >38°C	16 (18.0%)	12 (13.5%)	28 (31.5%)	24 (43.6%)	22 (40.0%)	46 (83.6%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

Our examinations demonstrated that the main factor leading to the development of suppurative cholangitis in patients with cholelithiasis was choledocholithiasis. Acute suppurative cholangitis developing as a complication of cholelithiasis arose in 82 patients (56.9%) as a result of choledocholithiasis and chronic calculous cholecystitis, and in 62 patients (43.1%) as a result of acute calculous cholecystitis and choledocholithiasis; of these, 29 patients had acute destructive cholecystitis complicated by peritonitis of varying extent (7 diffuse, 22 local) (Table 2.4).

Table 2.4

Clinical Presentation of Acute Suppurative Cholangitis

Clinical Presentation of ASC	Study Group	Comparison Group	Total
Choledocholithiasis + chronic calculous cholecystitis	48 (57.8%)	34 (55.7%)	82 (56.9%)
Acute destructive cholecystitis + choledocholithiasis With peritonitis: - Diffuse - Local	36 (39.6%) 17 4 13	26 (42.6%) 12 3 9	62 (43.1%) 29 7 22

*Note: * Difference between indicators is statistically significant (p <0.05)*

Signs of concomitant pathology of other organs and systems observed in patients are presented in Figure 2.1. As illustrated, the diagnosed comorbidities indicated the severity of the general condition, the large number of

complications adversely affecting treatment outcomes, and the multiplicity of systemic diseases in patients with suppurative cholangitis.

Comorbidities were identified in 97 patients (67.4%): primarily cardiovascular system disease in 59 (41.0%), chronic obstructive pulmonary disease in 21 (14.6%), obesity in 48 (33.3%), diabetes mellitus in 12 (8.3%), and other conditions in 19 (13.2%). Two or more concomitant conditions were identified in 54 patients (32.7%) (Figure 2.1).

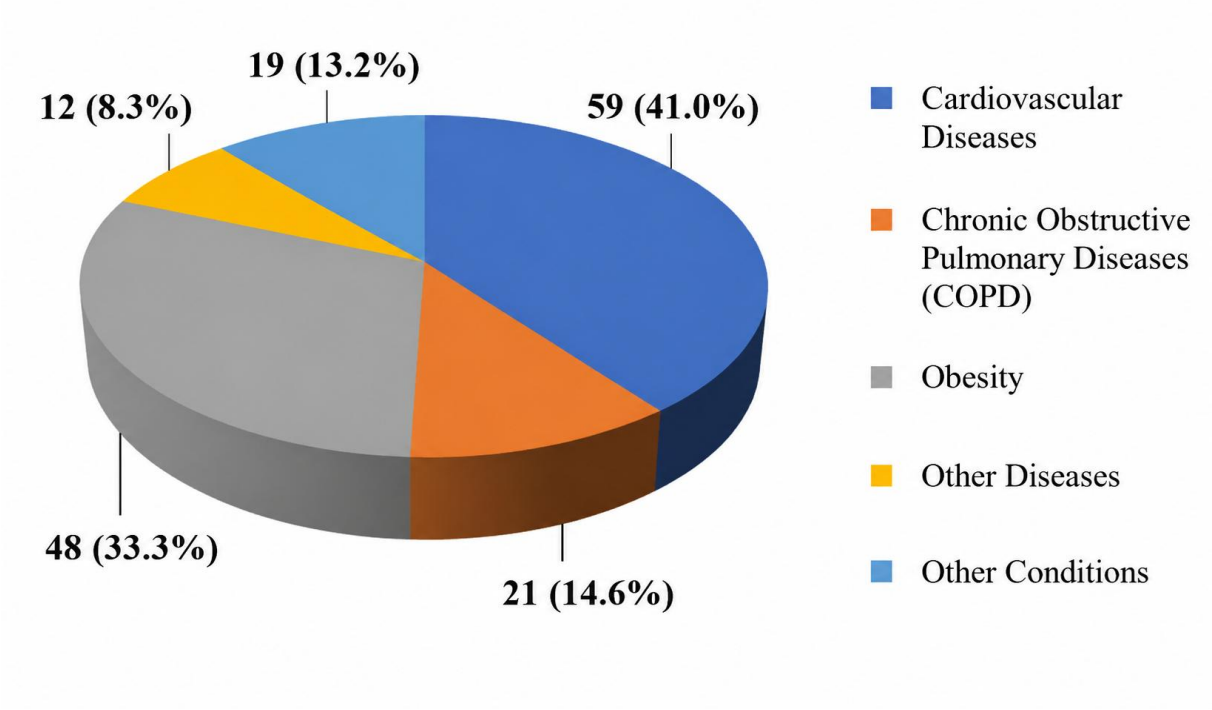


Figure 2.1. Distribution of patients according to concomitant diseases

Treatment of patients in the study group was conducted in accordance with the severity grading criteria for acute suppurative cholangitis proposed at the Tokyo Consensus Conference (2006). Based on these criteria, mild-grade ASC was identified in 54 patients (65%), moderate-grade in 18 (21.6%), and severe-grade in 11 (13.2%) (Table 2.5).

Table 2.5

Severity Grade Criteria for Cholangitis (Tokyo, 2006)

ASC Severity Grade	Severity Grade Criteria	No. of Patients
Mild acute cholangitis	Acute cholangitis that responds to initial conservative (including antibacterial) therapy within the first 24 hours	54 (65%)

Moderate acute cholangitis	Acute cholangitis not responding to initial conservative (including antibacterial) therapy within the first 24 hours, without organ dysfunction	18 (21.6%)
Severe acute cholangitis - Cardiovascular system - Nervous system - Respiratory system - Kidneys - Liver - Blood	Acute cholangitis not responding to initial conservative (including antibacterial) therapy within the first 24 hours, with dysfunction of one organ or system: - Hypotension controlled with dopamine >5 μg/kg/min or any dose of dobutamine - Altered consciousness - PaO_2/FiO_2 ratio <300 - Plasma creatinine >0.176 mmol/L - INR >1.5 - Platelet count $<100\times10^9$/L	11 (13.2%)

Diagnosis of acute suppurative cholangitis was made on the basis of clinical presentation (Charcot's triad, Reynolds' pentad), laboratory findings, and instrumental examination (sonography, ERCP, MR cholangiography). The definitive diagnosis was established on the basis of characteristic changes in the wall of the bile ducts and in bile, together with identification of the biliary microflora.

Figure 2.2. Patient D., 63 years. Image: thickening of the hepaticocholedochal wall, discharge of bile with fibrin threads through a choledochotomy incision

§2.2. General Characteristics of Research Methods

All patients examined and treated at the 1st Clinical Base of Samarkand State Medical Institute were first assessed by a surgeon, anaesthesiologist-

resuscitologist, and therapist for evaluation of objective status and identification of disease-specific clinical manifestations. The subsequent stage involved determination of disease criteria for prescribing laboratory and instrumental investigations in patients with acute suppurative cholangitis. The disease criteria included: abdominal pain (primarily in the right hypochondrium and epigastrium), nausea, fever, and jaundice; a history of chronic cholecystitis, cholelithiasis, or chronic pancreatitis; and dilatation of the hepaticocholedochus and the presence of choledocholithiasis confirmed by at least one radiodiagnostic examination.

§2.2.1. Results of Clinical-Laboratory Examination Methods

Laboratory examinations included complete blood count with determination of erythrocyte count, haemoglobin level, haematocrit, absolute leucocyte count, and differential leucocyte count in all patients.

The following parameters were determined in biochemical analyses: bilirubin and its fractions, urea, creatinine, total protein and its fractions, albumin/globulin (A/G) ratio, liver-specific enzymes--markers of cytolysis (AST and ALT), de Ritis coefficient (AST/ALT), cholestasis markers (GGT and ALP), blood glucose; coagulation parameters--plasma recalcification time, ethanol test, plasma fibrinolytic activity, fibrinogen, prothrombin index, thrombin time. Testing for hepatitis B and C was performed when indicated.

Bacteriological examination was performed to determine the characteristics of the biliary microflora, establish its role in the aetiology of acute suppurative cholangitis, and monitor the composition of the biliary microflora dynamically. Bacteriological examination of bile was performed in 123 patients. Microflora was identified in 117 patients; bile was sterile in only 6 patients (4.8%). The methodological protocol comprised two stages: pre-laboratory (bile collection and plating) and laboratory (identification of microflora composition and degree of biliary contamination). In the pre-laboratory stage, particular attention was paid to proper specimen collection. Bile from the biliary duct was used as the test material. Specimens were collected under aseptic conditions to prevent contamination by normal flora. In the preoperative period, bile was collected via an endoscope catheter introduced into the choledochus during ERCP or duodenoscopy, as well as through NBD. A volume of 2-3 mL of bile was sent for bacteriological analysis. In the postoperative period, specimens of bile flowing from external drains placed in the hepaticocholedochus were examined for dynamic monitoring of biliary

sanitation. Bacteriological cultures of bile were performed using classical microbiological technique in the bacteriological laboratory of the clinical-diagnostic department of the 1st Clinical Base of SamSMI. Qualitative analysis of bacteriocholia was performed on days 1, 3, 7, and 10 and before drain removal. The laboratory stage consisted of identification of microflora and quantitative characterisation of bile composition, calculated by the formula:

$$\mathbf{C = n \times A \times 5}$$

where C = number of microbial bodies per 1 mL of bile; n = number of colonies grown; A = dilution factor.

Analysis of the microbial spectrum of bile in suppurative cholangitis demonstrated the predominant growth of conditionally pathogenic organisms in cultures--primarily Gram-negative enteric flora--as well as the frequent co-occurrence of aerobic flora with non-clostridial anaerobic bacteria (Table 2.6).

Table 2.6

Biliary Microflora Characteristics in Acute Suppurative Cholangitis

Biliary Microflora	Number of Patients	%
Aerobic and facultative anaerobes	89	72.4
E. coli	51	41.5
Pseudomonas aeruginosa	4	3.3
Proteus vulgaris	10	8.1
Staphylococcus	8	6.5
Streptococcus	2	1.6
Enterobacter	3	2.4
Klebsiella	13	10.6
Obligate anaerobes	74	60.2
Bacteroides fragilis	26	21.1
Bacteroides melaninogenicus	18	14.6
Fusobacterium mortifortum	15	12.2
Peptococcus	11	8.9

*Note: * Difference between indicators is statistically significant (p <0.05)*

The observations demonstrated that the diagnostic value of bacteriological examination is high, allowing for accurate assessment of the sensitivity of the

flora to specific antibacterial agents and enabling timely initiation of therapeutic measures.

§2.2.2. Instrumental Examination Methods

Radiodiagnostic and endoscopic examination methods were employed among the instrumental examinations. Radiodiagnostic methods used included ultrasonography (USG), comprehensive MRI, and--when indicated--MSCT and ERCP. Information about the examinations performed is presented in Table 2.7.

Table 2.7

Information on Radiodiagnostic and Endoscopic Examinations Performed

Radiodiagnostic Method	Study Group		Comparison Group	
	Abs.	%	Abs.	%
Transabdominal ultrasonography (TAUS)	83	100	61	100
Magnetic resonance imaging (MRI) and/or MRCP	38	45.8	-	-
Endoscopic retrograde cholangiopancreatography (ERCP)	27	32.5	-	-
Multislice computed tomography (MSCT)	13	15.7	2	3.3
Oesophagogastroduodenoscopy	75	90.4	42	68.9

*Note: * Difference between indicators is statistically significant (p <0.05)*

As shown in Table 2.7, patients in the study group had greater access to modern radiodiagnostic techniques. The primary methods used in patients were ultrasonography, MRI with MRCP, and ERCP.

Transabdominal Ultrasonography

Transabdominal ultrasonography was performed in all patients of both the study and comparison groups as the initial stage of radiodiagnostics to identify pathological processes in the hepatobiliary region. The majority of examinations were performed using multifunction real-time ultrasound units (Mindray DC-3, SonoScape S50) with a 3-5 MHz convex transducer in two perpendicular planes.

Examinations in patients were performed electively in the morning in the fasting state, and without preparation in emergency situations. During the examination, in addition to assessment of the biliary tract, the liver and its porta

hepatis, spleen, duodenum, and the wall of the stomach were also evaluated. It should be noted that ultrasonography performed without preparation in emergency settings required significantly more time (approximately 1.5-2 times more) for visualisation of the distal biliary tract and pancreas due to the associated difficulties.

In 19 patients (13.2%) hospitalised in emergency settings and examined without preparation, assessment of the biliary tract was difficult and did not always yield the expected results. Analysis of ultrasonographic examinations of the biliopancreatoduodenal region allowed detection of hepaticocholedochal dilatation ranging from 9 to 23 mm in 106 patients (73.6%) (Figure 2.4). The mean hepaticocholedochal diameter was ±1.8 mm. Unsatisfactory detection of common bile duct dilatation in the remaining 38 patients (26.4%) was associated with the severity of the general condition and inadequate (or absent) preparation. It should be noted that primarily the proximal portions of the hepaticocholedochus were assessed, since visualisation of its distal portions was difficult in many instances. An important ultrasonographic finding was dilatation of the intrahepatic bile ducts, identified in 89 patients (61.8%) (Figure 2.4).

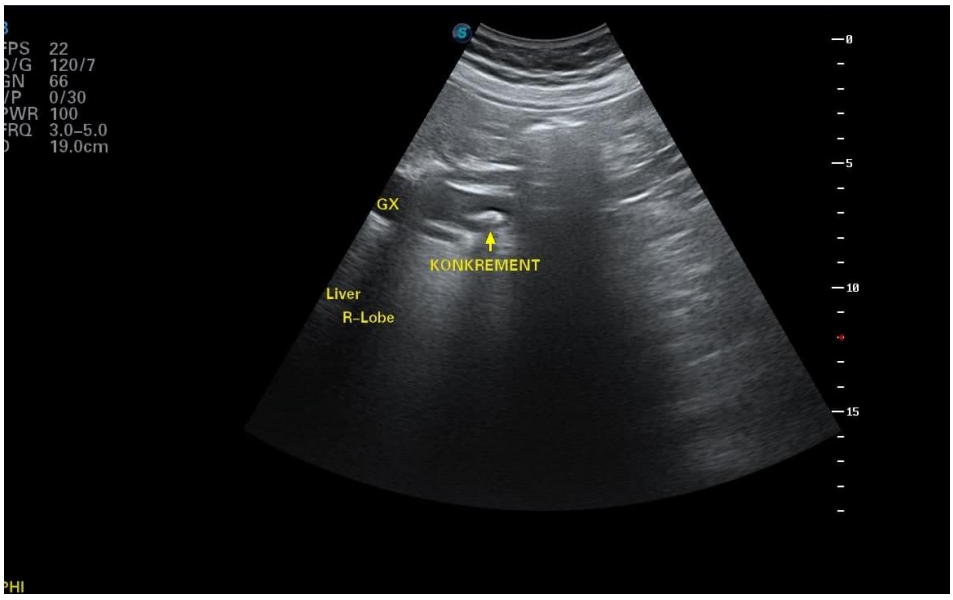


Figure 2.4. Patient Kh., 59 years. Echographic appearance of hepaticocholedochal and intrahepatic bile duct dilatation and a stone in the distal choledochus.

In cases where ultrasonographic results were unsatisfactory, advanced imaging modalities--MRCP, MSCT, and ERCP when indicated--were employed as the subsequent stage of investigation.

Magnetic Resonance Imaging

Examinations were performed using a "Magnetom Sola" tomograph (Siemens, Medical Systems, Germany), with a high-field magnet induction of 1.5 Tesla, enabling rapid acquisition of high-tissue-contrast images of adjacent structures. Examinations were performed with the patient in the supine position, face toward the tomograph tunnel, in a state of physiological rest and in the fasting state. In emergency settings, examinations were performed without preparation and were primarily limited to MRCP. Scanning was performed using a 32-channel phased-array surface body coil, ensuring high image quality (Figure 2.5).

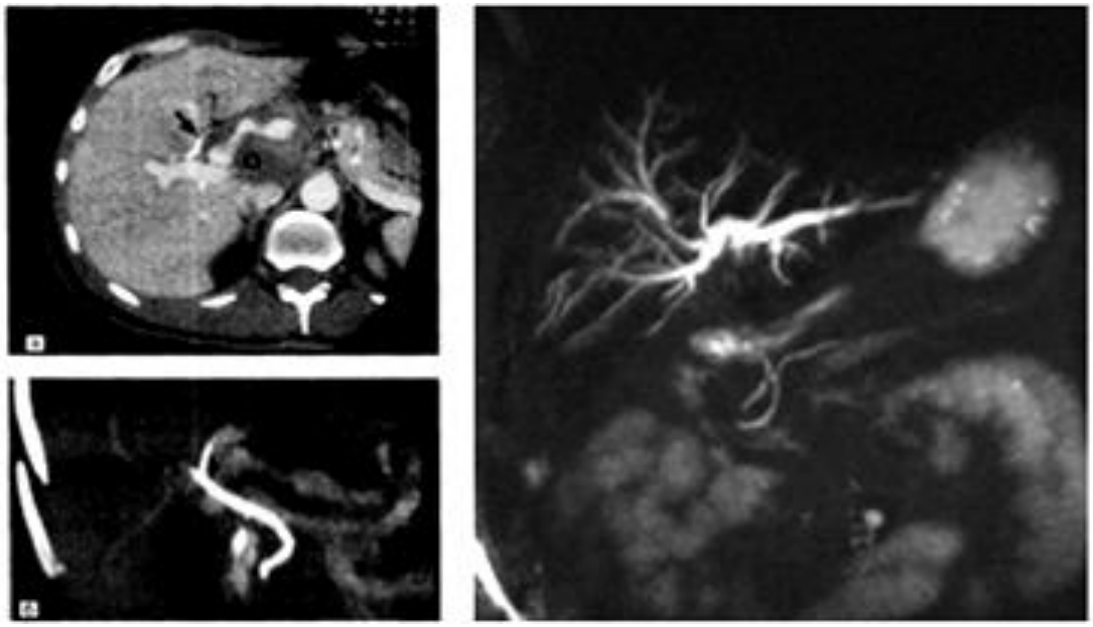


Figure 2.5. Patient D., 52 years. MRCP - ectasia of intrahepatic and extrahepatic bile ducts; concretions in the choledochus.

As the first stage of examination, conventional MRI was performed in the appropriate manner. Primary localisation was performed along the midline of the abdomen using a light reference and according to the position of the coil axis. For slice positioning, tomograms were first acquired using the "localizer" rapid acquisition programme based on gradient echo pulse sequence. The conventional MRI protocol incorporated T1 and T2 weighted sequences acquired in two (or three) planes, supplemented by the fat suppression technique. These sequences were implemented using breath-holding or respiratory triggering.

It should be noted that breath-hold sequences enabled acceleration of the examination. Respiratory triggering was used in patients in severe condition. In patients under 60 years of age, the hepaticocholedochal diameter was considered dilated if it exceeded 8 mm (>10 mm after cholecystectomy); in patients over 60 years, the thresholds were 9 mm and 12 mm, respectively. Images also provided information about stones of varying sizes in the common bile duct, tissue composition of detected formations, tissue oedema, and accumulated fluid. Based on the data obtained, the nature of obstruction of the common bile duct was pre-characterised.

Magnetic resonance cholangiopancreatography allowed detailed study of the anatomical variant of the biliary tree, detection of small stones in the biliary ducts (intraluminal and intramural formations), and assessment of the terminal portion of the common bile duct.

In our investigations, the diagnostic accuracy of MRCP performed in 38 patients for detection of choledocholithiasis and biliary ductal ectasia was 97.5%.

Multislice Computed Tomography

Radiographic computed tomography was performed in 15 patients using a Siemens SOMATOM Go Up multislice spiral tomograph capable of acquiring 64 sections per tube rotation. The standard protocol was used; scanning was performed in the fasting state. Initial native scanning was performed in the craniocaudal direction. Pre-contrast section thickness was 1.5 mm; for angiography--0.75 mm; reconstruction step was 1.5 mm and 0.75 mm, respectively. In the second stage, scanning was performed with bolus injection of contrast medium at 3.5-4 mL/sec using a "Medrad" automatic bolus injector, followed by image reconstruction. The contrast agent used was "Ultravist" (Bayer, Germany) with iodine concentration of 340-360 mg/mL, administered at 1 mL/kg body weight. Post-contrast scanning was performed in the arterial (20-30 seconds) and venous (60-70 seconds) phases. Section thickness and reconstruction step were both 1.5 mm. Pathological formations identified in the terminal common bile duct were assessed by their contrast enhancement characteristics. Multiplanar and volumetric reformation analysis enabled integral organ and tissue imaging, detection of common bile duct dilatation, and characterisation of the morphology of the liver, gallbladder, pancreas, and terminal common bile duct pathology. Detailed densitometric assessment

combined with contrast medium use further improved the overall effectiveness of CT diagnosis of biliary hypertension and its aetiology (Figure 2.6).

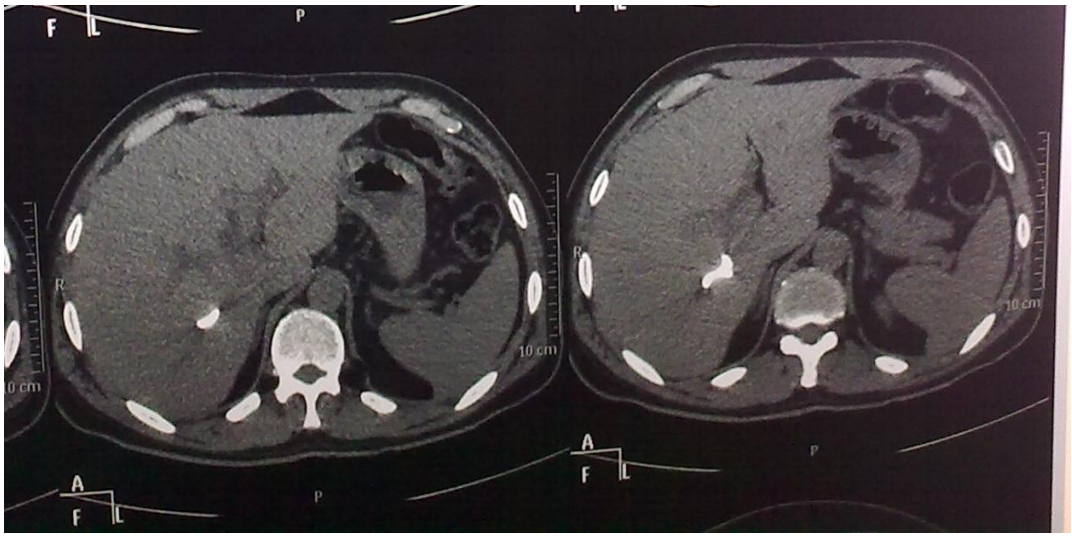


Figure 2.6. Patient Sh., 46 years. MSCT - an enlarged gallbladder and multiple stones in the choledochus are identified.

The value of MSCT performed in 13 patients from both the study and comparison groups was rated as 100%.

Endoscopic Retrograde Cholangiopancreatography

ERCP was performed in 27 of the examined patients (18.8%) for diagnostic and therapeutic purposes. Prior to the procedure, endoscopic examination of the oesophagus, stomach, and duodenum was performed. This examination was performed in the radiological-surgical suite using an Olympus Evis Exera TJF-160VR side-viewing videoduodenoscope according to the standard technique. Selective cannulation of the common bile duct was performed through the major duodenal papilla using an ERCP catheter over a guidewire, with injection of contrast medium under fluoroscopic control. In all 27 patients, the procedure was completed with a minimally invasive manoeuvre--endoscopic papillosphincterotomy (EPST)--using a fibre-type papillotome introduced into the common bile duct over a pre-placed guidewire. In all cases, an incision was made along the entire length of the longitudinal fold in the clockwise direction, with current delivered in ENDOCUT mode. This mode automatically controls current intensity according to tissue resistance. Use of ENDOCUT mode reduces the risk of haemorrhage and pancreatitis while maximally minimising post-coagulation oedema. Omnipaque (non-ionised triiodinated radiocontrast agent) solution with iodine concentration of 270, 300,

and 350 mg I/mL was used as the radiocontrast agent. Adverse reactions were observed less frequently with this agent than with ionised contrast agents.

Thus, patients underwent comprehensive clinical-biochemical, instrumental, and radiodiagnostic evaluation, which was sufficient for the diagnosis of suppurative cholangitis and for differential diagnosis between identified pathological changes and types of biliary hypertension (Figure 2.7).

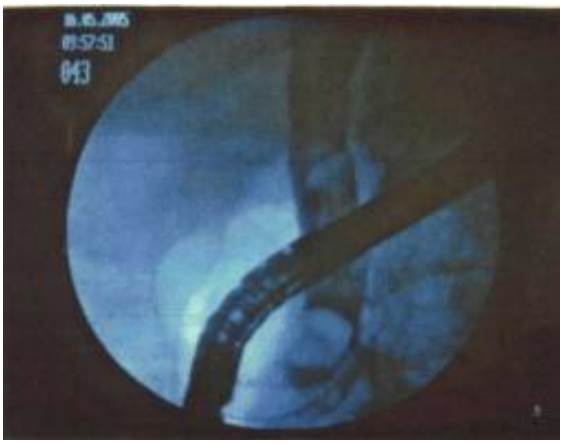


Figure 2.7. Patient I., 39 years. Endoscopic retrograde pancreatocholangiography.

CHAPTER III
OPTIMISATION OF THE TACTICAL AND TECHNICAL ASPECTS OF COMPLEX SURGICAL TREATMENT OF BENIGN SUPPURATIVE CHOLANGITIS

Surgical intervention was performed in 144 patients with acute suppurative cholangitis (ASC) arising as a complication of cholelithiasis, who were treated in the Surgical Department of the 1st Clinical Base of SamSMI between 2000 and 2019.

Acute suppurative cholangitis arising as a complication of cholelithiasis was caused by choledocholithiasis and chronic calculous cholecystitis in 82 patients (56.9%), and by acute calculous cholecystitis and choledocholithiasis in 62 patients (43.1%); of the latter group, acute destructive cholecystitis was complicated by various forms of peritonitis in 29 patients (7 diffuse, 22 local).

Patients were divided into two study groups in accordance with the research objectives. The comparison group comprised 61 patients (42.4%) who underwent surgery between 2000 and 2009 for acute suppurative cholangitis arising as a complication of cholelithiasis. The study group consisted of 83 patients (57.6%) treated between 2010 and 2019 using the surgical protocol implemented in clinical practice. Patients in both groups were comparable in age, prominence of clinical manifestations, and degree of severity.

In the preoperative and postoperative periods, patients received standard detoxification therapy, including intravenous infusions of 2,500-3,000 mL per day under diuresis monitoring: 5% glucose solution with insulin at 4 g of dry glucose, 0.9% sodium chloride solution, Ringer-Locke solution, Reamberin, Disol, Reosorbilact, and other crystalloid solutions. Intravenous infusions were supplemented by antibacterial therapy, primarily beta-lactam antibiotics (ceftriaxone, cefoperazone, imipenem, 1.0 g 2-3 times daily), fluoroquinolones (ofloxacin, levofloxacin 100 mL twice daily) in combination with metronidazole 100 mL twice daily, and analgesics: narcotic (promedol 2%-1.0 mL for the first 24 hours) and non-narcotic (ketorolac 1.0 mL, baralgin 0.5%-5 mL, spasmalgin 5.0 mL).

Analysis of the antibiotic sensitivity of micro-organisms encountered in suppurative cholangitis demonstrated that the highest sensitivity corresponded to ceftriaxone (85.2%), cefoperazone (83.1%), and levofloxacin (82.9%).

According to the literature, convincing evidence regarding the superiority of a particular antibacterial therapy regimen is lacking to date; however, the importance of adequate biliary sanitation in suppurative cholangitis must not be overlooked.

§3.1. Treatment Outcomes in the Comparison Group

In all 61 operated patients in the comparison group, surgical interventions were performed in the scope of cholecystectomy, choledocholithotomy, and external drainage of the choledochus; operations via wide laparotomy incision were performed in 48 patients (79%), and via minilaparotomy incision in 13 patients (21%) (Figure 3.1).

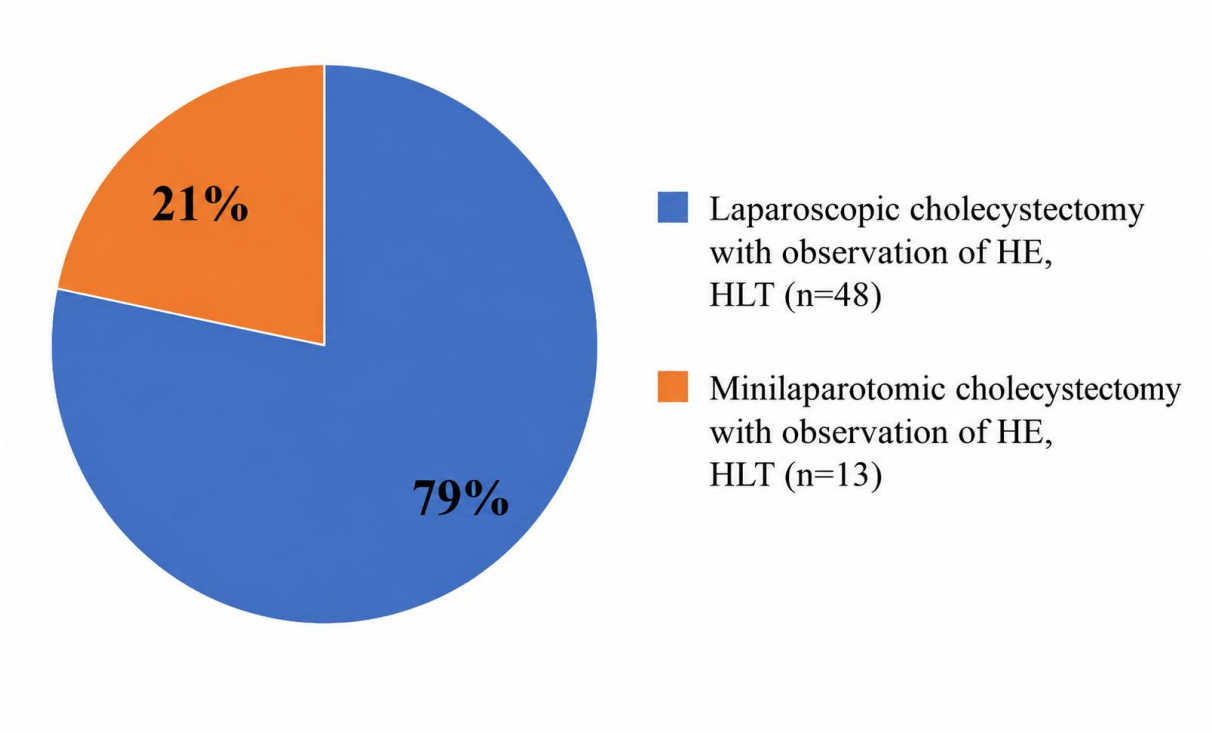


Figure 3.1. Types of surgical interventions in patients with ASC in the comparison group (n=61)

In this group, emergency cholecystectomy and choledocholithotomy were performed as urgent procedures (within 2-3 hours of hospitalisation) in 29 patients (47.5%) due to acute destructive cholecystitis; in 12 of these, the procedure was performed for acute destructive cholecystitis complicated by peritonitis. Additionally, emergency procedures were performed in 6 patients for rapidly progressive mechanical jaundice with acute obstruction of the main biliary ducts and severe pain syndrome.

Deferred urgent operations (within 2-3 days of hospitalisation) were performed in 32 patients (56%) in whom the clinical features of acute biliary obstruction predominated, without signs of destructive cholecystitis (Figure 3.2).

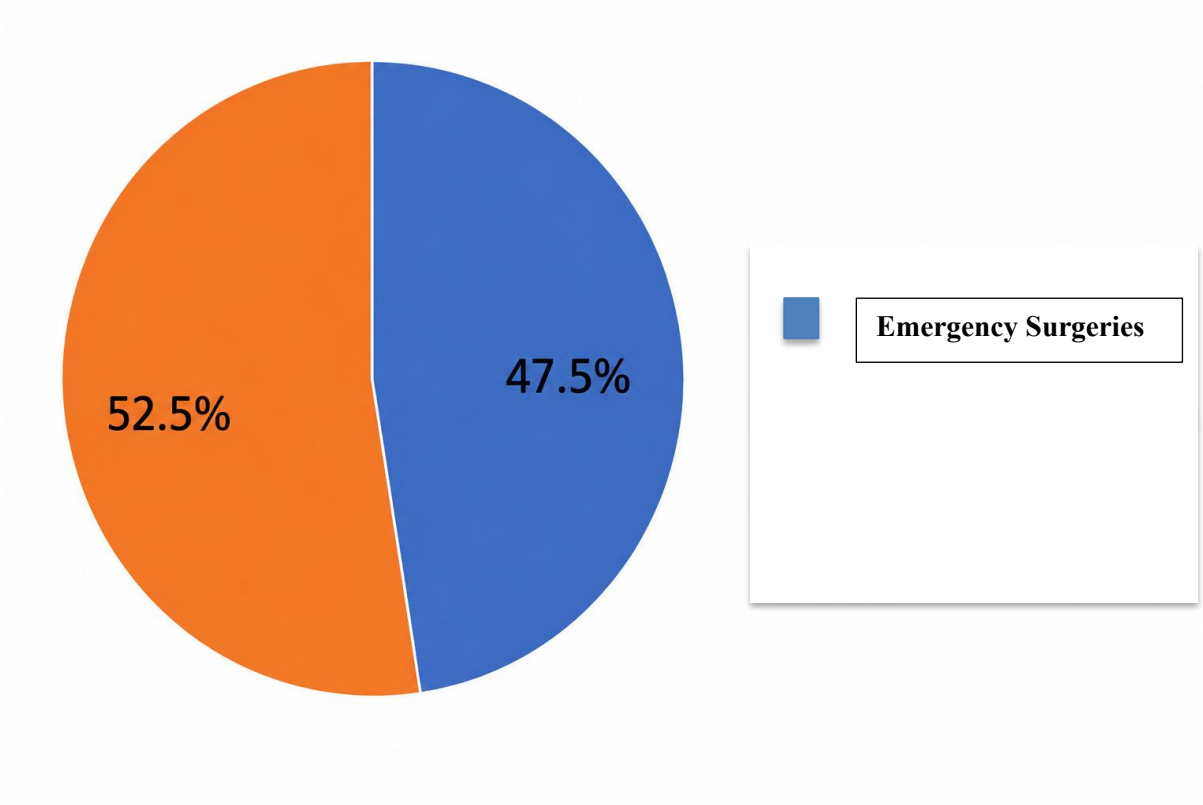


Figure 3.2. Timing of operations in the comparison group (n=61)

Analysis of the timing of operations in the comparison group revealed that postoperative complications and mortality were more frequent after emergency operations: mortality 13.8%, purulent-septic complications 37.9%. After deferred urgent operations, mortality was 3.1% and purulent-septic complications 11.7% (Table 3.1).

Table 3.1

Postoperative Mortality and Complication Rates According to Operation Type in the Comparison Group

Operation Type	No. of Operations	Mortality	Purulent-Septic Complications
Emergency operations	29 (47.5%)	4 (13.8%)	11 (37.9%)
Deferred urgent operations	32 (52.5%)	1 (3.1%)	4 (11.7%)
Total	61 (100%)	5 (8.2%)	15 (24.6%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

In the comparison group, the highest percentage of postoperative complications and mortality was observed when ASC was combined with acute destructive cholecystitis: mortality 14.8% and purulent-septic complications 44.4%. When ASC occurred with chronic calculous cholecystitis, mortality was 2.9% and purulent-septic complications 8.8% (Table 3.2).

Table 3.2

Mortality and Postoperative Complication Rates in the Comparison Group According to Clinical Presentation of ASC

Clinical Presentation of ASC	No. of Operations	Mortality	Purulent-Septic Complications
ASC + acute destructive cholecystitis	29 (44.3%)	4 (14.8%)	12 (44.4%)
ASC + chronic calculous cholecystitis	32 (55.7%)	1 (2.9%)	3 (8.8%)
Total	61 (100%)	5 (8.2%)	15 (24.6%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

Thus, in the comparison group, fatal outcomes (14.8%) and purulent-septic complications (44.4%) were observed primarily after emergency surgical interventions performed for ASC combined with acute destructive cholecystitis and peritonitis.

Among the most severe complications in the comparison group, cholangenic hepatic abscess and biliary sepsis were observed in 4 patients, all of whom died. Ongoing peritonitis resulted in a fatal outcome in 1 patient in our series. In the comparison group, the overall postoperative mortality was 8.2%, and purulent-septic complications were observed in 15 patients (24.6%) (Table 3.3).

Table 3.3

Causes of Mortality and Incidence of Purulent-Septic Complications in the Comparison Group

Cause of Death	Abs. (%)
Cholangenic hepatic abscess and biliary sepsis	4 (14.8%)

Peritonitis	1 (2.9%)
Total Deaths	5 (8.2%)
Purulent-Septic Complications	
Biloma	2 (3.2%)
External biliary fistula	5 (8.2%)
Cholemic haemorrhage	2 (3.3%)
Subhepatic and subphrenic abscess	5 (8.2%)
Wound suppuration	12 (19.6%)
Total Complications	15 (24.6%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

The unsatisfactory outcomes of surgical treatment of ASC were primarily associated with the development of biliary sepsis, underscoring the necessity of optimising the tactical and technical aspects of complex surgical treatment of this pathology.

§3.2. Optimisation of the Tactical and Technical Aspects of Surgical Treatment of Acute Suppurative Cholangitis Through the Use of Minimally Invasive Procedures

Treatment of 83 patients in the study group who underwent surgery between 2010 and 2019 for acute suppurative cholangitis arising as a complication of cholelithiasis was carried out with consideration of the criteria of the "Severity Classification of Acute Suppurative Cholangitis" proposed at the Tokyo Consensus Conference (2006). Based on these criteria, mild-grade ASC was recorded in 54 patients (65%), moderate-grade in 18 (21.6%), and severe-grade in 11 (13.2%) (Table 3.4).

Table 3.4

ASC Severity Grades in Patients of the Study Group (Tokyo Guidelines 2013, TG13)

ASC Severity Grade	Criteria for ASC Severity Grade	No. of Patients
Mild acute suppurative cholangitis	Acute cholangitis that responds to initial complex intensive (including antibacterial) therapy commensurate with severity within the first 24 hours	54 (65%)
Moderate acute	Acute cholangitis commensurate with	18

suppurative cholangitis	severity that does not respond to initial complex intensive (including antibacterial) therapy within the first 24 hours, without organ dysfunction	(21.6%)
Severe acute suppurative cholangitis - Cardiovascular system - Nervous system - Respiratory system - Kidneys - Liver - Blood	Acute cholangitis commensurate with severity that does not respond to initial complex intensive (including antibacterial) therapy within the first 24 hours, with dysfunction of one organ or system: - Hypotension controlled by dopamine >5 mg/kg/min or any dose of dobutamine - Altered consciousness - PaO_2/FiO_2 <300 - Plasma creatinine >0.176 mmol/L - INR >1.5 - Platelet count <100×10^9/L	11 (13.2%)

*Note: * Difference between indicators is statistically significant (p <0.05)*

Minimally invasive and open surgical interventions were performed considering both the severity grade criteria in patients with acute suppurative cholangitis and the presence or absence of acute destructive cholecystitis and peritonitis.

In the study group, minimally invasive decompressive interventions were performed as the first stage in 20 of the patients with moderate-grade (n=18) and severe-grade (n=11) ASC.

Specifically, in 9 patients with acute destructive cholecystitis, percutaneous transhepatic microcholecystostomy (PTMC) was performed under ultrasound guidance for gallbladder decompression. Subsequently, 5 of these patients underwent endoscopic papillosphincterotomy (EPST) and nasobiliary drainage (NBD).

Clinical case: Patient Z., 59 years of age, was admitted to the surgical department on 16.10.2019 (case history No. 7022/1025) complaining of pain in the right hypochondrium, rigors, fever up to 39°C, nausea and vomiting, icteric sclerae, and dark urine. Has been ill for 2 weeks. Associates the onset with excessive fatty food intake. History: recurrent paroxysmal right hypochondriac pain. In 2016, ultrasonography revealed cholelithiasis.

General condition: moderate severity. Skin and sclerae icterically tinged. Auscultation: bilateral vesicular breath sounds, no crackles. Heart tones muffled, accentuated second tone over the aorta. Pulse rhythmic, tense, 96 per minute. Tongue slightly dry, coated brown. Abdomen of normal shape, participates in respiration; palpation reveals local muscle guarding in the right hypochondrium with an enlarged, tender gallbladder fundus palpable. Murphy's sign and Ortner-Grekov sign positive. Liver and spleen not palpable. Stools normal. Micturition free.

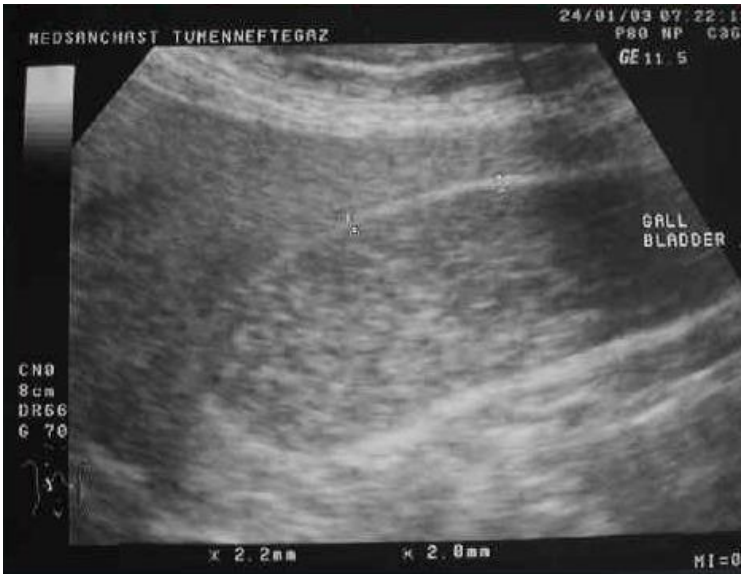


Figure 3.2. Patient Z., 59 years. Ultrasonography of the gallbladder and biliary tract.

Complete blood count: Hb 96 g/L; RBC 3.4×10¹²/μL; CP 0.8; platelets 230; WBC 9.7×10⁹/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 25 mm/h; Ht 24.

Biochemical blood analysis: total bilirubin 149.65 μmol/L; conjugated bilirubin 138.27 μmol/L; ALT 1.96 mmol/L; AST 1.34 mmol/L; thymol turbidity 2; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L.

Chest X-ray: no pathology detected.

Ultrasonography: gallbladder dimensions 15×8 cm; stones up to 1 cm in the lumen, one of which occluded the gallbladder neck (Figure 4.12). Choledochus diameter 1.9 cm; intrahepatic bile ducts not dilated.

With the diagnosis of "Acute calculous destructive cholecystitis, cholangitis, mechanical jaundice," and taking into account the severity of the patient's condition, microcholecystostomy under ultrasound guidance was fashioned on 17.10.2019 for decompression, with evacuation of 120 mL of pus. On 18.10.2019, EPST with NBD was performed for biliary decompression; a 0.5-0.6 cm soft stone and purulent thick bile were evacuated under pressure. Through the NBD, thick turbid bile continued to drain over the following 24 hours. The biliary tract was irrigated through the NBD for 10 days with 0.06% sodium hypochlorite solution, and detoxification therapy was administered. Seven days after microcholecystostomy and NBD placement, the patient's condition improved.

Complete blood count 8 days after NBD placement: Hb 94 g/L; RBC 3.2×10^{12}/μL; CP 0.8; platelets 230; WBC 6.5×10^{9}/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 15 mm/h; Ht 24. Biochemical blood analysis: total bilirubin 29.15 μmol/L; conjugated bilirubin 18.1 μmol/L; ALT 0.92 mmol/L; AST 1.34 mmol/L; thymol turbidity 2; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L.

On 27.10.2019, the patient underwent laparoscopic cholecystectomy under endotracheal anaesthesia.

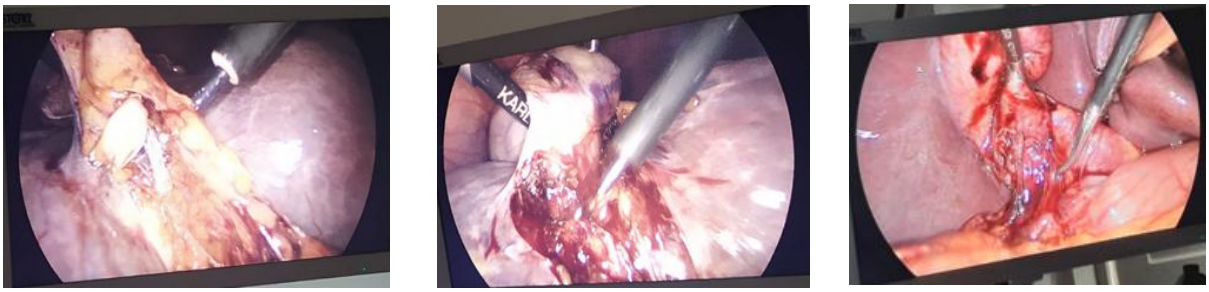


Figure 3.3. Stages of laparoscopic cholecystectomy (Patient Z., 59 years, case history No. 7022/1025).

The postoperative course was uneventful; the drain yielded approximately 5 mL of serosanguinous fluid on the first postoperative day. The drain was removed on postoperative day 2. The patient was discharged in satisfactory condition on the fourth postoperative day after LC (01.11.2019).

In the remaining 4 patients, PTMC allowed resolution of the clinical features of acute suppurative cholangitis. In 11 patients with ASC symptoms in the absence of clinical signs of acute cholecystitis, endoscopic transduodenal

interventions--EPST with lithoextraction and NBD--were performed as the first stage. In the second stage, cholecystectomy was performed in these 20 patients: LC in 13 and mini-laparotomy cholecystectomy (MLCE) in 7; in 4 cases, MLCE was combined with choledocholithotomy.

Emergency laparotomy, cholecystectomy, choledocholithotomy, and abdominal cavity sanitation were performed in 4 patients with clinical signs of peritonitis on an urgent basis.

Clinical case: Patient N., 48 years of age, was admitted to the surgical department on 24.05.2019 (case history No. 4677/342) complaining of pain throughout the abdomen, abdominal distension, dry mouth, rigors, fever, nausea and vomiting, icteric sclerae, acholic stools, and general malaise. Has been ill for 7 days.

General condition: severe. Skin and sclerae icterically tinged. Auscultation: bilaterally weakened vesicular breath sounds, no crackles. Heart tones muffled. Pulse rhythmic, tense, 105 per minute. Tongue dry, coated. Abdomen symmetric, does not participate in respiration; palpation reveals generalised pain and muscle guarding. Shchetkin-Blumberg, Murphy, Ortner-Grekov, and Mussi-Georgievsky signs positive. Liver and spleen not palpable. Acholic stools. Micturition free.

Complete blood count: Hb 78 g/L; RBC 2.2×10^{12}/μL; CP 0.7; platelets 210; WBC 12.1×10^{9}/μL; clotting time 2'30"-3'50"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 5%; lymphocytes 22%; monocytes 5%; ESR 26 mm/h. Biochemical blood analysis: bilirubin 126.6 μmol/L; ALT 0.98 mmol/L; AST 1.19 mmol/L; thymol turbidity 4; urea 8.36 mmol/L; residual nitrogen 19 g/L; creatinine 119.2 μmol/L; total protein 52.5 g/L.

Chest X-ray: no pathology. Ultrasonography: gallbladder 94×45 mm, wall thickness up to 8 mm, a stone of 9×13 mm in the neck region. Intrahepatic bile ducts mildly dilated, walls thickened; a stone 10×8 mm in the common bile duct. Bowel dilated. Approximately 300 mL of free fluid in the subhepatic space and pelvis.

With the diagnosis of "Acute calculous destructive cholecystitis, choledocholithiasis, acute suppurative cholangitis, mechanical jaundice, peritonitis," the patient underwent, on 25.05.2019, under general endotracheal anaesthesia: "Laparotomy. Cholecystectomy. Choledocholithotomy. Sanation and external drainage of the choledochus according to A.V. Vishnevsky. Sanation and drainage of the abdominal cavity." On postoperative day 1, the

drain yielded 70-80 mL of thick turbid bile. Bacteriological culture of bile identified E. coli, confirmed to be sensitive to cefotaxime. On postoperative day 2, to achieve early resolution of the biliary inflammatory process, the common bile duct was irrigated with 0.06% sodium hypochlorite solution. Following the 1st session of choledochal irrigation with 0.06% sodium hypochlorite solution, bile output was 240 mL; after the 2nd and 3rd sessions--370 mL and 560 mL, respectively--and progressively increasing day by day. Repeat bacteriological examination of bile revealed a significant reduction in microbial titre. After the 4th session of choledochal irrigation with 0.06% sodium hypochlorite solution, the signs of suppurative cholangitis were completely resolved.

Repeat complete blood count: Hb 74 g/L; RBC 2.0×10^{12}/μL; CP 0.7; platelets 243; WBC 8.1×10⁹/μL; clotting time 3'30"-5'50"; stab neutrophils 2%; segmented neutrophils 66%; eosinophils 3%; lymphocytes 24%; monocytes 5%; ESR 14 mm/h. Biochemical analysis: bilirubin 36.6 μmol/L; ALT 0.78 mmol/L; AST 0.91 mmol/L; thymol turbidity 4; urea 7.56 mmol/L; residual nitrogen 16 g/L; creatinine 89.2 μmol/L; total protein 55.3 g/L. Ultrasonography: intrahepatic bile ducts within normal limits, wall thickness 3 mm; drain tube identified in the choledochal lumen. The patient was discharged on postoperative day 7 in satisfactory condition with the choledochal drain in situ.

In a further 5 patients whose ASC clinical features intensified due to unsuccessful attempts at EPST, mini-laparotomy cholecystectomy was performed in combination with choledocholithotomy.

Clinical case: Patient Z., 65 years of age, was admitted to the surgical department on 12.02.2019 (case history No. 3062/525) complaining of pain in the right hypochondrium, rigors, fever up to 39°C, nausea and vomiting, icteric sclerae, and dark urine. Has been ill for 1 week. Associates the onset with fatty food intake. History: recurrent paroxysmal right hypochondriac pain. In 2013, ultrasonography revealed cholelithiasis.

General condition: moderate severity. Skin and sclerae icterically tinged. Auscultation: bilateral vesicular breath sounds, no crackles. Heart tones muffled. Pulse rhythmic, tense, 96 per minute. Tongue slightly dry, brownish coated. Abdomen of normal shape, participates in respiration; palpation reveals local muscle guarding in the right hypochondrium with an enlarged, tender gallbladder fundus palpable. Murphy's and Ortner-Grekov signs positive. Liver and spleen not palpable. Stools normal. Micturition free.

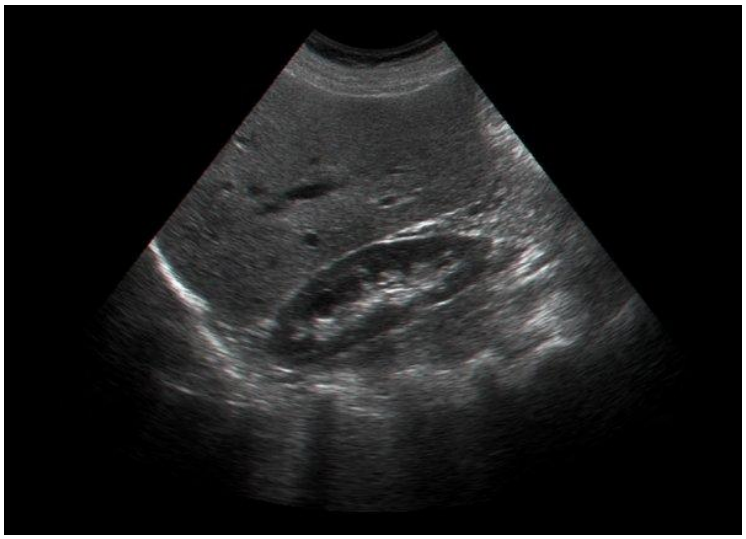


Figure 3.4. Patient Z., 69 years. Ultrasonography of the gallbladder and biliary tract.

Complete blood count: Hb 96 g/L; RBC 3.4×10¹²/μL; CP 0.8; platelets 230; WBC 9.7×10⁹/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 25 mm/h; Ht 24.

Biochemical blood analysis: total bilirubin 149.65 μmol/L; conjugated bilirubin 138.27 μmol/L; ALT 1.96 mmol/L; AST 1.34 mmol/L; thymol turbidity 2; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L.

Chest X-ray: no pathology.

Ultrasonography: gallbladder dimensions 12×4 cm; stones up to 1 cm in lumen, one stone impacted in the gallbladder neck (Figure 3). Choledochus diameter 0.8 cm; intrahepatic bile ducts not dilated. ECG: signs of ischaemia of the posterior wall of the left ventricular myocardium.

With the diagnosis of "Acute calculous obstructive destructive cholecystitis, mechanical jaundice, cholangitis," microcholecystostoma was fashioned under ultrasound guidance on 13.02.2019. An attempt to perform EPST for biliary decompression was made; placement of NBD drainage was not successful. Approximately 10 mL of purulent-mixed bile drained from the microcholecystostoma per day. Antibiotic therapy (ceftriaxone 1.0 IV ×2 daily), metronidazole IV, and detoxification therapy were administered for 7 days.

The patient's condition improved favourably 6 days after microcholecystostomy. Repeat blood count 8 days after microcholecystostomy:

Hb 86 g/L; RBC 3.2×10¹²/μL; CP 0.8; platelets 230; WBC 6.5×10⁹/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 20 mm/h; Ht 24. Biochemical analysis: total bilirubin 25.15 μmol/L; conjugated bilirubin 16.1 μmol/L; ALT 0.92 mmol/L; AST 1.04 mmol/L; thymol turbidity 2; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L.

On 20.02.2019, under endotracheal anaesthesia, cholecystectomy and choledocholithotomy were performed via a minilaparotomy incision. A 5 cm vertical transrectus skin incision was made. Abdominal exploration revealed the gallbladder adherent to the greater omentum; adhesions were divided sharply and bluntly. Subsequent exploration revealed adhesion of the duodenal wall to the Hartmann's pouch; the hepaticocholedochus was identified. Gallbladder dimensions: 15×6 cm. The hepaticocholedochus was dilated to 2 cm. Fundus-first cholecystectomy was performed. At the subsequent stage, choledocholithotomy was performed with evacuation of purulent bile under pressure; a 1.5 cm stone was extracted, and drainage was placed according to A.V. Vishnevsky. The subhepatic space was drained. The abdominal cavity was dried and the wound was closed in layers. An aseptic dressing was applied.

The postoperative course was uneventful; the drain yielded approximately 5 mL of serosanguinous fluid on postoperative day 1. The drain was removed on day 2. The wound healed by primary intention. The patient was discharged in satisfactory condition on the fourth postoperative day (26.02.2019).

Thus, two-stage surgical treatment was performed in 11 patients (61.1%) with moderate-grade and in 9 patients (81.8%) with severe-grade ASC (Table 3.5).

Table 3.5
Surgical Interventions Performed in Patients with Moderate and Severe Grade ASC in the Study Group (n=29*)

Diagnosis	Operation Type	No. of Patients	
ASC + acute destructive cholecystitis	PTMC, EPST and NBD → LC	2	9
	PTMC, EPST and NBD → MLCE	3	
	PTMC → MLCE + choledocholithotomy	4	

ASC + acute destructive cholecystitis + local peritonitis	Laparotomy, CE, choledocholithotomy, abdominal cavity sanation	4	
ASC + chronic calculous cholecystitis	EPST and NBD → LC	11	16
	MLCE + choledocholithotomy	5	

In mild-grade ASC, two-stage surgical treatment was performed in 13 patients (24.1%), and single-stage radical surgery in 41 patients (Table 3.6).

Table 3.6

Surgical Interventions Performed in Patients with Mild-Grade ASC in the Study Group (n=54)

Diagnosis	Operation Type	No. of Patients	
ASC + acute destructive cholecystitis	PTMC, EPST and NBD → LC	6	9
	PTMC, EPST and NBD → MLCE	1	
	PTMC → MLCE + choledocholithotomy	2	
ASC + acute destructive cholecystitis + local peritonitis	Laparotomy, CE + choledocholithotomy and abdominal cavity sanation	13	
ASC + chronic calculous cholecystitis	EPST and NBD → LC	3	32
	EPST and NBD → MLCE	1	
	MLCE + choledocholithotomy	28	

Percutaneous transhepatic microcholecystostomy (PTMC) was performed altogether in 18 patients (21.7%) in the study group. To ensure needle-tract hermeticity and prevent bile spillage into the abdominal cavity, the puncture was performed under ultrasound guidance through the hepatic parenchyma.

In all cases, drainage was performed using a stylet-catheter of 4F and 9F diameter with a terminal "basket."

In patients with moderate and severe grades of ASC who posed a high surgical-anaesthetic risk, emergency cholecystostomy was replaced by percutaneous transhepatic microcholecystostomy under ultrasound guidance as an alternative to surgical intervention. Indications for microcholecystostomy also arose in uncomplicated cases when conservative therapy was ineffective. When acute cholecystitis occurred with mechanical jaundice, gallbladder drainage achieved decompression of the biliary tract, thereby also resolving jaundice.

All percutaneous procedures under ultrasound guidance were performed using a SonoScape S50 1846 device operating in 3.5 MHz mode with a sector sensor in conjunction with a puncture attachment. The telemonitor of this device is equipped with an electronic matrix for displaying the puncture trajectory to the target organ (Figure 3.5).

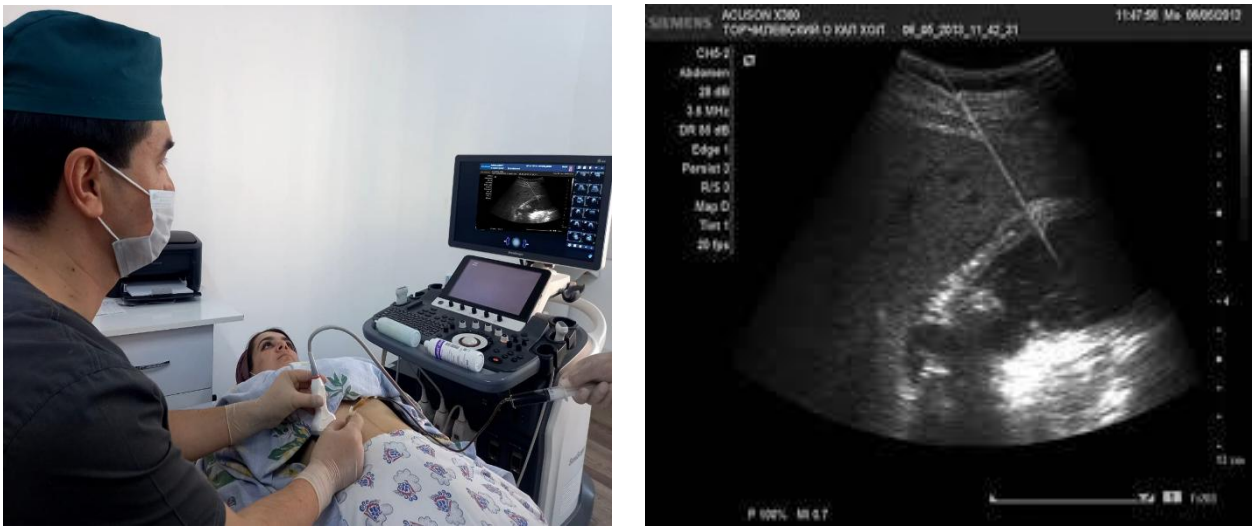


Figure 3.5. Performance of percutaneous transhepatic microcholecystostomy under ultrasound guidance.

In all cases, drainage was performed as a single-stage procedure using stylet-catheters 25 cm in length and 4F and 9F in diameter (French scale) with a terminal "basket." The catheter tip has a conical taper enabling secure fixation of the reinforced stylet. On placement of the stylet into the catheter, the "basket" blades straighten and do not impede catheter entry into the cavity (Figure 3.6).

Figure 3.6. Use of stylet-catheter for percutaneous transhepatic microcholecystostomy: a - puncture needle with catheter introduced into the gallbladder through the liver; b - position of catheter in the gallbladder lumen (diagram).

After stylet removal, the "basket" returned to its original position due to the material's memory, preventing catheter displacement from the cavity. All procedures were performed under ultrasound guidance in an aseptic setting in a specially equipped room. The patient's abdominal skin was treated with 3% alcoholic iodine solution. Local anaesthesia of the skin, subcutaneous tissue, and anterior abdominal wall muscles was performed at the planned puncture site using 0.25% novocaine or trimecaine solution (taking into account any drug allergy). The skin, subcutaneous fat, and aponeurosis of the external oblique abdominal muscle were incised with a double-edged scalpel 1-1.5 cm to allow unobstructed stylet-catheter passage. Gallbladder drainage was performed in a single precise movement while the patient held their breath, under ultrasound monitor control of the distal end of the stylet-catheter positioning (Figure 3.5). Once the position of the "basket" within the gallbladder lumen was confirmed, the instrument was halted; the catheter was maintained in position while the stylet was withdrawn. The drain was secured to the skin using two silk or nylon sutures. The puncture point on the gallbladder was selected taking into account the variability of its position and liver dimensions (presence or absence of hepatomegaly). In most patients, this procedure was performed through the subcostal margin along the mid-clavicular line.

Percutaneous transhepatic microcholecystostomy was performed through a segment of hepatic parenchyma in the projection of the gallbladder, 1-2 cm from its margin. In this manner, the puncture trajectory passes through the widest area between the body and fundus of the gallbladder. In selecting the puncture site, the accuracy of the chosen trajectory must be verified in both longitudinal and transverse ultrasound sections of the gallbladder. This is related to the variability of attachment of the posterior gallbladder wall to the liver.

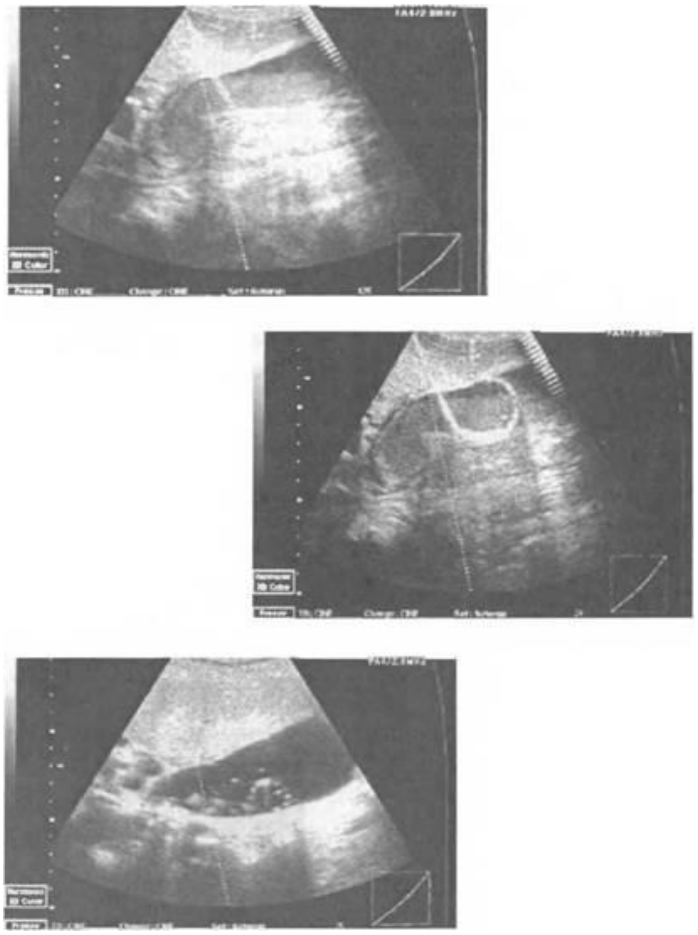


Figure 3.7. Sonogram. Stages of microcholecystostomy.

If the gallbladder adheres to the liver only by a thin line of the posterior wall, and trajectory selection is performed only in the longitudinal section, the stylet-catheter will pass through the liver and enter the gallbladder wall without an intrahepatic component. Consequently, bile from the gallbladder lumen may leak into the abdominal cavity. A similar risk of complication may also occur when transhepatic access to the gallbladder is not obtained. The variant of gallbladder attachment and the optimal puncture trajectory are assessed using a transverse gallbladder section. In this case, the puncture trajectory must be precisely directed toward the midpoint of the gallbladder section perimeter. The puncture transducer was positioned for the viewing plane to simultaneously pass through the hepatic parenchyma and the maximum longitudinal gallbladder section.

Following microcholecystostomy, the gallbladder fluid was completely aspirated, the cavity irrigated with physiological saline until effluent ran clear, and the drain connected to continuous drainage. Effluent from the drain was visually assessed and sent for bacteriological examination. Complete gallbladder

emptying was monitored sonographically. The catheter was irrigated 2-3 times daily with 20-30 mL physiological saline to maintain patency.

EPST was performed in 27 cases in the study group. Specifically, in 15 patients with ASC without clinical signs of acute destructive cholecystitis, EPST and NBD were performed as the first stage. In 12 patients in whom clinical signs of acute destructive cholecystitis predominated, this procedure was performed after PTMC.

Clinical case: Patient K., 63 years of age, was admitted to the surgical department on 12.04.2019 (case history No. 4841/582) complaining of pain in the right hypochondrium, rigors, fever up to 39°C, nausea and vomiting, icteric sclerae, and dark urine. Has been ill for 7 days. Associates the onset with fatty food intake. History: recurrent paroxysmal right hypochondriac pain.

General condition: moderate severity. Skin and sclerae icterically tinged. Auscultation: bilateral vesicular breath sounds, no crackles. Heart tones muffled, accentuated second tone in the aortic projection. Pulse rhythmic, tense. Tongue slightly dry, coated. Abdomen symmetric, participates in respiration; palpation reveals pain in the right hypochondrium and epigastrium. Murphy's and Ortner-Grekov signs positive. Liver and spleen not palpable. Stools normal. Micturition free.

Complete blood count: Hb 110 g/L; RBC 3.7×10^{12}/μL; CP 0.8; platelets 230; WBC 12.7×10^{9}/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 25 mm/h.

Biochemical blood analysis: total bilirubin 45.65 μmol/L; unconjugated bilirubin 24.27 μmol/L; ALT 0.96 mmol/L; AST 0.34 mmol/L; thymol turbidity 2; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L; ESR 30 mm/h.

Chest X-ray: no pathology.

Ultrasonography: gallbladder 8.0×4.0 cm; stones up to 1 cm in the lumen, one stone identified. Choledochus dilated to 1.2 cm; multiple stones up to 0.8 cm in the lumen; dilatation of intrahepatic bile ducts confirmed.

The patient was diagnosed with "Acute calculous cholecystitis, choledocholithiasis, cholangitis, mechanical jaundice," and on 14.04.2019, EPST with choledocholithoextraction was performed as the first stage; a 0.8 cm

stone and thick purulent bile were evacuated. NBD was placed for decompression.

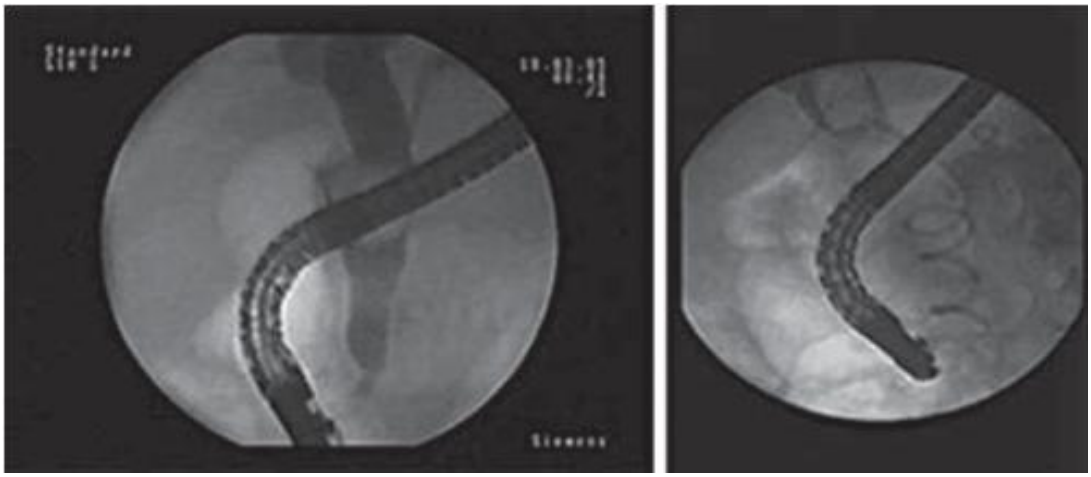


Figure 3.8. Endoscopic placement of nasobiliary tube: a) ERCP demonstrating stone in the choledochus; b) endoscopic placement of nasobiliary tube.

The biliary tract was irrigated through the NBD with 0.06% sodium hypochlorite solution for 5 days, and anti-inflammatory and detoxification therapy was administered. Repeat complete blood count 5 days after NBD placement: Hb 105 g/L; RBC 3.2×10^{12}/μL; CP 0.8; platelets 230; WBC 6.5×10^{9}/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 15 mm/h. Biochemical analysis: total bilirubin 22.15 μmol/L; conjugated bilirubin 7.1 μmol/L; ALT 0.92 mmol/L; AST 0.34 mmol/L; thymol turbidity 2; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L. The patient's condition improved; following resolution of the acute inflammatory signs, elective laparoscopic cholecystectomy was performed without technical difficulties.

The postoperative course was uneventful. The drain yielded approximately 5 mL of serosanguinous fluid on postoperative day 1 and was removed on day 2. The patient was discharged in satisfactory condition on the third postoperative day after LC.

EPST was performed in the endoscopic surgery department of SamSMI 1st Clinical Base using a standard duodenoscope, electrosurgical unit, and sphincterotome. In most cases, a pull-type sphincterotome was used--a plastic catheter containing a metal wire, with the distal end emerging externally and re-entering the sheath at the tip of the papillotome. The sphincterotome tension causes bowing of its distal end and positioning in the cutting configuration.

These sphincterotomes differ in catheter length and number of channels (for guidewire and contrast injection). A cutting wire length of 20-40 mm is variable. Greater cutting wire length ensures correct orientation within the major duodenal papilla (MDP). Sphincterotomes with an additional guidewire channel are most convenient, as they eliminate the difficulties of repeated cannulation with the sphincterotome after primary guidewire cannulation of the biliary tract, and additionally prevent instrument displacement from the MDP during dissection (Figure 3.9).

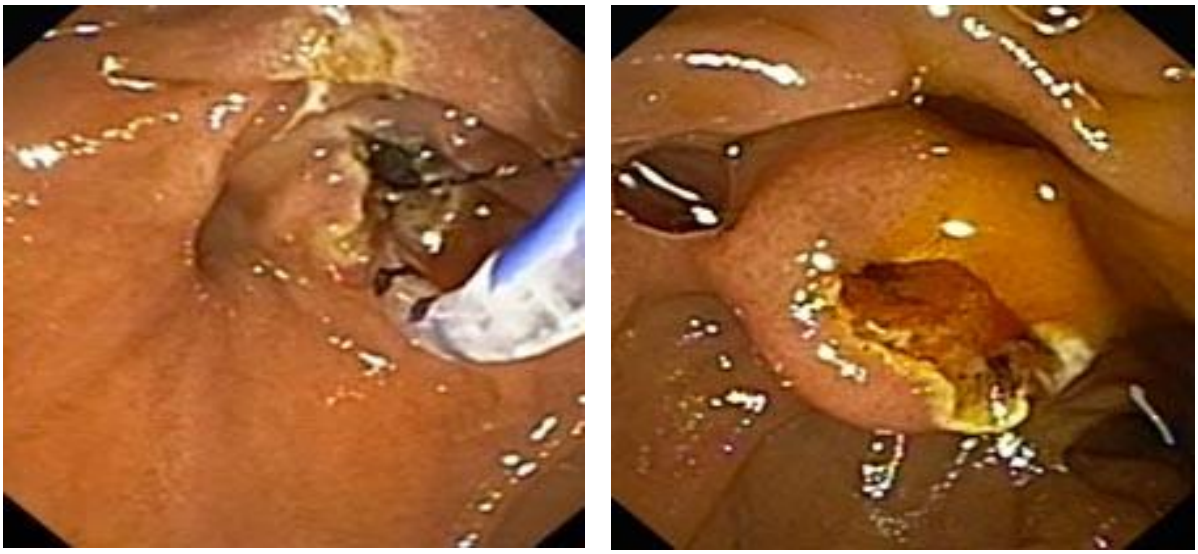


Figure 3.9. Patient D., 50 years. Stages of endoscopic papillosphincterotomy.

During papillosphincterotomy, adequate patient sedation (diazepam with narcotic analgesics or propofol) and elimination of peristalsis (atropine intramuscularly, metacin intravenously) are essential. A sudden patient movement or peristaltic wave during sphincterotomy may result in various complications and undesirable outcomes. Prophylactically, sandostatin and antibiotics were administered before the procedure.

Correct orientation of the cutting wire of the papillotome is the most critical aspect of EPST performance. It should ordinarily be oriented at 12 o'clock in the MDP, although the 11-1 o'clock range is also acceptable. In practice, the papillotome should be positioned at 6 o'clock in the MDP, with its tensioned portion at 12 o'clock. However, it is not always possible to achieve adequate contact of the cutting wire with tissue in the standard pulling technique with correct orientation. Furthermore, during each cutting movement, only a small portion of the cutting wire should be in contact with the tissue. When the tissue volume is large, the current disperses along the cutting wire, reducing its efficiency. The position of the duodenoscope plays a critical role in achieving

correct wire alignment. We consider optimal positioning of the papillotome in the lower visual field of the endoscope (in which case, the direction of the instrument channel is closest to the biliary tract direction). This is often achievable by advancing the instrument deeper into the duodenum, as if forming a long loop. Orientation of the cutting wire at 12 o'clock can also be achieved by manipulation of the instrument controls. As a rule, the elevator can be used during incision to ensure adequate contact of the wire with the tissue.

Incision was performed gradually (for adequate coagulation of the cut edges and control of incision length) using a series of brief current applications, progressively withdrawing the sphincterotome and thereby ensuring contact of the cutting wire tip with the tissue (Figure 3.10).

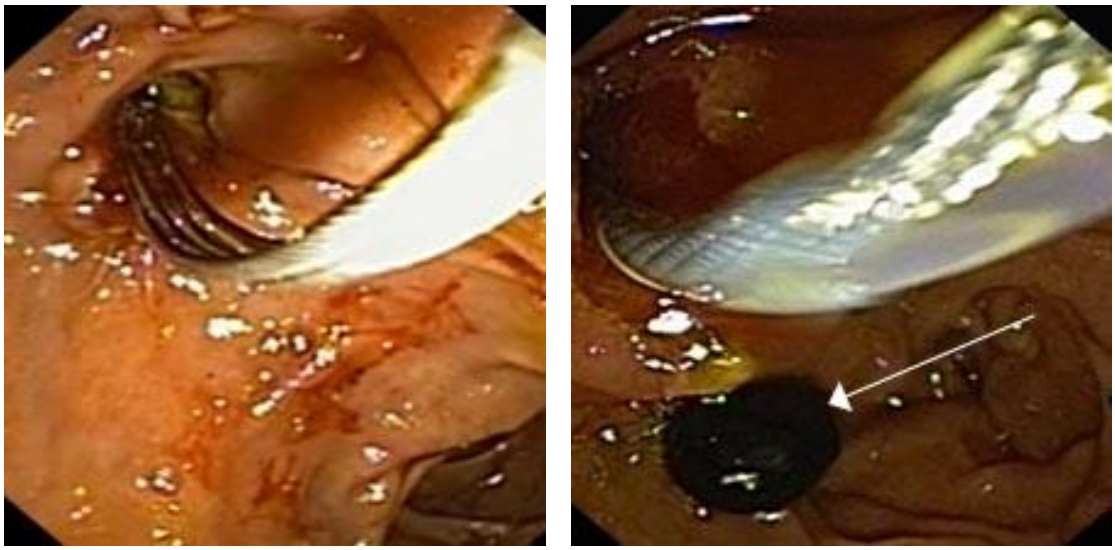
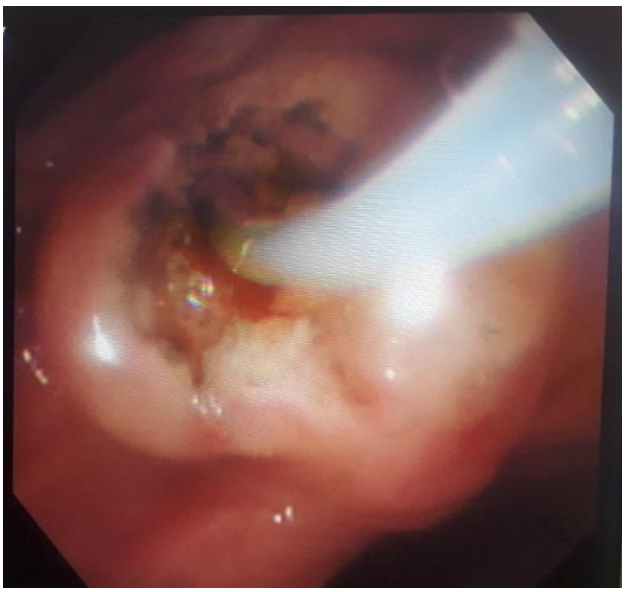


Figure 3.10. Stages of sphincterotomy.

In all cases, EPST was completed with placement of a nasobiliary tube (Figure 3.11).



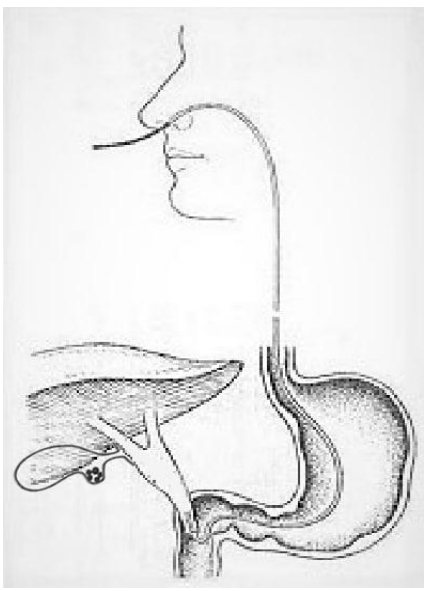


Figure 3.11. Endoscopic papillosphincterotomy and nasobiliary drainage placement.

It should be noted that in 9 patients with ASC, attempts at EPST and NBD placement were unsuccessful; in one case, the patient developed acute pancreatitis, which resulted in a fatal outcome.

Thus, two-stage surgical treatment was performed in 33 patients (39.7%) in the study group. After initial biliary decompression, cholecystectomy was performed in the second stage on postoperative days 7-12: LC in 22, MLCE in 11, and MLCE with choledocholithotomy in 6 patients.

In 50 patients (60.3%) of the study group with ASC concurrent with acute destructive cholecystitis and peritonitis, radical surgery--CE and choledocholithotomy--was performed via wide laparotomy in 17 patients and via mini-laparotomy in 33 patients.

LC was performed using instruments from "Karl Storz," and mini-incision CE using equipment from "SAN." Thus, LC was performed in 22 patients (26.5%), mini-incision CE in 44 patients (53%), and wide laparotomy CE in 17 patients (20.5%).

For mini-access CE, a 4-5 cm vertical transrectus incision was made below the right costal arch. Mirror retractors create a substantial working space, enabling visual control of the surgical process and free instrument manipulation. By changing the position of the mirror retractors and thereby expanding the field of interest, it is possible not only to perform cholecystectomy but also to extend the procedure: choledocholithotomy and external drainage of the choledochus (Figure 3.12).

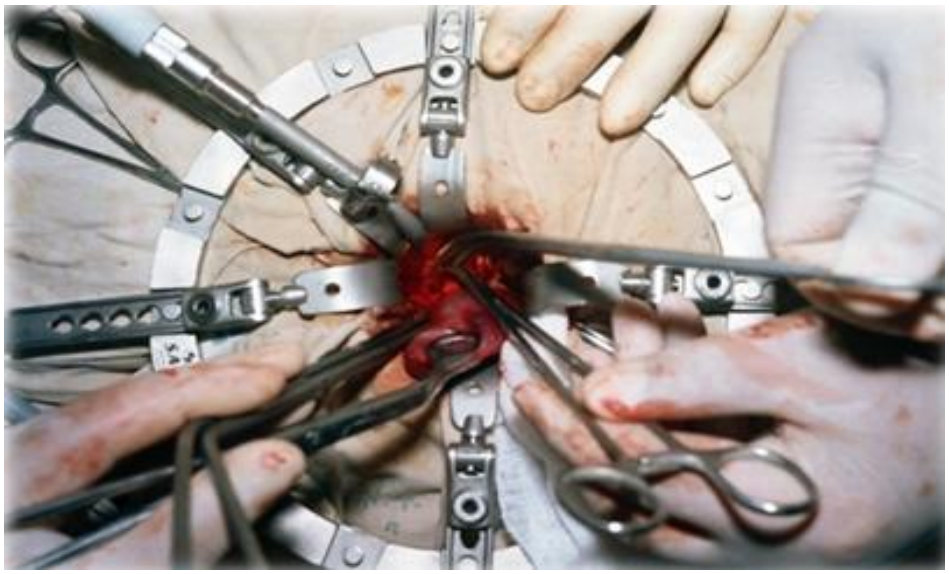


Figure 3.12. "Mini-assistant" instruments from the "SAN" company.

Use of a minilaparotomy incision for cholecystectomy is recommended when there are contraindications to laparoscopic intervention. This operative technique allowed gallbladder removal in the presence of inflammatory infiltrate and cicatricial changes in the hepatoduodenal ligament area, in cases of abdominal organ adhesion to the abdominal wall when early laparotomy had been performed, in obesity, and in intrahepatic gallbladder position.

In patients with cardiovascular and pulmonary comorbidities in whom pressurised pneumoperitoneum was not feasible, the mini-laparotomy approach is preferable.

Advantages of cholecystectomy via mini-laparotomy incision include: the surgical technique is analogous to open laparotomy, allowing visual control of operative stages and prevention of iatrogenic injury; the approach allows rapid conversion to open laparotomy when technical difficulties arise.

LC is performed under general anaesthesia with complete abdominal wall relaxation. The principal stages of endoscopic surgery are: creation of pneumoperitoneum, trocar and instrument insertion, abdominal cavity exploration, gallbladder dissection, identification and clipping of the cystic duct and cystic artery, followed by their transection; dissection of the gallbladder from its hepatic bed and extraction from the abdominal cavity (sometimes using a specimen bag) and placement of a drain in the subhepatic space. LC is performed according to the standard "critical view of safety" technique for

identification and dissection of the cystic duct and artery. For trocar insertion, an arcuate umbilical incision 1.5 cm above or below the umbilicus and three 0.5 cm incisions below the right costal arch are made.

In 4 patients with peritonitis, emergency laparotomy, CE, choledocholithotomy, and abdominal sanation were performed. In a further 5 patients whose ASC clinical signs intensified due to unsuccessful EPST attempts, mini-incision CE combined with choledocholithotomy was performed.

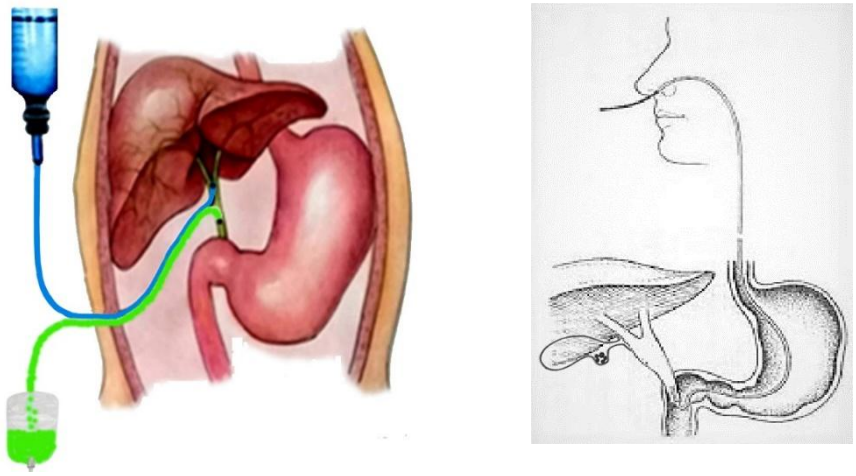
Thus, two-stage surgical treatment was performed in 11 patients (61.1%) with moderate-grade and in 9 patients (81.8%) with severe-grade ASC.

In the study group, all surgical interventions were completed with choledochal drainage: external drainage in 56 cases (67.5%) and NBD placement during endoscopic transduodenal intervention in 27 cases (32.5%).

§3.3. Intrabiliary Sanation via Drainage in the Treatment of Acute Suppurative Cholangitis

In the study group, all surgical interventions were completed with choledochal drainage: external drainage in 56 cases (67.5%) and NBD placement during endoscopic transduodenal intervention in 27 cases (32.5%).

In these patients, sanatory perfusion of the biliary tract was performed using the technique we developed, employing a 0.06% solution of sodium hypochlorite, to achieve resolution of biliary inflammatory signs and prevention of hepatic microabscess and abscess formation. Intrabiliary sanation was implemented via drain tubes placed in the hepaticocholedochus (HC) following choledocholithotomy (Figure 3.13).



A **B**

Figure 3.13. Schematic representation of sanatory perfusion of the biliary tract via HC drainage (A) and via nasobiliary drainage (B).

Following choledocholithotomy, a double-lumen (dual-channel) tube was placed in the biliary lumen; one of the channels directed toward the proximal HC (narrow lumen, 2 mm internal diameter) and the second (wider lumen, up to 5 mm) directed toward the distal HC.

Sanatory perfusion of the biliary tract was first performed with 400.0 mL of 0.06% anolyte solution of sodium hypochlorite (pH=6) until normalisation of biliary microflora. The 0.06% anolyte solution of sodium hypochlorite, being a strong oxidising agent, bound to the bile in the biliary tract, diluted it, and increased the volume of drainage output (Table 4.1).

Table 4.1
Statistical Significance of Differences in Bile Output (mL/day)

Days After Biliary Decompression	1	2	3	4	5	6
Without endobiliay sanation	41±1.2	70±2.2	121±3.4	210±5.3	250±7.7	280±6.5
After endobiliay sanation with sodium hypochlorite	40±1.4	100±3.5	200±4.7	340±7.2	370±7.6	420±7.1
Statistical significance of differences	-	$p>0.05$	$p<0.05$	$p<0.05$	$p<0.05$	$p<0.05$

*Note: * Difference between indicators is statistically significant ($p <0.05$)*

The sodium hypochlorite solution was prepared using an EDA-4 device. A STEL-MT-1 device was used for preparation of anolyte and catholyte solutions.

Results of bile viscosity assessment demonstrated that, in the study group, viscosity normalised 2±0.3 days after the start of sodium hypochlorite infusion, reaching an average of 0.5-0.6 conventional units; in the comparison group, bile viscosity normalised on day 5±0.4.

When the anolyte solution of sodium hypochlorite was introduced into the intrahepatic bile ducts, it diluted the bile and reduced the high microbial titre, thereby accelerating attainment of biliary sterility. Our investigations demonstrated that the "acidic" solution of sodium hypochlorite (anolyte)

possesses marked disinfectant properties and high antimicrobial activity. Additionally, administration of 400.0 mL of 0.06% anolyte solution of sodium hypochlorite reduced the microbial titre in bile cultures and continued to decrease consistently in subsequent days.

Microbiological examination of bile was performed on days 1, 3, and 5, and before drain removal. Escherichia coli (75.2%), Klebsiella (12.3%), and Enterobacter (8.1%) and their various combinations were the predominantly identified micro-organisms. After intrabiliary sanation, negative bile cultures were obtained in 72% of patients by day 5, and complete eradication of the microbial landscape was confirmed by day 12 (Figure 3.14).

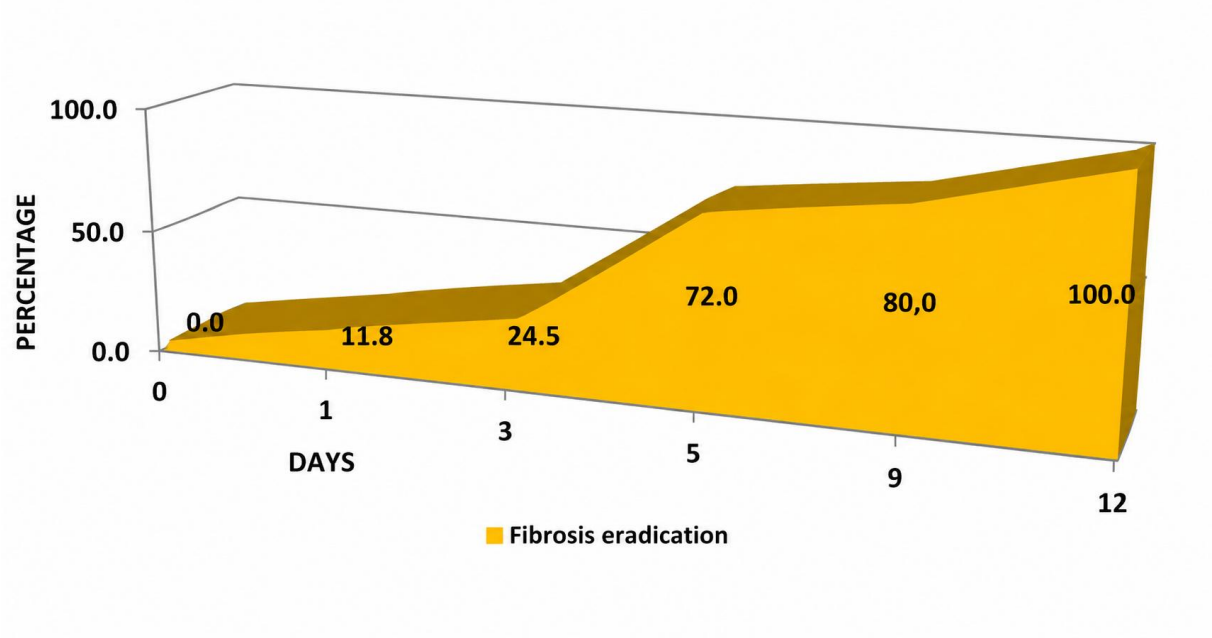


Figure 3.14. Dynamics of microbial landscape eradication in bile following intrabiliary sanation with sodium hypochlorite.

After obtaining a sterile or significantly reduced bile culture, biliary irrigation was continued with the catholyte solution of sodium hypochlorite (pH=8), which is a donor of active oxygen and also accelerates the regenerative process. The effectiveness of complex treatment of ASC was assessed by the rate of decline of biochemical blood parameters. Analysis of the results demonstrated that, in contrast to the comparison group, patients in the study group showed a dynamic decline in total bilirubin. Additionally, the results demonstrated earlier normalisation of AST level and alkaline phosphatase activity (Figure 3.15 a, b, c).

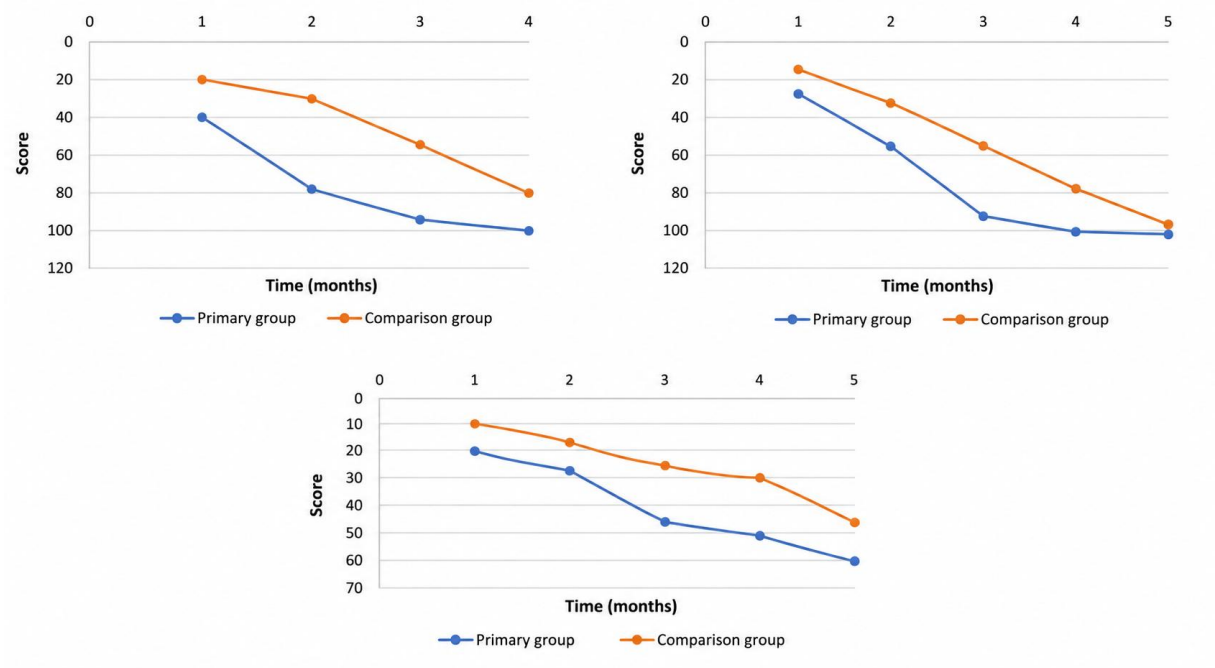


Figure 3.15. Dynamics of normalisation of total bilirubin (A), alkaline phosphatase (B), and AST (C) in the study groups (%/day).

CHAPTER IV. COMPARATIVE ANALYSIS OF TREATMENT OUTCOMES IN THE STUDY GROUPS

Results of comparative analysis demonstrated a significant reduction in mortality in the study group compared with the comparison group. Among the most severe complications in the comparison group, cholangenic hepatic abscess and biliary sepsis were observed in 4 patients, all of whom died.

Ongoing peritonitis resulted in a fatal outcome in 1 patient in our series. In all 61 operated patients of the comparison group, 5 fatal outcomes were recorded, yielding a mortality rate of 8.2%.

It should be noted that in the study group, 2 fatal outcomes occurred among 83 postoperative patients, yielding a mortality rate of 2.4%. The adverse outcome was attributable to acute pancreatitis as a complication of transduodenal endoscopic intervention in 1 patient, and to ongoing peritonitis in 1 patient (Table 4.1).

Table 4.1

Mortality in the Study Groups

Cause of Death	Study Group		Comparison Group	
	Abs.	(%)	Abs.	(%)
Cholangenic hepatic abscess and biliary sepsis	4	14.8%	-	-
Peritonitis	1	2.9%	1	1.2%
Acute pancreatitis	-	-	1	1.2%
Total	5	8.2%	2	2.4%

*Note: * Difference between indicators is statistically significant (p <0.05)*

In the comparison group, 15 patients (24.5%) developed purulent-septic complications in the postoperative period.

Additionally, biloma developed in 2 patients (3.2%) in the subhepatic region; these were drained by counter-aperture recanalisation. Bile leakage from the drain tubes placed in the subhepatic space occurred in 5 patients (11.4%); repeat surgery for drainage of subhepatic or subphrenic abscesses was required in 5 patients (8.2%). Cholemic intraperitoneal haemorrhage necessitating re-operation was recorded in 2 patients (3.2%). Postoperative wound suppuration occurred in 12 patients (19.6%).

In the study group, postoperative complications developed in 10 patients (12.1%). Biloma developed in the subhepatic region in 3 patients (3.6%) and was drained under ultrasound guidance.

Clinical case: Patient K., 48 years of age, case history No. 3948, presented to the clinic on 12.03.2019. On admission, the patient complained of pain in the right hypochondrium, abdominal distension, dry mouth, fever up to 39°C, intermittent rigors, nausea and vomiting. Has been ill for 10 days. Associates the onset with overeating. History: recurrent paroxysmal right hypochondriac pain on several occasions. Ultrasonography in 2018 revealed cholelithiasis.

On admission, general condition moderate severity; skin normal colour. Auscultation: bilateral vesicular breath sounds, no crackles. Abdomen of normal shape; right hypochondriac pain on palpation. Heart tones muffled, pulse rhythmic. Tongue slightly dry, white coated. Murphy's and Ortner-Grekov signs positive. Liver and spleen not palpable. Stools normal. Micturition free.

Complete blood count: Hb 85 g/L; RBC 2.7×10^{12}/μL; CP 0.8; platelets 230; WBC 12.7×10^{9}/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 25 mm/h. Biochemical blood analysis: total bilirubin 22.65 μmol/L; ALT 0.96 mmol/L; AST 0.34 mmol/L; thymol turbidity 4; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L. Chest X-ray: no pathology. Ultrasonography: gallbladder 8.5×4 cm, wall thickness 5 mm; stone up to 0.8 cm in the lumen; choledochus diameter 0.9 cm; thick bile sediment in the lumen; intrahepatic bile ducts not dilated.

Diagnosed with acute calculous cholecystitis and cholangitis. Conservative therapy resolved the pain syndrome and reduced inflammatory signs. On 14.03.2019, elective minilaparotomy cholecystectomy was performed without technical difficulties. On postoperative day 2, the patient reported pain recurrence in the right hypochondrium. No drainage output from the subhepatic drain. Ultrasonography showed approximately 100 mL of accumulated fluid in the subhepatic space. Given the absence of peritoneal signs, conservative management with dynamic monitoring was decided. On postoperative day 4 after MLCE, the patient reported intensified pain in the right hypochondrium and fever up to 37.9°C. Local peritoneal signs appeared. Ultrasonography revealed a circumscribed fluid level in the right hypochondrium, increased to 150 mL (Figure 4.1).

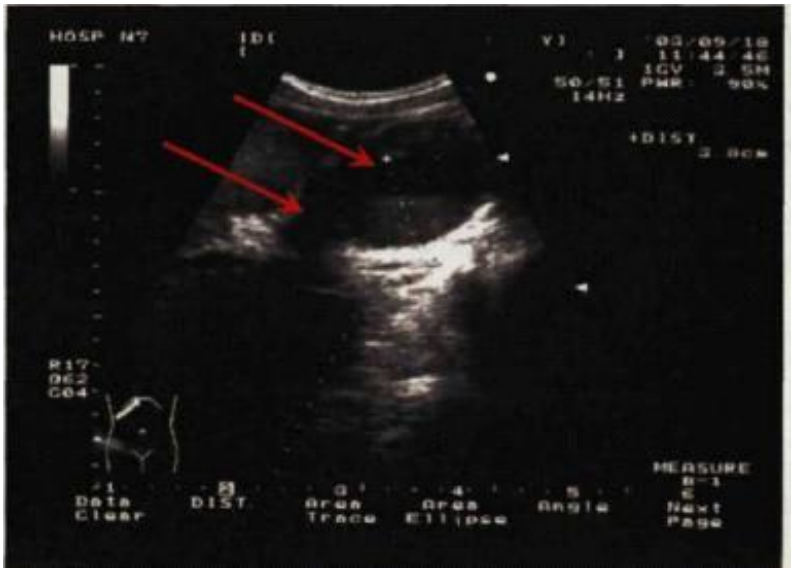


Figure 4.1. Patient K., 48 years. Sonogram on postoperative day 4 after mini-incision CE. Circumscribed subhepatic fluid accumulation of approximately 150 mL.

Puncture of the accumulated fluid under ultrasound monitoring was performed; approximately 150 mL of fluid was evacuated from the subhepatic space (Figure 4.2).

The postoperative course was smooth. Temperature normalised; peritoneal signs resolved. Control ultrasonography on postoperative day 7 showed no subhepatic fluid accumulation, and the drain was removed. Wound healing by primary intention. The patient was discharged in satisfactory condition.

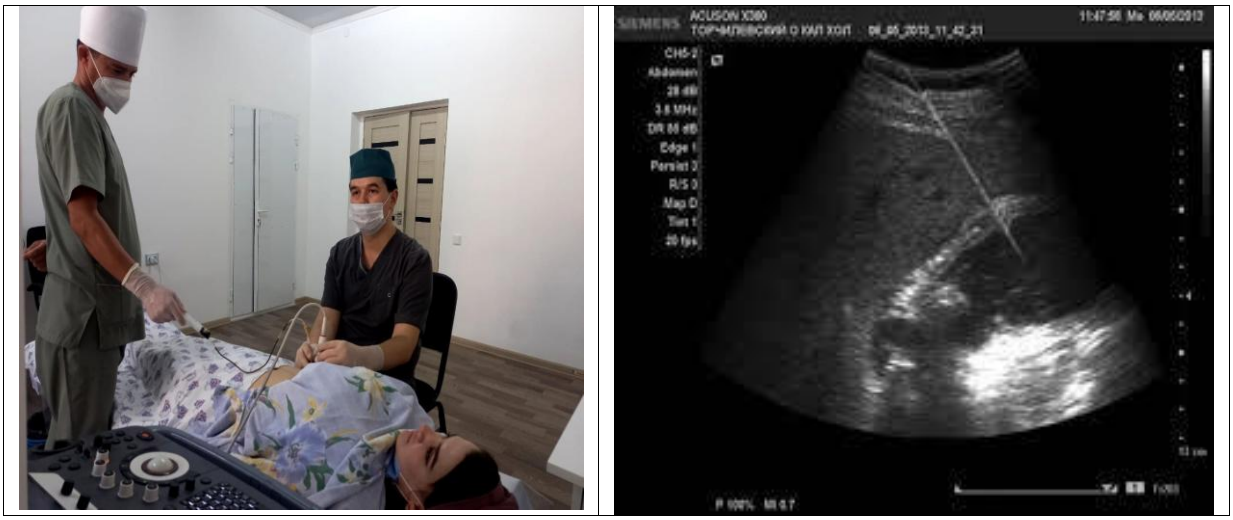


Figure 4.2. Patient K., 48 years. Puncture of biloma on postoperative day 4 after minilaparotomy CE under ultrasound guidance.

Cholemic haemorrhage at the puncture site of the gallbladder was observed in 2 patients (2.4%). An external biliary fistula developed in 2 patients. Relaparoscopy revealed inadequate clipping of the cystic duct remnant in 1 case (which was re-clipped), and bile leakage from the gallbladder bed in the second case (which was managed by coagulation).

Clinical case: Patient R., 53 years of age, case history No. 1306, was admitted as an emergency on 02.02.2020 with the following complaints: pain in the right hypochondrium, fever up to 39°C, rigors, nausea, and vomiting. Has been ill for 6 days. Associates the onset with fatty food intake. On admission, general condition moderate severity, skin normal colour. Auscultation: bilateral vesicular breath sounds, no crackles. Heart tones muffled, pulse rhythmic. Tongue slightly dry, white coated. Abdomen enlarged due to subcutaneous fat, participates in respiration; right hypochondriac pain on palpation. Murphy's and Ortner-Grekov signs positive. Liver and spleen not palpable. Stools normal. Micturition free.

Complete blood count: Hb 105 g/L; RBC 3.6×10^{12}/μL; CP 0.8; platelets 230; WBC 12.7×10^{9}/μL; clotting time 3'50"-4'00"; stab neutrophils 3%; segmented neutrophils 65%; eosinophils 1%; lymphocytes 20%; monocytes 7%; ESR 20 mm/h. Biochemical analysis: total bilirubin 19.65 μmol/L; ALT 0.96 mmol/L; AST 0.34 mmol/L; thymol turbidity 4; urea 4.66 mmol/L; residual nitrogen 17 g/L; creatinine 82.9 mmol/L; total protein 70.5 g/L. Chest X-ray: no pathology. Ultrasonography: gallbladder 10.5×6 cm, wall thickness 6 mm; stone up to 1.8 cm in the neck region; choledochus diameter 1.0 cm; thick bile in lumen; intrahepatic bile ducts not dilated.

Diagnosed with acute obstructive calculous cholecystitis and cholangitis. Conservative therapy yielded no response. On 03.02.2020, the patient underwent laparoscopic cholecystectomy. Final postoperative diagnosis: acute obstructive calculous phlegmonous cholecystitis. On postoperative day 2 after LC, the patient developed right hypochondriac pain, a single episode of vomiting, and nausea. More than 200 mL of bile drained from the tube in the subhepatic space. Objective examination revealed mild abdominal tenseness with right hypochondriac pain and developing peritoneal signs.

A decision was made to perform relaparoscopy. Pneumoperitoneum was created via a port 1 cm below the umbilical ring along the midline. Up to 60 mL of bile in the right iliac channel and more than 300 mL in the subhepatic region were identified. Inspection of the gallbladder bed and hepatoduodenal ligament

confirmed that bile was leaking from the cystic duct remnant. The abdominal cavity was sanitised and the cystic duct remnant was re-clipped. The operation was completed with abdominal drainage. The postoperative course was smooth; the abdominal drain was removed on day 3. The patient was discharged in satisfactory condition on postoperative day 5 after relaparoscopy.

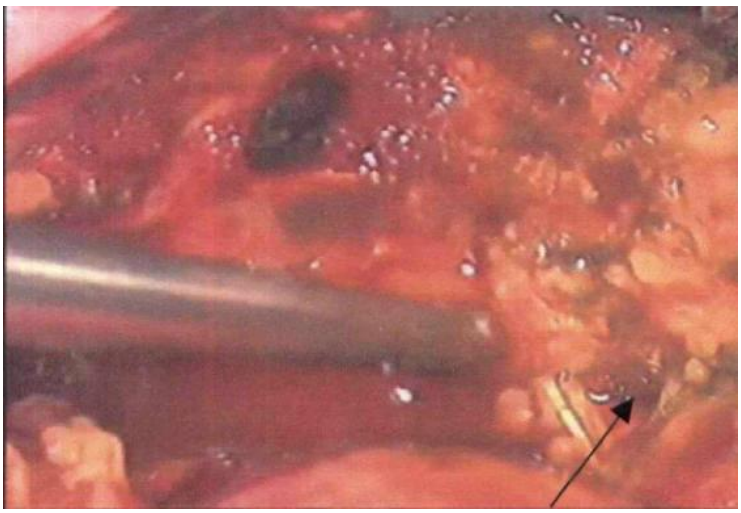


Figure 4.3. Patient R., 53 years. LC for ACC (day 2). Relaparoscopy showing bile accumulation in the subhepatic region due to cystic duct remnant insufficiency.

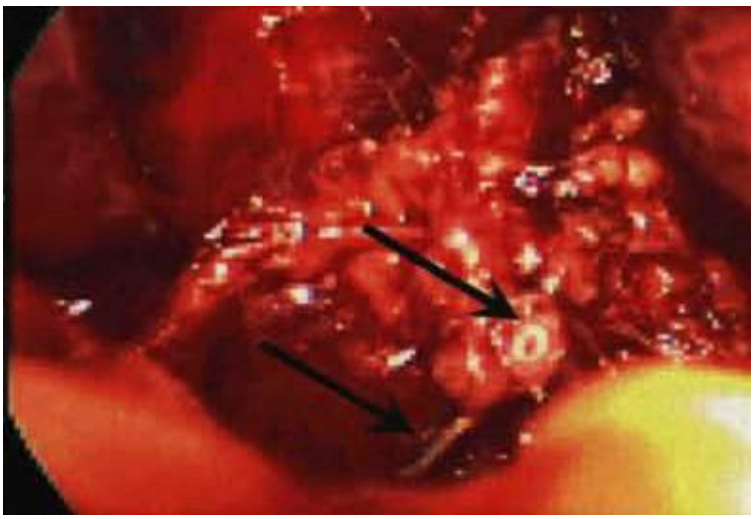


Figure 4.4. Patient R., 53 years. Additional re-clipping of the cystic duct remnant via relaparoscopy.

Duodenal haemorrhage after EPST was recorded in 1 patient and was arrested with conservative haemostatic therapy. A formed subphrenic abscess in 1 patient was managed by repeat puncture and sanation under ultrasound guidance. Wound suppuration occurred in 3 patients (Table 4.2).

Table 4.2

Causes and Incidence of Cholemic and Purulent-Septic Complications in the Study Groups

Purulent-Septic Complications	Comparison Group		Study Group	
	Abs.	(%)	Abs.	(%)
Biloma	2	3.3%	3	3.6%
External biliary fistula	5	8.2%	2	2.4%
Cholemic haemorrhage	2	3.3%	2	2.4%
Duodenal haemorrhage	-	-	1	1.2%
Subhepatic and subphrenic abscess	5	8.2%	1	1.2%
Wound suppuration	12	19.7%	3	3.6%
Total	15	24.6%	10	12.0%

*Note: * Difference between indicators is statistically significant (p <0.05)*

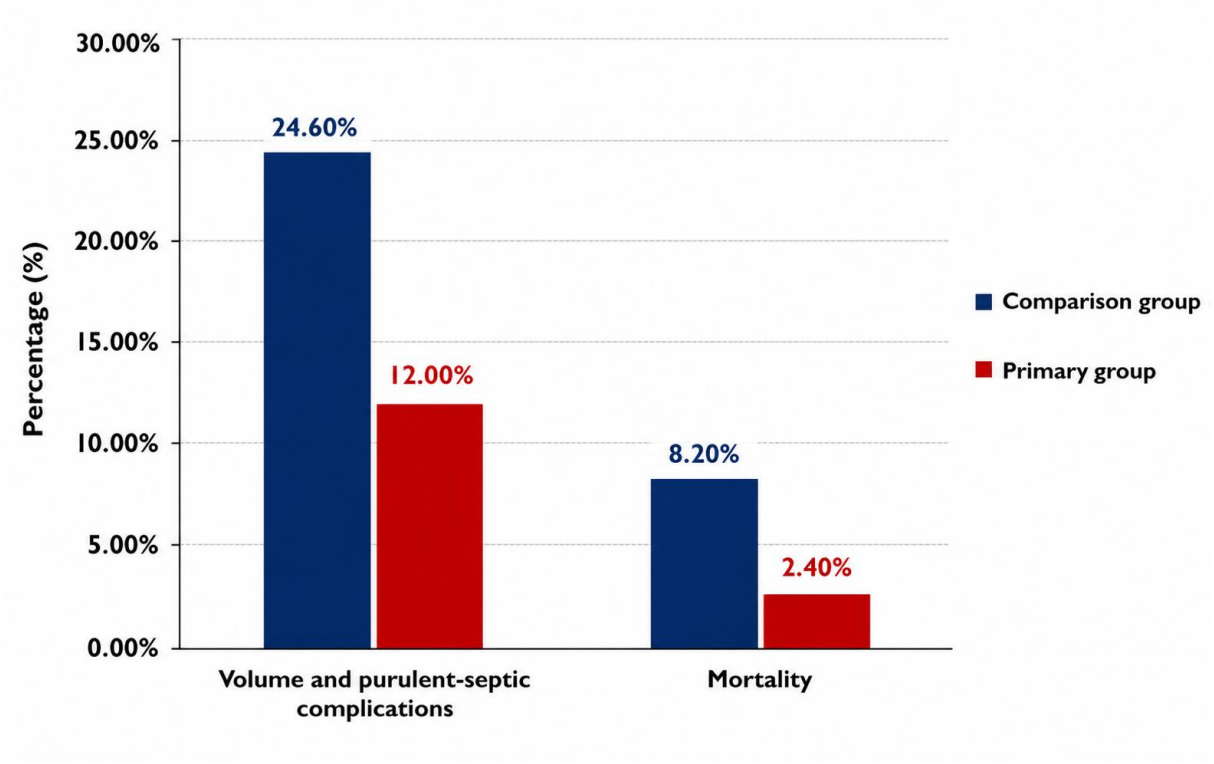


Figure 4.5. Results of complex surgical treatment of patients with acute suppurative cholangitis in both study groups.

In the study group patients, the staged surgical approach utilising initial decompressive intervention--taking into account the severity grade of ASC--

prevents cholestasis and purulent intoxication, while also enabling improvement of outcomes following radical surgery.

Thus, two-stage surgical treatment was performed in 33 patients (39.7%) in the study group. Of these, in 12 patients with acute obstructive cholecystitis concurrent with ASC, biliary decompression via MHCS and EPST with NBD was performed as the first stage. Following initial biliary decompression, cholecystectomy was performed as the second stage on days 7-12: LC in 22, MLCE in 11, and MLCE with choledocholithotomy in 6 patients.

In 50 patients (60.3%) of the study group with ASC concurrent with acute destructive cholecystitis and peritonitis, radical surgery--CE and choledocholithotomy--was performed via wide laparotomy in 17 patients and via mini-laparotomy in 33 patients.

LC was performed using "Karl Storz" instruments; mini-incision CE using "SAN" equipment (Figure 5). Thus, LC was performed in 22 patients (26.5%), mini-incision CE in 44 patients (53%), and wide laparotomy CE in 17 patients (20.5%).

All surgical interventions in the study group were completed with choledochal drainage: external drainage in 56 cases (67.5%) and NBD placement during endoscopic transduodenal intervention in 27 cases (32.5%).

In all 61 operated patients in the comparison group, surgical interventions were performed in the scope of cholecystectomy, choledocholithotomy, and external choledochal drainage; procedures via wide laparotomy incision were performed in 48 patients, and via mini-incision in 13 patients.

In this regard, diapeutic and endoscopic transduodenal interventions were required in 81.8% of severe-grade, 61.6% of moderate-grade, and 24.1% of mild-grade ASC patients.

Percutaneous transhepatic microcholecystostomy was used in a total of 18 patients (21.7%) in the study group in the surgical management of ASC. Puncture was performed under ultrasound guidance through the hepatic parenchyma to ensure hermeticity of the needle tract and prevent bile spillage into the abdominal cavity.

In all cases, drainage was performed using stylet-catheters of 4F and 9F diameter with a terminal "basket."

In the study group, EPST was performed in 27 cases. Specifically, EPST and NBD were performed as the first stage in 15 patients with ASC without

clinical signs of acute destructive cholecystitis. In 12 patients with predominating clinical signs of acute destructive cholecystitis, this procedure was performed after PTMC.

To resolve postoperative complications in the study group, minimally invasive interventions were performed: biloma in the subhepatic region in 3 patients (3.6%) was drained under ultrasound guidance. Relaparoscopy was performed for biliary fistula resolution in 2 patients. A subphrenic abscess in 1 patient was managed by repeat puncture and sanation under ultrasound guidance. Thus, in the study group, 6 of 10 patients (60%) with postoperative complications were managed with minimally invasive interventions.

Factorial analysis of acute suppurative cholangitis demonstrated that the principal cause of mortality was cholangenic hepatic abscess and biliary sepsis. Fatal outcomes (14.8%) and purulent-septic complications (44.4%) were observed primarily after emergency surgical interventions performed for ASC concurrent with acute destructive cholecystitis and peritonitis.

In patients of the study group, sanatory perfusion of the biliary tract via drainage using 0.06% anolyte and catholyte solutions of sodium hypochlorite resulted in early eradication of microbial contamination in bile cultures, normalisation of bilirubin, AST, and alkaline phosphatase levels, and more than doubled the rate of bile secretion.

Optimisation of the tactical and technical aspects of complex surgical treatment of ASC arising as a complication of cholelithiasis--through early resolution of cholangitis, prevention of hepatic abscess formation, and prevention of biliary sepsis--enabled improvement of treatment outcomes, with a reduction in purulent-septic complications from 24.5% to 12.1% and in mortality from 8.2% to 2.4%.

CONCLUSIONS

1. Factorial analysis of acute suppurative cholangitis demonstrated that the principal cause of mortality was cholangenic hepatic abscess and biliary sepsis. Fatal outcomes (14.8%) and purulent-septic complications (44.4%) were observed primarily after emergency surgical interventions performed for acute suppurative cholangitis concurrent with acute destructive cholecystitis and peritonitis.

2. The application of initial decompressive biliary interventions in acute suppurative cholangitis, taking into account the severity grade, allows arrest of cholestasis and purulent intoxication and improvement of outcomes after radical operations. Diapeutic and endoscopic transduodenal interventions were required in 81.8% of severe-grade, 61.6% of moderate-grade, and 24.1% of mild-grade ASC patients.

3. Sanatory perfusion of the biliary tract via drainage using 0.06% anolyte and catholyte solutions of sodium hypochlorite resulted in early eradication of microbial contamination in bile cultures, normalisation of bilirubin, AST, and alkaline phosphatase levels, and more than doubled the rate of bile secretion.

4. Optimisation of the tactical and technical aspects of complex surgical treatment of acute suppurative cholangitis arising as a complication of cholelithiasis--through early resolution of cholangitis, prevention of hepatic abscess formation, and prevention of biliary sepsis development--enables improvement of treatment outcomes, with a reduction in purulent-septic complications from 24.5% to 12.1% and in mortality from 8.2% to 2.4%.

LIST OF ABBREVIATIONS

HC	-	Hepaticocholedochus
BDT	-	Biliary drainage tract
CL	-	Cholelithiasis (gallstone disease)
LC	-	Laparoscopic cholecystectomy
MLCE	-	Mini-laparotomy cholecystectomy
MRCP	-	Magnetic resonance cholangiopancreatography
MRI	-	Magnetic resonance imaging
MSCT	-	Multislice computed tomography
MHCS	-	Microcholecystostomy
NBD	-	Nasobiliary drainage
ASC	-	Acute suppurative cholangitis
USG	-	Ultrasonography
CE	-	Cholecystectomy
EPST	-	Endoscopic papillosphincterotomy
ERCP	-	Endoscopic retrograde cholangiopancreatography
CBD	-	Common bile duct
MBD	-	Main (magistral) bile ducts
BS	-	Biliary sepsis
SIRS	-	Systemic inflammatory response syndrome
PTMC	-	Percutaneous transhepatic microcholecystostomy
PTCS	-	Percutaneous transhepatic cholangiostomy
PTHG	-	Percutaneous transhepatic cholangiography
AST	-	Aspartate aminotransferase
ALT	-	Alanine aminotransferase
ALP	-	Alkaline phosphatase
GGT	-	Gamma-glutamyltransferase
INR	-	International normalised ratio
MDP	-	Major duodenal papilla
MOF	-	Multiple organ failure
ICU	-	Intensive care unit

REFERENCES

1. Azizzoda Z.A. Acute parasitic suppurative cholangitis in patients with hepatic echinococcosis // Zdravookhraneniye Tadzhikistana [Healthcare of Tajikistan]. - 2019. - No. 1. - P. 5-12.
2. Aevuov M.E. Suppurative cholangitis in biliary surgery // Materialy nauchno-prakticheskoy konferentsii KazNII klinicheskoy i eksperimentalnoy khirurgii [Proceedings of the Scientific-Practical Conference of the KazNRI of Clinical and Experimental Surgery]. - Almaty, 2004. - P. 64-65.
3. Aliev Yu.G. Minimally invasive interventions in the surgical treatment of complications of cholelithiasis / Yu.G. Aliev // Khirurgiya. Zhurnal im. I.I. Pirogova [Surgery. I.I. Pirogov Journal]. - 2013. - No. 5. - P. 73-75.
4. Altiev B.K., Nazyrov F.G., Vakkasov M.Kh., Sadykov Kh.T. Complex treatment of suppurative cholangitis in patients with non-neoplastic obstruction of extrahepatic bile ducts // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2009. - No. 3. - P. 30.
5. Altiev B.K., Khozhiboev A.M., Khakimov B.B., Shelaev O.I. Technical features of endoscopic retrograde pancreatocholangiography and papillosphincterotomy in diverticula of the papillary region // Shoshilinch tibbiyot axborotnomasi [Bulletin of Emergency Medicine]. - 2010. - No. 4. - P. 19-23.
6. Aminov I.Kh. Effect of premedication type and risk factors on the development of acute pancreatitis after endoscopic retrograde cholangiopancreatography / I.Kh. Aminov, M.V. Churkin, V.I. Podoluzhnyi, K.A. Krasnov // Meditsina v Kuzbasse [Medicine in Kuzbass]. - 2014. - No. 3. - P. 21-27.
7. Anishchenko V.V. Single-port laparoscopic surgery / V.V. Anishchenko, M.N. Kotkina, A.I. Shevela // Almanakh Instituta khirurgii im. A.V. Vishnevskogo [Almanac of the A.V. Vishnevsky Institute of Surgery]. - 2011. - No. 1(6). - P. 38.
8. Antonyuk O.S. et al. Clinical manifestations of choledocholithiasis // Vestnik gigiyeny i epidemiologii [Bulletin of Hygiene and Epidemiology]. - 2021. - Vol. 25. - No. 1. - P. 62-65.
9. Akhaladze G.G. Pathogenetic aspects of suppurative cholangitis: why is there no systemic inflammatory response in mechanical jaundice? / G.G. Akhaladze // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2009. - No. 2. - P. 9-15.

10. Bagnenko S.F. Inflammatory diseases of the extrahepatic biliary ducts. A contemporary perspective / S.F. Bagnenko, S.A. Shlyapnikov, A.Yu. Korolkov // Infektsii v khirurgii [Infections in Surgery]. - 2008. - No. 1(6). - P. 13-17.
11. Bashirov R.A. "Zipper" effect--a complication of endoscopic papillosphincterotomy / R.A. Bashirov // Endoskopicheskaya khirurgiya [Endoscopic Surgery]. - 2013. - No. 19(6). - P. 39-41.
12. Boboev B.D. Role of endoscopic ultrasonography in the diagnosis of choledocholithiasis and inflammatory biliary strictures / B.D. Boboev // Vestnik khirurgii im. I.I. Grekova [Grekov's Bulletin of Surgery]. - 2012. - No. 3. - P. 39-41.
13. Boboev B.D. Contemporary aspects of diagnosis of cholelithiasis complicated by choledocholithiasis / B.D. Boboev, V.P. Morozov // Uchenyye zapiski SPbGMU im. I.P. Pavlova [Scientific Notes of I.P. Pavlov St. Petersburg State Medical University]. - 2011. - No. 1(18). - P. 5-9.
14. Boyko V.V. et al. Changes in physicochemical properties of bile in the development and manifestation of cholangitis. Acute cholangitis: possible trigger mechanisms // Novosti khirurgii [Surgical News]. - 2021. - Vol. 29. - No. 1.
15. Borisov A.E. Optimisation of standards of treatment of acute cholecystitis / A.E. Borisov, V.A. Kashchenko, K.G. Kubachev // Vestnik khirurgii im. I.I. Grekova [Grekov's Bulletin of Surgery]. - 2012. - No. 6. - P. 80-85.
16. Bubnova E.V. Diagnostic capabilities of radiodiagnosis of small hepaticocholedochal concretions: Cand. Med. Sci. Dissertation: 14.01.13 / Bubnova Yevgeniya Viktorovna. - St. Petersburg, 2011. - 136 p.
17. Burnevich E.Z. et al. Variant form of autoimmune liver disease (primary biliary cholangitis/autoimmune hepatitis overlap) associated with generalised sarcoidosis (clinical observations and literature review) // Terapevticheskiy arkhiv [Therapeutic Archive]. - 2019. - Vol. 91. - No. 1.
18. Bykov M.I. State of the antiradical defence system at the local level in benign biliary obstruction / M.I. Bykov // Meditsinskiy vestnik Yuga Rossii [Medical Bulletin of Southern Russia]. - 2015. - No. 2. - P. 15-19.
19. Bykov M.I. Improvement of prevention of acute post-manipulative pancreatitis at the current stage of development of endoscopic transpappillary surgery / M.I. Bykov, V.A. Porkhanov // Vestnik

Natsionalnogo mediko-khirurgicheskogo Tsentra im. N.I. Pirogova [Bulletin of the N.I. Pirogov National Medical-Surgical Centre]. - 2015. - No. 3. - P. 103-108.

20. Vayner Yu.S. Antegrade endobiliary operations in the treatment of patients with mechanical jaundice / Vayner Yu.S., Atamanov G.V., Veryatin L.S., Shidlovskaya E.V. // Almanakh Instituta khirurgii im. A.V. Vishnevskogo [Almanac of the A.V. Vishnevsky Institute of Surgery]. - 2017. - No. 1. - P. 664.
21. Vakhrushev Ya.M. Cholelithiasis as a possible manifestation of systemic digestive pathology / Ya.M. Vakhrushev et al. // Terapevticheskiy arkhiv [Therapeutic Archive]. - 2015. - No. 87(2). - P. 54-58.
22. Vakhrushev Ya.M. Cholelithiasis: epidemiology, risk factors, features of clinical course, prevention / Ya.M. Vakhrushev, M.A. Khokhlacheva // Arkhiv vnutrenney meditsiny [Archives of Internal Medicine]. - 2016. - No. 3(29). - P. 30-35.
23. Vitebsky Ya.D., Veselov A.Ya., Chernov V.F. Study of mechanisms of bile infection // Fiziologiya i khirurgiya pecheni [Physiology and Surgery of the Liver]. - Tomsk, 1982. - P. 48-49.
24. Vetshev P.S. Ways to improve surgical treatment results in patients with mechanical jaundice / P.S. Vetshev // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - Moscow, 2014. - 198 p.
25. Vilyavin M.Yu. Capabilities of spiral computed tomography and magnetic resonance imaging in the diagnosis of cholecystocholangiolithiasis / M.Yu. Vilyavin, N.Yu. Osipov // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2014. - No. 3(12). - P. 50.
26. Galperin E.I. Pathogenesis and treatment of acute suppurative cholangitis / E.I. Galperin // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2009. - No. 4. - P. 13-21.
27. Galperin E.I. Classification of severity of mechanical jaundice / E.I. Galperin // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2012. - No. 2. - P. 26-33.
28. Galperin E.I., Akhaladze G.G., Vetshev P.S., Dyuzheva T.G. Differentiated approach to the use of minimally invasive treatment methods in neoplastic mechanical jaundice // Annaly khirurgicheskoy

gepatologii [Annals of Surgical Hepatology]. - 2019. - Vol. 24. - No. 2. - P. 10-24.

29. Gostishchev V.K. Differential tactics in the treatment of suppurative cholangitis in patients with acute cholecystitis / V.K. Gostishchev, A.V. Kirillin, A.S. Vorotyntsev // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2004. - No. 2(9). - P. 118.
30. Gudieva I.R. Incidence of cholelithiasis in the Republic of North Ossetia-Alania / I.R. Gudieva // Molodoy uchonyy [Young Scientist]. - 2018. - No. 24(210). - P. 282-285.
31. Danilov S.A. Contemporary trends in the treatment of cholecystocholedocholithiasis / S.A. Danilov et al. // Vestnik SPbGU [Bulletin of St. Petersburg State University]. - 2011. - No. 3. - P. 52-60.
32. Degovtsov E.N. Single-stage minimally invasive surgical treatment of patients with cholecystocholedocholithiasis: Doctoral Dissertation: 14.01.17 / Degovtsov Evgeniy Nikolaevich. - Novosibirsk, 2011. - 234 p.
33. Dundarov Z.A. et al. Cholangiogenic infection in patients with cicatricial biliary strictures // Khirurgiya Belarusi na sovremennom etape [Belarusian Surgery at the Current Stage]. - 2018. - P. 55-57.
34. Durleshtyer V.M. Comprehensive application of endoscopic interventions in mechanical jaundice / Durleshtyer V.M. et al. // Almanakh Instituta khirurgii im. A.V. Vishnevskogo [Almanac of the A.V. Vishnevsky Institute of Surgery]. - 2017. - No. 1. - P. 101-102.
35. Zhanabekova A.K. Informative value of ultrasonography in the diagnosis of cholelithiasis / A.K. Zhanabekova // Vestnik KazNMU [Bulletin of KazNMU]. - 2014. - No. 2. - P. 4.
36. Zagidullina G.T. Contemporary technologies in the diagnosis of choledocholithiasis / G.T. Zagidullina, A.I. Kurbangaleyev // Prakticheskaya meditsina [Practical Medicine]. - 2015. - No. 4-2(89). - P. 45-49.
37. Zubareva N.A. Diagnosis of hepatic insufficiency in cholangiogenic sepsis / Zubareva S.V. et al. // Materialy XI syezda khirurgov Rossiyskoy Federatsii [Proceedings of the XI Congress of Surgeons of the Russian Federation]. - Volgograd. - 2011. - P. 518.
38. Ilyinsky I.M., Tsirulnikova O.M. Primary biliary cholangitis // Vestnik transplantologii i iskusstvennykh organov [Bulletin of Transplantology and Artificial Organs]. - 2021. - Vol. 23. - No. 1. - P. 162-170.

39. Ioffe I.V. Plasmapheresis in the complex treatment of mechanical jaundice caused by choledocholithiasis / I.V. Ioffe, V.P. Poteryakhin // Ukrainskiy zhurnal ekstremnoy meditsiny imeni G.O. Mozhaeva [Ukrainian Journal of Extreme Medicine n.a. G.O. Mozhaev]. - 2009. - Vol. 10, No. 1. - P. 122-125.
40. Karimov Sh.I. et al. Treatment of complications of transhepatic endobiliary interventions in mechanical jaundice caused by periampullary tumours // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2018. - Vol. 20. - No. 3. - P. 68-74.
41. Kasymov Sh.Z., Kurbaniazov Z.B., Davlatov S.S. Indirect electrochemical oxygenation of plasma in cholemic endotoxicosis // Materialy III syezda khirurgov Yuga Rossii [Proceedings of the III Congress of Surgeons of Southern Russia]. - Astrakhan. - 2013. - P. 120.
42. Korolkov A.Yu. et al. Cholangitis and biliary sepsis in cholecystocholedocholithiasis. Diagnostic criteria, management tactics in the emergency medical care department // Skoraya meditsinskaya pomoshch [Emergency Medical Care]. - 2018. - Vol. 19. - No. 1. - P. 31-35.
43. Kosayeva S.B. Contemporary views on the diagnosis and treatment of acute cholecystitis in persons over 60 years of age. Literature review / S.B. Kosayeva, M.Zh. Aymagambetov // Nauka i Zdravookhraneniye [Science and Healthcare]. - 2018. - No. 2(20). - P. 148-167.
44. Kotelnikova L.P. Surgical management of extrahepatic bile duct injuries / L.P. Kotelnikova et al. // Permskiy meditsinskiy zhurnal [Perm Medical Journal]. - 2014. - No. 4. - P. 26-32.
45. Krasilnikov D.M. Complications of laparoscopic cholecystectomy / D.M. Krasilnikov et al. // Prakticheskaya meditsina [Practical Medicine]. - 2016. - No. 4(96). - P. 110-113.
46. Kurbaniazov Z.B., Arziev I.A., Askarov P.A. Improvement of diagnostic and therapeutic tactics in early biliary complications after cholecystectomy // Vestnik nauki i obrazovaniya [Bulletin of Science and Education]. - 2020. - No. 13-3(91).
47. Kurbaniazov Z.B. Surgery of iatrogenic injuries of the main biliary ducts // Vestnik vracha [Physician's Bulletin]. - 2018. - No. 4. - P. 101.
48. Kurbaniazov Z.B., Askarov P.A. Analysis of surgical treatment results in patients with injuries of the main biliary ducts // Zdobutki

klinichnoyi i eksperymentalnoyi medytsyny [Advances of Clinical and Experimental Medicine]. - 2018. - No. 1. - P. 94-100.

49. Kurbonov K.M. Causes and management tactics for "fresh" bile duct injuries / K.M. Kurbonov et al. // Novosti khirurgii [Surgical News]. - 2016. - No. 2(24). - P. 120-124.
50. Levchenko N.V. Minimally invasive treatment of benign stenosis of the major duodenal papilla / N.V. Levchenko et al. // Meditsinskiy sovet [Medical Council]. - 2018. - No. 14. - P. 118-123.
51. Lukichev R.I. Contemporary approach to early diagnosis and treatment of choledocholithiasis / R.I. Lukichev et al. // Zdorovye - osnova chelovecheskogo potentsiala: problemy i puti ikh resheniya [Health as the Basis of Human Potential: Problems and Solutions]. - 2015. - No. 2(10). - P. 758-759.
52. Malakhova I.G. Acute cholangitis complicated by biliary sepsis: a clinical case with a favourable outcome / I.G. Malakhova, A.E. Shklyaev, I.Yu. Utkin // Arkhiv vnutrenney meditsiny [Archives of Internal Medicine]. - 2016. - No. 6(4). - P. 65-69.
53. Merzlikin N.V. Methods of treatment of choledocholithiasis / N.V. Merzlikin et al. // Byulleten sibirskoy meditsiny [Bulletin of Siberian Medicine]. - 2015. - No. 4(14). - P. 99-109.
54. Mikhaylova D.A., Nushtayeva S.A., Styazhkina S.N. Mechanical (obstructive) jaundice. Clinical case // Modern Science. - 2020. - No. 3-1. - P. 299-301.
55. Mikhin A.I. et al. Endoscopic treatment of elderly patients with complex choledocholithiasis // Endoskopicheskaya khirurgiya [Endoscopic Surgery]. - 2019. - Vol. 25. - No. 1. - P. 53-60.
56. Mizgirev D.V. et al. Bile infection and cholangitis in neoplastic mechanical jaundice // Infektsii v khirurgii [Infections in Surgery]. - 2018. - Vol. 16. - No. 1-2. - P. 120-125.
57. Mirzabekov S.G. Optimisation of treatment results of cholangitis in patients with mechanical jaundice // Byulleten meditsinskikh internet-konferentsiy [Bulletin of Medical Internet Conferences]. - 2018. - Vol. 8. - No. 4.
58. Nazarenko P.M. Our experience in the surgical treatment of acute biliary pancreatitis / P.M. Nazarenko et al. // Kurskiy nauchno-prakticheskiy vestnik "Chelovek i yego zdorovye" [Kursk Scientific-Practical Bulletin "Man and His Health"]. - 2017. - No. 4. - P. 57-66.

59. Nazirov F.G., Akilov Kh.A., Akbarov M.M. Tactics of treatment of patients with mechanical jaundice complicated by cholangitis and hepatic insufficiency // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2011. - No. 2. - P. 117-118.
60. Nichitaylo M.E. et al. Combined treatment of mechanical jaundice and cholangitis. - Kyiv: Publishing House "Zdorovya," 2005. - 168 p.
61. Osipov A.V. Antibacterial therapy in suppurative cholangitis / A.V. Osipov et al. // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2017. - No. 2. - P. 42-48.
62. Panfilov S.A. Diagnosis of diseases of the liver, biliary tract, pancreas, spleen with ultrasound duplex scanning. - Moscow: BINOM, 2003. - 208 p.
63. Samartsev V.A. Antibacterial therapy of biliary infections / V.A. Samartsev et al. // Annaly khirurgicheskoy gepatologii [Annals of Surgical Hepatology]. - 2015. - No. 2. - P. 64-71.
64. Shapkin Yu.G. Biliary decompression in the treatment of acute cholangitis / Yu.G. Shapkin et al. // Khirurgiya [Surgery]. - 2013. - No. 6. - P. 25-30.
65. Shulutko A.M. Minimally invasive surgery for acute cholecystitis and its complications / A.M. Shulutko, V.G. Agadzhanov. - Moscow: Medicine, 2008. - 212 p.
66. Khadzhibaev F.A. et al. Optimisation of surgical treatment of cholelithiasis complications // Vestnik neotlozhnoy i vosstanovitelnoy meditsiny [Bulletin of Emergency and Rehabilitation Medicine]. - 2018. - Vol. 19. - No. 2. - P. 117-122.
67. Ansaloni L. et al. 2016 WSES guidelines on acute calculous cholecystitis / L. Ansaloni et al. // World Journal of Emergency Surgery. - 2016. - N 11(25). - doi: 10.1186/s13017-016-0082-5.
68. Costi R. Diagnosis and management of choledocholithiasis in the golden age of imaging, endoscopy and laparoscopy / R. Costi, A. Gnocchi // World J Gastroenterol. - 2014. - N 20(37). - P. 13382-13401.
69. De Castro V. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography in suspected choledocholithiasis: A systematic review / V. De Castro et al. // Endosc Ultrasound. - 2016. - N 5(2). - P. 118-128.

70. Deo K. Laparoscopic Choledochotomy in a Solitary Common Duct Stone: A Prospective Study / K. Deo et al. // Minim Invasive Surg. - 2018. - P. 5.
71. Feng Q. Laparoscopic Transcystic Common Bile Duct Exploration: Advantages over Laparoscopic Choledochotomy / Q. Feng et al. // PLoS One. - 2016. - N 11(9). - P. 1-13.
72. Gomi H. Tokyo Guidelines 2018: antimicrobial therapy for acute cholangitis and cholecystitis / H. Gomi et al. // Journal of Hepato-Biliary-Pancreatic Sciences. - 2018. - N 25(1). - P. 3-16.
73. Hanau L. Acute (ascending) cholangitis / L. Hanau, N. Steigbigel // Infect Dis Clin North Am. - 2020. - N 14(3). - P. 521-546.
74. Harewood G. Cost analysis of magnetic resonance cholangiography in the management of inoperable hilar biliary obstruction / G. Harewood, T. Baron // American Journal of Gastroenterology. - 2019. - N 5(97). - P. 1152-1158.
75. Heuman D. Gallstones / D. Heuman // Medscape. - 2019. (https://emedicine.medscape.com/article/175667-overview)
76. Hope W. SAGES clinical spotlight review: intraoperative cholangiography / W. Hope et al. // Surg Endosc. - 2017. - P. 2007-2016.
77. Hungness E. Management of common bile duct stones / E. Hungness, N. Soper // J Gastrointest Surg. - 2016. - N 10. - P. 612-619.
78. Issa H. Successful Treatment of Mirizzi's Syndrome Using SpyGlass Guided Laser Lithotripsy / H. Issa et al. // Gastroenterology Res. - 2018. - N 5(4). - P. 162-166.
79. Jones M. Gallbladder Gallstones (Calculi) / M. Jones, C. Weir, Ghassemzadeh S. // Treasure Island (FL): StatPearls Publishing. - 2019. (https://www.ncbi.nlm.nih.gov/books/NBK459370/)
80. Joshi A. Four Susceptibility Loci for Gallstone Disease Identified in a Meta-analysis of Genome-Wide Association Studies / A. Joshi et al. // Gastroenterology. - 2016. - N 151(2). - P. 351-363.
81. Karvellas C. The impact of delayed biliary decompression and antimicrobial therapy in 260 patients with cholangitis-associated septic shock / C. Karvellas et al. // Aliment Pharmacol Ther. - 2016. - N 44. - P. 755-766.
82. Kenny R. Laparoscopic common bile duct exploration versus pre or postoperative ERCP for common bile duct stones in patients undergoing

cholecystectomy: Is there any difference? / R. Kenny, J. Richardson // Int J Surg. - 2014. - 12(9). - P. 989-993.

83. Kharbutli B. Management of preoperatively suspected choledocholithiasis / B. Kharbutli, V. Velanovich // Gastrointest Surg. - 2018. - N 11(12). - P. 1973-1980.
84. Kiriyama S. Clinical application and verification of the TG13 diagnostic and severity grading criteria for acute cholangitis: an international multicenter observational study / S. Kiriyama et al. // J Hepatobiliary Pancreat Sci. - 2017. - N 2. - P. 329-337.
85. Kleinubing D. Selective versus routine intraoperative cholangiography for cholecystectomy / D. Kleinubing et al. // The Cochrane Database of Systematic Reviews. - 2018. - doi: 10.1002/14651858.CD012971.
86. Lee T. Endoscopic treatments of endoscopic retrograde cholangiopancreatography-related duodenal perforations / T. Lee et al. // Clin Endosc. - 2013. - N 46(5). - P. 522-528.
87. Levy M. The Surviving Sepsis Campaign Bundle: 2018 update / M. Levy, L. Evans, A. Rhodes // Intensive Care Med. - 2018. - N 44. - P. 925-928.
88. Mandelia A. The Value of Magnetic Resonance CholangioPancreatography (MRCP) in the Detection of Choledocholithiasis / A. Mandelia et al. // J Clin Diagn Res. - 2013. - N 7. - P. 1941-1945.
89. Mattilla A. Cost-analysis and effectiveness of one-stage laparoscopic versus two-stage endolaparoscopic management of cholecystocholedocholithiasis: a retrospective cohort study / A. Mattilla et al. // BMC Surgery. - 2017. - N 17(79). - doi: 10.1186/s12893-017-0274-2.
90. Meeralam Y. Diagnostic accuracy of EUS compared with MRCP in detecting choledocholithiasis: a meta-analysis of diagnostic test accuracy in head-to-head studies / Y. Meeralam et al. // Gastrointest Endosc. - 2017. - N 86. - P. 986-993.
91. Nassar Y. Management of complicated gallstones in the elderly: comparing surgical and non-surgical treatment options / Y. Nassar, S. Richter // Gastroenterology Report. - 2019. - N 7(3). - P. 205-211.
92. Nicholas M. Complications of Endoscopic Retrograde Cholangiopancreatography: How to Avoid and Manage Them / M.

Nicholas, H. Firas // Gastroenterology & Hepatology. - 2013. - N 8(9). - P. 496-504.

93. Peery A. Burden of Gastrointestinal, liver, and pancreatic diseases in the United States / A. Peery et al. // Gastroenterology. - 2015. - N 149. - P. 1731.
94. Perales S. Comparative evaluation of magnetic resonance cholangiopancreatography and perioperative cholangiography in patients with suspect choledocholithiasis / S. Perales et al. // Arq Bras Cir Dig. - 2019. - N 32(1). - P. 1-4.
95. Qiu Y. Is preoperative MRCP necessary for patients with gallstones? An analysis of the factors related to missed diagnosis of choledocholithiasis by preoperative ultrasound / Y. Qiu et al. // BMC Gastroenterol. - 2015. - N 15(158). - P. 1-8.
96. Raith E. Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit / E. Raith et al. // JAMA. - 2017. - N 317(3). - P. 290-300.
97. Schacher F. Endoscopic retrograde cholangiopancreatography versus surgery for choledocholithiasis--A meta-analysis / F. Schacher et al. // Annals of Hepatology. - 2019. - N 18(4). - P. 595-600.
98. Shields H. Two Cases of Acute Cholecystitis and Symptomatic Choledocholithiasis in Two Women Less than 40-Years-of-Age with Hormonal Intrauterine Devices / H. Shields, H. Sidh // Gastrointestinal Medicine. - 2018. - doi: 10.1155/2018/2390213.
99. Singer M. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) / M. Singer // JAMA. - 2016. - N 3(315). - P. 801-810.
100. Taki-Eldin A. Outcome of laparoscopic cholecystectomy in patients with gallstone disease at a secondary level care hospital / A. Taki-Eldin, A. Badawy // Arq Bras Cir Dig. - 2018. - N 31(1). - P. 1347.
101. Testoni A. No treatment for asymptomatic gallbladder stones / A. Testoni // Endoscopy International Open. - 2017. - N 5. - P. 1151-1152.
102. Tomizawa M. Comparison of acute cholangitis with or without common bile duct dilatation / M. Tomizawa et al. // Exp Ther Med. - 2017. - N 13(6). - P. 3497-3502.

103. Venkatanarasimha N. Diagnosis and Management of Complications from Percutaneous Biliary Tract Interventions / N. Venkatanarasimha et al. // Radiographics. - 2017. - N 37(3). - P. 1004.