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CHARACTERISTICS OF CLINICAL MANIFESTATIONS IN POSTCHOLECYSTECTOMY SYNDROME

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ABSTRACT

The study was conducted on the basis of data obtained from a survey of 464 patients who underwent surgery to remove the gallbladder due to cholelithiasis. To develop a clinical classification of PCES and create an algorithm for examining these patients, the results of clinical, laboratory and instrumental studies of 388 patients who underwent inpatient treatment at the multidisciplinary clinic of Samarkand State Medical University in the period from 2018 to 2023, who were diagnosed with “Postcholecystectomy syndrome”, were analyzed. , selected by random sampling.

This work is a comprehensive study of postcholecystectomy syndrome (PCES) associated with postoperative consequences of laparoscopic cholecystectomy. The work analyzes clinical variants of PCES, including dyspeptic, pain, icteric, asymptomatic and Charcot variant. Particular attention is paid to the differential diagnosis between functional and structural disorders of the biliary tract using the concentration of cholecystokinin in blood serum. The study also discusses the significance of the lithogenic properties of bile, changes in humoral regulation and exocrine liver disorders in the formation of PCES. The work emphasizes the need for clinical monitoring and correction of biliary insufficiency in patients after cholecystectomy.

Key words: postcholecystectomy syndrome, cholecystokinin, cholecystectomy.

INTRODUCTION

Relevance of the Study. Gallstone disease (GSD) is one of the most frequently encountered gastrointestinal disorders, affecting 10-30% of the adult population and showing a growing trend among younger patients. Over the past 20 years, laparoscopic cholecystectomy has become the universally recognized "gold standard" in the surgical treatment of GSD. In Uzbekistan, approximately 30,000 to 50,000 such operations are performed annually. Among the primary advantages of this procedure are minimal invasiveness, a significant reduction in hospital stay, and shorter rehabilitation periods. However, one of the key criteria for evaluating new medical technologies is the long-term quality of life of patients after surgery.

According to studies, the proportion of patients with excellent long-term outcomes is 3%, good outcomes—65-85%, satisfactory—13-27%, and unsatisfactory—3-12%. Despite 26 years of laparoscopic practice, it is important to recognize that surgical intervention does not always fully compensate for the complex pathophysiological processes involved in GSD. Adequately and timely performed cholecystectomy eliminates the need for reoperation but does not exclude the necessity for prolonged pharmacological therapy.

Although the study of postcholecystectomy syndrome (PCS) has been ongoing for many years, many key issues related to its prevalence, diagnostic quality, and preventive measures remain unresolved. A particularly challenging aspect is the insufficient specificity of clinical symptoms of organic biliary tract pathology, which often leads to delayed diagnosis and worsened prognosis. The lack of an established clinical classification and clear diagnostic criteria for functional and organic disorders of the biliary tract complicates the development of differentiated treatment methods. Additionally, methods for predicting and preventing various disorders arising after cholecystectomy remain undeveloped.

Thus, the uncertainty surrounding issues related to the diagnostic structure, clinical classification of PCS, its prevalence, diagnostic methods, rehabilitation, and follow-up underscores the significance and determines the objectives of this study.

Objective of the Study. The aim of the study was to conduct a comprehensive investigation of postcholecystectomy syndrome (PCS) associated with postoperative consequences of laparoscopic cholecystectomy.

Materials and Methods of the Study. The study was based on data obtained from the examination of 464 patients who underwent gallbladder removal surgery due to GSD. To develop a clinical classification of PCS and create a diagnostic algorithm for these patients, clinical, laboratory, and instrumental study results of 388 patients treated at the multidisciplinary clinic of Samarkand State Medical University between 2018 and 2023 were analyzed. These patients, diagnosed with "postcholecystectomy syndrome," were selected using random sampling.

To analyze long-term outcomes and identify factors influencing the effectiveness of surgical treatment for GSD, 77 patients who underwent surgery in the surgical department and were followed up for five years postoperatively were examined. Inclusion criteria for this group required planned laparoscopic cholecystectomy without additional biliary tract interventions.

To identify various clinical forms of postcholecystectomy syndrome, a study involving 388 patients admitted to Samarkand State Medical University with the corresponding diagnosis between 2018 and 2023 was conducted. The study

included individuals of both sexes aged 25 to 82 years. The majority of participants were women—242 (62.3%), while men comprised 146 (37.7%). The main age group, accounting for 64.3%, consisted of patients aged 56 to 75 years.

Table 1

Age and Gender Distribution of Patients (n=388)

Age	Women Abs. number	Women %	Men Abs. number	Men %	Total Abs. number	Total %
25-30	4	1.3	1	0.6	5	1.12
31-40	38	9.9	4	1.12	42	10.8
41-50	44	11.7	21	5.3	65	16.7
51-60	71	18.5	49	12.7	120	30.8
61-70	68	17.6	62	15.8	130	33.5
71 and above	16	4.1	11	2.9	27	6.9

Based on the analysis of complaints and medical history of 388 patients, the following clinical forms of postcholecystectomy syndrome (PCS) were identified:

- Dyspeptic type, characterized by symptoms such as nausea, bitterness in the mouth, stool disturbances, and signs of "right hypochondrium syndrome."
- Pain type, presenting with spasmodic pain localized in the right hypochondrium.
- Icteric type, manifesting as periodic subictericity of the skin and sclera, along with "right hypochondrium syndrome."
- Charcot's variant, featuring acute pain, fever, and jaundice.
- Asymptomatic type, in which there are no specific complaints related to biliary tract diseases.

The distribution of patients across these clinical forms is presented in Figure 1.

The analysis of data shows that among patients with postcholecystectomy syndrome (PCS), the majority of cases are attributed to biliary-dyspeptic (45.8%) and pain (43.6%) types of the disease. A small proportion of patients presenting with symptoms typical of organic biliary tract lesions (icteric type – 4.5% and Charcot's variant – 2.4%) can be explained by the specific nature of the medical institution where the study was conducted and the elective nature of hospital admissions. Examination of 388 patients also revealed that in 73.5% of cases, various functional disorders in the biliary system were identified.

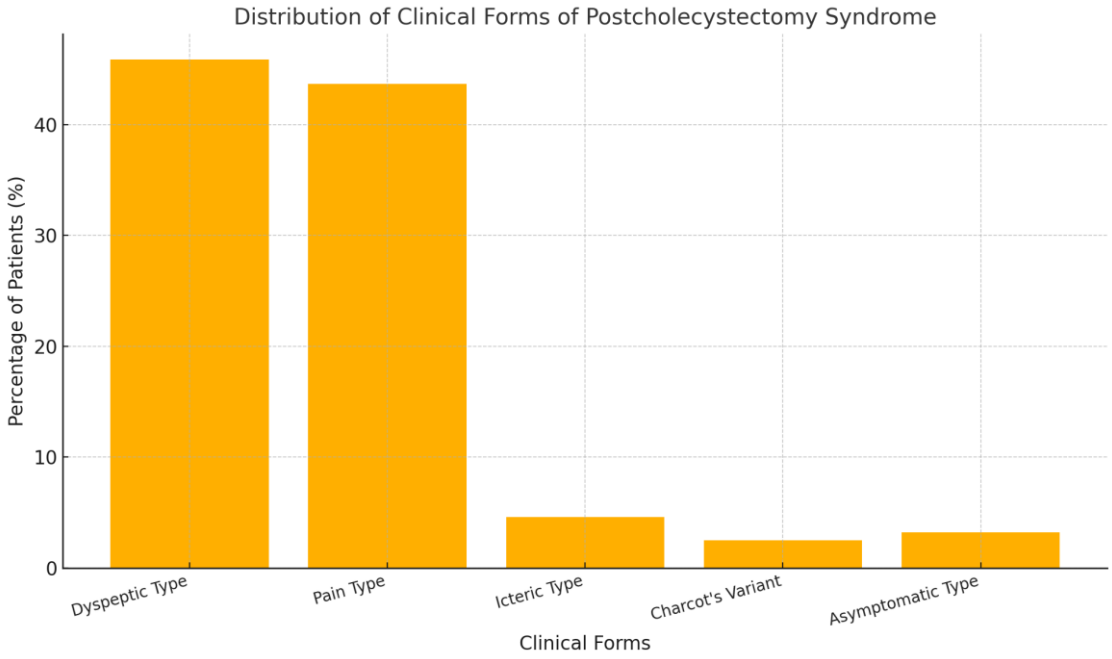

Fig. 1. Quantitative distribution of PCS patients by clinical variant

Among organic biliary tract disorders, the most common issue impeding normal bile outflow was stenosis of the distal common bile duct, found in 11.3% of cases. Stenosis was identified independently in 4.9% of cases and in combination with sludge in the common bile duct in 6.7% of cases. Choledocholithiasis was diagnosed in 10.2% of PCS patients. In 3.5% of cases, sludge without choledochal stenosis served as a mechanical obstacle to bile flow. A relatively small percentage of overall PCS cases included stones in an enlarged cystic duct stump (0.4%) and the presence of foreign bodies in the common bile duct (0.2%).

Thus, functional biliary system disorders were observed in 74.7% of cases, whereas organic pathologies accounted for 25.1%. The study also assessed the informativeness of clinical manifestations for various PCS types, confirming the relationship between the frequency of functional and organic disorders in the biliary tract.

It was found that among patients with PCS, different clinical forms occurred at varying frequencies, except for Charcot's variant, regardless of the presence or absence of organic changes in the biliary tract. A significant difference in distribution was observed only for the biliary-dyspeptic variant, which is more typical for functional disorders, and for the icteric variant, which is significantly more often associated with mechanical bile outflow obstruction. In the case of pain and asymptomatic variants, no statistically significant difference in the frequency of organic pathologies was found.

Thus, patients with PCS lack clear specificity of clinical symptoms, complicating the differential diagnosis of structural and functional biliary tract disorders. Identifying organic biliary tract pathology is of the greatest practical significance, as it often requires surgical intervention. To evaluate the sensitivity and specificity of ultrasound (US) in detecting organic pathology of the extrahepatic bile ducts in PCS patients, the results of transabdominal ultrasonography (TUS) were compared with those of endosonography (EUS) (see Fig. 3). According to TUS data, organic biliary tract pathology was identified in 16.6% of the 388 patients examined. In 18% of patients, difficulties arose with the complete visualization of the common bile duct (CBD). Endosonography of the pancreatobiliary zone was performed on patients with incomplete visualization of the CBD when its diameter exceeded 6 mm and/or alkaline phosphatase (ALP) levels were elevated (n=49), as well as on all patients with identified organic biliary tract pathology based on US results (n=65) to confirm the diagnosis and obtain additional information necessary for transpapillary interventions. Thus, the need for EUS amounted to 29.2% of all PCS patients (n=388).

Results of the Study.

Based on endosonography (EUS), hyperdiagnosis of organic biliary tract pathology initially diagnosed via ultrasound (US) was observed in 23 out of 258 patients (8.9%). Mechanical obstructions to bile flow were identified in 235 patients (91.4%). Among patients with inconclusive US results, organic biliary tract pathology was detected in 80% of cases. Overall, EUS revealed organic pathology of the extrahepatic bile ducts in 25.2% of cases. These findings confirm the rationale for using EUS as an additional diagnostic tool for the biliary tract.

The study determined the sensitivity and specificity of US in diagnosing organic biliary tract pathology. The sensitivity (Se) of US was 60.1%, and its specificity (Sp) was 62.9%.

To evaluate the long-term outcomes of surgical treatment for gallstone disease, 306 patients were examined. These patients underwent cholecystectomy for cholecystolithiasis in the surgical department of the multidisciplinary clinic at Samarkand State Medical University in 2023. Their condition was monitored for five years postoperatively.

Observation results showed that 157 out of 306 (51.3%) patients who underwent laparoscopic cholecystectomy (LC) reported no complaints over the five years following surgery. These patients were conditionally grouped as having a favorable outcome of surgical treatment for gallstone disease. However, in 149 out of 306 (48.7%) patients, no significant improvement in well-being was observed after surgery (see Fig. 2).

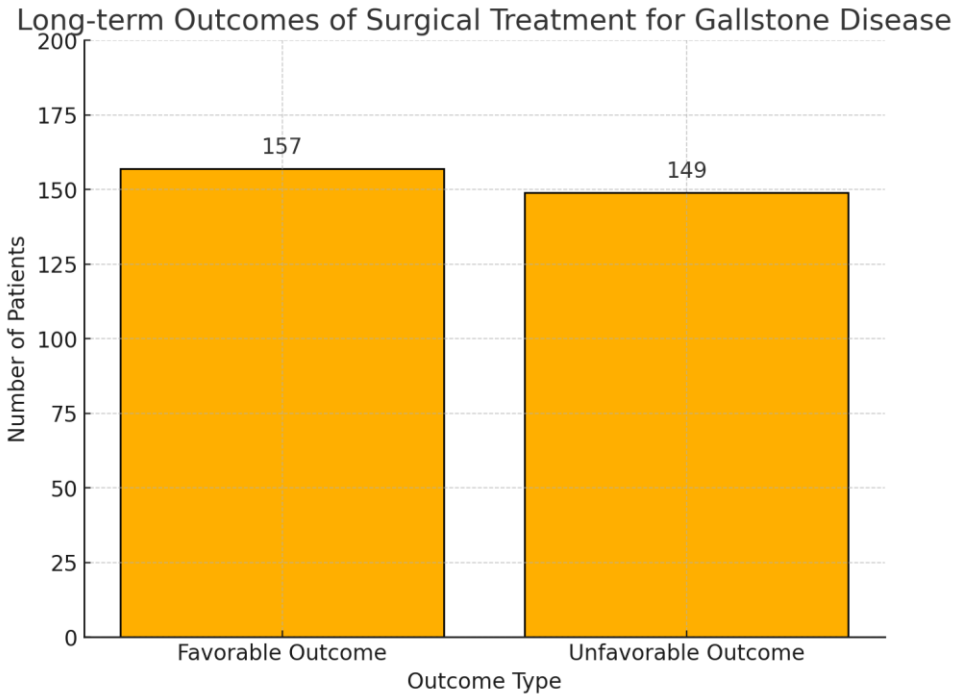

Fig. 2. Clinical outcomes of surgical treatment for gallstone disease based on patient follow-up data

During biochemical blood analysis and ultrasound (US) of the pancreatobiliary zone, 8 out of 157 (3.2%) patients with a favorable clinical outcome after surgical treatment for gallstone disease (GSD) were found to have dilation of the common bile duct (CBD) and an increase in the size of the pancreatic head. These findings were accompanied by elevated levels of alkaline phosphatase (ALP) and pancreatic trypsin-like protease (PTP). Notably, these changes were not observed during the preoperative evaluation prior to video-laparoscopic cholecystectomy (VLC).

During inpatient evaluation, based on endosonography (EUS), two patients were diagnosed with subcompensated stenosis of the distal CBD. No organic pathology of the extrahepatic bile ducts was detected in six patients. The laboratory and sonographic changes were interpreted as signs of sphincter of Oddi dysfunction and pancreatitis, requiring pharmacological correction at the current stage and further dynamic observation.

Thus, after laboratory and instrumental investigations, it was found that patients with a favorable outcome of surgical treatment for GSD constituted 48.7%. However, the detected organic biliary tract pathology allowed for the identification of a clinically asymptomatic variant of PCS, which accounted for 2.6% of cases (see Fig. 3).

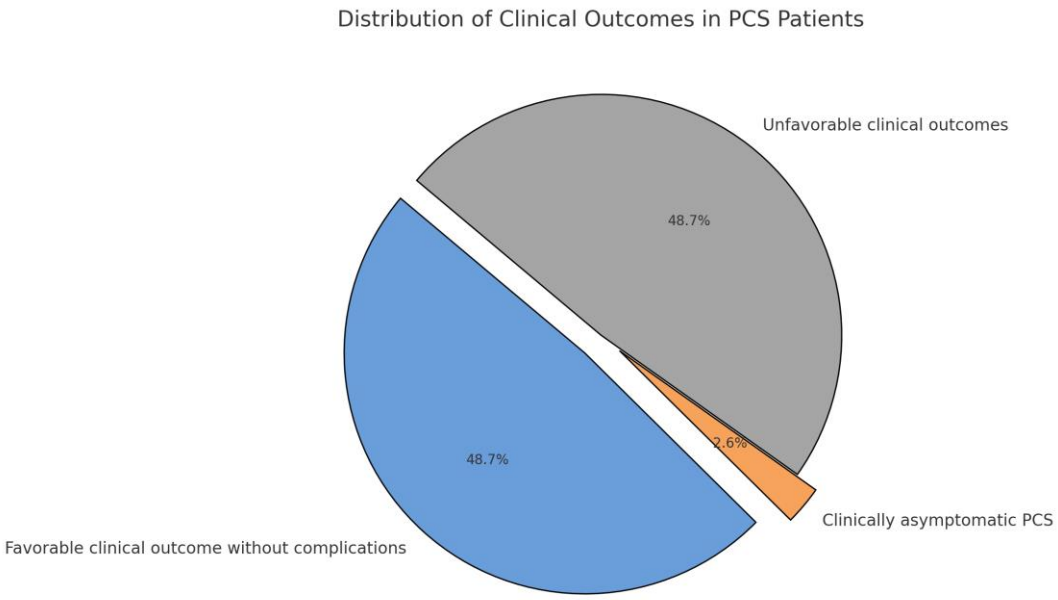

Fig. 3. Clinical outcomes of surgical treatment for gallstone disease based on clinical, laboratory, and instrumental study data

The results of the study highlight the necessity of regular follow-up for all patients who have undergone surgery for cholecystolithiasis, including those without clinical symptoms. This is essential for the timely therapeutic correction of biliary tract dysfunctions that may have existed previously or developed over time.

To identify the factors influencing the outcomes of surgical treatment for gallstone disease (GSD), patient complaints and examination results conducted immediately before video-laparoscopic cholecystectomy (VLC) were analyzed. Special attention was paid to the group with favorable treatment outcomes.

Based on the analysis of complaints from 77 patients with GSD prior to cholecystectomy, three types of clinical courses of the disease were identified: pain type (n=39), biliary-dyspeptic type (n=26), and "silent" type (n=11). Subsequently, clinical outcomes were analyzed based on these types of GSD courses (see Fig. 4).

Based on the conducted studies, it was established that among patients with a favorable outcome of gallstone disease (GSD) treatment, the pain type (61.3%) and clinically asymptomatic type (22.8%) were the most common in their medical history. The biliary-dyspeptic type of GSD was observed in this group in only 14.1% of cases, whereas it was registered in 52.9% of cases with an unfavorable outcome.

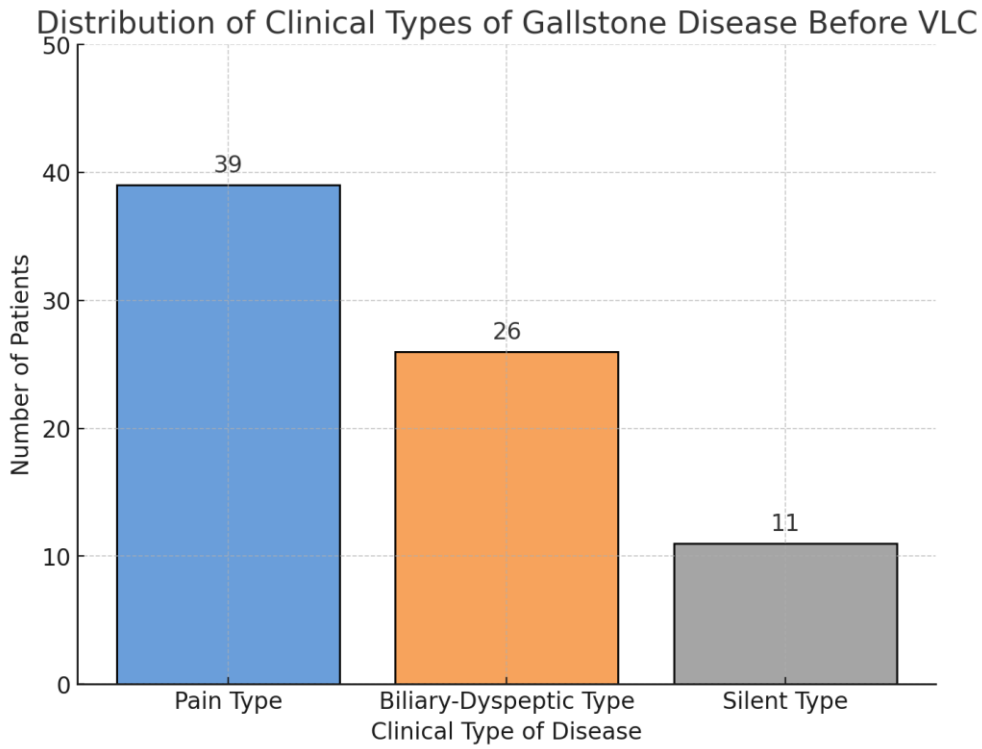

Fig. 4. Cholecystectomy outcomes based on the clinical course of gallstone disease before surgery

Thus, gallbladder removal in cases of the pain type of GSD, caused by the displacement of stones or the transit of microliths through the common bile duct, contributes to an increase in favorable outcomes of cholecystectomy. The predominance of the biliary-dyspeptic type of GSD among patients with unfavorable clinical outcomes indicates that this type of the disease is the least favorable in terms of prognosis.

A retrospective analysis of ultrasound data conducted during the preoperative stage showed that in the group with favorable clinical outcomes, almost one-third of patients (30.9%) had a reduced gallbladder contractility (GBC) of less than 50%, and 16.1% were diagnosed with an "non-functioning" gallbladder. In the comparison group, these indicators were 10.8% and 4.5%, respectively.

The results demonstrate that a reduction in gallbladder contractility (GBC) up to its "non-functioning" state is a prognostically favorable factor in the long-term outcomes after cholecystectomy. This is attributed to the gradual adaptation of the sphincter apparatus of the biliary tract to function under conditions of reduced GBC or a "non-functioning" gallbladder.

To determine the relationship between surgical treatment outcomes of GSD and the chemical composition of gallstones, the results of operative material analysis from 306 patients were evaluated. It was found that 229 patients (74.8%) underwent surgery for cholesterol stones (CS), 65 (21.2%) for pigment stones (PS),

and 12 (3.9%) due to mixed stones (MS). The study revealed that, in the long term, patients with a history of PS were significantly more likely to have favorable clinical outcomes after surgical treatment of GSD (87.7%, n=57). For CS, favorable outcomes were observed in only 40.2% (n=92) of cases. The worst prognosis was observed in patients operated on for MS, as 100% (n=12) required ongoing medical therapy over a 5-year follow-up period due to the presence of the biliary-dyspeptic variant of PCS (see Table 2).

Table 2

Clinical Outcomes of Surgical Treatment for Gallstone Disease Based on the Chemical Composition of Gallbladder Stones

Research Groups	Favorable Outcome Abs. (%)	Unfavorable Outcome Abs. (%)
PH (n=16)	**57 (87.7%)**	**2 (12.3%)**
XX (n=57)	**92 (40.2%)**	**34 (59.8%)**
PSFH GP (n=3)	**-**	**3 (100%)**
Total	**149**	**39**

Based on the results, a hypothesis was proposed regarding the possibility of predicting the outcomes of surgical treatment for gallstone disease (GSD) depending on the composition of gallstones. In pigment cholelithiasis, the likelihood of a favorable outcome is higher because the symptom complex associated with biliary insufficiency, which accompanies cholesterol cholelithiasis and gallbladder cholesterolosis in 100% of cases, is absent.

To confirm this hypothesis, the lipid composition and bile acid spectrum of operative bile from 13 patients were analyzed: 2 with pigment cholelithiasis, 4 with cholesterol cholelithiasis, 4 with a combination of cholesterol cholelithiasis and reticular gallbladder cholesterolosis, and 2 with polypoid-reticular cholesterolosis of the gallbladder. Operative bile from 2 patients with adenomatous and fibrous-adenomatous gallbladder polyps was used as the control group.

The study of the lipid composition of operative bile in pigment cholelithiasis and adenomatous polyps revealed that the cholesterol saturation index (CSI) was significantly higher in patients with cholesterol stones, particularly in cases combined with the reticular form of gallbladder cholesterolosis, compared to pigment stones and the absence of gallstones. In cases of lipid deposition in the form of reticular gallbladder cholesterolosis, the CSI was the highest.

The results convincingly demonstrate pronounced dyscholia in cholesterol-associated gallbladder pathology, including cholesterol cholecystolithiasis. This influences the clinical course during the postoperative period and the formation of variants of postcholecystectomy syndrome (PCS).

To assess the prognostic significance and likelihood ratio of the cholesterol saturation index (CSI) as a test for determining the clinical outcome of surgical treatment for GSD in the long term, the clinical symptoms (presence or absence of biliary dyspepsia syndrome) in the same patients were analyzed two years after cholecystectomy.

As shown in the table, patients with a high CSI two years after cholecystectomy were significantly more likely (80.5%) to experience biliary dyspepsia syndrome compared to those with normal CSI levels (18.7%).

Based on the obtained data, the predictive value of a positive test (CSIt) was found to be 80.5%, and the likelihood ratio was 4.1. This means that an increased CSI is four times more common in patients with biliary dyspepsia than in those without the syndrome. A high likelihood ratio of a positive test indicates that this test provides valuable information, just as a near-zero likelihood ratio does for a negative result (CSI-N).

The relative risk for the studied factor was 4.29, with a standard error of 0.53 and a 95% confidence interval ranging from 1.52988 to 12.0651. Thus, a relationship between the occurrence of the biliary-dyspeptic variant of PCS and an elevated CSI was established.

The study of the bile acid spectrum in operative bile from the same groups of patients revealed a statistically significant difference in the percentage of lithocholic acid in the group of patients with a combination of reticular gallbladder cholesterolosis and cholesterol cholecystolithiasis compared to other groups.

This finding has scientific and practical significance, as it is known that lithocholic acid suppresses bile acid synthesis, promoting gallstone recurrence. Therefore, patients with a combination of reticular gallbladder cholesterolosis and cholesterol cholecystolithiasis are at the highest risk of recurrent gallstone formation.

To study the effect of cholecystectomy on the secretion of gastrointestinal hormones, the concentration levels of CCK and secretin were analyzed in 13 patients who had undergone cholecystectomy at different times (1 to 10 years ago).

The study results demonstrated a significant difference in the average CCK concentration levels between patients with GSD and PCS. In the PCS group, the average CCK concentration was significantly higher than in the GSD group and the control group. The average secretin concentration in PCS patients showed only a tendency toward an increase.

Table 3

Average Levels of CCK and Secretin in Patients with GSD and PCS

Hormones	PHES (n=12) (M±m) ng/mL	GSD (n=30) (M±m) ng/mL	Control (n=8) (M±m) ng/mL
CCK	1.274±0.150*	0.641±0.080	0.731±0.070
Secretin	0.849±0.090	0.612±0.084	0.685±0.075

From Table 3, it can be seen that the average CCK concentration levels in the group of patients with gallstone disease (GSD) did not differ from those in the control group. A comparison of CCK concentration levels in GSD patients and the control group indicates that the presence of cholecystolithiasis, not complicated by organic biliary tract pathology, does not significantly influence the level of this hormone.

The CCK concentrations in the PCS group varied widely, ranging from 0.490 to 2.465 ng/mmol. Among the 12 patients with PCS, only 3 (27%) had CCK levels corresponding to the average values in the control group, while 9 (71%) had CCK levels exceeding 1.000 ng/mmol.

Based on these data, it can be concluded that most patients experience an increase in CCK concentration in the blood serum after cholecystectomy. The wide range of CCK concentration values in the PCS group suggests a potential dependence of hormone levels on the characteristics of PCS progression.

To determine the relationship between CCK levels and the clinical course of PCS, hormone concentration values were compared with clinical, laboratory, and instrumental examination data for the respective patients. Three groups of patients were identified with CCK concentration ranges from 0.5 to 2.0 ng/ml, within which significant differences were found in clinical-anamnestic data, biochemical blood test results, and ultrasound findings of the pancreatobiliary zone (see Table 4).

Table 4

Average Levels of CCK and Secretin in Patients with GSD and PCS Quantitative Distribution of Patients Based on CCK Concentration Levels (n=12)

Patient Group	Abs. (%)	Mean CCK Values (ng/mL) (M±m)
Group I (0.5–1.0 ng/mL)	4	0.834±0.079
Group II (1.1–2.0 ng/mL)	6	1.285±0.138
Group III (>2.0 ng/mL)	3	2.328±0.115

To investigate the relationship between CCK concentration and bile outflow conditions established after gallbladder removal, clinical and laboratory-instrumental data were analyzed in each group of PCS patients categorized based on CCK concentration ranges.

The analysis of clinical and anamnestic characteristics, as well as laboratory-instrumental data, showed that CCK concentration after gallbladder removal changes depending on the time since surgery and bile outflow conditions.

In the first year after cholecystectomy, CCK levels in patients were comparable to those in patients with GSD and preserved gallbladder function (GBF >50%), ranging from 0.5 to 1.0 ng/mL. After one year, due to adaptive-compensatory mechanisms, CCK concentration increased to 1.1–2.0 ng/mL, ensuring adequate functioning of the biliary tract sphincter apparatus and normal bile outflow. Clinically, this manifests as a favorable cholecystectomy outcome or a biliary-dyspeptic variant of PCS. Notably, similar CCK levels were observed in GSD patients with GBF below 50%, confirming the gradual adaptation of the biliary tract sphincter apparatus to conditions of reduced GBF or a "non-functioning" gallbladder.

In cases where bile outflow is impaired due to sphincter of Oddi spasm, further CCK elevation to 2.0–2.5 ng/mL occurs (subcompensation stage). This increase facilitates bile outflow under conditions of sphincter of Oddi hypertonicity. Laboratory-instrumental data in such patients revealed transient elevations in alkaline phosphatase (ALP) and common bile duct (CBD) dilation, which were corrected through pharmacological treatment.

The study results suggest the possibility of differential diagnosis between temporary bile outflow disorders caused by sphincter of Oddi dysfunction and organic obstruction such as distal CBD stenosis based on CCK levels.

Postcholecystectomy syndrome occurs in 51.3% of patients undergoing surgery in specialized gastroenterological hospitals, with functional disorders accounting for the majority (95.5%). Clinically, five variants of PCS were identified: dyspeptic (45.9%), pain (43.7%), icteric (4.6%), clinically asymptomatic (3.2%), and Charcot's variant (2.5%). Charcot's variant is specific to organic biliary tract pathology, while other variants can manifest in both functional and structural disorders.

Transabdominal ultrasonography demonstrated low sensitivity (60.1%) and specificity (62.9%) in diagnosing organic pathologies, emphasizing the need for additional methods such as endoscopic ultrasonography (EUS) in 29.2% of cases.

CCK levels after cholecystectomy indicate the adaptation of the biliary tract sphincter apparatus: with normal bile outflow, the concentration is 1.280±0.112 ng/mL, while with sphincter of Oddi spasm, it is 2.326±0.112 ng/mL.

CCK concentration is an important criterion for differentiating functional and structural biliary tract disorders: in sphincter of Oddi spasm, the CCK level is 2.326±0.112 ng/mL, while in distal CBD stenosis, it is 0.833±0.078 ng/mL.

The cholesterol saturation index (CSI) in cholesterol cholecystolithiasis combined with reticular gallbladder cholesterolosis is significantly higher (1.94±0.12 ng/mL) compared to pigment cholelithiasis (0.59±0.09 ng/mL) and cases without gallstones (0.51±0.11 ng/mL), supporting the need for correction of biliary insufficiency.

In patients with a combination of cholesterol cholecystolithiasis and reticular gallbladder cholesterolosis, a significant increase in lithocholic acid content (4.07±0.13%) was noted, indicating a high risk of gallstone formation and justifying the need for litholytic therapy.

Conclusion:

The incidence of postcholecystectomy syndrome is high and varies depending on functional and structural biliary tract disorders. The variety of clinical variants of this syndrome, including the asymptomatic type, underscores the importance of regular follow-up after surgical treatment of gallstone disease to prevent its development and provide timely intervention when necessary.

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