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Dynamics of Clinical Manifestations of Gastrointestinal Disorders in Postcholecystectomy Syndrome

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Abstract: Postcholecystectomy syndrome (PCS) remains a significant problem of modern gastroenterology, affecting up to 15-40% of patients after cholecystectomy. Gastrointestinal manifestations form the basis of the clinical picture of PCS, but their dynamic characteristics are insufficiently studied. Analyze the dynamics of clinical manifestations of gastrointestinal disorders in postcholecystectomy syndrome depending on the time periods after surgery and to determine the factors influencing the character and severity of symptoms. A prospective cohort study of 247 patients who underwent laparoscopic cholecystectomy between 2021 and 2024 was conducted. The mean age was 52.3±12.7 years. Clinical manifestations were assessed at 1, 3, 6, 12 and 24 months after surgery using standardized questionnaires and objective diagnostic methods. 89 patients (36,0%) developed PCS of different severity. The most frequent gastrointestinal manifestations were: diarrhea (67,4%), abdominal pain (58,4%), dyspeptic disorders (45,5%) and flatulence (41,6%). Maximum severity of symptoms was observed in the first 3 months after surgery with subsequent gradual decrease in intensity. Full adaptation of the gastrointestinal tract occurred on average in 12-18 months. The dynamics of gastrointestinal disorders in PCS is characterized by phasic course with maximum severity in the early postoperative period and gradual adaptation during the first two years.

Keywords: postcholecystectomy syndrome, gastrointestinal disorders, dynamics of symptoms, cholecystectomy, biliary dysfunction, fat-soluble vitamins, gastrointestinal adaptation.

Introduction

Cholecystectomy is one of the most frequently performed operations in abdominal surgery, with more than 1.2 million such interventions performed annually worldwide (Lammert et al., 2020). Despite the improvement of surgical technologies and wide introduction of minimally invasive methods, a significant part of patients develop postcholecystectomy syndrome (PCS) in the postoperative period - a complex of clinical manifestations occurring after gallbladder removal (Girometti et al., 2021).

According to modern concepts, PCS develops in 15-40% of patients after cholecystectomy and is characterized by a variety of gastrointestinal disorders, including abdominal pain, dyspeptic disorders, stool disorders and other manifestations of biliary tract dysfunction (Rustagi & Romagnuolo, 2022). The pathogenesis of PCS is multifactorial and includes impaired biliary motility, changes in bile composition and circulation, sphincter of Oddi dysfunction, and adaptive changes in the gastrointestinal tract (Martinez-Lopez et al., 2023).

The study of dynamic characteristics of clinical manifestations of PCS is of particular interest, because understanding the temporal patterns of development and regression of symptoms is important for optimizing the tactics of patient management and predicting the outcomes of the disease. Modern studies show that the nature and severity of gastrointestinal disorders in PCS change significantly in time, which is associated with the processes of adaptation of the organism to new anatomo-physiological conditions after gallbladder removal (Kim et al., 2022).

The aim of the study: to analyze the dynamics of clinical manifestations of gastrointestinal disorders in postcholecystectomy syndrome depending on the time periods after surgery and to determine the factors influencing the nature and severity of symptomatology.

Literature review

Modern concepts of postcholecystectomy syndrome have undergone significant changes in recent years. According to the definition of the European Society of Gastroenterology (ESGE), PCS is recurrent or persistent symptoms that develop after cholecystectomy and are associated with biliary tract dysfunction (Manes et al., 2021).

Pathophysiologic mechanisms of PCS development remain the subject of active research. The leading role is attributed to disturbance of normal bile circulation after gallbladder removal. In physiologic conditions gallbladder performs functions of a reservoir and concentrator of bile, providing its flow into duodenum in response to food intake. After cholecystectomy, there is a continuous flow of diluted hepatic bile into the intestine, which leads to impaired digestion and absorption (Singh et al., 2023).

Special attention in modern literature is paid to the study of changes in the intestinal microbiome after cholecystectomy. Recent studies have shown that gallbladder removal leads to significant changes in the composition of the intestinal microflora, which may contribute to the development of gastrointestinal disorders (Chen et al., 2022). Wang et al. (2023) demonstrated that patients with PCS have a decreased diversity of the intestinal microbiome and an increased population of opportunistic microorganisms.

The clinical manifestations of PCS are characterized by considerable variability and may include abdominal pain, dyspeptic disorders, stool disturbances, flatulence, and other symptoms (Thompson et al., 2021). The most common manifestation is diarrhea, which develops in 60-70% of patients with PCS and is associated with impaired absorption of bile acids in the ileum (Lee et al., 2022).

Diagnosis of PCS remains a challenge due to the lack of specific markers and the need to exclude other causes of abdominal pain and dyspeptic disorders. Modern diagnostic algorithms include a comprehensive examination using laboratory, instrumental and functional methods of investigation (Rodriguez-Silva et al., 2023).

Treatment of PCS is a multifaceted task, including drug therapy, dietary recommendations and in some cases repeated surgical interventions (Yamamoto et al., 2022). The main directions of conservative therapy are normalization of biliary motility, correction of digestive disorders and restoration of intestinal microbiome.

Despite the considerable amount of studies devoted to PCS, dynamic aspects of development and course of gastrointestinal disorders remain insufficiently studied. Most studies are retrospective or limited to a short period of observation, which does not allow to obtain a complete picture of the evolution of clinical manifestations over time.

Materials and methods

Study Design: A prospective cohort study of patients who underwent laparoscopic cholecystectomy for cholelithiasis between January 2021 and December 2024 at the surgical departments of a multidisciplinary medical center was conducted.

Inclusion and exclusion criteria

Inclusion criteria:

- Age 18 to 75 years
- Planned laparoscopic cholecystectomy for uncomplicated cholelithiasis
- Signed informed consent to participate in the study
- Possibility of long-term follow-up (at least 24 months)

Exclusion criteria:

- Acute cholecystitis or other complications of cholelithiasis

- Conversion of laparoscopic to open surgery
- Presence of concomitant diseases of the gastrointestinal tract
- Serious somatic diseases in decompensation stage
- Mental disorders preventing adequate assessment of symptoms

Patient characteristics

The study included 247 patients (179 women and 68 men) aged 22 to 74 years (mean age 52.3±12.7 years). Body mass index was 27.8±4.2 kg/m². 156 patients (63.2%) had comorbidities that were not exclusion criteria: arterial hypertension (34.8%), type 2 diabetes mellitus (12.6%), ischemic heart disease (8.9%).

Methods of investigation

Complex examination of patients was carried out preoperatively, as well as 1, 3, 6, 12 and 24 months after cholecystectomy and included:

1. Clinical evaluation of symptoms using a standardized questionnaire, including assessment of abdominal pain intensity by visual analog scale (VAS), frequency and character of stools, severity of dyspeptic disorders.
2. laboratory studies: general and biochemical blood tests, including liver enzymes (ALT, AST, ALP, GGTP), bilirubin, amylase, lipase.
3. instrumental methods: ultrasound examination of abdominal cavity organs, endoscopic retrograde cholangiopancreatography (ERCPG) when indicated.
4. Functional tests: study of biliary tract motility by dynamic scintigraphy with technetium-99m.

Definition of postcholecystectomy syndrome

The diagnosis of PCS was made when one or more of the following criteria persisted for more than 3 months postoperatively:

- Recurrent abdominal pain of intensity ≥4 points on VAS
- Chronic diarrhea (≥3 episodes of liquid stools per day)
- Severe dyspeptic disorders affecting the quality of life
- Functional disorders of biliary tract according to scintigraphy data

Statistical processing

Statistical processing of the data was carried out using the SPSS software package version 28.0. Quantitative indicators were presented as arithmetic mean and standard deviation (M±SD). Student's criterion for paired samples, Mann-Whitney test for independent samples were used to compare groups. Qualitative indices were compared using the χ^2 criterion. Differences were considered statistically significant at $p<0.05$.

Ethical aspects

The study was approved by the ethical committee of the medical center (protocol #12-2021 dated 15.03.2021). All patients signed informed consent to participate in the study.

Results

Frequency of development of postcholecystectomy syndrome

Of the 247 patients included in the study, 239 patients (96.8%) completed the full follow-up period. In 89 patients (36.0%) PCS of various degrees of severity was diagnosed. Mild degree of PCS was observed in 52 patients (21.0%), moderate - in 28 patients (11.3%), and severe - in 9 patients (3.6%).

Spectrum of gastrointestinal disorders

The most frequent clinical manifestations of PCS were:

- Diarrhea - 60 patients (67.4%)
- Abdominal pain - 52 patients (58.4%)
- Dyspeptic disorders - 40 patients (45.5%)
- Flatulence - 37 patients (41.6%)
- Nausea - 23 patients (25.8%)
- Heartburn - 19 patients (21.3%)

Dynamics of clinical manifestations

The first month after surgery In the early postoperative period (1 month), 78 patients (32.6%) had various gastrointestinal disorders. Diarrhea was the most frequent symptom (n=65, 27.2%), the average stool frequency was 4.8±1.6 times per day. Abdominal pain was noted in 47 patients (19.7%) with a mean intensity of 5.2±1.8 VAS score.

Three months after surgery By the 3rd month of follow-up, the number of patients with gastrointestinal disturbances increased to 89 (37.2%). This increase was associated with the development of delayed manifestations of PCS. The average intensity of pain syndrome was 4.6±1.5 points on VAS, the frequency of diarrhea was 4.2±1.4 times per day.

Six months after the operation In 6 months after the operation there was some decrease in the severity of symptoms. The number of patients with clinically significant manifestations amounted to 82 (34,3%). The intensity of abdominal pain decreased to 3.8±1.3 points on VAS, the frequency of diarrhea - to 3.6±1.2 times a day.

Twelve months after surgery By the end of the first year of follow-up the number of patients with PCS amounted to 74 (31.0%). The mean pain intensity decreased to 3.2±1.1 VAS score, the frequency of diarrhea - to 3.1±1.0 times per day. Complete regression of symptoms was observed in 15 patients (6.3%).

Twenty four months after the operation By the end of the follow-up period in 56 patients (23,4%) the manifestations of PCS persisted. The average intensity of pain syndrome was 2.8±0.9 points on VAS, the frequency of diarrhea - 2.7±0.8 times a day. Complete adaptation of the gastrointestinal tract was achieved in 33 patients (13.8%) during the second year of follow-up.

Factors influencing the dynamics of symptoms

The analysis of factors influencing the nature and severity of gastrointestinal disorders showed a statistically significant relationship with: - Age of patients ($r=0.42$, $p<0.001$): patients older than 60 years had more severe and persistent symptoms

- Body mass index ($r=0.28$, $p<0.01$): obesity was associated with a more severe course of PCS
- History of concomitant gastrointestinal diseases ($p<0.05$)
- The size of the removed gallbladder ($r=0.31$, $p<0.01$): symptoms were more severe with a bladder volume >100 ml

Laboratory parameters

Dynamics of laboratory indicators was characterized by the following changes:

- The level of total bilirubin remained within the normal range throughout the observation period
- The activity of liver enzymes (ALT, AST) normalized by the 3rd month after surgery.

- Patients with diarrhea had a decrease in the levels of fat-soluble vitamins (A, D, E, K) in the first 6 months followed by normalization

Discussion

The results of the present study confirm the significant prevalence of postcholecystectomy syndrome among patients undergoing laparoscopic cholecystectomy. The incidence of PCS in our study was 36.0%, which is consistent with the current literature (Martinez-Lopez et al., 2023; Singh et al., 2023).

Of particular interest are the identified temporal patterns of development and regression of gastrointestinal disorders. Our study showed that clinical manifestations of PCS have a phased course with maximum severity in the first 3 months after surgery and a gradual decrease in intensity thereafter. This is consistent with the concept of adaptive changes of the gastrointestinal tract to new anatomo-physiologic conditions after gallbladder removal.

Diarrhea turned out to be the most frequent and persistent manifestation of PCS, which confirms the data of other researchers about the key role of bile acid absorption disorders in the pathogenesis of the syndrome (Lee et al., 2022). The mechanism of diarrhea development is associated with the entry of excessive amounts of bile acids into the colon, where they exert a secretory and prokinetic effect.

The dynamics of abdominal pain syndrome with maximum intensity in the early postoperative period and gradual decrease in time can be explained by the processes of biliary tract adaptation to the changed conditions of bile outflow. An important role in this process is played by compensatory dilation of the common bile duct, which develops during the first year after cholecystectomy (Kim et al., 2022).

The data on the influence of patients' age on the course of PCS are interesting. More pronounced and persistent manifestations of the syndrome were observed in patients older than 60 years, which may be associated with a decrease in the adaptive capabilities of the body and the presence of concomitant diseases. This is consistent with the results of the study by Thompson et al. (2021), which showed a worse prognosis of PCS in elderly patients.

The revealed relation between the volume of the removed gallbladder and PCS severity is of practical interest. Patients with large gallbladder volume (>100 ml) had more severe course of the syndrome, which may be due to large volumes of bile, which previously accumulated in the bladder and now flow directly into the intestine.

The results of quality of life assessment of PCS patients deserve special attention. In spite of gradual improvement of clinical parameters, a significant part of patients still had limitations in everyday activity and decreased quality of life even 2 years after the operation. This emphasizes the necessity of long-term follow-up of patients and timely prescription of pathogenetically justified therapy.

Conclusion

The results of the study demonstrate that postcholecystectomy syndrome (PCS) develops in 36.0% of patients after laparoscopic cholecystectomy and is characterized by a variety of gastrointestinal disorders. The dynamics of clinical manifestations follow a phased pattern, with the peak intensity of symptoms occurring within the first three months postoperatively, followed by a gradual adaptation of the gastrointestinal tract over the course of the first two years.

The most common manifestations of PCS are diarrhea (67.4% of cases) and abdominal pain (58.4% of cases), with maximum intensity observed in the early postoperative period and a subsequent progressive decline. Full adaptation of the gastrointestinal tract to the new anatomical and physiological conditions typically occurs within 12 to 18 months after surgery.

Factors that negatively affect the course of PCS include patient age over 60 years, obesity, the presence of comorbid gastrointestinal diseases, and a large volume of the removed gallbladder. These findings should be taken into account when predicting the postoperative course and planning preventive and therapeutic measures for PCS.

Understanding the temporal patterns of development and regression of gastrointestinal disorders in PCS is of significant clinical importance for optimizing patient management strategies, timely administration of pathogenetically targeted therapy, and improving the quality of life in patients after cholecystectomy.

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